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ABSTRACT BOOK



Human Lumbar Discs are not sterile! - Defining the Normal Intervertebral Disc Microbiome

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Introduction: Traditionally, Central Nervous System, spinal cord, eye, fetus and Intervertebral Disc were considered to be sterile and immune privileged. With the advent of 16SrRNA sequencing, it has been proved that each of the above have a microbiome which plays an essential role in maintaining homeostasis. With increasing reports of sub-clinical infection as an etiology of disc degeneration and Modic changes, it remains unknown, whether lumbar discs are truly sterile. The primary aim of the study was to investigate the presence of Disc microbiome and its microbial composition.

Materials and Methods: In order to obtain true normal controls, intervertebral discs were collected from MRI normal brain-dead voluntary organ donors with no history of back pain. The study was performed after the approval of IRB. The discs were dissected in surgical sterile conditions and were snap frozen immediately to -160°C and the processed samples were subjected to total DNA extraction using QIAamp® DNA Mini Kit and enrichment using NEBNext® Microbiome DNA Enrichment Kit (Cat # E612S/L; New England BioLabs, Ipswich, MA). The purified DNA was amplified using v1-V9 specific primers and the sequencing was performed using Illumina MiSeq platform. Raw data was analysed using Bioinformatic tools such as Greengenes database and kraken2. Proteomic analysis was also performed to confirm bacterial presence.

Results: All the eight normal disc samples had bacteria. 42.75% OTUs were classified at the Kingdom level, 44% at Phylum level, 22.62% at Genus level and 5.5% at Species level. A total of 355 bacterial species were identified in normal discs which were distributed under five major phyla- *Proteobacteria*, *Parcubacteria*, *Firmicutes*, *Cyanobacteria* and *Actinobacteria*. 21 abundant genera including *Pseudomonas*, *Acinetobacter*, *Anoxybacillus*, *Sphingomonas*, *Bordetella*, and *Brevundimonas* were identified. At species level, the five most abundant bacteria identified were *Anoxybacillus kestanbolensis*, *Acinetobacter lwoffii*, *Sphingomonas yabuuchiae*, *Stenotrophomonas acidaminiphila* and *Pseudomonas veronii*. The much-discussed *Propionibacterium acnes* ranked ninth in abundance in the normal discs. Bacterial presence was confirmed through proteomics data by identification of bacteria specific proteins and vital enzymes.

Conclusion: This is the first metagenome study in world literature to document the entire microbiome of MRI normal disc. The results of this study prove that lumbar discs are not sterile structures as traditionally thought. This brings out the question of what spectrum of organisms could invoke sub-clinical infection and disc degeneration. In addition, the presence of *Propionibacterium acnes* in normal disc samples raises a doubt in its etiopathological role in disc degeneration. It would be interesting to analyze the microbiome of degenerated discs to analyze whether a differential microbial composition is associated with disc degeneration.

Kyphosis and early disc degeneration induced by paraspinal muscle insufficiency in female TSC1mKO mice

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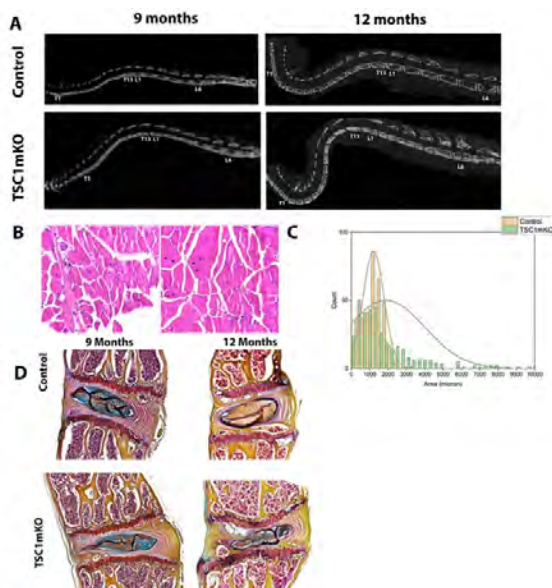
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INTRODUCTION: The progression of degenerative thoracolumbar kyphosis is known to be associated with intervertebral disc degeneration and sarcopenia. However, the cause-effect relationship remains unclear as human cohort studies are confounded by various comorbidities. TSC1 inhibitor muscle knockout (TSC1mKO) mice has constitutive activation of mammalian target of rapamycin complex 1 (mTORC1) leads to chronic muscle loss and kyphosis in later stages of their life cycle [1]. The aims of this study are to understand the roles of paraspinal muscle insufficiency, intervertebral disc degeneration and trabecular bone architectural changes in the development of kyphosis in female TSC1mKO mice.

METHODS: Twenty-four female mice were studied at 9 months (TSC1mKO, n = 3 and control, n = 7) and 12 months (TSC1mKO, n = 7 and control, n = 7), respectively. High resolution MicroCT was used to measure thoracolumbar kyphosis, disc height, and trabecular bone architecture. Myopathic changes in the paraspinal muscle were examined via H&E stain and Wheat Germ Agglutinin (WGA)/DAPI stain, and the extent of intervertebral disc degeneration was evaluated via FAST stain.



RESULTS: The H&E stained paraspinal muscle sections from female TSC1mKO mice shows signs of myopathic alterations at 12 months, including the presence of central nuclei, triangular fibres and vacuole formation (Figure 1A). WGA/DAPI stain analysis showed greater heterogeneity in muscle fiber size distribution (Figure 1B) and increase central nucleus formation/fiber in TSC1mKO mice compared to controls (TSC1mKO 20.0 ± 5.0% vs control 3.1 ± 3.2%, p=0.034). These confirm the TSC1mKO does accelerate paraspinal muscle insufficiency.

Development of thoracolumbar kyphosis is more significant in TSC1mKO mice than the control mice at 12 months (Figure 1C) (TSC1mKO 83.67 ± 17.18 vs control 52.23 ± 14.35°, p < 0.01). Comparing disc histological examination, mild NP cleft/fissure an early degeneration of the TSC1mKO mice disc is observed at 9 months before disc height loss is detectable on microCT (Figure 1D). At 12 months, AF clefts/fissure, more severe NP cleft/fissure and reduction of disc height are observed in TSC1mKO mice disc. The result matched with significantly greater reduction of disc height at L3/4 (TSC1mKO 166 ± 38µm vs control 235 ± 37 µm, p= 0.013) and L4/5 (TSC1mKO 164 ± 27 µm vs control 247 ± 59 µm, p= 0.027) in 12 months old TSC1mKO mice. Compared to the aging mice, vertebral bone density of lumbar spine is higher in 9 and 12 months old TSC1mKO mice (L4: 27.97 ± 9.17% vs 13.18 ± 5.57%, p=0.037) as there is increase trabecular thickness (113 ± 21

vs 81 ± 3µm, p= 0.0015) and number (2.45± 0.50 vs 1.25 ±0.59/mm, p=0.0046). This suggests that osteoporosis does not have an effect on the development of kyphosis.

DISCUSSION: This study demonstrates that paraspinal muscle insufficiency can accelerate the development of thoracolumbar kyphosis and cause early degeneration of the intervertebral disc. It provides a strong rationale for further study on the treatment of paraspinal muscle insufficiency to reduce susceptibility to degenerative thoracolumbar kyphosis and degenerative disc disease.

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Chromatin accessibility maps of human nucleus pulposus cells identify degeneration grade-specific epigenome signatures and gene regulatory networks

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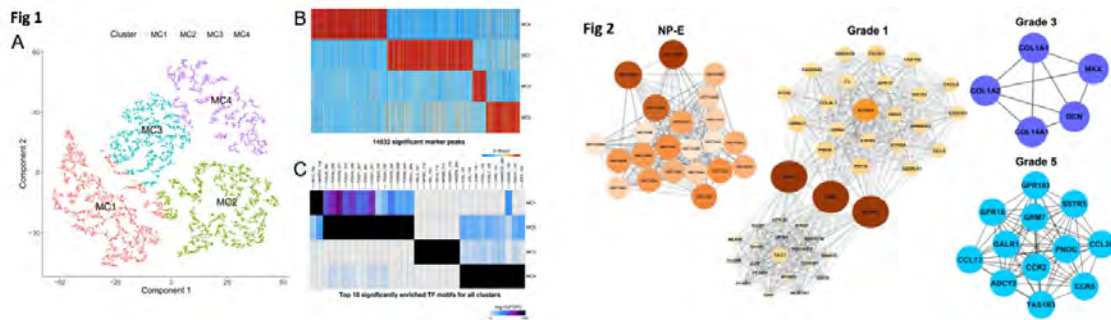
INTRODUCTION: Intervertebral disc degeneration (IDD) is characterized by substantial clinical heterogeneity despite relatively few conserved genetic alterations. To provide a basis for studying epigenome dysregulation in the setting of IDD, we present unbiased genome-wide single-cell (sc) chromatin accessibility maps for both healthy and degenerated human nucleus pulposus (NP) cells measured by the scATAC-seq assay, a first in the field.

METHODS: This study was approved by the ethics committees of Emory University (IRB# 00099028). Human NP cells were selected to reflect the clinical and biological heterogeneity of IDD, including those isolated from: (1) a Pfirrmann grade 1 disc (no degeneration) from an 18yo female, (2) a Pfirrmann grade 3 disc (mild/moderate degeneration) from a 35yo male, (3) a Pfirrmann grade 5 disc (severe degeneration) from a 66yo female. Additionally, notochordal cells from embryonic NP (ScienCell, CA) were included to provide an embryonic reference point (hereafter 'NP-E'). scATAC was performed using the 10X Genomics Chromium platform and libraries were sequenced (paired-end 40bp reads, Illumina NextSeq500). Peaks were identified for each cluster using ArchR using default parameters (FDA cutoff = 0.01, Log2FC cutoff = 1) and a Markov affinity-based graph imputation of cells (MAGIC) analysis was used to mitigate dropout noise. For gene regulatory network (GRN) inference, transcription factor binding motifs enriched among significant marker peaks (log₁₀(FDR)) were identified, followed by analysis with STRING (v11.0) and Cytoscape (v3.7.1).

RESULTS: After removing 1,481 nuclei (low-quality), 7,265 nuclei were retained for downstream analysis. **Figure 1A** presents these results visualized in 2-dimensional t-SNE space (MC1 = Grade5, MC2 = Grade1, MC3 = Grade3, MC4 = NP-E). We identified 14,832 peaks across all clusters exhibiting cluster-specific accessibility (**Fig 1B**). The top 10 most significantly enriched transcription factor binding motifs for each cluster is shown in **Fig 1C**. Finally, an interaction network analysis revealed significant functional networks involving diverse biological processes related to IDD (**Figure 2**). The NP-E and Grade 1 interaction networks were highly dense with histone genes being overrepresented in NP-E and biochemical pathway genes enriched in Grade 1 cells. The Grade 3 network was populated by Collagen and MKX genes, whereas multiple chemokines constitute the Grade 5 network.

DISCUSSION: We found distinct chromatin profiles for a variety of MRI-based degeneration grades, with each IDD grade having its own fingerprint of active GRNs being controlled at the epigenome level. This provides the best evidence to-date that epigenomic dysregulation may play a role in IDD pathogenesis. Footprinting analysis of transcription factor binding motifs and the imputation of GRNs for each IDD severity grade allowed for the determination of how GRNs and epigenetic states change as IDD severity progresses. Human NP cells isolated from either healthy, moderately, or severely degenerated IVDs had distinct epigenetic profiles on top of a shared core of *cis*- and *trans*-regulatory elements controlling each cell's epigenetic state. This data establishes a community resource for studying NP cell epigenome dysregulation in the setting of IDD and demonstrates the feasibility of epigenomic chromatin accessibility mapping of NP cells from clinical specimens.

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Rapamycin Ameliorates Age-Associated Intervertebral Disc Degeneration In Male Marmosets

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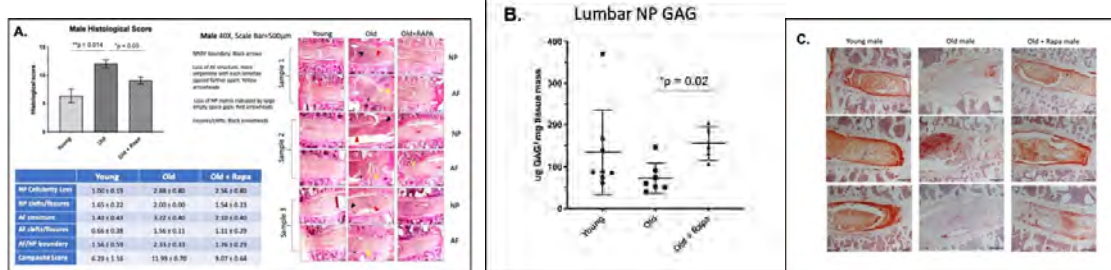
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INTRODUCTION: Age-associated intervertebral disc degeneration (IDD) is a major contributor to low back pain and physical disability of people older than 45 years in the US. Rapamycin has been shown in several animal models, including mammalian, to increase lifespan and decrease aging and age-associated pathologies, including cancer, cardiac and neurodegenerative diseases^{2,3,4,5}. Rapamycin is an FDA approved drug that inhibits mammalian target of rapamycin (mTOR) complex 1, which is a master regulator of cell growth and proliferation signals. However, it has not yet been determined if rapamycin treatment influences age-associated IDD. Hence, the goal of this study was to determine the effect of a one-year oral rapamycin treatment on IDD progression in old marmosets.

METHODS: Old male marmosets were given rapamycin using a delivery system that microencapsulates rapamycin in a eudagrit coating and is mixed into yogurt for feeding via a syringe to accurately account for each daily dose¹. As control, old animals were given empty eudagrit capsules delivered the same way, for one year. Spine specimens were collected from young (<5 years old), old (>10 years old) + vehicle, and old + rapamycin marmosets. Treatment was given for one year prior to sacrifice. Cellularity and histological structure was assessed using H&E staining. Disc proteoglycan (PG) content was assessed by aggrecan immunohistochemistry (IHC) and aggrecan fragmentation by Western Blot (WB). DMMB assay was used to quantify sulfated GAG. Autophagy was measured via WB for LC3-II, p62, Atg7, beclin-1, and Atg12-Atg5 expression. Student's t-test was used for significance, n=3-4.

RESULTS SECTION: Rapamycin treatment significantly decreased histological scoring for IDD characteristics compared to control old marmosets (Figure A.) Rapamycin treatment significantly restored older marmosets GAG levels and increased aggrecan IHC staining (Figure B,C, respectively). Similarly, rapamycin treatment decreased ADAMTS-mediated and MMP-mediated aggrecan fragmentation (data not shown). Rapamycin treatment did not significantly affect the autophagy markers LC3-II, Atg7, beclin-1, or Atg12-Atg5 expression, but it did significantly decrease p62 expression (data not shown).

DISCUSSION: Overall, rapamycin treatment significantly restored proteoglycan homeostasis and significantly improved histological score in marmosets. These results indicate that one-year daily rapamycin treatment delayed IDD progression in older marmosets. Interestingly, autophagy related proteins were not significantly increased in older marmosets treated with rapamycin, as rapamycin is a known inhibitor of mTOR, which is a negative regulator of autophagy. This finding warrants further study as rapamycin treatment has been shown to increase autophagy in other tissues. This is the first study to investigate the in vivo effects of rapamycin treatment on age-associated IDD in a nonhuman primate model and suggests rapamycin might be a viable treatment to improve IDD characteristics in patients.



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Expression and distribution of M1 and M2 macrophages in the degeneration process of human lumbar intervertebral disc herniation: A histological and clinical efficacy analysis

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Introduction: Macrophage phenotypic subtypes and association between M1/M2 positivity and clinical efficacy in relation to LDH have not been reported. Hence, it is important to determine the expression and distribution of M1, M2 macrophages in LDH and the association between M1/M2 positivity and clinical efficacy of LDH therapy.

Methods: Immunohistochemical analyses of M1 and M2 markers, induced nitric oxide synthase (iNOS) and CD206, respectively, were used to identify M1/M2 macrophages and analyze positivity and distribution in LDH patients. The association between positivity, clinical characteristics, and clinical efficacy was evaluated. Differences in the presence of M1 and M2 macrophages with or without modic changes (MCs), as well as in the high-intensity zone (HIZ), were also analyzed.

Results: iNOS and CD206 were expressed in all 79 consecutive LDH patients tested. Morphology and distribution of iNOS+ and CD206+ cells varied at different degenerative LDH stages. Furthermore, iNOS+ cells displayed a significantly decreasing trend in Pfirrmann grade and age, whereas CD206 positivity showed the opposite. Besides, iNOS+ showed a positive correction with visual analog scale (VAS) scores, while CD206+ exhibited positive correction with Oswestry disability index (ODI) on preoperative day 3. A significant increase in iNOS+ cells was observed in the HIZ, whereas more CD206+ cells were found in MC tissues.

Conclusion: M1/M2 positively in all LDH with different morphology and distribution suggested that these originated from recruited and resident macrophages. Significantly different expression in MCs and the HIZ and significant correlation with clinical efficacy indicated the important role of M1/M2 transition in the immune and inflammatory response in LDH. Management of M1/M2 transition may be a feasible approach for preventing LDH.

Paraspinal muscle contractile function is impaired with chronic spine disease: a study using the ENT1 KO mouse

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Introduction: Altered muscle structure and function are associated with various spine pathologies¹ and are therefore linked with a lowered quality of life for millions of patients annually. Commonly reported muscle adaptations to spine pathology include: muscle atrophy², fibre type changes³, increases in intramuscular fat and connective tissue³, and altered passive mechanical properties¹. However, the fundamental cellular mechanisms responsible for active spine muscle contraction and force production have never been investigated in any manner, let alone compared between healthy and pathological spine conditions, thus impeding proper prevention and resolution. The aim of the current work was to further develop our understanding of the mechanical interplay between spine pathology and the surrounding musculature by measuring the active contractile properties of the muscles surrounding the spine. This was performed using the *ENT1*^{-/-} mouse, which is shown to develop progressive mineralization of the fibrous connective tissues of the spine⁴. It was hypothesized that the active contractile properties of the spine muscles would be impaired in *ENT1*^{-/-} knockout (KO) when compared to wild-type (WT) mice.

Methods: Twenty-Four mice (12 *ENT1*^{-/-} (KO) and 12 wild-type (WT)) were sacrificed at 8 months-of-age. Lumbar multifidus and erector spinae were harvested from all animals, and the tibialis anterior (TA; control) was excised from 8 animals (4 *ENT1*^{-/-} and 4 WT). Single muscle fibres were maximally activated by immersion in a high-Ca²⁺ activating solution, and contractile measurements of specific force (maximal steady-state force normalized to cross-sectional area) active modulus (normalized stiffness) and unloaded shortening velocity (speed of shortening) were performed. Following the mechanical testing, fibre types were determined by measuring the myosin heavy chain (MHC) isoform using sodium dodecyl sulfate–polyacrylamide gel electrophoresis (SDS–PAGE). Differences in contractile properties between *ENT1*^{-/-} (KO) and WT mice were tested using unpaired two-tailed Students t-test with 0.05.

Results: The multifidus demonstrated decreases in specific force (Figure 1: type IIax: 36% decrease; type IIb: 29% decrease), active modulus (Figure 2: type IIax: 35% decrease; type IIb: 30% decrease) and unloaded shortening velocity (Figure 3: type IIax: 31% decrease) in the *ENT1*^{-/-} KO group when compared to WT controls. The erector spinae specific force was reduced in the *ENT1*^{-/-} mice when compared to WT (Figure 1: type IIax: 29% decrease), but active modulus and unloaded shortening velocity were unchanged. No differences were observed in the contractile properties of the TA muscle, validating that impairments observed in the spine muscles were specific to the underlying spine pathology and not the global loss of ENT1.

Discussion: The current work demonstrates, for the first time, a significant impairment in the active contractile function of the spine muscles, in particular the multifidus, associated with ectopic spine mineralization in *ENT1*^{-/-} (KO) mice. Earlier work demonstrated an inverse reciprocal relationship between the mechanical properties of the spine and the passive properties of the surrounding musculature⁵. This work expands these findings by demonstrating significantly impaired contractile function in the spine muscles of the *ENT1*^{-/-} mice, likely a consequence of the increased mineralization and stiffness present in their spines.

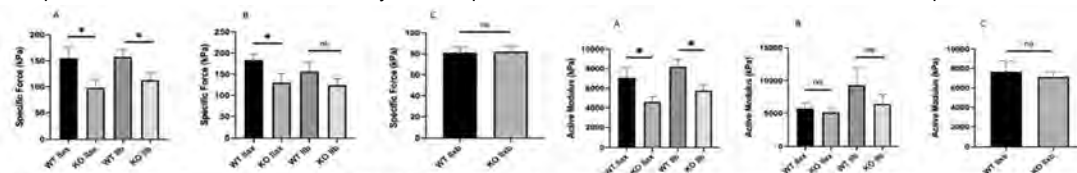


Figure 1. Specific force: A: multifidus (IIax WT n = 14, KO n = 15, IIb WT n = 21, KO n = 21) B: erector spinae (IIax WT n = 13, KO n = 13; IIb WT n = 18, KO n = 21) and C: TA (WT: n = 12, KO: n = 12). Values are presented as means ± SEM, and statistically significant differences (p < 0.05) are indicated by asterisks (*).

Figure 2. Active modulus: A: multifidus (IIax WT n = 14, KO n = 15, IIb WT n = 21, KO n = 21) B: erector spinae (IIax WT n = 13, KO n = 13; IIb WT n = 18, KO n = 21) and C: TA (WT: n = 12, KO: n = 12). Values are presented as means ± SEM, and statistically significant differences (p < 0.05) are indicated by asterisks (*).

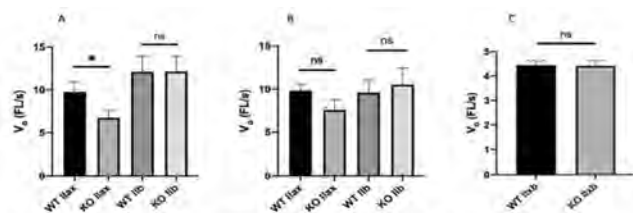


Figure 3. Unloaded shortening velocity (V_0): A: multifidus (IIax WT n = 14, KO n = 15; IIb WT n = 21, KO n = 21) B: erector spinae (IIax WT n = 13, KO n = 13; IIb WT n = 18, KO n = 21) and C: TA (WT: n = 12; KO: n = 12). Values are presented as means ± SEM, and statistically significant differences (p < 0.05) are indicated by asterisks (*).

Evaluating Senolytics as a treatment option for Lower Back Pain in SPARC-null mice

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INTRODUCTION:

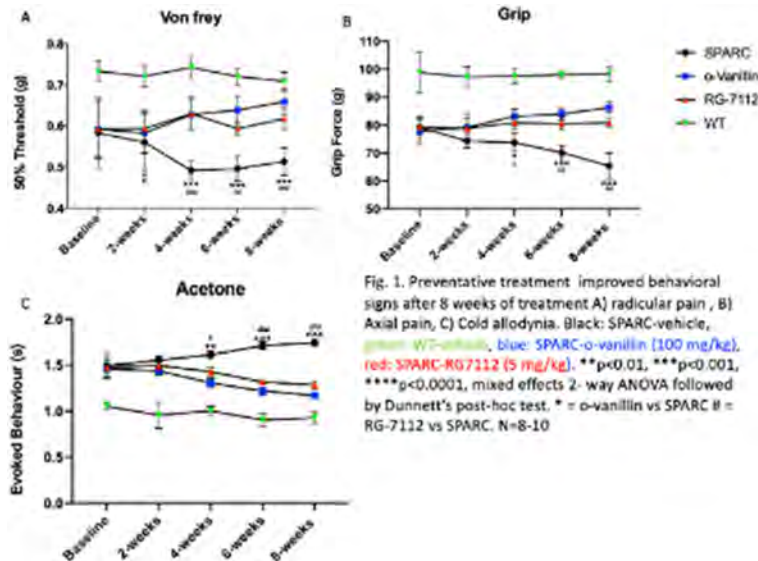
In ageing and degenerating IVDs, tissue homeostasis is disrupted by the accumulation of senescent cells producing inflammatory and nociceptive factors that cause pain and inflammation, along with proteases degrading the tissue. We propose senolytic drugs (RG-7112 & o-Vanillin) that target and remove senescent cells from the IVDs will improve tissue homeostasis and provide symptomatic pain relief. Currently, in a human IVD *in vitro* model we have seen a significant decrease in both gene expression and protein expression of senescent markers and inflammatory markers. One of the drawbacks of senolytic agents currently under investigation is their failure to target the same cell type in different species, or different cell types within a species. It is therefore imperative to test novel agents for effectiveness against senescent cell burden, and for potential deleterious side effects, in pre-clinical models with clinically relevant cells. The **overall objective** of this project is determining if senolytic drugs reduce pain and improve tissue homeostasis in middle-aged SPARC null mice with back pain *in vivo*. We **hypothesize** that senescent cells contribute to painful IVD degeneration and their presence prevents spontaneous and induced tissue repair. Therefore, removal of these cells will prevent further degeneration and pain and create an environment more favorable for tissue maintenance and even regeneration. This project will determine the potential for RG-7112 & o-Vanillin to remove senescent cells, promote tissue regeneration and reduce pain in a SPARC-null mice animal model.

METHODS:

Animals 5-6-month-old SPARC-null mice with signs of IVD degeneration and low back pain and age-matched wild-type will be used in this study. The mice will be randomized into treatment groups and drugs will be administered by oral gavage of Treatment 1: 5 mg/kg RG7112; Treatment 2: 100 mg/kg o-Vanillin or Treatment 3: saline as control, once a week for 8 weeks. Biochemical data will be assessed by repeated measures one-way ANOVA or two-tailed unpaired t-tests. Pain-like behavior data will be analyzed by repeated-measure 2-way-ANOVA. For two-way ANOVA the between groups variables will be strain and treatment group and the within group variable will be time.

RESULTS SECTION:

During pain behaviour analysis, we have seen that radicular pain (A), axial discomfort (B) and cold allodynia (C) have been significantly reduced as of 4 weeks of treatment in SPARC-null senolytic treated groups. Furthermore, we observe a greater behavioral effect of the senolytic treatments at the 8-week time point. Our preliminary data for the biochemical analysis of the cultured isolated IVDs has shown that SASP factors IL-6, IL-8 and TNF- α have been significantly reduced in treated groups.



DISCUSSION: Our goal is to demonstrate that these compounds can reduce the expression of pain behaviours, pain mediators and improve tissue homeostasis in a clinically relevant mouse model of lower back pain and IVD degeneration. If proven true, these therapies could revolutionize treatment of back pain for millions of patients worldwide and be one step closer to offering a preventative treatment for individuals at risk of lower back pain or avoid/prolong the need for invasive surgery.

Disc 'Dysbiosis' as a cause of Inflammaging and Lumbar Intervertebral Disc Degeneration – Revelations from Next Generation Sequencing Analysis

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Introduction: Apart from mechanical and genetic etiology, the possibility of sub clinical infection and inflammaging as a cause of disc disease and back pain is a raging controversy. The organisms implicated are fastidious and require stringent clinical atmosphere and have low positivity in traditional methods of culture and identification. The use of Next Generation Sequencing has revolutionized our ability to identify the presence of organisms even in low quantity and has thus questioned the traditional concept, that a healthy lumbar disc is sterile. The aim of the study was to analyze the microbiome of lumbar discs in health and disease

Materials and Methods: Eight Degenerated (DD) and eight control disc tissues (ND) were obtained from MRI normal spine segments harvested from voluntary organ donors. Sequence analysis of bacterial 16S rRNA genes containing the hypervariable V1-V9 regions were performed to study the composition of the human disc microbiome in health and disease using the Illumina MiSeq platform.

Results: All 16 samples had bacterial presence with varying diversity and abundance. Proteobacteria was the most abundant phylum of bacteria in both DD and ND. However, the Normal discs were characterized by a higher abundance of *Firmicutes* and *Actinobacteria* (protective gut commensals). At genus level, ND harbored 21 different abundant genera compared to only 13 in DD. *Pseudomonas* was abundant in DD (50%) and only 14.55% in ND. The second most abundant genus in ND, *Sphingomonas* (12.28%) was decreased in DD (4.68%). Beneficial bacteria like *Proteobacteria* (*Herbaspirillum* and *Devosia*), *Firmicutes* (*Lentibacillus*, *Planomicrobium* and *Virgibacillus*) and *Actinobacteria* (*Saccharopolyspora*) were present only in ND. A total of 355 species were identified in ND compared to only 346 in DD. *Blautia producta* (gut-microbe), *Propionibacterium granulosum* (skin-commensal) and *Sphingomonas yabuuchiae* (anti-tumoral) were found to be abundant in ND when compared to DD. In ND, 32 unique bacteria including known probiotics (*Bacillus coagulans* and *Bacillus clausii*) and bacteria with antimicrobial properties against *Pseudomonas aeruginosa* and *Staphylococcus aureus* (*Bdellovibrio bacteriovorus*) were present. Interestingly, pathogenic bacteria (*Prevotella tanneriae*, *Halomonas nitrophilus*, *Streptococcus alactolyticus*, *Streptococcus anginosus*, *Prevotella pallens*, *Avibacterium gallinarum* and *Enterobacter cowanii*) were present only in DD.

Conclusion: The relative abundance of bacteria varied significantly between ND against DD. Although *Pseudomonas* species were common to both groups, relative abundance was very low in ND. Further the presence of 32 unique bacteria in ND indicate differing ratios of protective and pathogenic bacteria in both groups implying 'Dysbiosis', a phenomena implicated in various diseases which is defined as any perturbation of the normal microbiome content that could disrupt the symbiotic relationship between the host and associated microbes resulting in disease. Our documentation of diverse pathogenic bacteria strongly supports 'Inflammaging' theory.

Effects of exosomes from mesenchymal stem cells on nucleus pulposus cells: a potential cell-free therapy.

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Introduction: Intervertebral disc degeneration (IDD) affects more than 80% of the population and is often linked to a reduction of the proteoglycan content within the nucleus pulposus (NP). Nutritional decline and accumulation of degraded matrix products promote the inflammatory process favoring the onset of disease. Several regenerative approaches based on mesenchymal stem cell (MSC) therapy have been explored. MSCs mediate their regenerative and immunomodulatory effects mainly through paracrine mechanisms regulating the homeostasis and behavior of recipient cells (1). Recently, paracrine factors and extracellular vesicles (EVs) such as exosomes have been described to play a fundamental role in the cross-talk between bone marrow MSCs and NP (2). EVs vehicle different molecules: proteins, nucleic acids and lipids involved in intercellular communication regulating the homeostasis of recipient cells.

The aims of this study were to evaluate the effects of human BM-MSCs derived exosomes on human NP cells (NPCs) and to analyze the effects of both conditioned media (CM) and MSCs-exosomes on an *in vitro* model of IDD.

Methods: Exosomes were isolated through a multistep ultracentrifugation and filtration of BM-MSCs conditioned media (CM), obtained by culturing MSCs in a serum exosomes-free medium for 48 hours. Exosomes morphology was characterized by transmission electron microscopy (TEM). The exosomes were quantified by bicinchoninic acid assay (BCA) and cryopreserved at -80 °C. hNPCs derived from surgical specimens were expanded and encapsulated in alginate beads and treated with growth medium (controls), exosomes, CM, with or without interleukin-1 beta (IL-1b). After 24 hours, gene expression levels of catabolic (MMPs, ADAMTs, TIMPs), anabolic (COL2A1, ACAN, SOX9) and inflammatory genes (IL-6, IL-1b, iNOS) were analyzed through real time-PCR. NPCs in alginate beads were stained with LIVE/DEAD viability assay and detected using confocal immunofluorescence microscopy. Data were analyzed using Graphpad prism 8 and expressed as mean ± S.D. One-way ANOVA analysis was used to compare differences among three or more groups.

Results: TEM analysis confirmed the cup-shaped vesicles in our preparations with a typical size of 50–130 nm in diameter. Live / dead staining suggested that cell viability increased after exosome treatment whereas decreased in presence of IL-1b. Gene expression levels resulted to be modulated. The expression of IL-6 and MMP 13 mRNA resulted downregulated after treatment with exosomes and CM whereas anabolic gene expression (COL2A1, ACAN, SOX9) increased compared to controls. Interestingly, exosomes were able to change anabolic and catabolic gene expression levels differently from CM.

Discussion: Our experimental conditions suggest that both exosomes and CM from BM-MSCs are capable to counteract the inflammatory stimuli of IL-1b on NPCs cultured in a 3D culture system. Moreover, proliferation increased while anabolic gene expression up regulated after exosomes treatment. BM-MSC derived EVs could be an interesting alternative strategy in intervertebral disc regeneration, overcoming the costs and translational limits of cell therapy to the clinical practice. However, due to many unknown pathophysiological processes in which exosomes are involved and the small amount of data will need further studies to confirm the ability of these nanoparticles to promote a long-term intervertebral disc health and homeostasis.

1. Teixeira et al. Immunomodulation of Human Mesenchymal Stem/Stromal Cells in Intervertebral Disc Degeneration Insights From a Proinflammatory/Degenerative Ex Vivo Model Spine: June 15, 2018 - Volume 43 - Issue 12 - p E673-E682
2. Xia et al. Mesenchymal stem cell-derived exosomes ameliorate intervertebral disc degeneration via anti-oxidant and anti-inflammatory effects. *Free Radic Biol Med.* 2019 Nov 1;143:1-15. Epub 2019 Jul 24.

Single-cell RNA-seq of human disc cells reveals new diagnostic and therapeutic biomarkers for intervertebral disc degeneration and back pain.

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INTRODUCTION: Single-cell RNA-seq (scRNA-seq) is a powerful tool for analyzing heterogeneous and functionally diverse cell populations. Visualizing scRNA-seq data can help us effectively extract meaningful biological information and identify novel cell subtypes. Low back pain continues to be a major public health problem worldwide. In this study, we used single-cell transcriptomic analysis to identify new specific biomarkers for nucleus pulposus (NP) and annulus fibrosus (AF) cells and to define cell populations within non-degenerating and degeneration human intervertebral discs (IVD).

METHODS: Straight from digestion, human NP and AF cells were separately isolated from non-degenerating (ND) and degenerate (D) discs of the same individual. Then, cells were subjected to droplet-based scRNA-seq using 10X Genomics platform. A total of 3134 (AFD), 3182 (AFND), 3665 (NPD) and 3918 (NPND) individual cells were profiled from ND and D discs respectively. Unsupervised clustering of the cells based on the gene expression profiles using the R seurat package (1) select the top 500 most altered genes and Uniform Manifold Approximation and Projection (UMAP) scRNA-seq visualization software constructs a high-dimensional graph representation of the data and identified the number of cell clusters. Differentially expressed genes between clusters were identified and classified with the R package and gene ontology analysis was performed using ToppGene (2). Candidate genes identified through scRNA-Seq were validated by rt-PCR. Immunohistochemistry and western blot analysis were used for validation at the protein level.

RESULTS: Here, we report both known and novel markers for NP and AF cell types and the lineage patterns controlling human disc degeneration pathogenesis. Cluster analysis based on differential gene expression delineated 8 cell subsets by comparing the scRNA-seq datasets from degenerate and healthy NP and AF cells. Gene expression profiles of IVDs at different stages of degeneration at single-cell resolution revealed that degeneration changes the frequency of disc-cell sub-populations. Specifically, we observed novel markers for disc degeneration and demonstrated a relationship between cell senescence and IVD degeneration using computational analysis. Notably, we propose MGST1, Vimentin, MT1G, MT1F, HILPDA, NDRG1, Ceruloplasmin, ATG7, ERFF1 and PTGS2 as novel specific biomarkers for distinguishing NP cells from AF cells. SOD2, SYF2 (p29) and CIRBP are proposed as predictive targets for the early diagnosis and treatment of disc degeneration. MGST1, Vimentin, SOD2 and SYF2 (p29) were validated as new biomarkers by immunohistochemistry and western blot.

Discussion: Our high-resolution single cell expression data provide new insights into disc cell phenotypes and markers of intervertebral disc degeneration that could improve diagnostic and be used to evaluate the effect of novel therapeutic options.

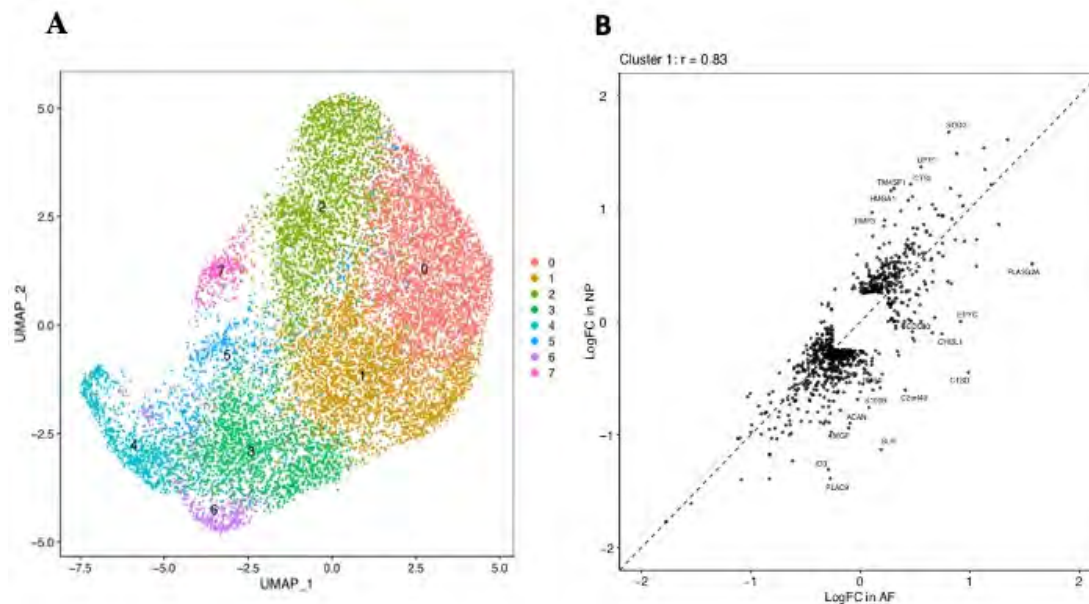


Figure A. NP and AF cells of degenerate and non-degenerate tissue of the same individual. Cells are clustered according to transcriptome similarity with 8 putative cell clusters identified.

Figure B. Gene expression correlation in NP vs AF cells. Scatter plot with genes detected at variable expression level in cluster 1.

1. Kiselev VY, Kirschner K, Schaub MT, et al. SC3: consensus clustering of single-cell RNA-seq data. *Nature Methods* 2017; 14: 483-86.
2. Satija R, Farrell JA, Gennert D, et al. Spatial reconstruction of single-cell gene expression data. *Nature Biotechnology* 2015; 33: 495-502.

Potential of MSC secretome to modulate degenerative changes in a loaded annulus fibrosus organ culture model

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INTRODUCTION: Failure of the annulus fibrosus (AF) is often associated with disc herniation and activation of the immune system. Mesenchymal stem/stromal cell (MSC)-based therapies have been proposed for disc degeneration/herniation-associated back pain, despite limited knowledge on their mechanism of action after transplantation. Hence, we investigated the impact of a cell-free therapeutic approach with MSC secretome on AF organ cultures (AF-OCs) exposed to mechanical overload and a pro-inflammatory environment¹.

METHODS: AF rings were isolated from bovine tails of 12-24 months-old animals (n=6-18). AF-OCs were exposed to upper-physiological cyclic tensile strain (CTS, 9 %, 1 Hz, 3 h/day) and 10 ng/mL interleukin (IL)-1 β (CTS+IL-1 β) in a 6-stations custom-made device¹. Sub-groups of stimulated AF-OCs were treated with either human MSC in co-culture or secretome produced by preconditioned human MSC (n=3, 1 female/2 male, age: 23 \pm 1.5 years; preconditioning: 10 ng/mL IL-1 β and 6 % O₂ for 48 h). Unstimulated AF-OCs were used as controls. AF cells gene expression for regulators of immune cell function, catabolic enzymes and matrix components was analyzed by real-time PCR using bovine primers. Interleukin (IL)-6 and metalloproteinase (MMP)-3 tissue distribution were analyzed by immunohistochemistry. Glycosaminoglycan, elastin and collagen tissue content were determined by biochemical assays. AF adhesive strength was quantified in the tissue using a peel-force test¹. Kruskal-Wallis test was used to determine differences between the groups in GraphPad Prism 7 software. P-values < 0.05 were considered significant.

RESULTS: Four days of CTS+IL-1 β stimulation up-regulated the expression of bovine immune response mediators *IL-6*, *IL-8* and *CD46* (p<0.05), and of catabolic enzymes *MMP-1* and *MMP-3* (p<0.01). In contrast, treatment of the CTS+IL-1 β -stimulated AF-OCs with the MSC secretome down-regulated the expression of these markers (p<0.05, Figure 1A). The changes in IL-6 and MMP-3 production were confirmed at protein level. In contrast, the MSC in co-culture only down-regulated *IL-8* expression (p<0.05). Interestingly, both the MSC in co-culture and the secretome contributed to a down-regulation of collagen type I (*COL1A1*) expression by the bovine AF cells (p<0.001), but only the secretome induced a significant decrease of total collagen content in the AF matrix (p<0.05, Figure 1B) and a decrease of the AF adhesive strength (p<0.05, Figure 1C), when compared to the CTS+IL-1 β stimulation alone. No differences were observed in glycosaminoglycan or elastin tissue content under the different stimuli.

DISCUSSION: AF cells presented a pro-inflammatory/degenerative phenotype, four days after CTS+IL-1 β stimulation. The MSC secretome had a stronger impact than the MSC in co-culture on decreasing the immune and catabolic response of AF cells activated by CTS+IL-1 β conditions. However, the secretome also contributed to a further decrease of collagen at gene/protein level and of the AF mechanical strength observed in the CTS+IL-1 β group. Using the MSC secretome as a therapeutic approach to modulate disc degeneration-associated inflammation seems to be an alternative option to MSC transplantation. Still, it requires further mechanistic investigations and evaluation of its long-term success *in vivo*, before moving to clinical trials. **Acknowledgements:** Ulm University (LSBN.0157).

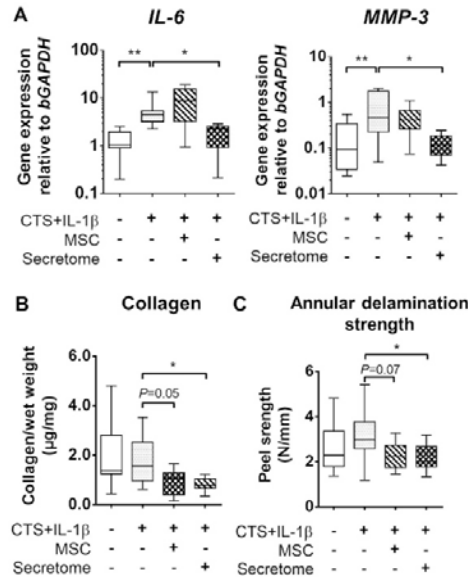


Figure 1. A) Relative mRNA expression of bovine *IL-6* and *MMP-1*. Results were normalised to expression level of bovine *GAPDH*. **B)** Collagen content in the AF tissues normalized to wet weight (μ g/mg). **C)** AF peel strength as function of displacement rate (N/mm). n = 6-18, *p<0.05, **p<0.01, ***p<0.001.

1. Saggese et al., Eur Spine J, 2019.

The effect of posterior lumbar spinal surgery on biomechanical properties of rat paraspinal muscles 13 weeks post-surgery

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Introduction: Paraspinal muscle is a key spine stabilizer, and iatrogenic muscle damage may lead to postoperative low back pain and functional disability [1]. The influence of surgery on paraspinal muscles is important, but few biomechanical studies have been done.

Aim: The purpose of this study is to evaluate the passive mechanical properties of paraspinal muscle after posterior spinal surgery in an animal model.

Methods: 12 Sprague-Dawley rats were divided equally into two groups, sham, and surgical injury. For the sham group, the skin and lumbodorsal fascia was incised at midline. For the surgical injury group, the paraspinal muscles were detached from the vertebrae, per normal surgical procedure. After 13 weeks from the initial surgery, multifidus and longissimus biopsies (5x5mm) at L1, L3, and L5 levels were harvested. Elastic modulus of 3 muscle fibers and 3 to 6 muscle fiber bundles of each muscle were tested biomechanically. Samples were put in a relaxing solution and tied to pins attached to a micro-level force transducer and manually stretched in 10% strain increments, separated by 4 minute-periods of load relaxation. For histological analysis, snap frozen samples were cryosectioned and stained for collagen I and perilipin positive cells. Images were analyzed for the deposition of collagen I and the quantity of perilipin positive cells. The data of both the multifidus and longissimus fibers and fiber bundles were compared using the Mann-Whitney test and the level difference of the passive stiffness of each muscle (L1, L3, and L5) was compared using a Friedman ANOVA (i.e. non-parametric one way) in SPSS software.

Results: 112 fibers and 137 bundles of the sham and 108 fibers and 142 bundles of the surgical injury group were tested. The elastic moduli of the multifidus and longissimus muscle fibers, as well as the longissimus fiber bundles, were not statistically different between the surgery and sham groups, (Figure 1, $p > 0.01$). However, the elastic modulus of the multifidus muscle fiber bundles was significantly greater in the surgical injury group (Figure 2, surgical injury group median 81 kPa, range 23-261; sham median 38 kPa, range 23-57, $p < 0.01$). For histology, only collagen I deposition in multifidus had a significant difference between the two groups (surgical injury group median 20.8%, range 11-26; sham median 5.8%, range 4-8; $p < 0.01$). The elastic modulus of the multifidus muscle fiber bundles in the surgical injury group was not significantly different between the spinal levels, but there was a trend toward significance (Figure 3; $p < 0.05$, L1 median 100 kPa range 55-368; L3 median 163 kPa range 27-764; L5 median 24 kPa range 16-110).

Discussion: Posterior spine surgery changes the passive mechanical properties of multifidus fiber bundles. Proximal fibrotic changes that result in stiffer muscle are likely important in post-operative complications like adjacent segment disease and proximal junction kyphosis. Future work will address the changes in muscle properties in people with spinal deformity.

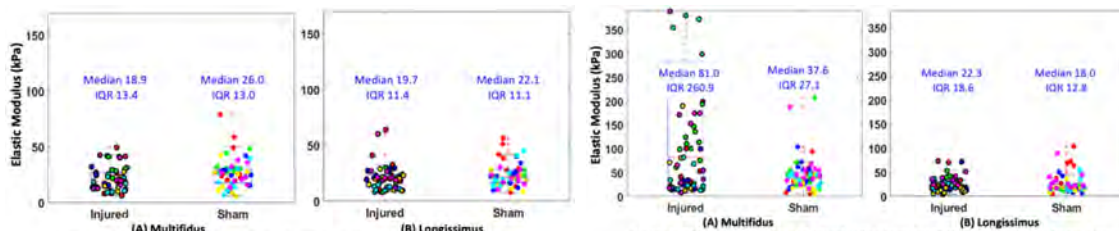


Figure 1. The Elastic Modulus of Muscle Fibers in Surgical Injury and Sham Group

Figure 2. The Elastic Modulus of Muscle Fiber Bundles in Surgical Injury and Sham Group

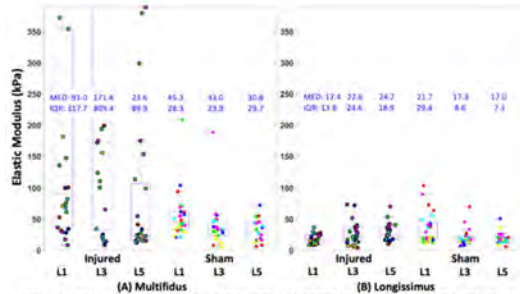


Figure 3. The Fiber Bundle Stiffness of Surgical Injury and Sham Group in each Spinal level

[1] Kawaguchi Y., Matsui H., Tsuji H., Spine 1996; Volume 21 Issue 8; 941-944

The Impact of Preoperative Cross-sectional Area of Psoas Muscle on Postoperative Outcomes of Adult Spinal Deformity Surgery

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Introduction: Proximal junctional kyphosis (PJK)/proximal junctional failure (PJF), which is caused by soft tissue or bony failure, is a critical challenge in ASD surgery. The cross-sectional area of psoas muscle has been used as a parameter of sarcopenia and reported to have a negative impact on clinical outcomes after lumbar surgery. However, it is unclear whether it also impacts outcomes of adult spinal deformity (ASD) surgery. The objective of this study was to examine the impact of preoperative cross-sectional area of psoas muscle on postoperative outcomes of ASD surgery.

Methods: ASD patients who were over 18 years old and underwent posterior fusion surgery with more than 5 levels with 6 months follow-up were included in this study. The cross-sectional area of psoas muscle was measured on T2-weighted axial images at L3/4 of preoperative MRI. Normalized total psoas area (NTPA) was calculated as total psoas area normalized to patient height. Outcomes were patient reported outcome measures (PROMs) (ODI, SRS-22) and radiographic parameters (PT, PI, SS, LL, SVA, C2-C7 SVA, C2-T3 SVA, TS, TK, TPA and Cobb angle) at pre-op and 6 months and prevalence of PJK/PJF at 6 months.

Results: The total of 65 patients were included in this study. Patients were divided into 2 groups [lower NTPA group (LG) and Higher NTPA group (HG)] at the point of the sex-specific lowest quartile of NTPA threshold (male 573 mm²/m², female 493 mm²/m²). There were no significant differences in PROMs between groups at all points, however, ODI and SRS-22 including all sub-items except for mental health were worse in the LG at 6 months, compared to the HG. (Table 1). In radiographic parameters, C2-C7 SVA was significantly higher and SS was significantly lower in the LG at pre-op and 6 months (Table 2). Prevalence of PJK was significantly higher in the LG, compared to the HG, while there were no patients with PJF in both groups (Table 3).

Conclusion: The decrease of psoas cross-sectional area on preoperative MRI significantly increased prevalence of PJK. It was also associated with higher C2-C7 SVA and lower SS before surgery and at 6 months.

		Low NTPA (n=16)	High NTPA (n=49)	P value
ODI	Pre	41.4 ± 21.5	34.4 ± 18.9	0.246
	6w	54.5 ± 23.5	46.1 ± 16.9	0.319
	6m	34.5 ± 20.3	26.1 ± 19.6	0.128
SRS-22 Function	Pre	3.1 ± 1.0	3.2 ± 1.0	0.474
	6w	2.4 ± 0.7	2.7 ± 0.6	0.238
	6m	3.4 ± 0.8	3.5 ± 0.9	0.405
SRS-22 Pain	Pre	2.6 ± 1.1	2.8 ± 1.0	0.596
	6w	2.0 ± 0.9	2.4 ± 0.8	0.186
	6m	3.0 ± 1.1	3.4 ± 0.9	0.192
SRS-22 Self image	Pre	2.5 ± 1.0	2.5 ± 0.8	0.837
	6w	3.2 ± 0.7	3.8 ± 0.9	0.068
	6m	3.6 ± 0.8	4.0 ± 0.8	0.051
SRS-22 Mental health	Pre	3.9 ± 0.8	3.5 ± 1.0	0.211
	6w	3.9 ± 0.9	3.7 ± 0.8	0.623
	6m	3.9 ± 0.7	3.8 ± 0.8	0.951
SRS-22 Satisfaction	Pre	2.5 ± 1.5	2.2 ± 0.8	0.900
	6w	3.9 ± 1.0	4.4 ± 0.6	0.271
	6m	4.3 ± 0.7	4.3 ± 0.8	0.700
SRS-22 Total	Pre	3.0 ± 0.9	2.9 ± 0.7	0.945
	6w	3.0 ± 0.6	3.3 ± 0.6	0.238
	6m	3.5 ± 0.7	3.8 ± 0.7	0.203

		Low NTPA (n=16)	High NTPA (n=49)	P value
C2-C7 SVA	pre	34.2 ± 14.8	26.4 ± 11.8	0.040
	6w	36.0 ± 19.5	28.3 ± 11.8	0.053
	6m	34.5 ± 17.4	28.9 ± 10.3	0.044
T1 slope	pre	32.5 ± 14.6	28.4 ± 15.5	0.309
	6w	21.8 ± 12.2	28.1 ± 13.1	0.715
	6m	29.7 ± 13.9	27.7 ± 13.4	0.707
TK	pre	38.4 ± 18.1	35.4 ± 21.7	0.578
	6w	48.1 ± 10.6	41.9 ± 14.2	0.273
	6m	45.6 ± 11.7	42.4 ± 13.1	0.573
TPA	pre	31.7 ± 15.1	26.9 ± 18.2	0.150
	6w	16.3 ± 13.6	16.9 ± 11.8	0.831
	6m	16.7 ± 14.0	17.8 ± 12.0	0.733
C2-T3 SVA	pre	70.9 ± 27.1	57.3 ± 24.2	0.107
	6w	72.6 ± 20.4	61.2 ± 22.1	0.337
	6m	68.5 ± 27.5	58.2 ± 20.8	0.269
PT	pre	26.0 ± 10.3	22.0 ± 11.8	0.180
	6w	17.9 ± 12.5	16.7 ± 9.3	0.207
	6m	49.0 ± 11.5	17.0 ± 9.4	0.939
SS	pre	25.0 ± 11.3	33.9 ± 12.7	0.013
	6w	33.2 ± 8.3	39.1 ± 10.9	0.059
	6m	30.9 ± 7.9	37.9 ± 10.5	0.025
PI	pre	51.0 ± 12.2	55.9 ± 13.4	0.292
	6w	51.1 ± 12.0	55.8 ± 13.5	0.300
	6m	49.9 ± 11.2	55.8 ± 13.7	0.189
LL	pre	-34.2 ± 17.4	-41.2 ± 20.5	0.102
	6w	-55.9 ± 7.8	-56.7 ± 14.4	0.451
	6m	-34.7 ± 8.5	-36.7 ± 14.8	0.398
SVA	pre	65.7 ± 64.0	57.3 ± 71.3	0.308
	6w	64.4 ± 42.9	17.2 ± 42.3	0.360
	6m	-3.0 ± 53.0	11.3 ± 46.7	0.366
Cobb angle	pre	14.1 ± 31.5	19.7 ± 31.5	0.659
	6w	8.4 ± 29.6	9.5 ± 26.9	0.938
	6m	12.2 ± 29.9	7.7 ± 29.4	0.651

	Low NTPA group (n=16)	High NTPA group (n=49)	P value
PJK	8 (50.0%)	9 (18.4%)	0.021
PJF	0 (0.0%)	0 (0.0%)	1.000

Thoracic Bone Mineral Density measured by Quantitative Computed Tomography in Patients undergoing Spine Surgery

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Introduction: The thoracic spine is a common location for vertebral fractures as well as instrumentation failure after long spinal fusion procedures. The association between those complications and bone mineral density (BMD) are well recognized. The current gold standard to measure spinal BMD is dual energy x-ray absorptiometry (DXA). However, due to the overlying sternum and ribs in the thoracic spine, DXA is limited to the lumbar spine. Quantitative computed tomography (QCT) circumvents several shortcomings of DXA and allows for level-specific BMD measurements. To the authors' knowledge, no investigation has comprehensively quantified the BMD of the entire thoracic spine in patients undergoing spine surgery. The objective of this study was to: 1) assess the reliability of thoracic QCT measurements, 2) determine possible level-specific BMD variation and 3) assess the correlation between BMDs of the spinal levels T1-T12.

Methods: Patients undergoing spine surgery from 2016-2020 at a single, academic institution with available preoperative thoracic spine CTs were included. Subjects with previous instrumentation at any thoracic level, concurrent vertebral fractures or a Cobb angle of more than 20 degrees were excluded. Asynchronous QCT measurements of T1-T12 were performed (Figure 1). To assess inter- and intra-observer reliability, a validation study was performed on 10 randomly selected patients. The interclass correlation coefficient (ICC) was calculated. A pairwise comparison of BMD was conducted and correlations between each thoracic level were evaluated.

Results: 60 patients (men, 51.7%) met inclusion criteria. The study population was 90% Caucasian with a mean age of 62.2 years and a mean BMI of 30.2 kg/m². The inter- and intra-observer reliability of the thoracic QCT measurements was excellent (ICC of 0.968 and 0.967, respectively). The trabecular BMD was highest in the upper thoracic spine and decreased in the caudal direction (T1=182.3 mg/cm³, T2=168.1 mg/cm³, T3=163.5 mg/cm³, T4=164.7 mg/cm³, T5=161.4 mg/cm³, T6=152.5 mg/cm³, T7= 43.5 mg/cm³, T8=141.3 mg/cm³, T9=143.5 mg/cm³, T10=145.1 mg/cm³, T11=145.3 mg/cm³, T12=133.6 mg/cm³) (Figure 2). The BMD of all thoracic levels cranial to T6 was statistically higher than the BMD of all levels caudal to T6 ($p < 0.001$). Nonetheless, significant correlations in BMD among all measured thoracic levels were observed, with a Pearson's correlation coefficient ranging from 0.74 to 0.97.

Discussion: Our results indicate significant regional BMD differences in the thoracic spine. This BMD variation might contribute to several clinically relevant phenomena: First, vertebral fractures have a bimodal distribution and occur most commonly at the thoracolumbar junction (T12-L1), with the midthoracic region (T7-T8) being the second most common site. In addition to mechanical reasons, this might be partially attributed to thoracic BMD that is lowest at T12, followed by T8. Second, optimal upper instrumented vertebra (UIV) for stopping long fusions to the sacrum and pelvis are controversial. The BMD of surgically relevant upper thoracic stopping points (T2-T4) was significantly higher than the BMD of lower thoracic stopping points (T10-T12). Besides stress concentration at the relatively mobile lower thoracic segments, the low BMD at these levels might contribute to previously suggested higher rates of junctional failures with short fusions.



Figure 1: Thoracic BMD measurement

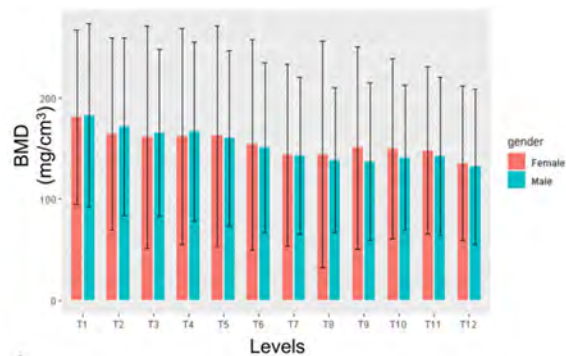


Figure 2: Mean BMD with standard deviation (SD) bar of the thoracic spinal levels by gender

Modic changes and endplate defects but not spinal stenosis affect low back pain in patients with lumbar spinal stenosis

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INTRODUCTION: Dural sac cross-sectional area has been reported to be associated with low back pain (LBP) in patients with lumbar spinal stenosis (LSS) and the general population. A previous study found that patients with LSS and sarcopenia reported more severe LBP than those without sarcopenia. However, in patients with LSS, the factors affecting LBP such as muscle mass, spinopelvic alignments, disc degeneration, and endplate defects have been poorly studied. The purpose of this study was to identify factors associated with LBP in patients with LSS.

METHODS: This cross-sectional study, which was conducted at the Spine Care Center, from September 2017 to March 2020, enrolled patients presenting with symptoms of neurogenic claudication caused by MRI-confirmed LSS. Patients with a history of previous spinal surgery or cognitive impairment were excluded. A numerical rating scale (NRS) of LBP, muscle mass measured using bioelectrical impedance using the InBody S10 (BioSpace, Seoul, Korea), and radiographic measurements (lumbar lordosis, pelvic tilt, pelvic incidence, sacral slope, and % slip) were collected. Schizas's spinal stenosis classification (7 grade), Pfirrmann disc degeneration grade (5 grade), Modic changes (3 types), endplate defects (3 types; focal, corner, and erosive defects), disc height and bulging (4 grade), and facet joint osteoarthritis (4 grade) were evaluated on MRI. Each grade of spinal stenosis, disc degeneration, disc height and bulging, and facet joint osteoarthritis were summed from L1/2 to L5/S. Each number of spinal stenosis (> grade 4), disc degeneration (> grade 3), Modic changes, and endplate defects were counted from L1/2 to L5/S. Correlational analysis was used to identify the relationships between severity of LBP and demographic data, muscle mass, and radiographic and MRI measurements. Regression analyses were used to examine the factors associated with severity and presence of LBP.

RESULTS: A total of 265 patients (122 men and 143 women, average age 72.7 y) were enrolled. Significant correlations were observed between severity of LBP and trunk muscle mass, appendicular skeletal muscle mass, pelvic tilt, the disc degeneration grade, the number of Modic changes, type 1 changes, and type 3 changes, the number of endplate defects, positive erosive endplate defects, and disc height ($P < 0.05$). Multiple regression analysis showed that appendicular skeletal muscle mass, the number of Modic type 1 changes, and type 3 changes, and the number of endplate defects predicted severity of LBP ($R^2 = 0.119$). Multivariate logistic regression analysis showed significant associations between presence of LBP (NRS > 3) with severity of stenosis (OR 0.94; 95% CI 0.88–1.00; $P = 0.04$), the number of Modic type 3 changes (OR 3.76; 95% CI 1.46–9.70; $P < 0.01$), and the number of end plate defects (OR 1.18; 95% CI 1.06–1.33; $P < 0.01$).

DISCUSSION: Lower muscle mass, disc degeneration, higher number of Modic changes and endplate defects are more closely associated with severity of LBP than severity and the number of spinal stenosis in patients with LSS. These results suggest that the cause of LBP in LSS patients is mechanical associated with muscle loss and disc degeneration, but not neurogenic.

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A Prospective, Three-Year Longitudinal Study of Modic changes of the Lumbar Spine in a Population-Based Cohort: the Wakayama Spine Study

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ABSTRACT

Introduction: Several studies have noted that Modic changes (i.e. subchondral vertebral bone marrow lesions) are one of the most clinically relevant lumbar imaging phenotypes on MRI that are highly associated with low back pain and disability. However, previous studies have largely been cross-sectional and prospective, longitudinal assessment of such phenotypes in the general population have been limited. The following study addressed the long-term three-year follow-up assessment of Modic changes of the lumbar spine based on an established population-based cohort.

Methods: We included 678 subjects (n=208 men, n=470 females) with a mean age of 62.1 years at baseline who were initially imaged in 2013 and re-assessed in 2016 as part of the Wakayama Spine Study of Japanese. Based on T1- and T2-weighted MRIs, we assessed for the presence of Modic types I, II, and III of each endplate from L1 to S1. The rate of change at each endplate was then analyzed over a period of three years. The incidence of Modic changes in the lumbar region was determined as an absence of Modic changes at baseline and signal changes in at least one endplate at follow-up. The progression of Modic changes in the lumbar region was defined by the presence of Modic type I or II at baseline and at least one endplate that had progressed to another Modic type upon follow-up. Finally, Modic degeneration in the lumbar region was considered to occur when type I, II, or III was present at baseline and at least one endplate had degenerated with regards to Modic type as measured at follow-up and as shown in **Figure 1**.

Results: A total of 3,390 endplates were included in the analysis. At baseline, type I, type II, and type III Modic changes in the overall lumbar spine were prevalent in 83 (2.4%), 375 (11.1%), and 77 (2.3%), respectively. At follow up, type I, type II, and type III Modic changes in the overall lumbar spine were prevalent in 58 (1.7%), 736 (21.7%), and 108 (3.2%), respectively. Over the course of three years, the number of endplates where Modic changes occurred, progressed, and degenerated were 395 (11.7%), 84 (2.5%), and 11 (0.3%), respectively. The highest levels of incidence, progression, and degeneration were observed in the following locations: 96 endplates at L2/3 (14.2%), 32 endplates at L5/S1 (4.7%), and 5 endplates at L2/3 (0.7%), respectively.

Discussion: To the best of our knowledge, this study was the first to detect Modic changes in the lumbar endplates of the general population over a three-year period. A high incidence and progression rate of Modic change were observed at the upper and lower levels of the lumbar lesion, respectively; however, degeneration hardly occurred. The follow-up period in this longitudinal study was only three years, which could potentially have limited the extent of the Modic changes observed in this study. Nevertheless, our findings shed light on the research of lumbar endplate changes. Large-scale longitudinal studies are needed to further validate our findings and address their clinical impact.

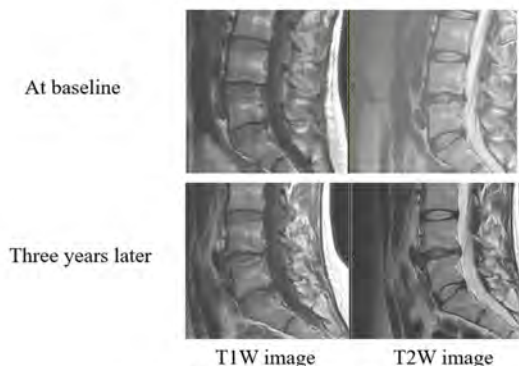


Figure 1. Modic degeneration
(From type II at baseline to type I three years later)

The lack of image-based dynamic components in Modic changes suggest that Modic changes are not actively involved in biomechanically induced pain

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Introduction:

Modic changes (MC) have gained increased interest as potential pain generators in low back pain (LBP). Recently, an increase in the MC area was reported in upright position compared to supine position with a correlation between area increase and induced pain in standing position (1). Hence, MRI during spinal loading have the potential to display changes not revealed on conventional supine examinations. Also, intervertebral discs and endplates have been shown to display dynamic behaviors in MRI, indicating different tissue characteristics between patients and controls that may add information in the search for image-based features linked to pain (2, 3). If, and how, the MRI signal in MC's changes during spinal loading remains to be established. The aim was therefore to investigate if spinal loading affects MC's in LBP patients in terms of MRI signal.

Methods:

In a cohort of 100 LBP patients, 43 individuals (23 male; mean age 45.7 years, range 29-66) had presence of MC's at MRI and, thus, were included. Lumbar MRI was performed in relaxed supine position followed by axial loading in supine position. The loading was induced with the Dynawell® compression device, applying 50% of the patient's body weight. On sagittal T2-weighted images, each MC was outlined using a free-hand polygonal tool (ITK-SNAP) (Fig.1), on each slice where at least 25% of the vertebrae was affected in either anteroposterior or craniocaudal direction. In vertebrae affected by MC's, a remote region-of-interest (mean size: 0.6cm²) was placed in tissue without MC's. The MC signal intensity (SI), normalized to CSF, and MC volume were registered and compared between MRI with and without spinal loading. MC's were classified into type (I-III). For mixed types, the dominant type (>50%) was registered. Reliability measurements for MC segmentation were performed using the intra-class correlation (ICC) coefficient.

Results:

A total of 94 MC's, 84% localized in L3-S1, were evaluated and distributed as follows; type I: 36.2% (n=34), type II: 58.5% (n=55) and type III: 35.3% (n=5). A higher SI (mean: -0.023, p=0.002) was induced during spinal loading in the remote region, while no significant SI change was detected in the MC's, neither in all MC's (mean: 0.020; p=0.308) nor when stratified for type. Neither did MC volume change between MRIs with (mean 1.87cm³; SD 1.5) and without spinal loading (mean 1.92 cm³; SD 1.5) (p=0.25), nor when stratifying for MC type. The ICC coefficients for intra-observer and inter-observer were excellent (0.97 respectively 0.98).

Discussion:

The load-induced SI change in vertebral regions not affected by MC's could be explained by the redistribution of water molecules in the dynamic hematopoietic bone marrow. The lack of similar dynamics in MC's, neither in SI nor in change of volume, likely reflect that MC's are not instantaneously influenced by biomechanical stress. Overall, these findings does not support the theory that MC's are actively involved in biomechanically induced pain.

Figure 1. Example of segmented Modic changes at MRI with (left) and without spinal loading (right)

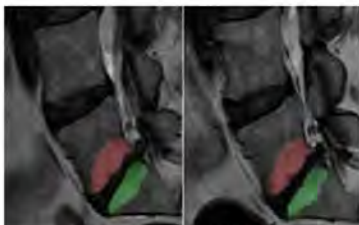
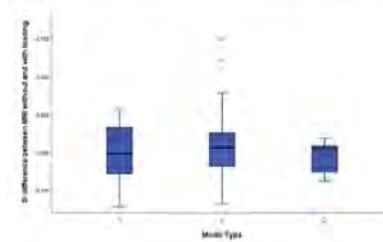


Figure 2. Box-plot of Signal intensity (SI) change in Modic changes between MRI without and with spinal loading



Integrative Analysis of Metabolomic, Genomic, and Imaging-based Phenotypes Identify Very Low Density Lipoprotein as a Potential Risk Factor for Lumbar Modic Changes

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Introduction: Low back pain (LBP) is the most common cause of disability worldwide. Modic changes (MC) are subchondral vertebral bone marrow lesions visible in spine magnetic resonance imaging (MRI), and are related to the development and severity of LBP. The etiology of MC remains elusive, but it has been suggested that altered metabolism may be a risk factor. Big data and omics approaches, including metabolomics (i.e. systemic metabolic profile), have gained significant traction in studying diseases, but have yet to be applied to MC. As such, study aimed to identify metabolomic biomarkers for MC phenotypes of the lumbar spine via a combined metabolomic-genomic approach.

Methods: A population cohort of 3,584 southern Chinese underwent MRI of the lumbar spine. Blood samples from subjects were genotyped with single nucleotide polymorphism (SNP) arrays (n=2,482) and serum metabolomics profiling using magnetic resonance spectroscopy (n=757), covering 130 metabolites that represent three molecular windows: lipoprotein lipids, low molecular weight, and lipid extracts. Genome-wide association studies (GWAS) were performed on each metabolite (i.e. 130 GWAS studies), to construct polygenic scores for predicting metabolite levels in subjects who had GWAS but not metabolomic data. Associations between predicted metabolite levels and MC phenotypes were assessed using linear regression and LASSO. Two-sample Mendelian randomization analysis was conducted to test for causal relationships between the potential metabolic biomarkers and MC.

Results: Of the participants, 20.4% had MC (10.6% type I, 67.2% type II, 22.2% mixed types). Significant metabolomic biomarkers for MC were the mean diameter of very low density lipoprotein (VLDL)/low density lipoprotein (LDL) particles and cholesterol esters/phospholipids in large LDL. Mendelian randomization showed that a decreased mean diameter of VLDL may lead to MC.

Discussion: Utilizing a panomics approach, this large-scale study is the first to address metabolomics in subjects with lumbar MC. Our causality studies implicate VLDL as being related to MC, thus substantiating a metabolic etiology to these clinically relevant phenotypes. Our study introduces the field of “spino-metabolomics” and also illustrates the power of integrative “omics” approaches to discover biomarkers for complex traits, paving the way for further studies on disease mechanisms and more personalized care for patients.

Does Preoperative Modic changes influence outcomes of Microdiscectomy: A prospective comparative cohort study

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Introduction

Microdiscectomy is the gold standard procedure performed for lumbar disc herniation with a high success rate (80%). However, in some patients, the preoperative back pain persists after microdiscectomy and leads to poor functional outcomes after surgery. The presence of pre-operative Modic changes has been correlated to poor outcomes by some authors. This study aims to elucidate the relationship between Modic endplate changes and clinical outcomes after a lumbar microdiscectomy.

Methods: A prospective comparative cohort study was performed in consecutive patients undergoing microdiscectomy for lumbar disc herniation (LDH) in a single centre after ethics committee approval. Patients between 18 to 65 years of age with symptomatic single-level disc herniation and failed a trial of conservative management were included. Patients with cauda equina syndrome and significant motor deficits were operated at the earliest and were also included. Patients with prior lumbar surgery, presence of lumbar instability, severe canal stenosis, facet hypertrophy, high risk for anesthesia, and patients who were lost to follow up during the study period were excluded. Pre-operative clinical and radiological parameters (Presence, location, size and type of Modic changes, Pfirrmann grading, Total endplate score (TEPS) were recorded. The pain was assessed by Numeric pain rating scale (NPRS), and functional assessment by Oswestry Disability Index (ODI). Minimal clinically important difference (MCID) in outcome was calculated for both the groups. Complications related to surgery were studied. Follow-up was done at six weeks, three months, six months and one year. Mac Nab criteria were used to assess patient satisfaction at one year. Statistical analysis was performed to understand the evenness of the distribution of variables across groups and to understand the relationship of Modic changes with functional outcomes.

Results: Out of 309 patients, 86 had Modic changes, and 223 had no Modic changes. Both groups had similar back pain (p-value: 0.07) and functional scores (p-value: 0.85) pre-operatively. Postoperatively patients with Modic changes had poorer back pain and ODI scores in the third month, sixth month and one year (p-value: 0.001). However, MCID between the groups were not significant (p-value- 0.18 for back pain and 0.58 for ODI scores). Mac Nab criteria at one year were worse in Modic patients (p-value: 0.001). No difference was noted among Modic types (Type 1 vs Type 2) in the pre-operative and postoperative pain and functional outcomes. Four patients in Modic group (4.7%) and one patient in the non-Modic group (0.5%) developed postoperative discitis (p-value: 0.009).

Conclusions: Our study found a negative association between the presence of Modic change in preoperative MRI and postoperative back pain, functional outcomes and patient satisfaction at one year in patients with lumbar disc herniation undergoing microdiscectomy. Modic changes were associated with higher grades of disc degeneration and higher Total endplate scores. However, no difference in clinical outcomes was seen between different types of Modic changes. Our study also found an increased incidence of postoperative discitis and the need for repeat procedures in patients with Modic changes.

DISC SPACE NARROWING INFLUENCES CLINICAL SYMPTOMS MORE IN WOMEN THAN MEN: THE WAKAYAMA SPINE STUDY

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Introduction: Disc space narrowing (DSN) has been the most commonly used specific finding to indicate degenerative disc in the lumbar imaging, DSN might be a clear sign of pathology in the lumbar disc. However, there were few studies to assess DSN by MRI in a population-based cohort. Low back pain (LBP) and leg symptoms due to degenerative lumbar spinal stenosis (LSS) is associated with impaired walking and other disabilities in the elderly. To date however, there has been no report about the association of leg symptoms due to LSS with structural changes in the spine as investigated MRI including DSN.

Aim: Our aim of this study is to clarify the prevalence of DSN and its association of the symptoms including LBP and leg pain with DSN assessed by MRI in a large population-based cohort.

Materials and Methods: This was a cross-sectional observational study of adults based in Wakayama, Japan using general population. All participants underwent lumbar spine MRI in a mobile unit (Excelart 1.5 T; Toshiba; Tokyo, Japan). DSN on MRI scan was assessed by one experienced orthopaedic surgeon (MT), who was blinded to participants' clinical status. The disc height was measured quantitatively at the midpoint of disc on the T2 sagittal images using the imaging software OsiriX (<http://www.osirix-viewer.com/>). All participants were asked the following question by the experienced orthopedic surgeon (YI): "In the past month, have you had pain that last on most days?" Those who answered "yes" were identified as having low back pain. The diagnostic criteria for leg pain were based on the LSS definition from the North American Spine Society (NASS) guidelines.

Results: Complete data were available for 962 participants (321 men, 641 women, mean age 66.3 years, range: 21-93 years). DSN at most levels were advanced at older age in total and disc height at L4/5 in women dropped dramatically after their menopause as compared to males. And disc height did not changed so much in their young in both genders. Age and BMI were significantly related to DSN at L2/3, 3/4, and 4/5, but smoking and alcohol was not. In current study, about 40% of all participants had chronic LBP and 10% had leg symptoms. Regarding those symptoms, DSN at any levels were not significantly associated with LBP in men, whereas, DSN at all levels other than L1/2 was significantly higher risk for LBP after adjustment for age, BMI, alcohol and smoking. Only DSN at L3/4 in women was significantly associated with leg symptoms after adjustment for all the same confounders.

Conclusion: In conclusion, our data highlighted the prevalence of DSN in both genders and the association of DSN with clinical symptoms. Estrogen deficiency may influence over the difference of trend of prevalence of DSN in both genders. Our findings also suggested that DSN in women was significantly higher risk for clinical symptoms.

Age and disc degeneration in low back pain: comparison of large cohorts of symptomatic and asymptomatic female subjects demonstrates interactions of age, spinal level and degenerative features

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Introduction

There is still little understanding of why a significant proportion of asymptomatic subjects have degenerate discs and other degenerative features. Even though there is strong evidence for the importance of psycho-social factors, the role of disc degeneration is thought to be paramount. Differences in the MRI grading schemes adopted by the various studies aiming to uncover the relationship between disc degeneration and pain, have hampered the efforts to compare results, or to combine cohorts for large genetic or comparative epidemiological studies. The capacity of human annotators to process large numbers of MRI images and re-grade large datasets consistently is a major limitation. This can in part be overcome using automated annotation, such as SpineNet.

Methods

The MRIs of two cohorts, one symptomatic (724 adult females with chronic low-back pain from a secondary care spinal- triage clinic), one asymptomatic (660 female subjects reporting no back pain for 3 months, selected from the TwinsUK population cohort) were analysed on the same objective scale using an automated analysis system (SpineNet (1)). We compared prevalence of intervertebral disc degeneration (Pfirrmann grades) and disc herniation, spinal stenosis, bone marrow and endplate changes (all binary: present/absent) between cohorts in relation to age and spinal level.

Results

There were distinct differences between the symptomatic and asymptomatic cohorts. Prevalence of severe degeneration (Pfirrmann grade 4 or 5) was 3-4 times greater in symptomatic subjects below 50-60yrs, but the difference between cohorts fell with increasing age (Fig 1). The prevalence of degenerative features varied with age and disc level and was markedly greater in symptomatic than asymptomatic subjects particularly at younger ages, and, apart from endplate defects, far greater in the lower (L4-L5) lumbar spine (Fig 2). The prevalence of these features was very low (<10%) in the upper lumbar discs (L1-L3), where it was similar in both groups. In both cohorts, the majority (>90%) of the endplate and marrow features were found only in discs with severe degeneration, whatever the overall prevalence. Co-existence of several degenerative features was evident in symptomatic discs, but many symptomatic discs (c.30-50%) showed no degenerative changes.

Discussion

Our data, while in broad agreement with many previous studies, highlights the complex interactions of age, spinal level and degenerative features. Comparing prevalence rates has been difficult from previous reports because of small studies with inconsistent annotation and definitions of age and spinal level. Here, we were able to determine marked differences in the prevalence of degeneration between the symptomatics and asymptomatics in the cohorts studied.

However, we were still unable to determine any features which might distinguish MRIs of symptomatics from those of asymptomatics. More refined means of defining degeneration, or for determining differences between degenerative features, might differentiate between asymptomatics and symptomatics, but our study was underpowered for such analyses once age and disc level were taken into account. Analysis of larger cohorts would allow such differentiation, but these require large asymptomatic cohorts for comparison which do not exist at present.

Reference

Jamaludin, et al. ESJ. 2017;26(5):1374-85

The longitudinal analysis to determine whether current sexual activities among elderly people affect low back pain in future

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INTRODUCTION

Japan is a one of the most rapidly aging country in the world. Low back pain (LBP) is the most frequent complaint among elderly in Japan, so LBP of the elderly is national burden. Exercise was reported to be effective for reduction of LBP, especially chronic LBP among elderly patients. We hypothesized that sexual activity in the elderly might also be effective in reducing LBP.

However, there was no study which investigated the association between sexual activity and LBP among elderly in Japan. The purpose of this study was to examine whether the presence of current sexual activities among elderly people affect LBP in future.

METHODS

The subjects were 317 elderly people (aged ≥ 65 years; 130 males, 187 females) who voluntarily participated in the longitudinal survey of the health status for elderly population living in a suburban community in Japan. It began from 2016 and aimed at investigating locomotive syndrome, sarcopenia, frailty, and LBP among elderly population. It was also designed to elucidate risk factors for these conditions. Based on the results of questionnaires, we classified those who had sexual intercourse within the past year into sexually active group, and those who did not have sexual intercourse in over a year into sexually inactive group. Baseline characteristics such as current visual analogue scale (VAS) of LBP, physical decline (the 25-question geriatric locomotive function scale [GLFS]) and marital status were compared between two groups. We investigate whether sexual activity among elderly people affect LBP in future using multiple regression analysis with the VAS of LBP in following year as the objective variable and age, gender, body mass index, baseline VAS of LBP, GLFS, marital status and the presence of current sexual activities as explanatory variables.

RESULTS

In total, 23.3% (N=74) of participants reported to have current sexual activity. The current VAS of LBP was significantly higher in the sexually inactive group than active group (22.8 mm vs. 12.4 mm, $p < 0.01$), but just 0.8% (N=2) of participants reported that their sexual activity was absent due to LBP. The sexually active group showed that they were younger (72.5 yrs. vs. 75.5 yrs., $p < 0.01$), less physical decline (GLFS: 5.7 pts. vs. 11.5pts., $p < 0.01$), more males (59.5% vs. 35.4%, $p < 0.01$), more married (90.5% vs. 72.4%, $p < 0.01$), and less likely to live alone (5.4% vs. 17.7%, $p < 0.01$). Multiple regression analysis showed that the presence of current sexual activity independently affected the VAS of LBP in following year ($\beta = -6.24$, $p = 0.01$).

DISCUSSION

This is the first to investigate the relationship of sexual activity and LBP among elderly in Japan. It was reported that age, marital status, and physical function were associated with the presence of sexual activity among elderly. Our results showed that even after adjusting for these factors, the presence of sexual activity among elderly people significantly affect the reduction of LBP. Just as exercise is favorable treatment for LBP, maintaining sexual activity in elderly may also be effective in reducing LBP.

Healthcare utilization and pain outcomes in individuals with low back pain: an observational study of a large dataset

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Introduction: Low back pain (LBP) is the single leading cause of disability around the world¹. In the past two decades, medical costs associated with the condition have continued to rise without an associated improvement in treatment outcomes or disability rates²⁻⁵. This alarming trend suggests that current treatment paradigms are ineffective in eliciting a positive change in patients with LBP. The purpose of this study was to determine the relationship between healthcare utilization and change in pain status for a large cohort of patients with LBP.

Methods: This was a retrospective, observational study in which data was collected from electronic health records (EHR), and included patients seen in an outpatient setting between January 2010–October 2020. Index visit was defined as the first outpatient visit that included a diagnostic code for LBP. Based on the minimum clinically important difference of two points using the Numeric Pain Rating Scale (NPRS)⁶, patients' recovery status was categorized as improved, worsened, or same. NPRS scores were extracted from most recent encounter prior to index visit and compared to the average of NPRS scores taken up to 365 days following index visit. Healthcare utilization was compared across groups and was based on rates of back surgeries, epidural steroid injections (ESI), opioid prescriptions, advanced imaging orders, and follow up encounters including bedded hospitalizations and emergency department (ED) visits, both within 365 days post-index visit.

Results: Data from 25,481 patients were included in this study. Based on patient reported change in NPRS scores, 20.3% of patients improved, 20.6% worsened, and 59.1% remained the same. Compared to those who worsened, those who improved were less likely to receive an opioid prescription (unadjusted 99% odds ratio: 0.87 [0.77, 0.98]) and advanced imaging (0.82 [0.74, 0.91]), but were just as likely to receive back surgery, ESI, be hospitalized, or visit the ED. Compared to those who remained the same, those who improved were less likely to receive back surgery, ESI, opioid prescription, advanced imaging, be hospitalized, or visit the ED (OR 99% confidence intervals range from [0.63-0.77] to [0.75-0.97]). Compared to those who remained the same, those who worsened were less likely to receive an opioid prescription (0.80 [0.73-0.89]), but were equally likely to have back surgery, ESI, advanced imaging, be hospitalized, or visit the ED.

Discussion: Despite high rates of utilization across all groups, less than a quarter of the study population improved, which is the same percentage that worsened. The majority of patients had no clinically significant change in pain over one year. Results suggest that healthcare utilization is not indicative of change in pain status and that the highest rates of utilization were seen in those that had no change in pain. These results emphasize the need for significant improvements to be made regarding delivery of value-based care for LBP treatment. Limitations to this study include lack of functional outcome measures to broadly assess recovery. In addition, pain scores extracted just prior to LBP diagnosis may not accurately reflect pain levels prior to initiation of treatment.

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The association between subphenotypes of low back pain and degenerative imaging findings in a cohort of young adults from the Raine Study

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Introduction: The association between lumbar spine imaging findings and low back pain remains unclear due to important limitations of previous studies, such as a lack of clearly defined low back pain phenotypes and large variation in age. Prospective, properly matched studies focusing on young adults, their pain profiles and degenerative outcomes on imaging are uncommon. Also, little is known with respect to the different subphenotypes of low back pain and the development of lumbar degenerative changes. As such, the following study investigated the association between lumbar spine MRI findings and previous low back pain 5-year trajectories in young adults based from the Raine Study.

Methods: Young adults (Gen2) from the Raine Study, an ongoing birth cohort study of 2,868 children born between 1989 and 1991, were selectively recruited at the age of 27. We identified 78 'case' participants with a previously identified 'consistent high disabling low back pain' trajectory from age 17 to 22 years and 78 'control' participants from a trajectory with consistently low pain over the same time period, matched for sex, age, body mass index, physical activity levels and work physical demands. All participants underwent a standardised lumbar MRI scan 5 years later, at age 27, from which imaging phenotypes were extracted (e.g. disc degeneration/herniation, endplate abnormalities, facet changes, stenosis, etc). Primary analyses used unconditional logistic regression, adjusting for covariates used in the matching process, to investigate the relationship between the presence of each imaging finding and being a case or control. Secondary analyses explored those relationships based on the number of spinal levels with each MRI finding.

Results: The odds for being a case compared to a control were higher in those with disc degeneration (Pfirrmann grade >3; OR=3.21, 95%CI:1.60-6.44; p=0.001) or those with a herniation (OR=1.90, 95%CI:0.96-3.74; p=.065). We also found that the association became substantially stronger when either disc degeneration or herniation was present at two or more spinal levels (OR=5.56, 95%CI:1.97-15.70; p=0.001, and OR=5.85, 95%CI:1.54-22.25; p=.009, respectively). The other investigated MRI findings were not associated with greater odds of being a case, suggesting that they manifest in older age and are not related to the pain profiles of the young.

Discussion: Our longitudinal study based on the established Raine Study Birth Cohort noted that subphenotypes of low back pain are associated with distinct MRI features of lumbar disc degeneration and herniation in young adults. Further investigation of their potential prognostic and causal roles is indicated.

Epidemiology of lumbar degenerative phenotypes of children and adolescents: a large-scale imaging study

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Introduction: Recently, there has been a rise in children and adolescents developing low back pain and/or sciatica. With decreased physical activity, increased weight gain, and increased psychological stress globally, the burden of musculoskeletal pain will continue to become more prevalent. Degenerative lumbar spine changes as noted on MRI can occur in children and adolescents but such reports have been sporadic. As such, the following study was performed to identify the incidence and MRI phenotypes of the lumbar spine in children and adolescents.

Methods: 597 children and adolescents (2,985 lumbar discs) with lumbar MRIs from a university hospital were included in the study. T1- and T2-weighted lumbar images from L1/2 to L5/S1 were analyzed in axial and sagittal planes. Global phenotype assessment was performed of each level and based on established nomenclature protocols.

Results: The cohort of children and adolescents consisted of 57.29% (342) boys and 42.71% (255) girls, with an average age as 10.75±5.25 years (range: 0 to 18 years). The prevalence of imaging findings of LDD and LDH were 2.2% and 5.8%, respectively. Modic changes and high-intensity zone were absent in this cohort.

Discussion: Our large-scale study provides evidence on the prevalence and features of incidental changes in lumbar spine MRI in children and adolescents. Lumbar disc degeneration emerged as early as the first decade of life without additional specific phenotypes, including Modic changes and high-intensity zone. The study provides much needed information of a unique age group that is often under-represented but equally of great importance as adults.

Do both morphometric and mechanical characteristics of lumbar multifidus in people with chronic low back pain differ from those of asymptomatic counterparts?

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Introduction: Lumbar multifidus muscle (LMM) is an important spinal stabilizer that may affect the development/maintenance of chronic low back pain (CLBP). Muscle atrophy and/or increased fatty infiltration of LMM among people with CLBP are assumed to indicate suboptimal function or biomechanical properties of LMM although this premise has not been verified. The current study aimed to investigate whether people with CLBP displayed both altered morphometric and biomechanical properties of LMM as compared to age- and gender-matched asymptomatic controls.

Methods: Individuals with (n=78) and without CLBP (n=73) underwent lumbar magnetic resonance imaging (MRI) and ultrasonography to examine LMM morphometry. Total cross-sectional areas (CSAs) and lean muscle CSAs of bilateral LMM from L4 to S1 levels were manually measured to estimate bilateral LMM volume using a customized MATLAB program. Bilateral parasagittal thickness of LMM at L4/5 and L5/S1 at rest and during contralateral leg lifts in a prone position were measured from brightness-mode ultrasound videos. The percentage thickness change of LMM at L4/5 and L5/S1 levels during contralateral leg lifts were calculated from the formula: $(\text{thickness}_{\text{contracted}} - \text{thickness}_{\text{rest}}) / \text{thickness}_{\text{rest}} \times 100\%$. The shear modulus (stiffness) of bilateral LMM at L4/5 and L5/S1 at rest and during contralateral leg lifts were measured by supersonic shear wave imaging. Morphometric and biomechanical properties of LMM between people with and without CLBP were compared by Mann-Whitney U tests.

Results: The mean pain intensity of the CLBP cohort was 4 out of 10 using numeric rating scale. Bilateral total or lean muscle CSAs of LMM at L4-5 ($p=0.01$), L5-S1 ($p<0.01$), and total LMM volume across L4-S1 levels ($p=0.02$) among people with CLBP were significantly greater than those of asymptomatic controls. The resting thickness at L4-5 in people with CLBP was significantly higher ($p=0.05$) than asymptomatic individuals. Compared to asymptomatic controls, people with CLBP displayed significantly smaller percentage LMM thickness change during contraction at L4-5 ($p<0.01$) and L5-S1 ($p<0.01$). There were no significant between-group differences in the contracted thickness, and resting or contracted stiffness of LMM at L4/5 and L5/S1. Total CSA (r range: 0.32-0.50) or thickness (r range: 0.55-0.67) of LMM at L4/5 and L5/S1 as measured from MRI was significantly correlated with the corresponding LMM resting thickness as measured from ultrasonography in both groups.

Discussion: Our CLBP cohort displayed significantly greater bilateral CSAs, volume, and resting thickness of LMM than asymptomatic controls, which contradict previous studies. However, like prior research, our CLBP participants demonstrated significantly smaller percentage thickness change of LMM during submaximal LMM contraction. Although speculative, the increased dimensions of resting LMM in our CLBP cohort may indicate pain-related muscle spasm. Interestingly, significant between-group differences in LMM morphometry were not accompanied by between-group differences in LMM stiffness, indicating that LMM morphometry cannot be used as a surrogate to estimate functions or mechanical property of LMM in people with CLBP. Future research should investigate whether baseline morphometric and/or biomechanical characteristics of LMM can predict the prognosis/trajectory of LBP in people with or without CLBP, and/or explore novel subphenotyping of LBP patients for more personalized spine care.

Pelvic Compensation Accompanying Spinal Malalignment and Back Pain-Related Factors in a General Population

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INTRODUCTION: When the center of gravity of elderly people with decreased trunk flexibility moves forward, it often takes posture to maintain standing by pelvic compensation. Therefore, it is not enough to evaluate global alignment with only the sagittal vertical axis (SVA), but it is also important to simultaneously evaluate pelvic tilt (PT). In this study, we focused on the combination of C7 SVA and PT and aimed at evaluating the standing posture of elderly people and investigating the factors related to postural abnormality. **METHODS:** This was a cross-sectional study using an established population-based cohort in Japan. Of the 1575 subjects who participated in the second survey of the cohort study, 1090 (349 men, 742 women, mean age 67.4 y.o.) underwent sagittal whole-spine radiography in a standing position. The cut-off value for the diagnosis of sarcopenia followed the proposal of the Asian Working Group for Sarcopenia. Presence of LBP within one-month, VAS of LBP and ODI were evaluated via self-administered questionnaire. **Statistics:** The participants were divided into the following four groups on the basis of PT and SVA: normal group (PT<20°; SVA<50mm), compensated group (PT≥20°; SVA<50mm), noncompensated group (PT<20°; SVA≥50mm), and decompensated group (PT≥20°; SVA≥50mm). The latter three categories were defined as "malalignment", and the characteristics of and factors related to each group were examined. **RESULTS:** The prevalence of malalignment was increased by age group as follows: less than 50 y.o., 19%; 50s, 29%; 60s, 40%; 70s, 53%; over 80 y.o., 69%. This prevalence was significantly higher in women over 60 y.o. The number of people in each group and the average age per group were 597 and 64.2 y.o. in the normal group; 323 and 68.7 y.o. in the compensation group; 50 and 74.5 y.o. in the non-compensated group; and 120 and 76.8 y.o. in the decompensated group, respectively. The male ratio was 38% in the normal group; 21% in the compensated group; 58% in the non-compensated group; and 20% in the decompensated group, respectively. There was a significant difference in the prevalence of LBP, VAS, ODI%, and the prevalence of sarcopenia among the four groups although it was not significant between the non-compensated group and decompensated group in the stratified analysis. On multivariate analysis, all three groups with malalignment were associated with the presence of LBP and related disability (ODI%≥21). Moreover, decompensated group was significantly associated with sarcopenia. **DISCUSSION:** This study reveals that pelvic compensatory function for the postural abnormality changes with age. Moreover, the results of observation suggest that this compensatory effect differs between men and women. Regardless of whether the SVA was kept within 50 mm, the group with pelvic retroversion contained many women. This may be due to the differences in spinal flexibility and muscle strength by gender. Furthermore, the results of this study suggest that personnel with pelvic compensation is at increased risk for LBP and related disorders, even if SVA is maintained within normal range. In terms of public health, exercise therapy interventions for compensated groups may be effective.

Factors contributing to biomechanical changes in the lumbar spine following spaceflight and incidence for post-spaceflight intervertebral disc herniation

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Introduction

To understand the mechanistic relationship between prolonged exposure to microgravity and an elevated risk for lumbar disc herniation following spaceflight, we conducted a longitudinal study tracking spinal health of 12 NASA astronauts before and after approximately 6-months on ISS. We hypothesized that both pre-existing spinal pathology and multifidus muscle atrophy following spaceflight cause risks for post-flight chronic low back pain and disc herniation. Results from this study are valuable for both: 1) illuminating longitudinal mechanisms and risk factors for developing low back pain and disc herniations, and 2) informing countermeasures to reduce the incidence of disc herniation in astronauts.

METHODS

With IRB approval, advanced imaging data were collected for 12 NASA astronauts at three separate time points relative to 6-months in space on ISS: 1) within a year before launch ('pre-flight'), 2) within a week after return to Earth ('post-flight'), and 3) between 1 and 2 months after return to Earth ('recovery'). Paraspinal muscle size and composition, disc degeneration and hydration, and pathology were measured by 3T MRI. Quantitative fluoroscopy evaluated segmental kinematics of the lumbar spine in flexion/extension and lateral bending. Patient-reported outcomes for pain and disability, along with clinical notes, were used to assess post-flight symptoms and incidence of symptomatic disc herniation.

RESULTS

Six of 12 subjects experienced symptoms associated with a new or existing (and previously asymptomatic) lumbar disc protrusion or extrusion following spaceflight. We did not find any consistent changes in disc hydration in relation to spaceflight, nor any associations with the incidence of disc herniation. Multifidus muscle quality (relative fraction of muscle tissue compared to fat and fibrotic tissue within the total muscle area) significantly decreased following spaceflight in the lower lumbar spine with specific changes at L4L5 (-6.2%, p=0.03) and L5S1 (-4.6%, p=0.007) associated with the incidence of disc herniation (p<0.05). However, decreased muscle size (total area and lean muscle only area) occurred at the same levels and did not associate with the incidence of disc herniation. Flexion/extension range of motion (ROM) significantly decreased at L2L3 (-17.2%, p=0.006) and L3L4 (-20.5%, p=0.02) following spaceflight. Decreases in ROM among the upper three segments of the lumbar spine associated with the incidence of disc herniation (-24.1%, p=0.01). Existing endplate pathology associated with reduced segmental ROM (p=0.02) and was mostly present in the upper three segments of the lumbar spine (see Figure 1).

Discussion

These results are part of the final report for a 10-year study investigating the effects of spaceflight on the lumbar spine and risk for disc herniation. In conclusion, we found the incidence of lumbar disc herniation is associated with paraspinal muscle quality changes, lumbar ROM reductions, and pre-existing spinal endplate irregularities. These findings suggest differential effects of spinal stiffness and muscle loss in the upper versus lower lumbar spine regions that may specifically provoke risk for symptomatic disc herniation in the lower lumbar spine following spaceflight.

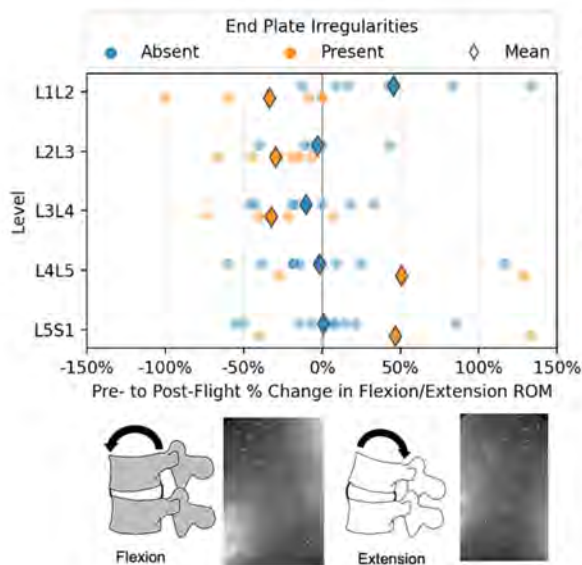


Figure 1: Percent changes in pre- to post-flight flexion/extension ROM per spinal level. Pre- to post-flight decreases were significant for L2L3 (-17.2%, p=0.006) and L3L4 (-20.5%, p=0.02). Additionally, we found that the presence of endplate irregularities associated with decreased ROM (p=0.02), which are particularly prevalent in the upper three segments of the lumbar spine.

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The Nocebo Effects of an MRI Report on the Patient and the Benefit of Reassurance - Results from a Randomized Clinical Trial of 44 patients

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Introduction: The overuse of MRI has led to an increasing number of interventions and surgeries for low back pain (LBP). With the increasing exposure of medical information and medical terminologies from the Internet, the nocebo effects of an MRI report on the patient's perception of his spine and functional outcome of treatment is pertinent. We probed the effects of MRI report and the benefits of reassurance by analyzing the clinical and functional outcomes of conservative treatment in non-specific chronic LBP.

Methods: 44 patients with chronic non-specific mechanical LBP of minimum 12 weeks, with no red flags and no underlying psychological abnormality (GHQ-12 score of <10), were randomized to Group-A who had a full factual explanation of their MRI findings, and Group-B who were reassured that their MRI was completely normal with only incidental findings. Patients with significant pathologies such as tumor, infection, severe stenosis, instability, sacroiliitis, and disc extrusions were excluded. The severity of pain (Visual Analogue Scale-VAS), the perception of their status of spine and disease (Pain Self Efficacy Questionnaire-PSEQ-2), and functional status (Short form Survey-SF-12) were measured at the first consult, after exposure to the MRI report, and at six weeks of identical medical and physiotherapy regime.

Results:

Patients in both groups were comparable in demographic and disease characteristics at the first consultation. However, following exposure and detailed explanation of the MRI report, Group-A had a decrease in PSEQ score (from 8.19+1.8 to 7+2.04), showing a negative perception of disease and catastrophization. Group-B had improved perception of their spine status (8.13+1.7 to 8.9+1.8) on reassurance. The difference in alteration of perception between the groups was more significant ($p=0.002$).

Following similar conservative therapy for six weeks, differences within and between the groups in VAS, PSEQ-2, and SF-12 showed that Group-A continues to have the deteriorating effect of a negative perception. In Group-A, VAS significantly increased to 6.19+1.7 from 5.33+1.4 ($p=0.006$), whereas it decreased from 5.96+1.1 to 2.43+0.8 in Group B ($p<0.001$). Similarly, the perception of illness deteriorated from PSEQ-2 of 8.19+1.8 to 6.19+1.9 ($p<0.001$) in Group-A compared to an improvement from 8.13+1.7 to 10.87+1.1 in Group B ($p<0.001$). The functional status of patients in Group-A deteriorated from SF-12-PCS of 43.8+7 to 38.8+8.8 and improved significantly from 41.9+6.6 to 47.3+6.5 in Group B. SF-12 MCS deteriorated from 44.7+7.5 to 39.2+8.8 in Group-A compared to an improvement from 43.4+5.5 to 49.6+5.0 in Group-B. The effect size was larger in MCS than PCS, indicating that the mental effects were more significant than physical effects. The results document that patients who were not alarmed about their MRI report had a better perception of their spine condition and also showed greater functional improvement for the same treatment.

Conclusion

Routine MRI reports produce a negative perception and poor functional outcomes in LBP. The reassurance of incidental findings in MRI reports and focussed clinical reporting might provide significant benefits in patients with non-specific LBP.

Progression of lumbar disc degeneration on MRI is not associated with occurrence of LBP, and LBP related QOL: an epidemiological study with 10-year follow-up

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【Introduction】

No conclusions have yet been reached regarding the association between low back pain (LBP) and lumbar spine MRI findings. The purpose of this study was to evaluate relationship between progression of lumbar disc degeneration on MRI and occurrence of LBP, and LBP related QOL over a 10-year period in the local residents.

【Methods】

One hundred sixty-one participants (51 males and 110 females, mean age was 62.6 years) were eligible for lumbar spine MRI at baseline survey in 2004 and 10-year follow-up in 2014. Disc degeneration was evaluated by the Schneiderman classification (4 grades from 0-3) and the Disc Degenerative Disease (DDD) score, which is the sum of the Schneiderman's grades between each of the L1-2 to L5-S1. The participants were divided into three categories based on DDD score changes for 10 years: no change, mild change, and severe change. Roland-Morris Disability Questionnaire (RDQ) was defined as norm-based score, and less than 50 points was assessed as low quality of life compared to the national norm. The chi-square test and Kruskal-Wallis test were used for statistical examination, and a p value less than 5% was used as statistical significance in this study.

【Results】

One hundred fifty-eight participants could be followed up their LBP, and there were 72 (45.6%) in no change, 46 (29.1%) in the mild change, and 40 (25.3%) in the severe change group. Twenty-five participants had LBP at baseline, and 16 of them was still suffering from LBP 10 years later. There was no significant difference in the distribution of persistent LBP among the three groups (7/11=63.6% in no change vs 4/8=50% in the mild vs 5/6=83.3% in the severer group, p=0.77). One hundred thirty-three participants had no LBP at baseline, and 56 of them had a new onset of LBP after 10 years. There was no significant difference in the distribution of new LBP onset among the three groups (26/61=42.6% vs 17/38=44.7% vs 13/34=38.2%, p=0.85). Moreover, in the 121 participants who were available for RDQ follow up, there were 55 (45.5%) participants in no change, 33 (27.3%) in the mild change, 33 (27.3%) in the severe change group. There was no significant differences of mean RDQ score at baseline (53.9 vs 51.3 vs 52.6 p=0.71) and after 10 years (57.9 vs 58.0 vs 58.2 p=0.81), and those of the distribution of RDQ scores less than 50 points at baseline (12/55=21.8% vs 10/33=30.3% vs 10/33=30.3% p=0.66) and after 10 years (6/55=10.9% vs 4/29=13.8% vs 4/29=13.8%, p=0.97).

【Discussion】

In this study, no association was found between 10-year DDD score change and occurrence of LBP, norm-based RDQ scores, and prevalence of lower national norm of RDQ score. It is concluded that progression of lumbar disc degeneration on MRI was not directly associated with LBP and LBP-related QOL. Further studies including other MRI findings should be needed to validate these results.

Extensive Subphenotyping of Lumbar Modic Changes and their Association with Low Back Pain in a Large Population-Based Cohort: the Wakayama Spine Study

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Introduction: Lumbar magnetic resonance imaging (MRI) phenotypes such as Modic changes are clinically impactful. Previous studies have classified Modic changes differently, sometimes using 'type I' and 'type I/II' or 'type II/III' and 'type II' interchangeably. No population-based study has previously examined the respective associations between types I, I/II, II, II/III, and III and the presence and intensity of lower back pain (LBP). Hence, we aimed to examine both the prevalence of the five types of Modic change throughout the lumbar region and the associations between LBP presence and intensity and the Modic change types in a large population.

Methods: Of the 952 participants enrolled in the Wakayama Spine Study in 2013, 814 subjects (246 men; 568 women; mean age, 63.6 years) were included. Endplate changes observed by MRI were classified using the Modic classification system of types I, I/II, II, II/III, and III. LBP was defined as current, continuous back pain lasting 48 hours or more in the past month. We assessed the prevalence of the Modic types at each lumbar disc level. Analysis of variance was used to assess the association between the LBP Visual Analog Scale (VAS) score and Modic types I, I/II, II, II/III, III, and those with no Modic changes. Multivariate logistic regression models were used in the following manner: to evaluate the association between each Modic type and the presence of LBP; to compare the associations between the types to those without Modic change; and to adjust for age, sex, body mass index, and the presence of disc degeneration and high intensity zones as previously defined. Additionally, we performed a multivariate logistic regression analysis of the association between Modic types I and I/II.

Results: We observed Modic changes in the lumbar spines of 63.5% (n = 516) of the participants, with types I and I/II, II and II/III, and III observed in 29.2% (n = 151), 66.3% (n = 343), and 4.5% (n = 23), respectively. The mean LBP VAS scores were 23.9±26.3, 12.6±21.3, 12.7±23.6, and 9.9±19.4 in participants with types I and I/II, II and II/III, III and those with no Modic changes, respectively. Furthermore, the LBP VAS score was significantly higher in patients with type I/II than in those with type I (28.0±28.2 vs. 18.4±22.6, p<0.05). Associations were found between Modic types I and I/II and the presence of LBP (odds ratio [OR]: 2.46; 95% confidence interval [CI]: 1.60-3.81). Furthermore, Modic type I/II was more significantly associated with LBP than was Modic type I (OR: 1.99; 95% CI: 1.02 - 3.91).

Discussion: Type I/II Modic changes were significantly associated with LBP with a stronger pain intensity than type I. To our knowledge, this is the first large population-based study on the association between extensive Modic changes types and LBP. Our study substantiates that Modic changes overall are clinically relevant phenotypes, but subphenotype analyses revealed specific patterns with LBP that need to be taken into account for any future study addressing Modic changes as well as to address mechanisms related to pain generation.

Influence of lumbar developmental spinal stenosis on back pain, leg pain and disability – prospective cohort 2206 subjects

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Introduction: Low back pain (LBP) and radiating leg pain are two common health problems around the world. Lumbar developmental spinal stenosis (DSS) may play an important role in pain generation. It is described as pre-existing narrowed vertebral canals at multiple lumbar levels with earlier onset of neurological compromise. To date, the interactions of DSS with different radiological phenotypes in causing pain are poorly understood. Although many spinal phenotypes are postulated to be possible pain generators, their clinical presentations are often poorly associated with the imaging profiles. The contribution of DSS in generating pain alone is also unknown. Its impact on clinical outcomes related to LBP, radicular leg pain and disability is unknown

Methods: A prospective cohort of 2206 subjects with demographics, lifestyle factors and magnetic resonance imaging (MRI) was studied. Information related to LBP and radiating leg pain was recorded as follows: age of onset, any pain experienced in the past month (30 days) and year (365 days). Clinical and radiological information regarding subjects' demographics, workload, smoking habit and various MRI phenotypes including disc degeneration, DSS, facet morphology were assessed. Pain-related disability was assessed by Oswestry Disability Index (ODI) and Roland-Morris Disability Questionnaire (RMQ). Quality of life was assessed by 36-Item Short Form Survey (SF-36). Predictive models for LBP and radicular leg pain yielded clinical and imaging risk factors.

Results: Of the 2206 subjects, 153 had DSS. Mean age was 51.9 years with mean BMI of 23.7. There were 847 (38.4%) males and 1359 (61.6%) females. 1590 (72.1%) subjects had LBP in the past year and 1251 (56.7%) had LBP in the past month. 904 (41.0%) subjects had radicular leg pain in the past year and 672 (30.5%) had radicular leg pain in the past month. Up to 959 (43.5%) subjects had severe pain. Subjects with DSS had more severe LBP, radiating leg pain and pain-related disability, and lower quality of life ($p < 0.05$). Besides, subjects with spondylolisthesis had 1.5 (95% CI=1.0-2.3; $p=0.048$) and 1.7 (95% CI=1.0-3.0; $p=0.033$) times higher odds of LBP in the past month and year respectively. Individuals with DSS had 1.4 (95% CI=1.0-2.1; $p=0.048$) and 1.8 (95% CI=1.3-2.6; $p=0.001$) times higher odds of radiating leg pain in the past month and year respectively. No association was observed with disc degeneration, facet joint morphology, Modic changes or high intensity zones.

Discussion: This large population-based study identified DSS, spondylolisthesis as risk factors of acute and chronic pain. DSS is likely to cause radiating leg pain as a pre-existing narrowing of the spinal canal predisposes the subject to nerve root compression. These factors should be considered for decision-making during management planning.

PREDICTING THE LIKELIHOOD OF COMPLICATIONS IN PATIENTS UNDERGOING SURGERY FOR DEGENERATIVE DISORDERS OF THE LUMBAR SPINE – MODEL DEVELOPMENT

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Introduction

Previous studies have identified several factors influencing the likelihood of incurring a complication during spine surgery for degenerative disorders of the lumbar spine. These include previous spine surgery, age, comorbidity, complexity of the surgery, BMI, smoking, and others. The aim of this study was to identify predictors from a large international spine registry and develop a multivariable model to predict the probability for perioperative complications, with a view to creating an online tool to accompany the registry and assist with preoperative decision-making.

Methods

The data were extracted from EUROSPINE's International Spine Tango Registry. Medical history and surgical details had been documented using the Tango surgery form, as had surgical and general medical complications arising between admission and discharge. Separate prediction models were built for surgical and general complications. Predictors were age, gender, previous spine surgeries at the same level, additional pathologies, BMI, smoking status, comorbidity, prophylaxis, technology used and Mirza surgical invasiveness score. For model development, all predictors were included simultaneously in a multiple logistic regression. A complete-case approach was taken. The discriminative ability of each model was assessed as the area under the receiver operating characteristic curve (AUC), and 95% confidence intervals. Plots were used to assess the calibration of the models.

Results

Data were available for 68'111 patients operated between Jan. 2012 and Dec. 2017. 43'461 were patients with degenerative lumbar disorders, aged 18 to 95 years, and 23'873 of them were available for complete case analysis. A general medical complication was reported in 766/23'873 (3.2%) patients, most commonly postoperative kidney/urinary problems (202; 0.8%) and a surgical complication in 2559/23'873 (10.7%), most commonly dural tear (1653; 6.9%). The most important predictor for surgical complication was previous surgery at the same level (odds ratio 1.96; 95% CI 1.76 – 2.18, p-value < 0.001); for general complications, it was the ASA-Score (ASA-2 odds ratio 1.59; 95% CI 1.21 – 2.14; p-value = 0.001, ASA-3 odds ratio 3.09; 95% CI 2.27 – 4.25; p-value < 0.001, ASA-3 odds ratio 5.80; 95% CI 3.03 – 10.59; p-value < 0.001)

The AUC for the model was 0.74 (95% CI: 0.72-0.75) for general complications and 0.63 (95% CI: 0.62-0.64) for surgical complications. Calibration was good up to predicted probabilities of 0.30 and 0.25, respectively.

Discussion

In general, complications were relatively rare. Surgical complications could be predicted with less discriminative ability than general complications. Reoperation at the same level was strongly predictive of surgical complications and a higher ASA-score, of general complications. The regression coefficients from the predictor models will be integrated into a tool that should be externally validated by future Spine Tango registry participants and ultimately used to provide patients with a more personalised prediction of the likelihood of incurring a complication during surgery.

Evaluation of the association between "appropriate use of surgery" and patient-rated outcome in degenerative spondylolisthesis: a prospective, controlled, multicentre study.

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INTRODUCTION: Many treatment failures in spine surgery are attributable to poor patient selection and the application of inappropriate treatment. Identifying appropriate candidates for surgery is important to optimise outcomes and prevent unnecessary risk and expense. Appropriate Use Criteria (AUC) serve to help clarify the indications for a procedure. The aim of this study was to evaluate the short-term outcomes of patients with lumbar degenerative spondylolisthesis (LDS) classified as appropriate or otherwise for surgery using a recently developed appropriateness algorithm(1).

METHODS: This was a prospective, controlled, multicentre (5 in Switzerland; 1 in USA) study of 737 patients (493 surgical and 244 nonsurgical controls; 70±10y; 67% female) with a first follow-up (FU) after treatment. The AUC were used to judge the appropriateness of surgery for each patient, based on the presenting symptoms and a constellation of other variables documented at baseline. Patients completed the Core Outcome Measures Index (COMI) at baseline and 3 months' FU. The care plan (surgery or nonsurgical care) was decided at the discretion of the treating physician, as per their normal practice and irrespective of the criteria. The data were analysed using repeated measures ANCOVA.

RESULTS: According to the AUC, surgery of some type was considered appropriate (A) in 143/493 (29%), uncertain (U) in 230/493 (47%) and inappropriate (I) in 120/493 (24%) of the surgical patients; it was A in 43/244 (18%), U in 94/244 (38%) and I in 107/244 (44%) of the nonsurgical patients. As per convention, the A and U groups were combined for comparison with the I group. There was a significant interaction ($p=0.02$) between the change in COMI score from baseline to 3mo FU in relation to treatment group and appropriateness for surgery: the benefit of surgery over nonsurgical care was greater in patients for whom surgery was considered A/U (2.9-point greater reduction in COMI) than in those for whom it was I (1.8-point greater reduction). In patients A/U for surgery, the COMI minimal clinically important change (MCIC) score was reached by 76% who got surgery and 27% who got non-surgical care; in those who were I for surgery, it was reached by 61% patients who got surgery and 26% who got non-surgical care.

DISCUSSION: The AUC were able to successfully identify patients who derived greater benefit from surgery at the first follow-up. The literature suggests that the early outcome heralds the longer-term results, but the findings should nonetheless be confirmed by further analyses of the 12 mo-FU data. Validation of the AUC for surgery for LDS should support their widespread adoption for quality improvement in spine surgery.

1. Mannion et al (2014) Eur Spine J. 23(9):1903-17.

Risk factors for symptomatic adjacent segment disease following lumbar fusion: A systematic review and meta-analysis

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INTRODUCTION: Adjacent segment disease (ASD) is a late complication of lumbar fusion that leads to chronic pain and revision surgery. Given the growing number of fusion operations and the severity of ASD, numerous studies have investigated the risk factors for symptomatic ASD. However, no systematic reviews have summarized these factors, which can inform clinical decision-making and establish further research direction. Therefore, this review aimed to summarize the risk factors for symptomatic ASD after lumbar fusion.

METHODS: A systematic database search including CINAHL, Cochrane Library, EMBASE, MEDLINE, and Web of Science was conducted from inception to December 2019. Two reviewers independently screened and extracted data from relevant primary studies. Newcastle-Ottawa quality assessment scale was adopted for critical appraisal. Meta-analyses were conducted to summarize potential risk factors. Odds ratio (OR) with confidence intervals (CI) was used to compare the characteristics between patients with and without symptomatic ASD.

RESULTS: Of 665 identified citations, 16 studies comprising 3,553 patients were included. The mean prevalence of symptomatic ASD among included studies was 13.4±5.5%, while the mean ASD-related reoperation rate was 11.2±7.4%. Four, 11, and 1 studies were classified as low, moderate and high methodological quality, respectively. The included studies identified 21 demographic, 8 surgical, and 49 radiographical risk factors for ASD. Twenty-two meta-analyses were conducted to summarize common risk factors identified in the included studies. Given numerous investigated risk factors, only those significant risk factors with moderate level of evidence were reported and discussed in the current review. The meta-analysis revealed moderate evidence to support that high body mass index (3 studies; n=438; pooled MD=2.77kg/m²; 95%CI=1.68kg/m²-3.85kg/m²; p<0.01), facet joint violation (2 studies; n=867; OR=30.30; 95%CI=17.62-52.10; p<0.01), anterior shift of the preoperative lumbosacral sagittal plumb line (4 studies; n=952; pooled MD=7.01mm; 95%CI=4.96mm-9.06mm; p<0.01), decreased preoperative lumbar lordosis (11 studies; n=2,014; pooled MD= -4.19°; 95%CI = -6.66° to -1.71°; p < 0.01), preoperative adjacent disc degeneration (8 studies; n=1,877; pooled OR=1.91; 95%CI=1.19-3.06; p<0.01), decreased preoperative adjacent disc height (4 studies; n=395; pooled MD= -0.69mm; 95%CI= -1.26mm to -0.11mm; p=0.02), anterior shift of the postoperative lumbosacral sagittal plumb line (4 studies; n=952; pooled MD=3.98mm, 95%CI = 2.46-5.49mm; p<0.01), reduced postoperative lumbar lordosis (9 studies; n=1,639; pooled MD= -5.50°; 95%CI = -7.59° to -3.40°; p<0.01), and increased postoperative lumbopelvic mismatch (2 studies; n=231; pooled MD=4.56°; 95%CI=0.95°-8.17°; p=0.01), postoperative pelvic incidence (4 studies; n=475; MD=3.69°; 95%CI=0.67-6.71, =0.02), and postoperative pelvic tilt (5 studies; n=507; MD=3.20°; 95%CI=1.68°-4.71°; p<0.01) were significantly related to ASD.

DISCUSSION: This is the first meta-analysis to summarize evidence regarding various modifiable and non-modifiable risk factors for symptomatic ASD following lumbar fusion. While age or preoperative degeneration of patients undergoing lumbar fusion cannot be altered, it is possible to lower the risk of symptomatic ASD by modifying other risk factors. Specific considerations should be given to the preoperative adjacent segment degeneration, proper sagittal lumbopelvic realignment, and the minimization of intra-operative iatrogenesis injuries. Future prospective research is warranted to evaluate the effects of modifying these risk factors on lowering the development of symptomatic ASD among high-risk patients.

Prospective comparison of the accuracy of the New England Spinal Metastasis Score (NESMS) to legacy scoring systems in spinal metastases

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INTRODUCTION:

We developed the New England Spinal Metastasis Score (NESMS) as a simple, informative, scoring scheme that could be applied to both operative and non-operative patients. The performance of the NESMS to other legacy scoring systems has not previously been compared using appropriately powered, prospectively collected, longitudinal data. We sought to compare the predictive capacity of the NESMS to the Tokuhashi, Tomita and Spinal Instability Neoplastic Score (SINS) in a prospective cohort, where all scores were assigned at the time of baseline enrollment.

METHODS:

We enrolled 202 patients with spinal metastases who met inclusion criteria between 2017-2019. One-year survival was our primary outcome; 3-month mortality and ambulatory function at 3- and 6-months were considered secondarily. All prognostic scores were assigned based on enrollment data, which was also assigned as time-zero. Patients were followed until death or survival at 365 days after enrollment. Survival was assessed using Kaplan-Meier curves and score performance was determined via logistic regression testing and observed to expected plots. The discriminative capacity (c-statistic) of the scoring measures were compared via the z-score.

RESULTS:

When comparing the discriminative capacity of the predictive scores, the NESMS had the highest c-statistic (0.79), followed by the Tomita (0.69), the Tokuhashi (0.67) and the SINS (0.54). The discriminative capacity of the NESMS was significantly greater (p-value range: 0.02 to <0.001) than any of the other predictive tools. The NESMS was also able to inform independent ambulatory function at 3- and 6-months, a function that was only uniformly replicated by the Tokuhashi score.

DISCUSSION:

The results of this prospective validation study indicate that the NESMS was able to differentiate survival to a significantly higher degree than the Tokuhashi, Tomita and SINS. The NESMS was also able to inform independent ambulatory function at 3- and 6-months, a function that was only uniformly replicated by the Tokuhashi score. We believe that these findings endorse the application of the NESMS to the care of patients with spinal metastases.

“Readmission-free survival” in metastatic spine tumour surgical patients: A novel concept

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Introduction

Outcomes commonly used to ascertain success of metastatic spine tumour surgery (MSTS) are 30day complications/mortality and overall/disease-free survival. We believe a new effective outcome indicator after MSTS would be the absence of unplanned hospital readmissions (UHR) after index-discharge. We introduce the concept of “readmission-free survival” (ReAFS), defined as ‘the time duration between hospital discharge after index-operation and first UHR/death’. We postulate that an ideal ReAFS should be equal to remaining life expectancy of the patient after index-surgery. The aim of our study was to identify factors influencing ReAFS in MSTS-patients.

Methods

We retrospectively analysed 266 consecutive patients (age \geq 18 years) who underwent MSTS between 2005–2016 with a follow-up for a minimum of 2years or until their demise, whichever was earlier. Approval was obtained from Institutional Review Board prior to study commencement. Demographics, oncological characteristics, procedural, preoperative, and postoperative details were collected. ReAFS of patients within two-years or till demise, were reviewed. Perioperative factors predictive of prolonged ReAFS were evaluated using multivariate regression analysis.

Results

A total of 230-patients met criteria for analysis. The mean age was 60.1 \pm 11.8 years; 47.8% were females. Mean preoperative haemoglobin was 11.93 \pm 1.96g/dL. Majority had at least two preoperative comorbidities. Median Tokuhashi score was 8. An Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score of 1 was observed in 38.8% of patients. Majority of primary tumours were lung followed by breast, and haematological. 74% of the cohort underwent open surgery with a median of five levels instrumented and one level decompressed. Of the 230-patients, 201 had an UHR or died during the study period, whilst one in eight (29/230) had no UHR. Initial univariate (Kaplan-Meier) analysis revealed that patients with preoperative haemoglobin $>$ 12g/dL had a median ReAFS of 182days (95%CI 82.8–281.1) while those with $<$ 12 had a median of 66days (40.5–91.4) ($p=0.005$). Patients with ECOG $<$ 3 had a median ReAFS of 138days (90.9–185.0), versus 30days (0–75.7) for those with ECOG $>$ 3 ($p<0.001$). Patients who underwent preoperative radiotherapy had a median ReAFS of 48days (22.5–73.5) while those without preoperative RT had 134days (84.2–183.7) ($p=0.016$). Metastatic spine disease from primary lung tumours had the shortest ReAFS of 51days (21.9–80.0). Conversely, having breast or prostate primaries had average ReAFS of 230days (49.4–410.5) and 322days (0.0–677.3), respectively ($p=0.004$). An ReAFS of 111days (63.5–158.5) was observed when comorbidities were $<$ 4, as opposed to 47days (18.8–75.2) when comorbidities exceeded 4 ($p=0.062$). Multivariate analysis revealed that preoperative haemoglobin \geq 12g/dL ($p=0.029$); ECOG score of \leq 2 ($p=0.026$); primary breast ($p=0.003$) and haematological ($p<0.001$) cancers; comorbidities $<$ 4 ($p=0.030$); absence of preoperative radiotherapy ($p=0.033$); and a shorter postoperative length of stay ($p=0.025$) significantly prolonged the ReAFS.

Discussion

Readmission-free survival is a novel concept in MSTS, which relies on patient’s general condition, appropriateness of interventional procedures, and underlying disease burden. Additionally, it may indicate the successful combination of a multi-disciplinary treatment approach. This information will allow oncologists and surgeons to identify patients who may benefit from increased surveillance following discharge to increase ReAFS. We envisage that ReAFS is a concept that can be extended to other surgical oncological fields.

Comparison of opioid use in multilevel lumbar spinal fusion patients before and after implementation of an institutional opioid minimizing program

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INTRODUCTION

Opioid prescribing for patients undergoing orthopedic procedures has been identified as a major contributor to the current opioid crisis in the United States. The rising awareness and more restrictive prescribing guidelines are beginning to affect the practice of medicine. Physicians are looking for alternative methods to effectively control acute pain and improve the treatment of chronic opioid patients. In line with these efforts, hospitals are establishing interventions and policies to address the national epidemic at the institutional level. Our hospital implemented new clinical, regulatory and policy guidelines in 2017 directed toward minimizing opioid use and prescribing while providing adequate analgesia after orthopedic surgery. These included clinical guidelines for managing opioid naïve and opioid tolerant patients and/or those with substance abuse disorder, educational programs for patients and prescribers, and surgery-specific prescribing recommendations to limit unnecessary prescribing of opioids. The aim of this study was to describe changes in opioid use and prescribing associated with the implementation of opioid minimizing initiatives in patients undergoing multilevel lumbar fusion.

METHODS

A retrospective before-and-after analysis of 268 patients who underwent multilevel lumbar fusion at an orthopedic surgery specialty hospital in New York City. The study included data collected between January 1 2016 – December 31 2016 (prior to institutional implementation) and between January 1 – December 31 2019, (after full institutional implementation) The electronic medical records and office notes were retrospectively reviewed for opioid use before and after surgery, and converted to equianalgesic doses (morphine equivalent dose, MED, and expressed as milligrams of morphine per day, mg/day). The primary outcome was postoperative opioid consumption during the hospital stay and the opioid prescribed upon hospital discharge. The secondary outcomes were length of hospital stay (LOS), opioid-induced side effects, and numeric rating scale (NRS) pain scores. Demographic and perioperative characteristics were compared between the intervention group and control cohort using Wilcoxon signed rank test for continuous variables and fisher's exact test for dichotomous variables and set the statistical significance at $p < 0.05$.

RESULTS

A total of 268 multilevel lumbar fusion patients were included in this analysis. 141 (52.6%) patients had surgery in 2016 and 127 (47.4%) underwent surgery in 2019. We found a statically significantly lower opioid consumption during the hospital stay ($p < 0.0001$) and at discharge ($p < 0.0001$) in 2019 compared to 2016 with statistically significant lower side effects ($p = 0.03$) in 2019. Additionally, preoperative opioid consumption was statistically significantly lower in 2019 ($p = 0.003$). There was no difference in the LOS and NRS pain scores in 2016 and 2019 ($p = 0.21$ and $p = 0.33$).

DISCUSSION

This study found that after the clinical and policy interventions, opioid consumption, prescribed opioids upon hospital discharge and opioid-related side effects were lower. Despite these gains, there were no changes in reported pain associated with surgery and LOS was unchanged. Our findings demonstrate the efficacy of institutional implementation of a set of interventions to address the national opioid epidemic at the local level.

Preoperative Cross-sectional Area of Psoas Muscle Impacts Postoperative Functional Outcomes of Posterior Lumbar Surgery

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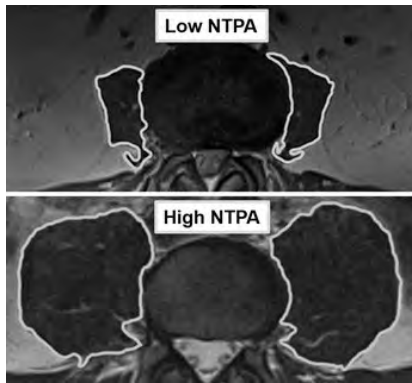
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Introduction: The decrease of psoas cross-sectional area has been reported to be a predictor of increased risk of mortality and complications in spine surgery. However, there is no consensus on which level should be selected to measure it on MRI. Additionally, it is unclear whether the psoas size impacts postoperative functional outcomes after lumbar surgery. The objective of this study was to determine the optimal level for the measurement of psoas cross-sectional area and examine its impact on short-term functional outcomes of lumbar surgery with posterior approach.

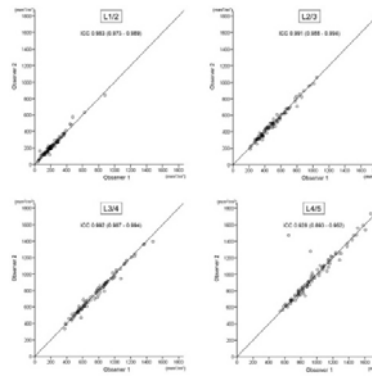
Methods: Patients who underwent minimally invasive posterior lumbar surgery for degenerative diseases with more than 6 months follow-up were included in this study. The cross-sectional area of psoas muscle was measured at each intervertebral level on T2-weighted axial images of preoperative MRI by 2 observers (Figure 1). Normalized total psoas area (NTPA) was calculated as total psoas area normalized to patient height. Intraclass Correlation Coefficient (ICC) was calculated to evaluate inter-rater reliability of NTPA at each level. Patient reported outcome measures (PROMs) including Oswestry disability index (ODI), visual analog scale at back (VAS back) and leg (VAS leg), short form 12 physical component summary (SF-12 PCS) and mental component summary (SF-12 MCS) and patient-reported outcomes measurement information system physical function (PROMIS PF) were collected at pre-op, 2 weeks, 6 weeks, 3 months and 6 months.

Results: The total of 215 patients were included in this study. ICC at L3/4 [0.992 (95%CI 0.987-0.994)] was the higher than those at the other 3 levels [L1/2 0.983 (0.973-0.989), L2/3 0.991 (0.986-0.994), L4/5 0.928 (0.893-0.952)] (Figure 2). The median NTPA at L3/4 was 892 (789-1077) mm²/m² in males and 612 (522-691) mm²/m² in females. NTPA in females was significantly lower than that in males (p < 0.001). Patients were divided into 2 groups at the point of the sex-specific lowest quartile of NTPA at L3/4 threshold. There were no significant differences in preoperative PROMs except for SF-12 MCS, however, all of them were significantly worse in the low NTPA group at postoperative points (Table 1). In terms of SF-12 MCS, preoperative score was significantly better in the low NTPA group, however, no significant differences were found at all postoperative points. Multivariate logistic regression showed low NTPA was an independent predictor of high ODI and VAS leg at 6 months (Table 2).

Conclusion: The decrease of psoas cross-sectional area on preoperative MRI had a negative correlation with short-term functional outcomes of posterior lumbar surgery. NTPA, which is a highly reliable and easy to assess, may be useful for a decision making for more effective treatment based on muscle health in each patient.



	Low NTPA group (mm ²)	High NTPA group (mm ²)	P value
ODI			
pre-op	38.6 ± 10.6	32.2 ± 20.2	0.089
2 weeks	38.4 ± 21.3	37.8 ± 20.1	0.300
6 weeks	38.5 ± 16.3	37.2 ± 19.0	0.682
3 months	38.9 ± 20.3	37.1 ± 18.6	0.639
6 months	23.8 ± 18.8	13.3 ± 15.2	0.014
VAS back			
pre-op	4.9 ± 2.0	5.4 ± 3.2	0.345
2 weeks	4.0 ± 2.8	3.8 ± 2.8	0.190
6 weeks	3.3 ± 2.7	2.8 ± 2.3	0.022
3 months	3.0 ± 2.7	2.9 ± 2.3	0.622
6 months	2.8 ± 2.5	2.0 ± 2.3	0.048
VAS leg			
pre-op	4.4 ± 2.1	4.3 ± 3.1	0.120
2 weeks	3.2 ± 2.1	3.4 ± 3.1	0.784
6 weeks	2.8 ± 2.6	2.3 ± 2.6	0.487
3 months	2.5 ± 2.5	1.9 ± 2.3	0.166
6 months	2.3 ± 2.3	1.3 ± 2.2	0.003
SF-12 PCS			
pre-op	31.0 ± 7.2	31.5 ± 8.1	0.374
2 weeks	31.7 ± 8.9	31.4 ± 8.4	0.821
6 weeks	34.9 ± 10.1	33.3 ± 10.0	0.051
3 months	38.9 ± 11.8	42.3 ± 11.1	0.179
6 months	47.1 ± 10.8	48.2 ± 10.8	0.812
SF-12 MCS			
pre-op	52.4 ± 11.5	47.8 ± 11.6	0.002
2 weeks	50.8 ± 10.5	50.3 ± 11.0	0.847
6 weeks	54.1 ± 10.2	52.4 ± 10.5	0.342
3 months	56.0 ± 9.8	57.8 ± 9.4	0.680
6 months	54.9 ± 9.1	57.8 ± 9.5	0.021
PROMIS PF			
pre-op	38.8 ± 7.2	39.0 ± 8.2	0.878
2 weeks	38.0 ± 8.4	37.6 ± 8.8	0.858
6 weeks	38.5 ± 7.1	41.4 ± 8.2	0.048
3 months	43.7 ± 10.0	44.8 ± 10.0	0.367
6 months	47.8 ± 9.9	47.2 ± 9.7	0.628



	Odds ratio (95% CI)	P value	VIF
ODI (> 20.0)			
BMI (> 30.0)	1.74 (0.79-3.82)	0.166	1.009
NTPA (low NTPA group)	2.50 (1.23-5.08)	0.011	1.009
VAS back (> 3.4)			
Gender (male)	0.67 (0.33-1.33)	0.248	1.000
Smoking	1.48 (0.70-3.08)	0.314	1.004
NTPA (low NTPA group)	1.64 (0.77-3.51)	0.204	1.004
VAS leg (> 3.4)			
BMI (> 30.0)	2.25 (0.89-5.70)	0.087	1.012
NTPA (low NTPA group)	3.65 (1.68-8.61)	0.001	1.012
SF-12 PCS (< 50.0)			
BMI (> 30.0)	1.95 (0.77-4.94)	0.160	1.016
Smoking	0.82 (0.31-1.27)	0.193	1.004
History of previous lumbar surgery	1.69 (0.74-3.87)	0.213	1.048
Number of surgical levels (multiple)	0.83 (0.26-1.52)	0.303	1.016
NTPA (low NTPA group)	2.11 (0.93-4.78)	0.074	1.040
SF-12 MCS (< 50.0)			
BMI (> 30.0)	0.61 (0.25-1.52)	0.289	1.000
PROMIS PF (< 50.0)			
CCI (> 1)	1.49 (0.54-4.10)	0.438	1.028
Type of surgery (with fusion)	1.70 (0.81-3.60)	0.163	1.025
NTPA (low NTPA group)	1.93 (0.76-4.90)	0.167	1.004

The extent, nature, and consequences of loss to follow-up in a long-established single-centre spine surgery registry of over 15'000 patients

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INTRODUCTION: Patient-rated outcome measures are integral to the assessment of treatment success and an essential part of the documentation in surgical registries. Lack of compliance with follow-up (attrition) can threaten the validity of the outcomes reported in registry studies. Prior research indicates that demographic, socioeconomic, and medical factors may all contribute to attrition. These same characteristics are often also predictors of outcome. We studied the extent, nature and consequences of drop-out in a long-established, single-centre spine registry.

METHODS: Data were analysed from 15'264 consecutive patients (60±17y; 46% men) who had undergone spine surgery in our Spine Center 1.1.06-31.12.17. Data were documented prospectively using EUROSPINE's Spine Tango Registry forms. Surgeons had completed a Surgery Form (clinical history, surgical measures, complications) for 99.1% cases. The proportion of patients completing a Core Outcome Measures Index (COMI) ("completers") was 90% preoperatively, 89% at 3 mo follow-up (FU), and 86% at 12 mo FU. At the two FUs, patients also rated the Global Treatment Outcome (GTO) ("how much did the operation help your back problem"; response categories: helped a lot, helped (=good outcome), helped only little, didn't help, made things worse (=poor outcome)). We determined: (1) baseline characteristics of 12-mo responders vs non-responders, (2) 12-mo outcome in responders vs delayed responders (those responding only after further reminders; typically lost to follow-up in standard registry protocols), and (3) 3-mo outcome of 12-mo responders vs non-responders. Analyses included Chi-square, ANOVA and multivariable regression.

RESULTS: The most notable independent predictors (each $p < 0.001$) of being a 12-mo non-responder were: lower age, non-Swiss, having semi-/private insurance, higher ASA, worse baseline COMI, and previous surgery. 19% patients received a reminder and half of them finally returned a questionnaire. The outcome of these delayed responders was worse than that of responders (74% vs 78% good GTO, respectively; $p=0.008$). The "non-responders at 12-mo FU" had shown a worse outcome at their 3-mo FU than had the "responders at 12-mo FU" (respectively, 66% vs 80% good GTO; $p < 0.0001$). All COMI results reflected those of GTO.

DISCUSSION: Although non-responders were relatively few in the present cohort (14% at 12-mo FU), they displayed distinctive characteristics and their early outcome was significantly worse than that of responders. Without the resources to contact non-responders, outcome in registries will likely be overestimated, and falsely optimistic results reported. Knowing the risk profiles of non-responders may help to focus efforts to reduce attrition and improve the validity of registry data.

Decompressive surgery without instrumented fusion in patients with low-grade degenerative spondylolisthesis patients: long-term patient reported outcome

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Introduction: Degenerative spondylolisthesis is a condition where one vertebra slips over another due to facet joint degeneration and intervertebral disc degeneration. It is generally accepted that surgical treatment is preferred over non-surgical treatment in clinically relevant lumbar spinal stenosis. However, if spinal stenosis is accompanied by degenerative spondylolisthesis, the surgical technique to use remains debatable. Low-grade degenerative spondylolisthesis is considered a risk factor for instability requiring instrumented fusion in addition to decompression. In this long-term cohort study, clinical outcome of patients who underwent decompressive surgery without instrumented fusion is assessed.

Methods: Questionnaires concerning pain, functionality and perceived recovery were sent to 250 patients with degenerative spondylolisthesis that were merely decompressed after a mean follow up period of 9 years. As a control group, a randomly selected cohort of 200 patients with spinal stenosis without spondylolisthesis, who had received decompressive surgery in the same period, was considered. Demographic characteristics, surgical technique, indication and incidence of reoperation and patient reported outcome measures were assessed.

Results: At follow up, the mean ODI was 23.6 ± 20.15 in the spondylolisthesis group and 23.4 ± 20.9 ($p = 0.957$) in the stenosis group. The EQ-5D was respectively 0.74 ± 0.28 and 0.75 ± 0.24 ($p = 0.793$) in the spondylolisthesis and stenosis group, and the ZCQ score was respectively 48.2 ± 18.8 and 49.6 ± 18.5 % ($p = 0.646$). After 9 years of follow up, 69% of spondylolisthesis patients were satisfied with their surgery compared to 68% in the stenosis group ($p=0.855$), according to the Likert-scale. Although response rates in the spondylolisthesis and stenosis group were 43 and 32% respectively, but reoperation rates (12 versus 15%) were in agreement with the reoperation rate in the total group (17 versus 12%; $p=0.729$).

Discussion: This long-term follow-up cohort study demonstrated a comparably satisfactory clinical outcome between spinal stenosis patients and low-grade degenerative spondylolisthesis stenosis patients, after the regimen of first decompression and adding fusion if necessary, in a second intervention procedure. Even after 9 years of follow up patients from both groups are generally satisfied with the treatment they received. Decompressive surgery is in most cases of lumbar spinal stenosis with and without degenerative spondylolisthesis an effective treatment and adding instrumented spondylodesis as a routine is not recommended.

Intervertebral disc repair with autologous nucleus pulposus-derived MSCs transplantation: a controlled clinical trial by 5-year follow-up

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INTRODUCTION: Intervertebral disc degeneration is irreversible with no efficacious treatment available currently. Lumbar disc herniation treated by discectomy results in a significant loss of disc material and disc height. Biological restoration through nucleus pulposus-derived MSCs transplantation might offer a potential to achieve functional integration of disc metabolism and mechanics. We demonstrated that reinsertion of MSCs slowed disc degeneration and significantly up-regulated the viability of NP cells in pre-clinical studies^[1-2]. This study aimed to assess the safety and efficacy of autologous NP-derived MSCs transplantation and the regenerative restoration ability in clinical outcome after lumbar discectomy.

METHODS: Subjects were 30 patients aged from 20 to 55 years. All patients had been diagnosed lumbar disc herniation and been given the discectomy. Nucleus pulposus were collected and cultured in GMP condition. Fifteen patients were given the transplantation of autologous NP-derived MSCs to the index intervertebral disc by a minimally invasive procedure 4 weeks postoperatively. The other fifteen patients were no transplantation of MSCs as a control group. The study was approved by the hospital ethics committee. The safety was assessed by symptom and blood assay, and the efficacy was assessed by the VAS scores, JOR scores, ODI Index and Sf-36 Index. The repair and regeneration of herniated disc was assessed by X-ray and Magnetic resonance imaging T2, the ratio value of the grayscale (RVG) was used to evaluate the disc degenerative degree.

RESULTS: No complication were observed after autologous NP-derived MSCs transplantation. All functional scores at two groups, including VAS scores, JOR scores, ODI Index and SF-36 Index, had the significant improvement comparing with pre-operation during 5 years clinical follow-up. Furthermore, all functional scores hadn't the significant difference between two groups in different observing points postoperatively. X-ray results showed that the height of intervertebral disc at two groups hadn't the significant difference. At 5 years post-transplantation, on T2-weighted magnetic resonance imaging, the index intervertebral discs RVG was 73.3 ± 13.6 in autologous NP-derived MSCs transplantation group compared with 43.6 ± 9.7 in control group. ($p < 0.05$).

DISCUSSION: Autologous nucleus pulposus-derived MSCs transplantation showed the safety and efficacy in clinical trial by 5-year follow-up. This result indicate that the MSCs-treated disc had the higher water contents and relevant to repairing or retarding disc degeneration biologically after discectomy.

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Viable Disc Tissue Allograft Supplementation in the Treatment of Degenerated Intervertebral Discs the One Year Results of a Randomized Control Trial

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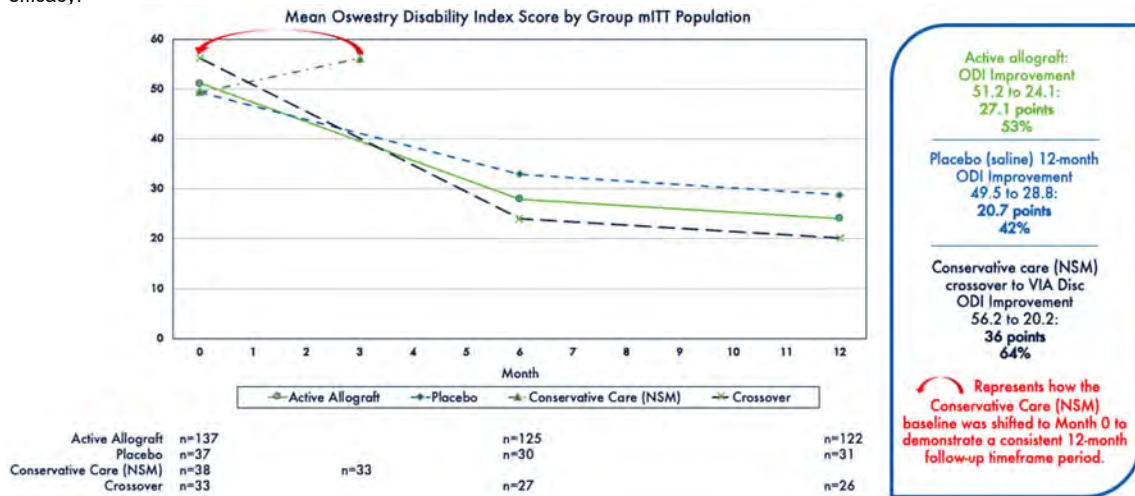
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Introduction: A viable disc tissue allograft has been developed to supplement tissue loss associated with degenerative lumbar disc disease and the development of chronic discogenic lower back pain (CLBP). This unique viable disc allograft was injected into painful degenerated discs to evaluate safety and to determine whether it can improve pain and function in patients from CLBP.

Materials and Methods: A prospective, multicentered, blinded randomized, clinical trial (RCT) for subjects with single level or two-level degenerative lumbar disc disease was conducted. 218 patients with chronic low back pain secondary to single-level or two-level degenerative disc disease were enrolled in the study. Patients had back and leg pain for a minimum of 6 months that was recalcitrant to nonoperative treatment modalities. Subjects were blinded and randomized to receive intradiscal injections of either viable disc allograft or saline or to continue with non-surgical management (NSM). Standardized clinical outcome instruments were used, including Oswestry Disability Index (ODI) and Visual Analogue Scale of Pain Intensity (VASPI). Plain radiographs and MRI scans were used to assess disc space height and spinal alignment, and to determine the degree of disc degeneration. The NSM group could cross over to the allograft group after 3 months. Patients were assessed at 6 and 12 months. Patient adverse events were continuously assessed.

Results: At 12 months, clinically meaningful improvements in mean VASPI and ODI scores were achieved in both the investigational allograft and saline groups; however, the mean clinical outcomes were not statistically significant between the treatment groups. At one year in the investigational allograft group, pain improved 54% and was accompanied by a 53% improvement in ODI. NSM subjects following crossover attained a 65% improvement in pain at 12 months combined with a 64% improvement in ODI. a responder analysis demonstrated, a clinically meaningful reduction in ODI of ≥ 15 points at 12 months that was statistically significant; 76.5% of subjects randomized to allograft being responders ($p = 0.03$) when as compared to 56.7% in the saline group. In the allograft group, 11 safety adverse events occurred in 141 subjects (3.5%).

Conclusions: This large, prospective blinded RCT demonstrated safety and results suggesting that viable disc tissue allograft may be a beneficial non-surgical treatment for patients that have chronically painful lumbar degenerative discs. Subjects treated with viable disc tissue allograft exhibited significantly higher functional responder rates than the saline arm indicating promising benefits for patients with painful lumbar degenerative discs. The safety profile of the supplemental allograft was demonstrated to carry a risk similar to discography. Further studies are required to confirm efficacy.



Supervised exercise therapy versus unsupervised exercise for patients with lumbar spinal stenosis: one-year follow-up of a randomized controlled trial

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INTRODUCTION: Supervised physical therapy for patients with lumbar spinal stenosis (LSS) has been reported to lead to better short-term outcomes in terms of disability and leg pain than unsupervised exercise.¹ However, it is unclear whether these short-term effects persist and whether patients with LSS who receive supervised physical therapy are less likely to undergo surgery than those performing unsupervised exercise. The purpose of this study was to assess the 1-year follow-up outcomes of LSS patients treated with supervised physical therapy or unsupervised exercise.

METHODS: Patients presenting with symptoms of neurogenic claudication caused by LSS were randomized to a physical-therapy group (PT group), which performed supervised physical therapy twice a week for 6 weeks, or a home-exercise group (HE group). PT sessions included manual therapy, stretching and strengthening exercises, cycling, and body weight-supported treadmill walking. All patients were asked to undertake an HE program. Patients in the HE group visited a physical therapist to determine whether they performed home exercise once a week for 6 weeks. The primary outcome was the difference in improvement in symptom severity scores on the Zurich Claudication Questionnaire (ZCQ) at 1 year. Secondary outcomes included: physical function on the ZCQ; pain indicated using a numerical rating scale; and scores on the Medical Outcomes Study 36-item Short-Form General Health Survey, Hospital Anxiety and Depression Scale, Pain Catastrophizing Scale, and the Tampa Scale for Kinesiophobia. Scores, mean changes, and surgery rate after 1 year were compared between the groups. A *P*-value <0.05 was considered significant.

RESULTS: Forty-three patients (20 men and 23 women, average age 72.3 years) were randomly allocated to the PT group and 43 (19 men and 24 women, 73.2 years) to the HE group. At 1-year follow-up, 2 patients in the PT group and 1 patient in the HE group had dropped out because of health problems or death. One patient in the PT group and nine patients in the HE group underwent decompression surgery during the 1-year follow-up period. At baseline, there were no significant differences between groups for age, gender, BMI, duration of symptoms, MRI findings or outcome measures (*P*>0.05). At 1-year follow-up the PT group showed significant improvements compared with the HE group for ZCQ symptom severity (adjusted mean difference –0.3; 95% confidence interval [CI]: –0.5 to –0.01, *P*=0.04), ZCQ physical function (adjusted mean difference –0.3; 95% CI: –0.6 to –0.04, *P*=0.03). The surgery rate at 1 year was lower in the PT group than in the HE group (7.0% vs. 23.3%; adjusted odds ratio 0.2 [0.04–0.9] *P*=0.04).

DISCUSSION: Six weeks of supervised physical therapy for patients with LSS produced significant improvements in symptom severity and physical function compared with unsupervised exercise over 1 year of follow-up. Furthermore, patients with LSS receiving supervised physical therapy were less likely to undergo surgery within 1 year. Patients with LSS should be treated with intensive and supervised exercise programs to obtain the maximum benefits from exercise therapy.

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Cone of Economy Classification: Evolution, Concept of Stability, Severity Level, and Correlation to Patient-Reported Outcome Scores

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Introduction: Preoperative functional data is a crucial component of determining patient disability and prognosis. Patient-reported outcomes measures (PROMs) have been developed to aid in quantifying the level of debilitation in spine patients but have various limitations. The cone of economy (CoE) has been theorized to be the foundation of biomechanical changes that leads to increased energy expenditure and disability in spine patients. Correlating CoE measurements to PROMs and classifying alterations in balance can help provide objective measurements to improve preoperative decision making. The purpose of this study was to determine a classification system for CoE measurements that defines clinically significant changes in altered balance and to assess if the CoE measurements directly impact PROMs.

Methods: We conducted a non-randomized cross-sectional study of 423 patients with symptomatic spine pathology. Patients were given a series of PROMs preoperatively including VAS, ODI, Tampa Scale for Kinesiophobia (TSK), Fear and Avoidance Beliefs Questionnaire (FABQ), and Demoralization (DS). The functional balance was tested in this group using a full-body reflective marker set to measure the head and center of mass (CoM) sway.

Results: PROMs scores were correlated with the magnitude of the CoE measurements. Patients were separated by the following proposed classification: CoM coronal sway >1.5cm, CoM sagittal sway >3cm, CoM total sway > 30cm, head coronal sway > 3cm, head sagittal sway > 6cm, and head total sway > 60cm. Patients with spine pathology's ODI score strongly correlated with CoM and head sway and the VAS back did not correlate. Primary balance measures for this study included head and CoM coronal and sagittal sway, and total sway. Patients were separated by the following proposed classification based on the mean and standard deviation of previously published healthy controls: CoM coronal sway >1.5cm, CoM sagittal sway >3cm, CoM total sway > 30cm, head coronal sway > 3cm, head sagittal sway > 6cm, and head total sway > 60cm. Significant differences between groups were noted in the ODI (<0.001), FABQ physical activity (<0.001-0.009), DS (<0.001-0.023), and TSK (<0.001-0.032) across almost all planes of motion for both CoM and head sway. The moderate back VAS and leg VAS were significantly different between the severe and moderate altered balance groups for coronal CoM and head sway (p = 0.001-0.016) but were less sensitive to alterations in sagittal balance (p = 0.08-0.7). The ODI was most sensitive to the difference between groups across CoM and head sway planes with a mean ODI of 47.53-49.56 (p < 0.001) in the severe group vs. 36.62-39.35 (p < 0.001) in the moderate group.

Conclusions: By classifying CoE measurements by the cutoffs proposed, clinically significant alterations in balance can be quantified. Furthermore, this study demonstrates that across spinal pathology, higher magnitude CoE and range of sway measurements correlate with worsening PROMs. The Haddas' CoE classification system in this study helps to identify patients that may benefit from surgery and guide their postoperative prognosis.

Table 1. Haddas' Cone of Economy Classification: Summary of comparison of patient-reported outcome measures between cone of economy moderate to severe scores among symptomatic spinal degeneration cohorts

	Score	Low back VAS	leg VAS	ODI	Tampa Scale for Kinesiophobia (TSK)	Fear and Avoidance Beliefs Questionnaire (FABQ) Physical Activity	Fear and Avoidance Beliefs Questionnaire (FABQ) Work	Demoralization (DS)
Head Coronal Sway (3 cm)								
Moderate	1.91	4.87	4.03	39.35	40.47	16.80	13.94	17.47
SD	0.60	3.34	3.59	16.90	7.95	6.06	11.17	13.54
N	241	241	241	241	241	241	241	241
Severe	5.71	5.65	4.95	49.17	42.95	18.59	17.10	24.58
SD	2.63	3.06	3.30	15.67	8.65	6.03	12.70	17.91
N	182	182	182	182	182	182	182	182
p Value	<0.001*	0.015*	0.005*	<0.001*	0.003*	0.003*	0.007*	<0.001**
Head Sagittal Sway (6)								
Moderate	4.60	4.93	4.26	38.73	40.29	16.99	14.31	18.36
SD	0.98	3.35	3.61	16.38	7.50	5.98	10.64	14.44
N	204	204	204	204	204	204	204	204
Severe	9.17	5.45	4.56	47.77	42.63	18.07	16.15	22.38
SD	2.83	3.16	3.39	16.59	8.90	6.18	12.96	16.93
N	219	219	219	219	219	219	219	219
p Value	<0.001*	0.104	0.386	<0.001*	0.004*	0.069	0.116	0.010*
Head Total Sway (60 cm)								
Moderate	45.95	4.76	4.00	37.75	40.93	16.67	14.22	17.00
SD	8.74	3.56	3.56	16.12	7.80	6.56	11.10	13.18
N	210	210	210	210	210	210	210	210
Severe	102.53	5.64	4.83	49.14	42.09	18.42	16.33	23.90
SD	41.09	3.08	3.39	16.13	8.83	5.50	12.65	17.57
N	213	213	213	213	213	213	213	213
p Value	<0.001*	0.005*	0.016*	<0.001*	0.157	0.003*	0.072	<0.001**

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

PREVALENCE AND CHARACTERISTICS OF A SPINAL SAGITTAL MALALIGNMENT IN PATIENTS WITH OSTEOPOROSIS

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Introduction: Patients with osteoporosis often report intermittent low back pain (LBP). Whether osteoporosis causes LBP remains controversial because the pathological mechanism is still not fully understood. Several factors, including high bone turnover, vertebral fractures, and low muscle mass, are reported risk factors associated with both LBP and osteoporosis. In the current study, we hypothesized that a spinal sagittal malalignment, due to vertebral fractures in patients with osteoporosis, induced LBP.

Aim: To elucidate the prevalence of spinal sagittal malalignments, relationships between a spinal sagittal malalignment and vertebral fractures, as well as the characteristics of patients with osteoporosis and a spinal sagittal malalignment.

Materials and Methods: 260 patients with osteoporosis were included in this study. Sagittal vertical axis (SVA), pelvic tilt (PT), and pelvic incidence minus lumbar lordosis (PI-LL) were measured in addition to the number of vertebral fractures using whole-spine lateral radiographs. According to the SRS-Schwab classification of adult spinal deformity, SVA>40 mm, PT>20 degrees, or PI-LL>10 degrees defined a spinal sagittal malalignment. The prevalence of a spinal sagittal malalignment was evaluated by the number of vertebral fractures. In patients without vertebral fractures, we assessed bone mineral density (BMD), bone turnover markers, including BAP and TRACP5b, the Controlling Nutritional Status (CONUT) score, and LBP scores. The Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ) consists of 5 functional scores: LBP, lumbar function, walking ability, social life function, and mental health. Higher scores indicate a better condition. Visual analogue scale (VAS) scores measure LBP. A comparison was made between the spinal sagittal malalignment group and the normal alignment group for each measurement.

Results: 205 out of 260 (78.8%) patients had a spinal sagittal malalignment. The prevalence of a spinal sagittal malalignment in patients with 0, 1, or ≥ 1 vertebral fractures was 71.5%, 86.0%, and 86.3%, respectively. The CONUT scores and the VAS score for LBP in patients without vertebral fractures was significantly higher in the spinal sagittal malalignment group than in the normal alignment group ($p < 0.05$). All 5 JOABPEQ functional scores in the spinal sagittal malalignment group were significantly lower than those in the normal alignment group ($p < 0.05$). No significant differences were observed between the spinal sagittal malalignment group and the normal alignment group for BMD and bone turnover markers ($p > 0.05$).

Conclusion: In the current study, the majority of patients with osteoporosis had a spinal sagittal malalignment, and even in patients without vertebral fractures, more than 70% patients have spinal sagittal alignment malalignment. According to previous reports, low muscle mass may induce a spinal sagittal malalignment. Low muscle mass might be one potential risk factor for spinal sagittal malalignment in patients without vertebral fractures. Further study focused on muscle mass would be needed.

Patients with osteoporosis and a spinal sagittal malalignment had low nutrition status, LBP that was independent of BMD, bone turnover markers, and vertebral fractures in this study. These findings suggest that a spinal sagittal malalignment is one potential risk factor for LBP in patients with osteoporosis. In addition, we should pay attention to nutrition status in osteoporosis treatment.

Global Balance of the Spine, an Independent Contributor to Physical Function and Falls in Older Adults: the SAFE Cohort Study

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Introduction

Falls are common among older adults and remain the leading cause of fractures. They may result from several intrinsic and extrinsic risk factors. Among them, the role of the global balance of the spine has never been fully established. We conducted a preliminary cross-sectional analysis to determine the association between global balance of the spine, physical function and falls in community-dwelling older adults.

Methods

The SAFE study is an ongoing prospective, longitudinal cohort study conducted in Geneva (Switzerland) among community-dwelling adults aged ≥ 65 years without history of instrumented spinal surgery. All subjects underwent a comprehensive assessment battery including: full skeleton 2D/3D radiographs in the standing position by EOS® low-dose biplane X-ray imaging system, DXA imaging, clinical examination, fall history in the past 12 months, and physical function tests. Spino-pelvic parameters collected included, among others, the spino-sacral angle (SSA) and the C7-central sacral line (C7-CSL) distance for sagittal and coronal balance, respectively.

Results

In this preliminary analysis, 50 subjects (mean age, 74 years; 76% female) were included. Among them, 18 (36%) reported one or more falls in the past 12 months, 19 (38%) reported a history of low-trauma fracture, 15 (30%) were osteoporotic, while 12 (24%) had a Short Physical Performance Battery (SPPB) score ≤ 9 . Global sagittal balance was independently associated with physical performances after controlling for potential confounders (adjusted regression coefficient for SPPB score and SSA= 0.09, 95% CI [0.03, 0.16]; $p=0.007$), as well as some sagittal pelvic and lumbar curve measures. In addition, imbalanced subjects or balanced subjects thanks to compensations had more falls as compared to balanced subjects with no compensation (IRR=1.46, 95% CI [0.13, 2.79; $p=0.031$]). After controlling for age, sex, comorbidities, vertebral fractures and SPPB score, increased C7-CSL distance was independently associated with increased fall risk (OR=2.28, 95% CI [1.06, 4.92]; AUC=0.79, 95% CI [0.65, 0.92]).

Conclusions

The findings of this study suggest that global balance of the spine is an independent contributor to physical impairments and falls in older adults. Further analysis from this longitudinal cohort study will reveal the role of compensating mechanisms in the sagittal plane, and should help to clarify whether global balance of the spine relates to incident falls and fractures in older adults.

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Learning-based coronal spine alignment prediction using smartphone-acquired scoliosis radiograph images

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Introduction: Previous work on the automated coronal alignment detections had either unsatisfied accuracy or limitations to image qualities and/or curve patterns. Thus, we aim to develop an easily accessible automated CA prediction system irrespective of image quality, with no restrictions on curve patterns.

Methods: 367 consecutive patients attending our scoliosis clinic were recruited and their coronal X-rays were re-captured using mobile phones (Figure 1). Five-fold cross-validation was conducted (each with 294 randomly selected images to train a neural network SpineHRNet for endplate landmarks and end-vertebrae detection, the remaining 73 images to test). The predicted heatmaps of vertebral landmarks were visualized to enhance interpretability of the SpineHRNet. Per-landmark absolute distance (L2) errors and recall of landmark detection were calculated to assess the accuracy of the predicted landmarks. Further computed CAs were quantitatively compared with spine-specialists measured ground truth (GT).

Results: The average L2 error and the recall of the detected endplates landmarks were minimal being 2.8 pixels and 0.99. The predicted CAs were all significantly correlated with GT ($p < 0.01$). Compared with GT, the mean absolute error was 3.73-4.15° and standard error of the SpineHRNet was 0.8-1.7° for the predicted CAs at different spinal regions.

Discussion: This is the first study on smartphone taken coronal X-rays to accurately predict vertebral landmarks of the scoliotic spine and automatically compute the CAs at different regions. SpineHRNet's applicability is evidenced by five-fold cross-validations, which may be used with telemedicine to facilitate fast and reliable auto-diagnosis and follow-up.

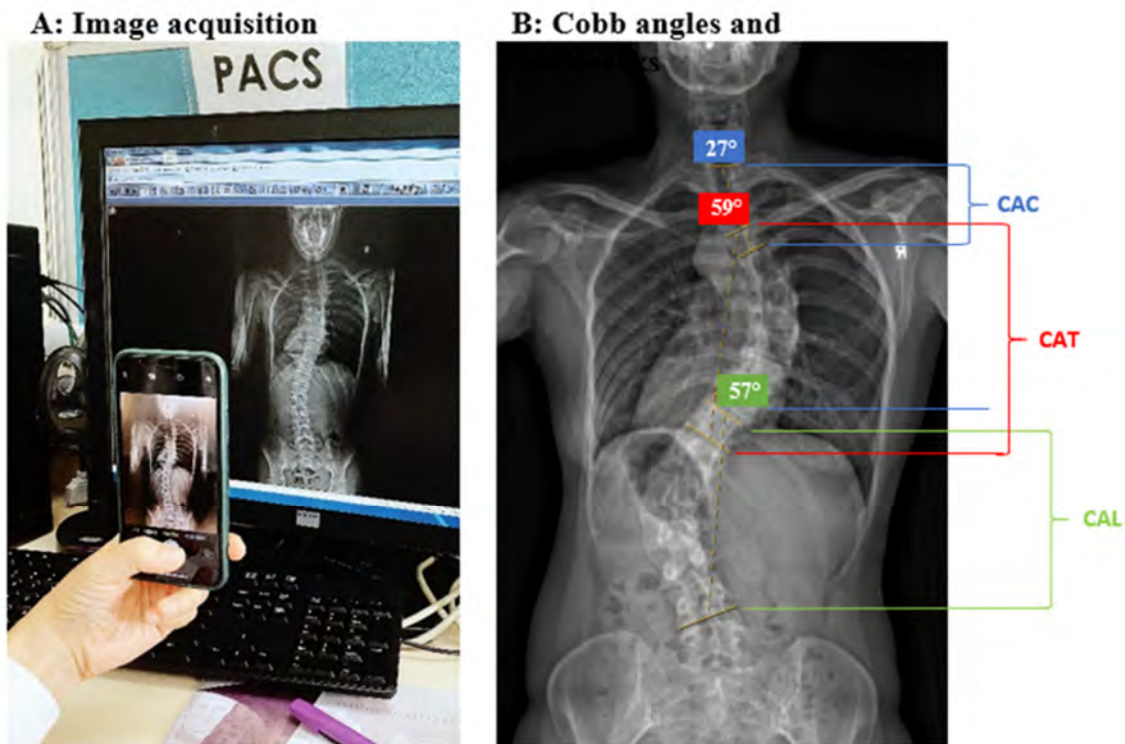


Figure 1. Example of the image acquisition process, end vertebra and Cobb angles. The images were acquired by using smart phones and screenshots of the X-rays displayed on the PACS (A). Cobb angles (CAs) measured by the angles formed by lines drawn at the upper and lower endplates of the upper and lower end vertebrae (the most tilted vertebrae from the apical vertebra) respectively, with CAC, CAT, CAL representing CAs at different regions of the spine (B) can be automatically detected through SpineHRNet.

What are the risk factors for low back pain flares and does this depend on how flare is defined?

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INTRODUCTION: Although risk factors for new low back pain (LBP) episodes and acute-to-chronic transition have been identified, risk factors for flares of LBP remain largely unknown. This case-crossover study aimed to identify; i) risk factors LBP flares; and ii) whether risk factors differed when flare is defined by pain increase (pain-defined flare: PDF) or identified by participants according to a broader flare definition that considered emotions and coping (self-reported flare: SRF).

METHODS: 126 participants with LBP for >3 months were included. Candidate risk factors and flares (PDF/SRF) were assessed daily using a smartphone application for 28 days. Data on exposure to risk factors one-, two- and three-days preceding PDF/SRF were compared to control periods. Conditional logistic regression estimated associations between risk factors and PDF/SRF.

RESULTS: Odds of PDF and SRF were increased by poor sleep quality and morning pain. Good sleep quality reduced odds of flare. Odds for increased pain (PDF), but not SRF, were increased after days with higher afternoon and evening pain, fatigue, fear of physical activity and leisure physical activity.

DISCUSSION: LBP flare has been largely ignored but is more reflective of the LBP experience than conventional definitions of acute, sub-acute and chronic LBP. This study highlights risk factors for flare, and that these differ depending on whether flare is defined by pain alone (PDF) or a broad multidimensional definition (SRF). Potential targets to reduce the intensity/frequency of LBP flares are identified, with strong indication for the potential role of sleep intervention to mitigate LBP flare risk.

A Novel Inducible System to Regulate Transgene Expression of TIMP1

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Introduction: Intervertebral disc degeneration (IDD) is a common contributor to low back pain. IDD occurs secondary to inflammatory and oxidative stress that upregulates matrix metalloproteinase (MMP) activity. Previous gene therapy studies have used human tissue inhibitor of metalloproteinase 1 (hTIMP1) to inhibit MMP activity and effectively treat IDD in animal models. However, unregulated gene expression may have negative side effects. We developed a recombinant adeno-associated viral (AAV) gene vector, AAV-NFκB-hTIMP1, that only expresses the hTIMP1 transgene under conditions of stress.

Methods: Rabbit annulus fibrosus (AF) and nucleus pulposus (NP) cells were transfected or transduced with AAV-CMV-hTIMP1, which constitutively expresses hTIMP1, or AAV-NFκB-hTIMP1, which was designed to only express hTIMP1 under conditions of stress. Disc cells were selectively treated with IL-1β. NFκB activation was verified by nuclear translocation. hTIMP1 mRNA and protein expression were measured by RT-PCR and ELISA, respectively. MMP activity was measured by following cleavage of a fluorogenic substrate. Student's t-test with significance set at p<0.05 was used to identify differences between mean hTIMP1 mRNA expression, hTIMP1 protein expression, and MMP expression.

Results: IL-1β stimulation activated NFκB demonstrating that IL-1β was an appropriate surrogate for inflammatory stress. Stimulating AAV-NFκB-hTIMP1 cells with IL-1β increased hTIMP1 expression compared to unstimulated cells. AAV-CMV-hTIMP1 cells demonstrated high levels of hTIMP1 expression regardless of IL-1β stimulation. hTIMP1 expression was comparable between IL-1β stimulated AAV-NFκB-hTIMP1 cells and AAV-CMV-hTIMP1 cells. MMP activity was decreased in AAV-NFκB-hTIMP1 cells compared to baseline levels or cells exposed to IL-1β.

Discussion: AAV-NFκB-hTIMP1 is a novel inducible transgene delivery system. NFκB regulatory elements ensure that hTIMP1 expression occurs only with inflammation, which is central to IDD development. Unlike previous inducible systems, the AAV-NFκB-hTIMP1 construct is dependent on endogenous factors, which minimizes potential side effects caused by constitutive transgene overexpression. It also prevents the unnecessary production of transgene products in cells that do not require therapy. Unstimulated disc cells transfected or transduced with AAV-NFκB-hTIMP1 did exhibit some basal hTIMP1 expression, which resulted in decreased MMP activity. It is likely that this basal hTIMP1 expression was associated with cellular stress from the transduction or transfection process. This inducible system, which utilizes endogenous factors to control protein production, can serve as a template for creation of new approaches towards effective and safe gene therapy for other inflammatory disease states.

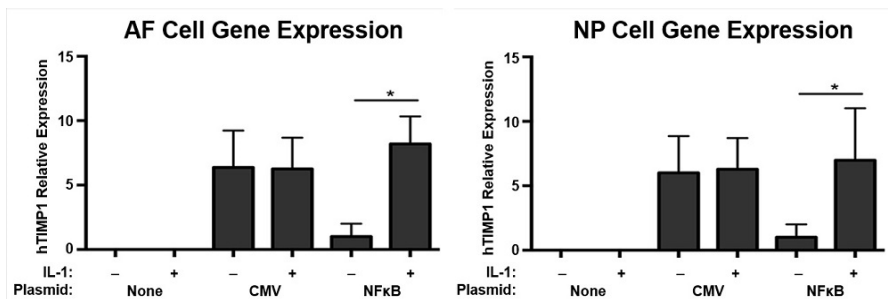


Figure 1. hTIMP1 mRNA expression in disc cells transfected with plasmids as measured by RT-PCR

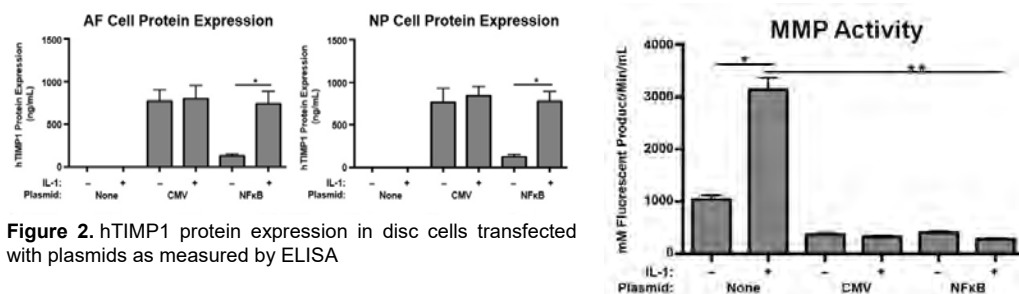


Figure 2. hTIMP1 protein expression in disc cells transfected with plasmids as measured by ELISA

Figure 3. MMP enzymatic activity in disc cells transfected with plasmids

***In vivo* sagittal motion of the lumbar spine in low back pain patients: a radiological big data study**

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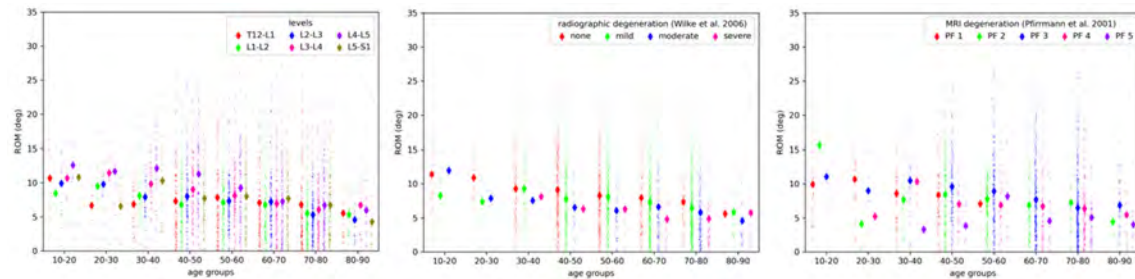
Introduction. We investigated the flexion-extension range of motion and center of rotation of lumbar motion segments in a large population of 602 patients (3612 levels), and the associations between lumbar motion and other parameters such as sex, age, and intervertebral disc degeneration.

Methods. Lumbar radiographs in flexion-extension of 602 patients suffering from low back pain and/or suspect instability were collected; magnetic resonance images were retrieved and used to score the degree of disc degeneration for a subgroup of 354 patients. Range of motion and center of rotation were calculated for all lumbosacral levels with in-house software allowing for high degree of automation. Associations between motion parameters and age, sex, spinal level and disc degeneration were then assessed.

Results. The median range of motion was 6.6° (range 0.1-28.9°), in good agreement with *in vivo* and *in vitro* literature data. Associations between range of motion and age as well as spinal level, but not sex, were found. Disc degeneration determined a consistent reduction of the range of motion (Figure). The center of rotation was most commonly located at the center of the lower endplate or slightly lower. With progressive degeneration, centers of rotation were increasingly dispersed with no preferential directions.

Discussion. The present data constitute the largest analysis of the *in vivo* motion of the lumbar spine in flexion-extension currently available, covering a wide range of clinical scenarios in terms of age and spinal degeneration. In general, an agreement between the novel and published data was found in terms of range of motion and center of rotation. Among the novel findings of the study, we were able to demonstrate that ageing determines a reduction of the mobility of the lumbar spine independently of the presence of degeneration, and that in degenerative levels centers of rotation are dispersed around the center of the intervertebral space with no preferential directions. We also demonstrated that ranges of motion measured in *in vitro* experiments are in good agreement with those *in vivo*.

Figure caption. Scatter plots showing the association between age groups and range of motion (ROM) subdivided by spinal levels (left), degrees of degeneration based on radiographs (Wilke et al. 2006) (center) and based on magnetic resonance imaging (Pfirrmann et al. 2001) (right).



A systematic review on the risk factors for chronic low back pain in older adults

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INTRODUCTION: Since chronic low back pain (CLBP) is a major musculoskeletal problem affecting up to 68% of adults aged 60 years or older, there is a growing number of studies investigating risk factors for CLBP in older adults so as to prevent or manage such pain. However, no systematic review has summarised relevant evidence on this topic. Accordingly, the current review aimed to summarise the evidence regarding the risk factors for CLBP in seniors.

METHODS: Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medline, Embase, and PsycINFO were searched from inception to July 26, 2020. Studies were included if they investigated risk factors for CLBP in older adults aged 60 years or older (together with relevant statistics). CLBP should last for at least 1 month consecutively. Five reviewers conducted the abstract and full-text screening, and data extraction in such a way that each paper was read by two independent reviewers. The methodological quality of cross-sectional studies and cohort studies was assessed by the Appraisal tool for Cross-Sectional Studies (AXIS), and Quality In Prognosis Studies (QUIPS), respectively. The level of evidence for each risk factor was synthesised based on established criteria.

RESULTS: The search yielded 6,015 citations. Following duplicates removal, 5,647 abstracts and 368 full-text articles were screened. Six cross-sectional studies, one retrospective cohort study, and four prospective cohort studies (involving 50,246 participants) were included. Seven and four included studies had moderate and poor methodological quality, respectively. Thirty-nine potential risk factors were investigated by the included studies. Limited evidence suggested that the presence of comorbidity (e.g., chronic obstructive pulmonary disease) was related to a higher 12-month prevalence of CLBP in older adults (adjusted odds ratios (AORs) ranging from 1.2 to 1.5). Similarly, there was limited evidence that the presence of lumbar disc narrowing (AORs ranging from 1.5 to 2.5) or vertebral body osteophytes (AORs ranging from 1.2 to 1.6) increased the likelihood of a higher point prevalence of CLBP in seniors. Very limited evidence supported that female (AOR=1.5), retired due to illness (AOR=2.6), anxiety (AOR=1.7), depression (AOR=2.0), mental disorders (AOR=1.6), knee osteoarthritis (AOR=1.4), severe facet osteoarthritis (AORs ranging from 1.2 to 2.2), widespread pain or leg pain (AOR ranging from 1.1 to 2.0), and poor expectation of recovery (AOR=1.2) were independently related to a higher 12-month prevalence of CLBP in seniors. Likewise, very limited evidence substantiated that prior injury of lower body (AOR=1.6) and family history of body pain (AOR=1.7) were correlated with the higher point prevalence and lifetime prevalence of CLBP in older adults, respectively.

DISCUSSION: Although many studies attempted to determine modifiable and non-modifiable risk factors for CLBP in older adults, many identified risk factors only have very limited to limited evidence because each of these factors was only investigated by one or two studies. The current review highlights the importance of validating the identified risk factors in different cohorts of older adults, and investigating the effectiveness of altering some modifiable risk factors (e.g., psychology or patient expectation) in managing CLBP in older adults.

Epidural Steroid Compared To Placebo Injection In Patients With Sciatica: A Systematic Review And Meta-analysis

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Introduction:

Epidural steroid injections (ESI) are an established treatment to relieve symptoms in patients with lumbar radiculopathy with highly increasing utilization rates worldwide. However, there is no consensus on the superiority of steroid in comparison with epidural and non-epidural placebo injections raising concerns about the justification of the extensive use ESI treatment. The purpose of this review and meta-analysis is to determine whether epidural injections with steroids are better than epidural or non-epidural placebo injections in improving symptoms of leg pain, back pain and functional status at 6 weeks, 3 months and 6 months follow-up.

Methods:

The PubMed, Embase, Cochrane Library and Web of science databases were systematically searched for randomized-controlled trials comparing ESI to epidural or non-epidural placebo. All included trials assessed patients with sciatica and compared transforaminal (TF), interlaminar (IL) or caudal steroid injections with epidural or non-epidural placebo injections. Risk of bias was assessed using the Cochrane RoB 2 tool. The primary outcomes were leg pain, back pain and functional status as continuous and proportional data. Secondary outcomes included pain medication use and adverse events. The primary outcome measures were pooled using a random-effects model for three follow-up periods and sensitivity analyses were performed. Secondary outcomes were described qualitatively. Quality of evidence was graded in accordance with GRADE classification.

Results:

Seventeen out of 732 articles were included. Heterogeneity between studies varied from low to substantial. Epidural steroid injections were superior compared to epidural placebo at 6 weeks and 3 months for leg pain, though the minimally clinical important difference (MCID) was not met (GRADE: low to moderate-quality). For back pain, there was no difference between ESI and placebo with the exception of non-epidural placebo at 3 months (GRADE: moderate-quality). For functional status, ESI was superior to epidural placebo at 6 weeks, though again MCID was not met. For other comparisons, differences were smaller and non-significant. Sensitivity analysis demonstrated patients with radiologically confirmed lumbar disc herniation to benefit more than clinically diagnosed patients at 6 weeks, whereas overall TF and IL injections were slightly more effective than the caudal route. Proportions of treatment success were not different between treatments. ESI reduced analgesic intake in some studies. Complication rates of (non-)epidural injections are low.

Discussion:

Assessment of current literature demonstrates that ESI induces larger improvements in pain and disability on the short term compared to epidural placebo, although the MCID is not met. For longer follow-up or for comparisons with non-epidural placebo no strong conclusions can be drawn due to the quality of evidence and limited number of studies. Epidural injections can be considered a safe therapy. The paucity of literature precluded unequivocal identification of subgroups of sciatica patients that benefit most from ESI. Based on the current evidence, ESI can be used as short-term pain management therapy in clinical practice to relieve leg pain and improve functional status, although the benefits are limited and small complications can occur.

Biomarkers as a predictive tool for the outcome of pain and function in acute low back pain.

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Introduction

Low back pain (LBP) is a common musculoskeletal condition and a major cause of disability worldwide. Previous studies have found associations of biomarkers with pain and pain-related disability in patients with LBP. The purpose of this study was to explore the possible predictive association between serum biomarkers and the clinical outcomes of pain and disability in patients with acute axial LBP treated with spinal manipulation or standard medical care.

Methods

107 adults with a new episode of LBP within the 3 months prior to enrollment were recruited from a single academic center. Individuals were randomized into three groups: one of two different types of spinal manipulation (manual-thrust or mechanical-assisted) or usual medical care. All investigators involved were blinded to treatment assignment. 90 of these 107 participants consented to have blood samples obtained immediately before the beginning of treatment and after 4 weeks of intervention. Seven biomarkers were analyzed from these samples: neuropeptide Y (NPY), tumor necrosis factor-alpha (TNF α), substance P (SubP), ESelectin, regulated upon activation, normal t-cell expressed and presumably secreted (RANTES) (with ELISA), vitamin D, and c-reactive protein (CRP) (with standard clinical lab procedure). Primary clinical outcomes were pain (von Korff pain scale), and disability (Oswestry Disability Index, ODI); both were measured at baseline and 4 weeks. Pearson's r was used to study the linear association of initial levels of biomarkers with both outcomes scores at baseline and with improvement in outcomes scores from baseline to 4 weeks (end of treatment). Baseline correlations were computed for the full sample (n=90), whereas correlations for outcomes improvement were computed for each study group separately because of differing effects of the three interventions.

Results

Significant associations were found between initial Vitamin D levels and baseline pain ($r=.29$; $p=.007$), initial CRP levels and baseline pain ($r=.33$; $p=.001$), and initial CRP levels and baseline ODI ($r=.22$; $p=.039$). Significant associations between initial biomarker levels and improvement in ODI were observed for TNF α ($r=.36$; $p=.047$) and Vitamin D ($r=.39$; $p=.030$). No significant correlations were found between initial biomarker levels and pain improvement in any study group.

Discussion

These seven biomarkers represent only a small portion of the potential variety that may be identified as potential candidates for predicting outcomes or influencing the treatment. Previous work suggests that panels of biomarkers may provide greater predictive power than any single biomarker alone. Moreover, combining molecular biomarkers with clinical metrics may likely prove to be the most useful approach in identifying patients, sub-classifying them according to their phenotype, and developing an individualized treatment plan to deliver the most appropriate intervention with the best timing. Overall, the associations that we observed do not point at direct mechanisms but are likely dependent on a more comprehensive set of physiological and clinical interactions that are still not understood. More research is thus warranted in this area.

A Study on the Clinical Features of Interspinous Ligament Lesion in Adolescent Patients with Low Back Pain

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INTRODUCTION: Among adolescent patients with low back pain, there are some patients who feel backache on trunk extension and rotation, which is characteristic to spondylolysis, but don't have spondylolysis. They sometimes have high signal intensity in interspinous ligament on MRI STIR images. The purpose of this study was to examine the clinical features of adolescent patients who had MRI findings in interspinous ligaments.

SUBJECTS and METHODS: We included 156 adolescent patients with low back pain (Apr.2017-May.2020; men 101case, women 55case; mean age 15.1y) in this study. MRI was performed on all the patients, and CT scans if necessary. We recorded the pain during trunk flexion, extension, rotation and side-bending. We also recorded tenderness on spinous process and straight leg raising test (SLRT). We defined interspinous ligament lesion as positive (ISL(+)) when there was high intensity on STIR images with low intensity on T1-weighted images. These clinical findings, age and gender were compared between ISL(+) group and the other diagnoses groups.

RESULTS: There were 39 ISL(+) patients and 93 spondylolysis patients, 9 lumbar disc herniation (LDH), 6 facet joint fluid, 5 endplate lesion (EL) and without abnormal images were 4. In each diagnosis group, the number of women was 20, 19, 4, 3, 3, 4, respectively. ISL(+) had higher rates of women than spondylolysis significantly. The average age was 14.7, 15.5, 15.9, 14.2, 14.7, 13.9-year-old respectively, and there was no significant difference between ISL(+) and the other groups. About examination findings, pain during trunk flexion was more seen significantly in ISL(+) than spondylolysis (33/39: 19/93). However, almost all ISL(+) patients and spondylolysis patients felt pain during trunk extension, rotation, side bending. There was no significant difference. Also, almost all spinous process tenderness was seen in both group without significant difference. SLRT of ISL(+) was significantly lower than LDH group.

DISCUSSION: Interspinous ligament connects adjacent spinous processes. It consists of three parts, and it is arranged so that the spinous processes are not separated and limits the flexion of facet joints. Interspinous ligament lesion is famous as Baastrup disease, which means bursitis of ligament and relates "kissing spine". Robbert reported that the disease associated with age, central canal stenosis, disc bulging and anterolisthesis. However, in ISL(+) group in our study, all patients were young, and no patient but one had disc degeneration. So we think pathology of ISL(+) may be different from Baastrup disease. Fujiwara revealed that interspinous ligament lesion of low intensity on T1 and high intensity on T2-weighted images (same as ISL(+)) was proliferation of cells and vascular invasion by histologic examination. We think ISL(+) is like sprain. Therefore, pain on forward bending is stretching stress and pain on backward bending is induced by compression between spinous processes. To relieve this condition, it's necessary to increase the stability of lumbar spine and the mobility of the rib cage and hip joint. When seeing adolescent patient with low backpain, we should keep this lesion in our mind.

Axial loading during MRI induce lumbar foraminal area changes and may have the potential to improve diagnostics of nerve root compromise

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Introduction:

Lumbar foraminal stenosis is a common cause of radiculopathy with a prevalence of around 10 % [1]. Assessment of potential foraminal stenosis is conventionally performed with MRI in a supine position. This might influence the diagnostic accuracy, as the symptoms mainly are provoked at standing. MRI with spinal loading might unmask pathology not revealed in patients in a supine relaxed position [2]. If and how, the intervertebral foramina are affected during spinal loading remains to be established. The aim was to investigate if and how axial loading affects the area of lumbar intervertebral foramina measured on MRI.

Methods:

In 89 low back pain (LBP) patients lumbar MRI was performed in both relaxed supine position (unloaded MRI), and during axial loading in supine position (loaded MRI). The mean age was 43 years (range 27-66 years) and included 56 men and 33 women. Axial loading of about 50 % of the patient's bodyweight was applied using a Dynawell® compression device. The area of the intervertebral foramina L3/L4 - L5/S1 (in total 534 foramina) was determined bilaterally in the sagittal T2-weighted sequences by using a free-hand polygonal tool (Figure 1). If a foramina was included in more than one sagittal image, the image with the smallest foraminal area was used. The qualitative grading system (grade 0-3) described by Lee et al [3] was used to assess foraminal stenosis, where grade 0 refers to absence of stenosis and grade 3 represents severe stenosis.

Results:

A large variation in load-induced changes in foraminal area were seen with a range of 58% increase to 42% decrease. Overall, a mean reduction between unloaded and loaded MRI of 2.2% (mean 0.89 cm² and 0.87 cm² respectively) was seen (p = 0.002). Stratified for lumbar level, a reduction in area during loading was found for L3/L4 and L4/L5 foramina (mean change 0.03cm²; p = 0.036 and 0.03 cm²; p=0.004 respectively) but not for L5/S1. Also with the qualitative stenosis grading of the foramina, differences between unloaded and loaded MRI was seen (p <0.001). With unloaded MRI, the number of foramina within each grade 0-3 was; 448, 77, 8 and 1 respectively. In 25% of the foramina, a change in foraminal stenosis grade (higher or lower grade) occurred with loaded MRI, with a higher grading determined in 19% of all foramina (p <0.001). Intra class correlation coefficient for foraminal area measurement was 0.96 for intra observer agreement and 0.76 for inter observer agreement.

Discussion:

Overall only a small reduction in mean foraminal area was induced in this group of LBP patients without radiculopathy. However, the wide range of load-induced foraminal area change demonstrated a large dynamical influence on the lumbar foramina. It is likely that MRI performed with spinal loading may unmask nerve root affection, not seen in an unloaded position, and could thus improve the diagnostics when conventional MRI findings do not match with clinical symptoms of lumbar radiculopathy.

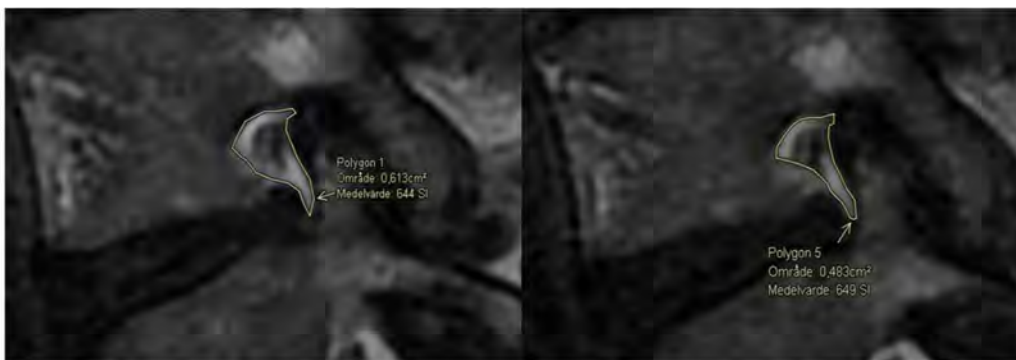


Fig. 1. Example of measurement of the right L4–5 foraminal area at unloaded MRI (left) and with axial loading (right).

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SP506

Women with lumbar degenerative spondylolisthesis demonstrate delayed abdominal reflex latency

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Introduction: Degenerative spondylolisthesis (DS) is a degenerative spinal condition that contributes to low back pain (LBP), disability and reduced quality of life. DS affects women more than men and is related to multiparity. LBP and abdominal muscle dysfunction are common during pregnancy, making parity-induced abdominal muscle impairments a potential causal factor. Considering the role of the lumbopelvic musculature in stabilizing the spine, it is conceivable that these muscles will be impaired in women with DS.

Aim: The aim of this study was to determine if lumbopelvic muscle function is impaired in women with DS.

Materials and Methods: A total of 95 women (DS=31, without DS=64) participated. All women underwent medical imaging to diagnose DS. Lumbopelvic muscle function was assessed in a laboratory setting using: Abdominal Muscle Test (AMT), Hip Extensor Test (HET), and Quick Release (QR). AMT assessed abdominal muscle strength over four levels of difficulty, which we then categorized as high or low abdominal muscle strength. HET assessed lumbopelvic neuromuscular control, which was scored as positive or negative based on specific abnormal movement patterns. QR assessed muscle reflex latencies (onset and offset of muscle activity) of the trunk flexors (abdominal) and trunk extensors (erector spinae) from electromyographic signals following a sudden release of isometric force in either flexion or extension. Muscle reflex latencies were averaged across muscle groups and 5 trials. Differences between groups for the AMT and HET were evaluated using binary logistic regression models with age as a covariate. QR muscle reflex latencies were assessed using ANCOVA with age as a covariate. Statistical significance was set at $p \leq 0.05$.

Results: Women with DS were significantly older than women without DS (64.7 ± 6.6 vs. 59.7 ± 7.5 years, $p=0.03$). When controlling for age, there were no significant differences between groups for the AMT or HET tasks (all $p > 0.05$). For QR flexion, women with DS had significantly longer offset latency for their abdominal muscles than women without DS ($p=0.003$, 160.3 ± 54.3 vs. 128.3 ± 56.5 ms, respectively). No significant difference in extensor offset latency was observed for QR extension ($p=0.42$). Further, onset latencies were not significantly different between groups during QR flexion (erector spinae) or extension (abdominals) ($p=0.34$ and $p=0.26$, respectively).

Conclusions: Women with DS demonstrated delayed abdominal offset reflex latencies during a sudden trunk perturbation, which provides additional evidence of impaired abdominal muscle function in this patient population. Because of the cross-sectional design of the study, it is not possible to determine if delayed reflex latencies are causal factors in the development of DS or adaptive neuromuscular strategies to compensate for a loss of spinal stiffness. Further investigations into the role of lumbopelvic muscle function in the development and treatment of DS is warranted.

SP507

Influences of limited flexibility of the lower extremities and occurrence of low back pain in adolescent baseball players: a prospective cohort study

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INTRODUCTION

Limited flexibility of the lower extremities, such as hamstring tightness, has long been suggested as a physical risk factor for low back pain (LBP) among adolescent athletes. However, few prospective cohort studies have examined the direction of causality for this relationship. The purpose of the present study was to investigate the relationship between limited flexibility of the lower extremities and the occurrence of LBP among high school baseball players.

METHODS

The present study was a prospective cohort study involving high school baseball teams among all local communities in our prefecture of Japan in October 2015 to September 2016. Participants comprised 335 baseball players (80 pitchers, 255 fielders) from 43 high school baseball teams who had undergone baseline medical evaluations (a self-completed questionnaire and physical examination). Occurrence of LBP during a 1-year follow up, and associations with measurements of flexibility of the lower extremities such as straight-leg-raising angle (hamstring tightness), Thomas test (iliopsoas tightness), heel-buttock-distance (quadriceps tightness), and passive range of motion of the hip were investigated. We calculated odds ratios (OR) and 95% confidence intervals (CI) to examine the longitudinal association between 12 potential risk factors at baseline and LBP occurrence the following year, using univariate and multivariate logistic regression analyses. The following were analyzed as potential risk factors: position (pitcher vs. fielder), previous episodes of LBP, and hamstring tightness, iliopsoas tightness, quadriceps tightness, limitation of hip internal rotation, and limitation of hip external rotation on both sides. All tests used were two-sided, and P values of less than 0.05 were considered statistically significant.

RESULTS

In total, 296 players (88.4%) participated in the 1-year follow-up survey, with 147 of the 296 players (49.7%) reporting the occurrence of LBP during follow-up. Numbers of players with LBP peaked in November 2015 (n = 52), then decreased and were lowest in March 2016 (n = 9) to June (n = 6), then gradually increased again towards September 2016 (n = 23) during follow-up. After adjusting for factors associated with LBP using logistic regression modeling, significant associations between previous episodes of LBP (OR, 2.87; 95%CI, 1.71–4.82; P<0.0001), hamstring tightness on the non-throwing arm side (OR, 2.86; 95%CI, 1.17–6.94; P=0.018), and LBP were found.

DISCUSSION

Hamstring tightness on the non-throwing arm side was identified as a potential risk factor for LBP in high school baseball players. These results may provide guidance in the development of future prevention programs.

Loads at adjacent segment level before and after surgery – combined clinical and simulation study of 205 adult spinal deformity patients

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INTRODUCTION

Restoration of normal sagittal alignment is one of the goals of adult spinal deformity (ASD) surgery. Various measures have been proposed to assess sagittal alignment, among them Global Alignment and Proportion (GAP) score which has promising accuracy in predicting mechanical complications after surgery (Yilgor, 2017, JBJS Am). Postoperative mechanical failure in ASD can be attributed to excessive forces due to the change in loading conditions of the proximal segment caused by biomechanical effects of spinal realignment and fusion. The investigation of spinal loads in relation to postoperative sagittal alignment may provide insight into factors contributing to the development of proximal junctional disorders.

The aim of this combined clinical and computational study was to investigate the relationship between (1) postoperative **change** in load at the proximal segment and **change** in GAP, as a measure of spine alignment correction, and (2) postoperative proximal segment absolute loads and postoperative GAP score in ASD patients. We hypothesised that (1) greater correction is related to greater reduction in compressive loads, but higher posterior shear, and (2) higher GAP scores are related to higher loads at the proximal segment, which might be indicative of potential mechanical failure.

METHODS

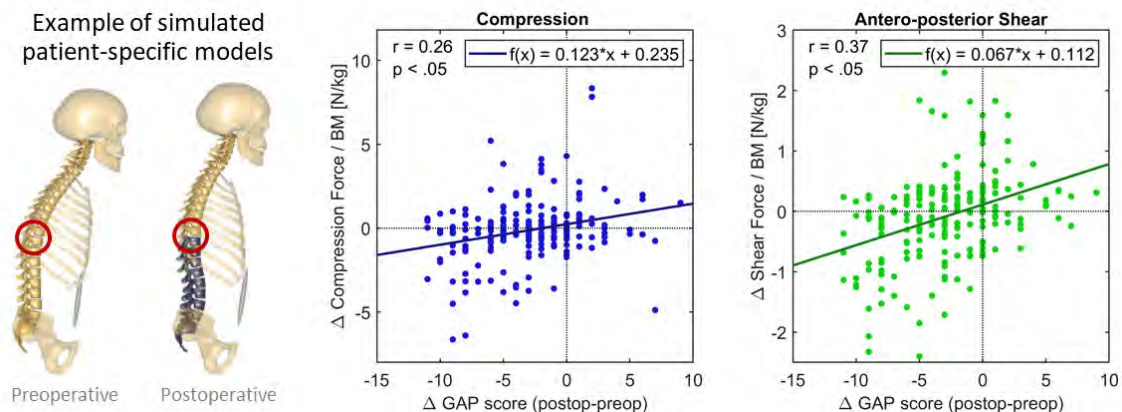
A previously validated musculoskeletal (AnyBody) model of the thoracolumbar spine (Ignasiak, 2016, J Biomech) was used without and with fusion (Ignasiak, 2018, ESJ), to simulate pre- and postoperative spinal biomechanics, respectively. The model was modified to represent patient-specific sagittal alignments, based on measured pelvic incidence, sacral slope, global tilt, L1-S1 and L4-S1 lordoses, T10-L2, T5-T12 and T2-T12 kyphoses angles. Compression and shear forces at the proximal adjacent segment (or corresponding level for prep condition) were predicted for upright standing for individual patients using preoperative and postoperative alignment measurements and fusion details. In total, 205 patients were analysed (156 female, 49 male; age 52.1±19.2 years; upper and lower instrumented vertebra: UIV=T2-L3, LIV=T12-Sacrum/Iliia).

RESULTS

The changes (postop-preop) in alignment, given by the changes in GAP score, correlated with the changes in compressive ($r=0.26$; $p<0.05$) and shear loads ($r=0.37$; $p<0.05$) (Figure). Due to large variability in fusion configurations within the sample, the relationship between absolute postoperative loads and GAP score was evaluated only for the most common subset, those with fusions from T10 to sacrum or ilia (N=27). Significant positive correlations were found between GAP and compressive ($r=0.51$; $p<0.05$) and shear ($r=0.51$; $p<0.05$) forces at the proximal segment.

DISCUSSION

Weak-to-moderate positive associations were found between changes in sagittal alignment (GAP score) after surgery and changes in compression and shear forces at the proximal segment. In patients with T10-sacrum/ilia fusion, greater sagittal imbalance (higher GAP scores) was found to be related to greater loads at the adjacent segment. A larger sample size is needed to test whether this relationship holds true for other fusion configurations. To our knowledge, this is the first study of spinal loads estimated for real patient-specific thoracolumbar alignments, analysing a large patient cohort pre- and post-operatively, which may provide insights into the causes of mechanical complications after ASD surgery.



Peri-operative complications of open spine surgery in the elderly over 90 years of age

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Introduction. Increased life and health expectancy have led to indications for open spine surgeries in patients aged 90 years or older. Although peri-operative risks in nonagenarian patients who undergo open spine surgery for degeneration disorder or spinal trauma is of great interest, the prevalence of complications in this group remains unclear. The aim of this study was to examine the peri-operative complications of open spine surgery in the elderly over 90 years of age. In addition, we assessed the difference of peri-operative complications between degeneration disorders and spinal traumas.

Methods. Pre- and intra-operative characteristics including American Society of Anesthesiologists (ASA)-physical status (PS) class, type of surgery, and complications within 30 postoperative days were retrospectively collected from over 90 year-old patients who underwent open spine surgery between April 2004 and July 2019 at our spine centers. Those with balloon kyphoplasty, percutaneous surgical procedures, infections or tumors were excluded.

Results. Of 12,380 patients who underwent spine surgeries, 48 patients (0.4%) met the inclusion criteria of this study. All were in ASA-PS class 2 (69%) or 3. The pathologies were trauma in 22 cases (45.8%), lumbar spinal stenosis in 18 cases (37.5%), cervical spondylotic myelopathy in 4 cases (8.3%), degenerative lumbar spondylolisthesis in 2 cases (4.2%), thoracic myelopathy in 1 case (2.1%), and degenerative cervical spondylolisthesis in 1 case (2.1%). Major complications (surgical site infection, heart failure, pneumonia, gastrointestinal bleeding, sepsis, vascular embolism, stroke, renal failure) occurred in 13 cases (27.1%) and the rate of overall peri-operative complications was 79.2% (38 patients). One patient who underwent cervical stabilization for cervical fracture dislocation died during hospitalization due to respiratory disorder. The rates of major complications and overall peri-operative complications were 3.6% and 14.3% in degenerative group and they were 45.5% and 81.8% in trauma group, respectively (Figure 1). Especially in trauma group, respiratory disorder occurred in 7 cases (31.8%), delirium in 11 cases (50%), and urinary tract infection in 5 cases (22.7%) (Table 1).

Discussion. Our hypothesis was that patients of spinal trauma have a poorer outcome as compared with the patients of degeneration disorders; potential differences between the 2 groups were assessed by means of statistical tests. Consequently, although the peri-operative complications rate reached 79.2% in overall patients and 81.8% in spinal trauma cases, the complication rate in degenerative disorder was relatively low as 14.3%. Open spine surgery for degenerative disorders can be relatively safe even in patients aged 90 years or older, whereas the risks of peri-operative complications including respiratory disorder and delirium were high in spinal trauma cases.

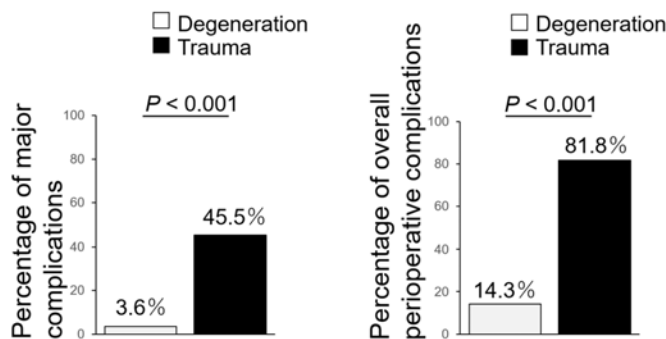


Figure 1

Table 1. Incidence of individual complications in the degeneration and trauma groups

	Degeneration group (n=26)		Trauma group (n=22)	
	Number of cases	%	Number of cases	%
Major complications				
Respiratory disorder	0	0	7	31.8
Deep surgical site infection	1	3.6	1	4.5
Cardiac event	0	0	2	9.1
Renal failure	0	0	1	4.5
Gastrointestinal hemorrhage	0	0	1	4.5
Minor complications				
Delirium	2	7.1	11	50.0
Urinary tract infection	2	7.1	5	22.7
Decubitus	2	7.1	2	9.1
Death	0	0	1	4.5

Risk Factors for Adjacent Segment Degeneration Following Lumbar Fusion: A Meta-analysis

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INTRODUCTION: Adjacent segment degeneration (ASDeg) is a common postoperative complication after lumbar fusion surgeries. Previous studies have described numerous risk factors for adjacent segment degeneration although clinically applicable risk stratification and prevention of such outcomes has remained elusive. The aim of the current review was to summarize the evidence regarding the risk factors that are related to an increase in ASDeg after lumbar fusion surgeries.

METHODS: Five databases (CINAHL, Cochrane Library, EMBASE, MEDLINE, and Web of Science) were searched from inception to July 7th, 2019. Two independent reviewers screened the abstracts and full-text articles (**Figure 1**). Intra- and inter-observer reliability was calculated using Cohen's kappa with a minimum cutoff value of 0.80 before the next screening step was performed. Any disagreements were discussed between the two reviewers and resolved by consensus. Relevant data regarding participants' characteristics, study design, follow-up time points, and identified risk factors were extracted from the included studies. The two reviewers also independently appraised the methodological quality of cohort studies and cross-sectional studies using Quality In Prognosis Studies tool, and Appraisal tool for Cross-Sectional Studies, respectively.

RESULTS: A total of 643 citations that were identified and 118 were screened for full text. Nineteen studies involving 1,962 patients were included. Seventy-three potential demographic, surgical, and radiographic risk factors for ASDeg following lumbar fusion were identified. Although individual studies reported significant risk factors in each category, meta-analysis of 11 selected studies only found 3 significant risk factors. There was strong evidence that patients with ASDeg at ≥ 5 -year follow-up were significantly older than those without ASDeg (3 studies, $n = 449$, mean difference: 3.38 years, 95% CI: 0.15 to 6.62). Moderate evidence suggested that those with ASDeg had significantly greater preoperative pelvic incidence (2 studies, $n = 148$, mean difference: 13.82 degrees, 95% CI: 5.93 to 21.70 degrees) and pelvic tilt (2 studies, $n = 148$, mean difference: 5.42 degrees, 95% CI: 2.46 to 8.39 degrees) than those without ASDeg at ≥ 5 -year follow-ups.

DISCUSSION: Older age, and greater preoperative pelvic incidence and tilt are significant risk factors for ASDeg in patients ≥ 5 years after surgery. Although our meta-analysis did not find any other significant risk factors for developing ASDeg, individual studies found increased BMI, decreased segmental and lumbar lordosis, pre-existing facet degeneration, and posterior lumbar interbody fusion as potential risk factors. Surgeons should take these factors into account when explaining the postoperative risk of ASDeg to patients and closely follow patients with potential risk factors to ensure the provision of timely interventions.

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A retrospective analysis of patients with early deterioration of general condition after spinal metastasis surgery: Could we predict the early deterioration with the preoperative blood test?

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INTRODUCTION: Spinal metastasis is a growing problem in patients with cancer. We have previously reported the efficacy of spinal metastasis surgery for maintaining or improving quality of life by alleviating pain and preserving neurologic function. On the other hand, spinal metastasis patients often have reduced general condition and might get even worse early after spinal metastasis surgery. The aim of current study was to retrospectively investigate prognostic factors of early deteriorated general condition after spinal metastasis surgery from the preoperative blood test.

METHODS: One hundred twenty-three patients with spinal metastasis with spine surgery from November 2013 to August 2018 were included. We defined the patients who were dead or had worsened Performance Status (PS) one month after surgery as early deterioration group (E-group) and the other patients as improvement group (I-group). Age, gender, the preoperative blood test items such as C-reactive protein (CRP), lactate dehydrogenase (LDH), Alkaline Phosphatase (ALP), serum albumin (Alb), calcium adjusted for albumin level (Ca), hemoglobin (Hb), platelet (Plt), prothrombin time (PT) were studied. Cut off value was determined by receiver operating characteristic curve (ROC curve) using Youden index.

RESULTS: The overall patients had median survival time of 4.9 months and had significantly improved PS one month after surgery (preoperative and postoperative median PS were 3 and 2, respectively). E-group contains 10 patients (8.2%). Six patients had died and 4 patients had worsened PS. Spinal surgery, including some complications such as malposition of screws, did not cause the early deterioration. Although age and gender did not show significant difference between the two groups, E-group had significantly higher CRP (mean 5.17 mg/L vs. 0.83 mg/L), LDH (mean 308 U/L vs. 206 U/L) and Ca (mean 10.1 mg/dL vs. 9.6 mg/dL) ($p < 0.05$) and significantly lower Alb (mean 2.7 g/dL vs. 3.5 g/dL) compared to I-group ($p < 0.01$). Cut off value and the area under the curve of ROC curve of each items were as follows: CRP 4.17 mg/L, 0.858, LDH 257 U/L, 0.741, Ca 10.1 mg/dL, 0.774, Alb 3.1 g/dL, 0.767. All the patients whose all 4 blood test items mentioned above did not reach the cut off values belonged to I-group.

DISCUSSION: About 8% of patients who had spinal metastasis surgery had early deterioration of general condition after surgery. The current study indicated that some blood test items might be helpful to detect the patients with the risk of early deterioration of general condition after spinal metastasis surgery. Further studies are needed to create the optimal medical care system of spinal metastasis.

The “spinal metastasis invasiveness index”: A novel scoring system to assess surgical invasiveness

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Introduction: The variability in surgical treatment of similar metastatic spine disease(MSD) cases across different institutions can be attributed to lack of universal treatment algorithms. An objective index would be useful to predict important outcomes in metastatic spine tumour surgery(MSTS) and help in making informed treatment decisions. The aim of this study was to develop a novel surgical invasiveness index for MSTS that can serve as a standardized tool in predicting quantifiable outcome measures associated with the magnitude of surgery such as intraoperative estimated blood loss(EBL) and surgical duration.

Methods: We conducted a retrospective review of 261-patients who underwent MSTS between 2005–2015. Demographic, clinical, oncological, and procedural data were collected. We decided to use operative time and EBL as direct measures of surgical invasiveness and forewent length of hospital stay, adverse events, and unplanned readmission as these could be due to sequelae of patients' oncological disease process and not surgical invasiveness itself. Binary logistic regression, using median values for surgical duration and intraoperative EBL, was used to determine statistical significance of variables to be included in the “spinal metastasis invasiveness index”(SMII). The corresponding weightage of each of these variables was agreed upon by experienced spine surgeons. Multivariate regression analysis was used to predict operative time and EBL while controlling for demographic, procedural, and oncological characteristics.

Results: The mean age of the patients was 59.7±11.5 years with near equal gender distribution. The cohort had an average of 6.2±2.9 levels instrumented and 1.8±1.3 levels decompressed, with 12.3% anterior-only surgeries, 76.6% posterior-only, and 11.1% combined. Average EBL was 824.5±685.4 mL, and average operative time was 253.4±113.3 minutes. The variables that reached statistical significance and hence, included in the SMII with their corresponding weightage were: total corpectomy from any approach (4/level), hemicorpectomy from any approach (3/level), pediclectomy (2/pedicle), posterior decompression (2/level), anterior column support (cement spacer, graft and cage) (2/level attached to and replacing vertebral bodies), open posterior instrumentation (2/level), posterior percutaneous surgical fixation (1/level), and vertebroplasty (1/level). Of all the preoperative variables, tumor vascularity and embolization have the largest influence on blood loss. Hence, hypervascular tumors (renal, thyroid, hepatocellular) were awarded a modifier of 2/level decompressed, separately scored for anterior and posterior column. Similarly, for absence of preoperative embolization, we awarded a modifier of 1/level, separately scored for anterior and posterior column (Table 1). The newly developed SMII strongly predicted extended surgical duration($R^2=0.28, p<0.001$) and high intraoperative blood loss($R^2=0.18, p<0.001$). When compared with a previously established surgical invasiveness index, the SMII accounted for more variability in outcomes. For every unit increase in score, there was a 42 mL increase in mean blood loss($p<0.001$) and 5-minute increase in mean operative time($p<0.001$).

Discussion: This is the first study to date to develop a novel “surgical invasiveness index” specific to MSD population. Long surgical duration and high intraoperative blood loss were strongly predicted by the newly developed SMII. The use of SMII may help in preoperative risk assessment and allow surgeons to gauge intraoperative blood loss and surgical duration of their proposed procedures, thus aiding in resource management.

Table 1. Components used to calculate the SMII

Factors	Points Assigned
Total Corpectomy ^a	4 points per level
Hemicorpectomy ^a	3 points per level
Anterior column support (cement spacer/graft/cage)	2 points per level spanned to replace the vertebral body/bodies
Pediclectomy	2 points per pedicle
Posterior decompression	2 points per level
Posterior instrumentation	
Open	2 points per level
Minimally invasive	1 point per level
Vertebroplasty	1 point per level
Modifiers:	
Hypervascular primary tumor (thyroid, renal, liver, gallbladder)	2 points per level decompressed ^{a,b}
No preoperative embolization	1 point per level decompressed ^{a,b}

^aRegardless of type of approach, ^bCount separate for anterior and posterior decompression

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Can collective intelligence improve the outcome of spine surgery?

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INTRODUCTION: The outcome of surgery for degenerative disorders of the spine is inferior to that of interventions for degenerative disorders of the hip or knee¹. One of the reasons for this may be the relatively greater uncertainty with respect to diagnosis and the indication for spine surgery, with correspondingly inappropriate treatment plans. The aim of this study was to assess whether agreement versus disagreement in surgical plan between two surgeons was associated with patient rated outcome.

METHODS: This was a retrospective study of prospectively collected data from 64 consecutive patients with lumbar spinal stenosis (35 m, 29 f; mean age 71 ± 8 yrs) who had undergone posterior decompression with or without additional instrumented fusion. The radiological dataset was anonymised, as were the patient outcomes. Only the chief complaint of the patient was noted. An experienced surgeon reviewed the dataset and established his own chosen treatment plan. Patients were then retrospectively grouped into agreement and disagreement groups: patients were placed in the agreement group if the surgery proposed by the second reviewing surgeon concurred with that which had actually been performed according to the plan of the primary surgeon. Completely different plans, with no overlap at all, were considered disagreement. The multidimensional Core Outcome Measures Index (COMI), was completed by patients before and 1 year after surgery and used to indicate the extent of clinical improvement. Patients also answered single questions on global treatment outcome.

RESULTS: In total, 40 (62.5%) of the patients were in the agreement group and 24 (37.5%) in the disagreement group. Age, gender, and chief complaint before surgery did not differ between the groups ($p > 0.05$). Overall, the agreement group had better outcomes than the disagreement group: respectively, reduction in COMI score, 3.5 ± 2.8 vs 2.0 ± 3.0 ($p = 0.048$); reduction in back pain, 2.8 ± 2.9 vs 0.4 ± 2.4 ($p = 0.001$); reduction in leg pain 3.1 ± 3.8 vs 1.8 ± 3.0 ($p = 0.19$); reduction in intensity of chief pain complaint (back or leg), 3.5 ± 3.2 vs 1.0 ± 2.7 ($p = 0.003$); global treatment outcome, 72.5% vs 53.2% ($p = 0.13$); achievement of minimum clinically important change score for COMI, 65.0% vs 42.0% ($p = 0.07$)

DISCUSSION: If two experienced spinal surgeons independently (blindly) agree on the treatment plan, it may increase the success rate of surgery, as measured by the patient rated outcome according to COMI. This should be evaluated in a prospective study.

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Can We Predict the Cone of Economy Measurement using Only a Force Plate?

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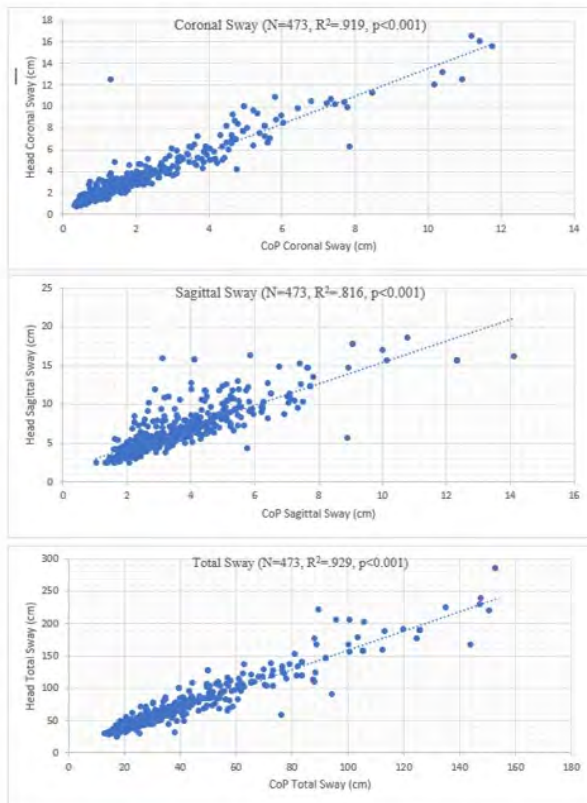
Introduction: Currently, most spinal deformity surgeons rely on static radiographic parameters for alignment, balance, and outcomes data alongside patient reported outcome measures. The cone of economy (CoE), the stable region of upright posture, can be objectively measured to determine the efficiency and balance of the spine. Motion capture technology is currently used to collect data to calculate CoE, but this requires expensive and complex equipment, which is a barrier to widespread adoption and clinical use of CoE measurements. Force plates, which measure pressure, are less expensive and can be used in a clinical setting. The purpose of this study was to develop a new method for estimating CoE using a force plate rather than traditional motion capture.

Methods: Motion capture and a force plate were used to quantify the CoE of 473 subjects (423 spinal surgical candidates, 50 health controls; 271 Females; Age: 58.60±15.27; Height: 1.69±0.13; Weight: 81.07±20.91), and a linear multiple regression model was used to predict CoE using force plate data in a human motion laboratory setting. Patients stood with feet together in a natural position for a full minute while measures of sway and center of pressure were recorded. All raw data were exported from the Vicon video system and imported into a custom laboratory algorithm using Matlab for processing.

Results: The selected CoP variable regression models successfully predicted CoE measurements. The variables that were used to predict vertical CoE were CoP coronal sway, CoP sagittal sway, and CoP total sway. The coefficient of determination for the head total sway model indicated that 87.0% ($F(3,469)=1044.14$, $p<0.001$) of the variance in the dependent variable was explained by CoP coronal, sagittal, and total sway and were significant predictors of head total sway ($p<0.006$). The coefficient of determination for the head sagittal sway model indicated that 69.2% ($F(3,469)=351.70$, $p<0.001$) of the variance in the dependent variable was explained by CoP coronal, sagittal, and total sway and were significant predictors of head sagittal sway ($p<0.003$). The coefficient of determination for the head coronal sway model indicated that 85.2% ($F(3,469)=899.27$, $p<0.001$) of the variance in the dependent variable was explained by CoP coronal, sagittal, and total sway and were significant predictors of head coronal sway ($p<0.001$).

Discussion: Center of pressure sway was highly correlated with CoE total, sagittal, and coronal sway and successfully predicted CoE in healthy controls and spine patients using regression analysis. The overall goal of this study was achieved by providing surgeons with a practical method for producing objective global balance data via CoE prediction from a force plate. Several benefits are anticipated from this quantitative tool to assist with pre-operative planning for patient-specific alignment objectives and also prognostic information, recovery monitoring, and treatment data. More physicians may consider incorporating this technology into their clinical practice as force plates are relatively affordable, portable, and straightforward to use.

Figure 1. Correlation between Cone of Economy (CoE) to Center of Pressure (CoP)



Risk factors of worsening global spinal mal-alignment after osteoporotic vertebral fracture.

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Introduction

The global spinal mal-alignment was reported as the risk for the occurrence of vertebral fracture and the cause of backpain. Patients with osteoporotic vertebral fracture (OVF) sometimes show global spinal mal-alignment. Objective of this study is to show the change of global spinal alignment after OVF and to clarify the risk for progression of global spinal mal-alignment.

Methods

Fifty-three patients conservatively treated and followed for 96 weeks after new single-level thoracolumbar OVF were enrolled. Conservative treatment was conducted using soft lumbosacral orthosis plus osteoporosis drugs, either weekly alendronate (BP) or daily teriparatide (TPD) randomly assigned for 24 weeks, and followed without orthosis continuously for more than 72 weeks using BP. Patients were divided into two groups depending on the change of pelvic incidence minus lumbar lordosis (PI - LL) from 24 weeks to 96 weeks after OVF. Stepwise multinomial logistic regression analysis was used to identify associations between the risk of worsening global spinal alignment and the patients background status as age, past vertebral fracture, local kyphosis at fractured vertebra, union status, and global spinal alignment containing the distance between C7 plumb line to the center of OVF (C7PL-OVF) at 24 weeks.

Results

PI-LL was $19.3^\circ \pm 14.6^\circ$ at 24 weeks, $9.5^\circ \pm 16.2^\circ$ at 48 weeks, $10.3^\circ \pm 17.1^\circ$ at 72 weeks, and $9.8^\circ \pm 16.7^\circ$ at 96 weeks after OVF. Change of PI-LL from 24 weeks to 96 weeks after OVF showed bimodal with the boarder at -10 degrees. The improved PI-LL group (n = 28) was defined as the change of PI-LL over 10 degrees, and the worsening PI-LL group (n = 25) was defined as the change of PI-LL under 10 degrees, respectively. The factors showed $p < 0.2$ between the improved PI-LL group and the worsening PI-LL group were age (71.7 ± 1.3 and 75.5 ± 1.4 , $p = 0.060$), past vertebral fracture (40.0 %, 19.2 %, $p = 0.145$), union rate at 24 weeks (86.7 %, 69.2 %, $p=0.191$), pelvic tilt ($20.2 \pm 1.5^\circ$, $26.2 \pm 1.6^\circ$, $p = 0.008$), sagittal vertical axis (36.4 ± 8.2 mm, 72.6 ± 8.8 mm in ($p = 0.004$), and C7PL-OVF (43.9 ± 7.6 mm, 70.5 ± 8.1 mm, $p = 0.020$). Stepwise multinomial logistic regression analysis showed C7PL-OVF > 60mm (odds ratio; 12.6 (95%CI; 2.5 - 63.3), $p = 0.002$) and past vertebral fracture (odds ratio; 8.7 (95%CI; 1.5 - 49.7), $p = 0.015$) were the factors for the worsening PI-LL.

Discussion

Global spinal mal-alignment as 20° of PI-LL at 24 weeks changed to normal alignment as 10° at 48 weeks and maintained it until 96 weeks after OVF. Local greater kyphosis caused by OVF did not show the risk for worsening PI-LL, compensated by other lumbar segments. C7PL-OVF > 60 mm was the candidate to prevent restoration of normal global spinal alignment. Larger C7PL-OVF means greater moment at OVF, and needs more muscle strength to maintain global spinal alignment.

Age and Gender Related Differences in Gait Amongst Patients with Degenerative Spinal Disorders

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Introduction: Gait mechanics is a crucial component that impairs the function and quality of life in patients afflicted with various spinal pathologies. Novel techniques in motion capture have furthered our understanding of cone of economy (CoE) based balance measurements and dynamic gait parameters. While the literature has begun to explore gait differences in comparison to healthy patients, there is little information about age and gender related differences in gait amongst patients with spine pathology. Understanding how age and gender affect dynamic measurements in afflicted patients will provide better standards to compare the clinical severity of altered. Therefore, the purpose of this study is to examine age and gender dependent effects on altered gait in various spine disorders.

Methods: We conducted a non-randomized prospective study of 414 patients with symptomatic spine pathology and 65 healthy controls. Patients were divided into 4 categories based on their age: adolescents (12-20), young adults (21-40), adults (41-60), and elderly (>60). Patients were also divided by their gender: male vs. female. A series of over-ground gait trials were then performed by each patient using a full body external reflective marker set to determine gait mechanics.

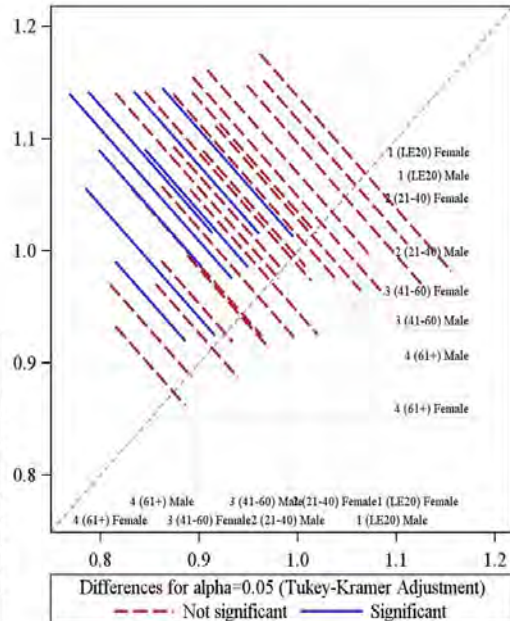
Results: Amongst patients with degenerative spine disorders, elderly and adult spine patients were found to walk slower in comparison to other age groups (p <0.001) (Table 1). Furthermore, elderly and adult patients had less cadence, longer stride time (p <0.001), and longer stride time (p <0.001) when compared to younger populations. The elderly demographic also had longer single support time (p 0.027), shorter stride length (p <0.001), and lower gait deviation index (GDI) (p 0.014) when compared to the adult group. When a similar analysis was conducted in healthy controls, elderly volunteers were still noted to have slower walking speed (p 0.004), less cadence (0.003), and longer stride time (0.001) compared to younger age groups. The differences that were seen in the affected adult group were not as notable in the healthy control population. Regarding gender differences in gait mechanics, female patients with spine disorders were noted to have more cadence (p <0.001), shorter single support time (p <0.001), shorter double support time (p 0.05), and shorter stride length (p <0.001) in comparison to male patients. A similar analysis in healthy controls showed that female patients have more cadence (p 0.005), shorter stride time (0.005), and shorter single support time (p 0.043) in comparison to males.

Conclusions: This study demonstrate that across spinal pathology, elderly (age >60) and adult (age 41-60) patients have worse gait mechanics and speed compared to younger patients. In particular, adult patients with spine disorders have more significant age-related gait differences when compared to healthy controls. Regarding gender, female patients have some differences in gait mechanics such as cadence and support time but overall speed and GDI is not significantly different from males. As gait analysis becomes a more important tool in decision making, understanding the expected age and gender related differences in spine pathology will help quantify the severity of altered gait in individual patients.

Interaction (Gender X Age Group)

Age Group	Gender	Walking Speed LSMEAN	95% Confidence Limits	
Adolescents	Female	1.079	1.004	1.154
Adolescents	Male	1.058	0.958	1.159
Young Adults	Female	1.038	0.979	1.097
Young Adults	Male	0.990	0.916	1.065
Adults	Female	0.955	0.919	0.992
Adults	Male	0.929	0.886	0.973
Elderly	Female	0.851	0.811	0.890
Elderly	Male	0.897	0.858	0.937

pValue Least Squares Means for effect (Age Group * Gender)									
Dependent Variable: Walking Speed									
Age Group	Gender	1	2	3	4	5	6	7	8
Adolescents	Female		1.000	0.990	0.723	0.059	0.014	<0.001	<0.001
Adolescents	Male			1.000	0.963	0.547	0.279	0.004	0.064
Young Adults	Female				0.976	0.229	0.058	<0.001	0.001
Young Adults	Male					0.992	0.864	0.028	0.389
Adults	Female						0.978	<0.001	0.224
Adults	Male							0.078	0.946
Elderly	Female								0.464
Elderly	Male								



Impact of Lumbar Fusion Length on Sitting Spino-pelvic Balance: Multi-segmental Versus Mono-segmental

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Introduction: Lumbar fusion is an effective surgical intervention for the treatment of various lumbar degenerative diseases. It renders the fixed spine immobile in a sagittal alignment that is considered to be the most ideal position for the spine. The standard data of the sagittal parameters in the standing position have been well established. Analysis of spinopelvic sagittal balance, however, remains largely unclear in the sitting posture. In addition, it is well known that the fusion length is significantly associated with functional disability. Therefore, we perform this study to evaluate the effect of spinal fusion on the spinopelvic sagittal alignment and to assess the impact of fusion length upon sitting and standing spinopelvic sagittal alignment in patients with lumbar degenerate diseases.

Methods: The current study recruited 26 patients who had undergone lumbar fusion, consisting of 11 with one-level fusion (mono-segmental group) and 15 with fusion of two or more levels (multi-segmental group). And the control group comprised 20 adults who had no previous spinal fusion surgery. For the control group, long-cassette lateral radiographs of the spine and pelvis were obtained in standing and sitting positions. In mono-segmental and multi-segmental groups, the abovementioned radiographs were obtained 12 months after fusion surgery. Spinopelvic parameters of patients were assessed: Sagittal vertical axis (SVA), Pelvic tilt (PT), Sacral slope (SS), Pelvic incidence (PI), Thoracic kyphosis (TK), Lumbar lordosis (LL), and Proximal femur angles (PFA).

Results: There were no statistical differences in mean age, sex, and BMI among the three groups. Although the three groups demonstrated no differences for standing sagittal parameters, we observed statistical differences in sitting TK ($P=0.035$), sitting LL ($P=0.043$) and sitting SVA ($P=0.019$) among the three groups. There were significant differences in the dynamic changes of several sagittal spinopelvic parameters from standing to sitting position between three groups. The multi-segmental group had the least change in SVA ($P=0.016$), PT ($P=0.043$), and LL ($P=0.009$), with a compensatory increase in TK ($P=0.021$). Moderate to strong correlations were found between the change in the LL and those in the SVA ($r=-0.548$, $P=0.001$), PT ($r=-0.600$, $P=0.001$), and SS ($r=0.623$, $P=0.001$).

Conclusion: Lumbar fusion limits the lumbar mobility and this impact increases with the fusion length. Multi-segmental spinal fusion significantly affects the ability to compensate postural changes. The pelvic tilt and thoracic kyphosis increases compensatively to rebalance the spinopelvic profile in the sitting position.

An Active Hybrid Model of the Human Lumbosacral Spine: Facet Joint Integration in a Multi-Objective Optimization of Muscle Forces

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INTRODUCTION The definition of single or multiple objective functions to solve muscular redundancy problems remains a challenge in musculoskeletal (MS) modeling. A common technique in musculoskeletal optimizations is the minimization of the sum of squared or cubed muscle stresses. However, multi-objective optimizations including joint structures remain limited. In this study, we extend the existing optimization of muscle forces in the human lumbosacral spine (LSS) to a multi-objective optimization including both muscle stresses and forces computed in a single functional spinal unit (FSU) with focus on facet joint forces.

METHODS An active hybrid model of the LSS is built in Artisynt (www.artisynt.org) – a software to simulate the dynamics of active and passive structures by coupling rigid-body with finite element (FE) models. The skeletal geometry adapted from the Visible Human Project of the US National Library of Medicine has been modified to fit an average physiology. A passive model of the ligamentous LSS including ligaments, intervertebral discs and facet joints has been extended by a muscle set covering multifidus, erector spinae, psoas major, quadratus lumborum and abdominals (Figure 1). The definition of muscle fascicles is based on recently developed musculoskeletal models.

To optimize redundant muscle forces in the LSS model, a quasi-static study in upright standing position is performed. Beyond the objective of minimized muscle stresses squared, two additional objectives have been added to the implemented tracking controller. These include the minimization of compressive forces squared of a single FSU in both the intervertebral disc and facet joints. A detailed comparison is made by varying the weights of the competing objectives named above, leading to Pareto optimal solutions.

RESULTS In general, the selection of objectives for optimizations affects the determination of redundant muscle forces. Correlating with previous findings, the intervertebral disc compression force is found to present an influencing factor in muscle force prediction. In addition, the results suggest an essential effect of integrating facet joint compression force as one objective. The Pareto front indicates a non-linear relation between the three computed objective functions. It is therefore concluded that not only compressive forces in the intervertebral disc but also in the facet joints appear to be important when determining redundant muscle forces.

DISCUSSION Considerable insight has been gained within this study concerning the multi-objective optimization of muscle forces in the LSS with focus on facet joint compressive forces. Future work may include the study of additional objective functions like ligament forces, joint stresses or shear forces. Furthermore, work is needed on integration of multiple FSU into the optimization. The introduced active hybrid model enables the study of complex interactions between passive and active structures in the LSS. Moreover, it provides a framework to overcome inherent limitations of conventional FE and MS models.

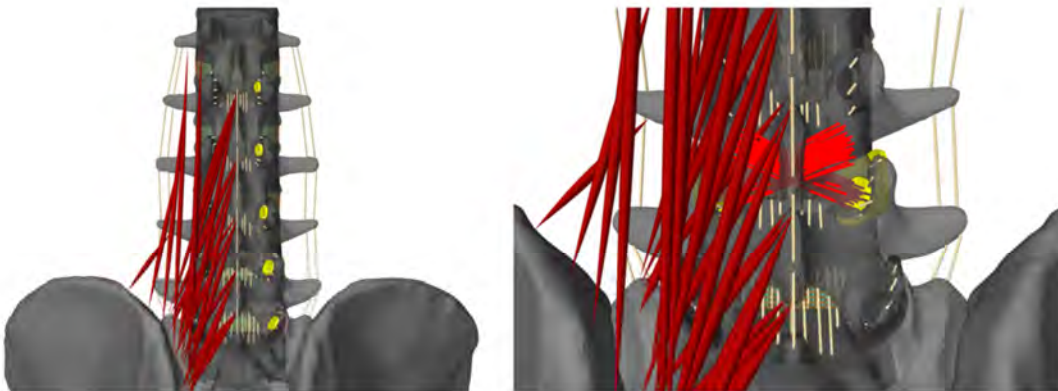


Figure 1: Extract of the active hybrid model of the lumbosacral spine with one-sided muscle groups of lumbar multifidus and lumbar erector spinae shown (left). Facet joint reaction forces during extension (right).

Deficits in proprioceptive reweighting in middle-aged people with chronic low back pain and asymptomatic people: a cross-sectional study

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Introduction: Compared to asymptomatic individuals, young (age range: 18-25 years) and older adults (mean age:75.5±5.1 years) with chronic low back pain (CLBP) show difficulty in reweighting proprioceptive signals from lumbar multifidus and calf muscles for standing balance control when these muscles were vibrated. However, it remains unclear if similar deficits in lumbar proprioception/repositioning sense exist in middle-aged individuals with CLBP. Therefore, the current study aimed to: (1) compare the relative proprioceptive reweighting (RPW) and lumbar reposition errors in young (18-44 years) and middle-aged people (45-65 years) with CLBP with reference to age- and gender-matched healthy controls; and (2) evaluate the correlation between RPW and lumbar repositioning errors in young and middle-aged patients with and without CLBP.

Methods: Individuals with (n=78) and without CLBP (n=73) underwent postural sway tests on a force-plate with visual occlusion to evaluate the relative reliance on trunk proprioception for the balance control. The test consisted of standing on: (1) the force plate with vibration to bilateral L5/S1 multifidi; (2) the force plate with vibration to bilateral calves; (3) a foam with vibration to bilateral L5/S1 multifidi; and (4) a foam with vibration to bilateral calves. Sagittal displacements of the center of pressure (COP) before and after vibration were recorded. The proprioceptive reweighting ability of an individual was estimated by RPW. RPW was the ratio of absolute value of COP displacement during calf vibration to the sum of absolute values of COP displacements of multifidi and calves during respective vibrations. Higher RPW values indicate more reliance on calf proprioceptive signals for balance control. Additionally, participants underwent lumbar repositioning tests in sitting by reproducing target lumbar flexion/extension positions thrice. The average repositioning errors were used for analysis. Between-group differences were compared using Mann-Whitney U test. Correlation between RPW and lumbar repositioning errors was assessed by Spearman's rank correlation test

Results: Young individuals with CLBP had significantly higher RPW than age matched asymptomatic controls when standing on the force plate ($p = 0.006$) and foam ($p = 0.017$). Conversely, there was no significant difference in RPW between middle-aged people with and without CLBP when standing on both the force-plate and foam. Interestingly, both young and middle-aged individuals showed no significant difference in lumbar repositioning errors. Likewise, RPW values were not related to lumbar repositioning errors in people with or without CLBP regardless of age.

Discussion: Our results validated that young individuals with CLBP relied less on lumbar proprioception for balance control as compared to age- and gender-matched asymptomatic counterparts. However, middle-aged individuals regardless of their CLBP status exhibited decreased reliance on lumbar proprioception and increased reliance on calf muscles for balance control. Although speculative, our findings suggest that asymptomatic middle-aged individuals start to lose their proprioceptive reweighting ability. They may be at higher risk of developing LBP in the future. Further investigation is warranted to determine if the altered proprioceptive reweighting ability in middle-aged people occurs at spinal and/or supraspinal levels. Future research should also examine if baseline RPW values can predict future CLBP development.

Lumbar disc degeneration and vertebral fracture at thoracolumbar junction are risk factors for chronic low back pain with disability: 7 years' follow-up of the Wakayama Spine Study

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Introduction: It is still controversial about the relationship between the degenerative changes on MRI and chronic low back pain (CLBP). Disc degeneration (DD), vertebral deformity due to osteoporotic fracture, and spinal stenosis have been reported as possible causes of CLBP. However, these degenerative changes are often coexisting and may confound each other as the cause of CLBP.

AIM: To elucidate the risk factors of CLBP among degenerative changes on MRI in a general population

Methods: This is a longitudinal study using an established population-based cohort in Japan. A total of 1009 subjects who participated in the baseline survey of the Wakayama Spine Study (AD 2008-9) were subjected to the MRI evaluation. Lumbar DD (Phirrmann's classification: grade 1-5), and morphometric fracture of the vertebral bodies (semi-quantitative method: SQ grade 0-3) were evaluated on the sagittal MRI. Lumbar spinal stenosis (Suri's classification: grade 0-3) was evaluated on the axial MRI. In the third survey of the Wakayama Spine Study (AD 2015-6), we followed-up 663 subjects (Men 219, Women 444, age at the baseline 62±13 years old) and got the information on the presence of CLBP (continued more than 3 month) and Oswestry Disability Index (ODI). The relationship between the degenerative changes at the baseline and the presence of chronic LBP with disability (ODI%≥21) after 7 years was determined using multiple logistic regression analysis including mental component summary scale of the SF-8, smoking habit, age, sex, and body mass index (BMI) as the explanatory variables.

Results: The prevalence of disabled CLBP was 91/663 (13.7%). Significant risk factors at baseline for the disabled CLBP after 7 years were age (+1 year, odds ratio 1.07 [95% CI 1.03-1.10]), sex (female, 3.69 [1.83-7.44]), BMI (+1kg/m², 1.11 [1.02-1.20]), sum of the lumbar disc degeneration grade (L1/2 – L5/S, +1point, 1.14 [1.01-1.30]), and sum of the SQ grade at the thoracolumbar junction (T11-L1, +1point, 1.32 [1.10-1.60]).

Conclusion: Lumbar DD and vertebral fracture at thoracolumbar junction were risk factors for CLBP with disability in the general population. Other factors that may cause CLBP have been reported in addition to our evaluated items. The lack of them is the limitation of this study. However, we consider the results of this study extremely important both epidemiologically and clinically, because there are few longitudinal studies on spinal degeneration and related disability.

AI-based automated detection of traumatic thoracolumbar fractures on sagittal X-rays

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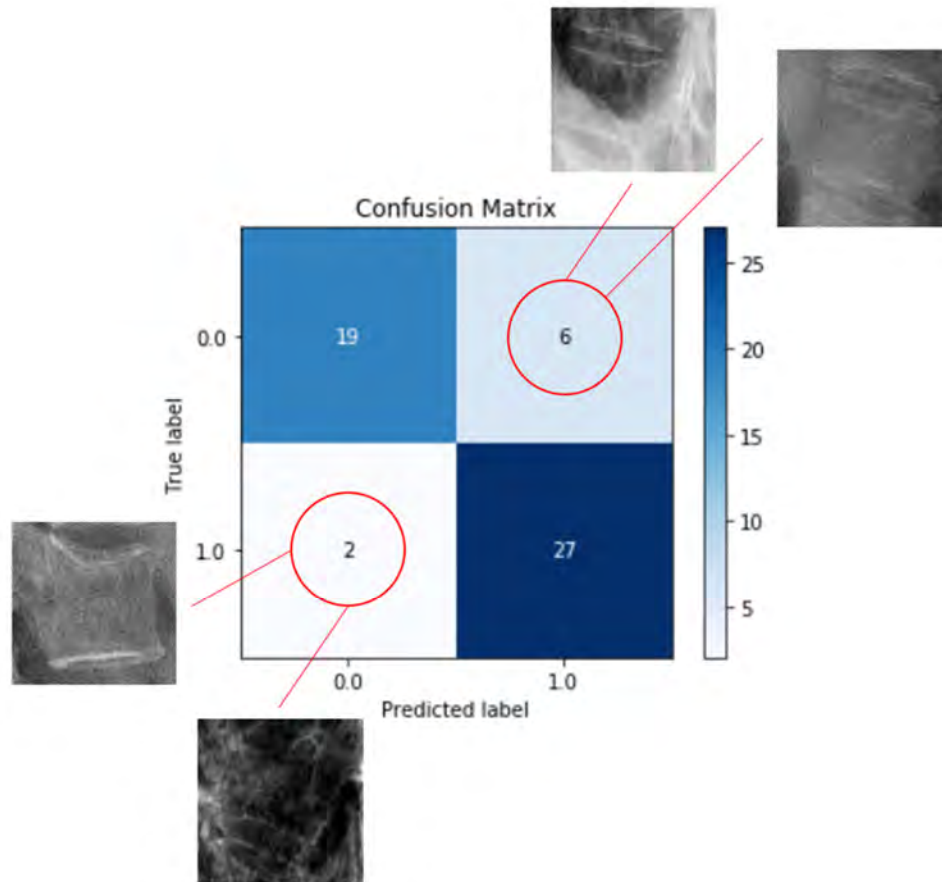
Introduction. Traumatic thoracolumbar fractures are frequently encountered in emergency wards, and their identification is mandatory for correct treatment. However, their detection is challenging on planar radiographs resulting in significant rates of missed diagnoses (30%), thus requiring second-level diagnostic imaging (CT and MRI) which is however time and resource consuming. Being able to reliably detect fractures in simple radiographic projections would therefore have a significant impact on healthcare.

Methods. We collected sagittal radiographs, CT and MRI scans of the thoracolumbar spine of 362 patients exhibiting traumatic fractures. Three expert spine surgeons labelled the dataset by drawing a Region of Interest (ROI) around each fractured vertebra and a non-fractured one and to indicate the corresponding class (fracture/no-fracture) on sagittal X-Rays, using CT and MRI to confirm the presence of the fracture. From this dataset, 297 X-Ray images of fractured vertebrae and 275 showing no fracture were annotated. The dataset was then used to train, validate and test a deep learning classifier based on the Resnet architecture.

Results. Among the 54 images constituting the test set, 85% were correctly classified in the respective classes (Figure). Precision and recall were 0.82 and 0.93 respectively.

Discussion. The machine learning-based classifier proved to be able to detect thoracolumbar fractures on planar radiographs in an accurate and reliable manner; we expect that the achieved performance would further improve by enlarging the training database. The use of deep learning could enhance the detection of fractures on simple radiographic projections, benefiting settings in which tomographic images are not readily available such as emergency conditions or developing countries and guiding the clinician in selecting patients in need of second-level imaging.

Figure caption. Confusion matrix describing the performance of the classifier, and depicting some examples of incorrectly classified images. True and predicted labels: "0.0": non-fractured; "1.0": fractured.



Learning-based fully automated prediction of lumbar disc degeneration progression with specified clinical parameters and preliminary validation

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Introduction: Lumbar disc degeneration (LDD) may be related to aging, biomechanical and genetic factors. Despite the extensive work on understanding its etiology, there is currently no automated tool for accurate prediction of its progression. We aim to establish a novel deep learning-based pipeline to predict the progression of LDD-related findings using lumbar MRIs.

Methods: We utilized our dataset with MRIs acquired from 1,343 individual participants (taken at the baseline and the 5-year follow-up timepoint), and progression assessments (the Schneiderman score, disc bulging, and Pfirrmann grading) that were labelled by spine specialists with over ten years clinical experience. Our new pipeline was realized by integrating the MRI-SegFlow and the Visual Geometry Group-Medium (VGG-M) for automated disc region detection and LDD progression prediction correspondingly (Figure 1). The LDD progression was quantified by comparing the Schneiderman score, disc bulging and Pfirrmann grading at the baseline and at follow-up. A 5-fold cross-validation was conducted to assess the predictive performance of the new pipeline.

Results: Our pipeline achieved very good performances on the LDD progression prediction, with high progression prediction accuracy of the Schneiderman score (Accuracy: $90.2 \pm 0.9\%$), disc bulging (Accuracy: $90.4\% \pm 1.1\%$), and Pfirrmann grading (Accuracy: $89.9\% \pm 2.1\%$).

Discussion: This is the first attempt of using deep learning to predict LDD progression on a large dataset with 5-year follow-up. Requiring no human interference, our pipeline can potentially achieve similar predictive performances in new settings with minimal efforts.

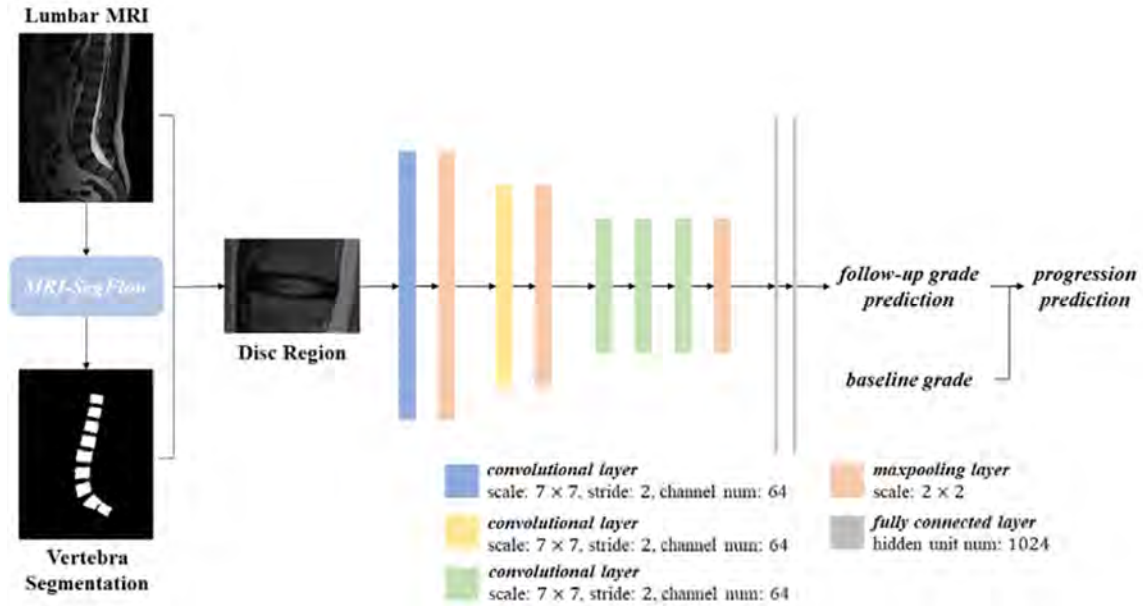


Figure 1: The pipeline of our pathology progression prediction method. MRI-SegFlow was used for the disc region detection using the protocol described in our recent published in prior to the VGG-M. The follow-up grade could be directly predicted from this pipeline. In comparison with the baseline grade, whether the pathology would progress was predicted.

Disc Height Assessment and Inter-observer Variability Using Auto-segmentation

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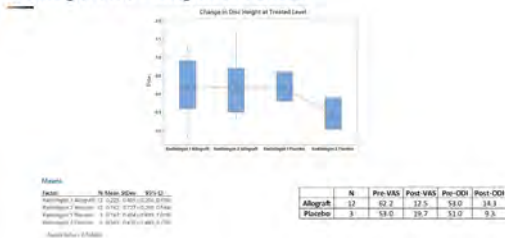
3. SmartSoft Ltd., Varna, Bulgaria

Introduction Degenerative disc disease causes changes in nucleus pulposus and annulus fibrosis composition and compromises the structural integrity of the disc. There are additional alterations of metabolic activity and biochemical function of the disc. A recent study evaluated whether viable allograft supplementation could replace tissue lost to disc degeneration and measured the effect on pain reduction and functional improvement.^[1] Allograft supplementation of the degenerated disc achieved a marked reduction in pain, an improvement of function and a resolution of symptoms in in both the allograft and saline cohorts. While the anatomic changes were encouraging, interobserver consensus failed to provide a definitive anatomical difference. This study evaluated auto-segmentation assessment of disc height following tissue supplementation.

Methods The study was a RCT evaluating saline vs. supplemental allograft over 1 year for VAS, ODI, and MRI differences. MRI analysis assessed all lumbar discs, comparing not only the treated levels but those adjacent for disc height in the sagittal plane. Two board-certified radiologists, blinded to the treatment, and level or levels treated, measured all lumbar disc levels in a mid-sagittal central location. A comparison was made with auto segmentation software which has attained ISO 13485:2016, European Commission Seal of Excellence, to read, segment, measure and classify MRI images. Disc height was measured at the anterior margin, mid-central sagittal, and at the posterior margin. Three para-sagittal measurements were averaged to determine height.

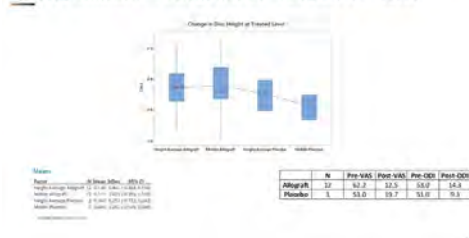
Results

Radiologist 1 & 2 – Allograft vs. Placebo



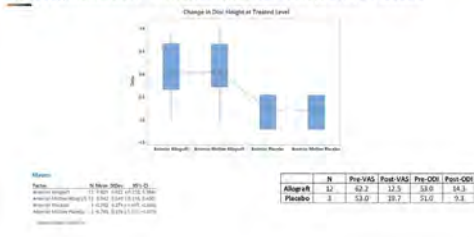
There was considerable interobserver variability between the radiologists that contributed to the readings not reaching consensus. Readings were made independently with pre-arranged criteria as near-central sagittal as possible (Figure 1).

Autosegmentation – Average Middle – Allograft vs. Placebo



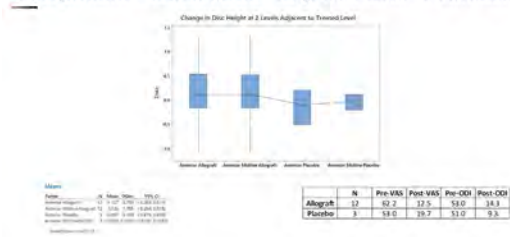
Auto-segmentation height measured centrally paired with one of the readers (Figure 2), but the anterior and posterior assessments produced additional information.

Autosegmentation – Anterior Midline – Allograft vs Placebo



Anterior disc height was maintained at 12 months with the allograft while it was lost at the posterior margin (Figure 3).

Autosegmentation – Anterior Midline – Allograft vs Placebo – 2 levels above



When measured at the posterior margin, anterior difference of disc height with the allograft compared similarly to the saline treated. This trend persisted 2 levels above the treated levels, with allograft maintaining or increasing anterior and saline supporting posterior increase (Figure 4)

Discussion Anterior height was stable or increased over 12 months at the treatment level in the allograft-treated while it decreased in the placebo-treated disc. In central and posterior disc height measurement, both the allograft and the placebo disc height remained constant or increased. These differences were also seen up to 2 levels above index level. Anterior height increase with the allograft coupled with posterior height change in the saline-treated disc without an increase in anterior height suggests the clinical gain noted in the 12-month data (Figures 1 – 4) is supported by an anatomical changes at the treated level and levels up to 2 levels rostral.

[1] Beall DP, Wilson GL, Bishop R, and Tally W. VAST Clinical Trial: Safely Supplementing Tissue Lost to Degenerative Disc Disease. International Journal of Spine Surgery April 2020, 7033; DOI: <https://doi.org/10.14444/7033>

Predicting Disc Re-Herniation After Lumbar Decompression: A Machine Learning Approach

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Introduction: Surgical treatment of herniated lumbar intervertebral discs is a common procedure worldwide. However, re-herniated nucleus pulposus (re-HNP) may develop, complicating outcomes, and patient management. The purpose of this study was to utilize machine-learning (ML) analytics to predict lumbar re-HNP, whereby a personalized risk factor scoring scheme can be developed as a clinical tool.

Methods: A retrospective study was conducted at a single center of 2,630 consecutive patients that underwent lumbar microdiscectomy (mean follow-up: 22 months). Various preoperative patient pain/disability/functional profiles, imaging parameters, and anthropomorphic/demographic metrics were noted. An Extreme Gradient Boost(XGBoost) classifier was implemented to develop a predictive model identifying patients at risk for re-HNP. The model was exported to a web application software for clinical utility.

Results: There were 1,608 males and 1,022 females, 114 of whom experienced re-HNP. Primary herniations were central (65.8%), paracentral (17.6%), and far lateral (17.1%). The XGBoost algorithm identified multiple re-HNP predictors and was incorporated into an open-access web application software, identifying patients at low or high risk for re-HNP. Preoperative duration of symptoms, pelvic incidence-lumbar lordosis mismatch, and elevated body mass index were the strongest predictors.

Discussion: Our predictive modeling via an ML approach of our large-scale cohort is the first study, to our knowledge, that has identified significant risk factors for the development of re-HNP after initial lumbar decompression. We developed the **Re-herniation after Decompression (RAD) Score** that has been translated into an online screening tool to identify low-high risk patients for re-HNP. Additional validation is needed for potential global implementation.

A novel tool to provide predictable alignment data irrespective of source and image quality acquired on mobile phones: what engineers can offer clinicians

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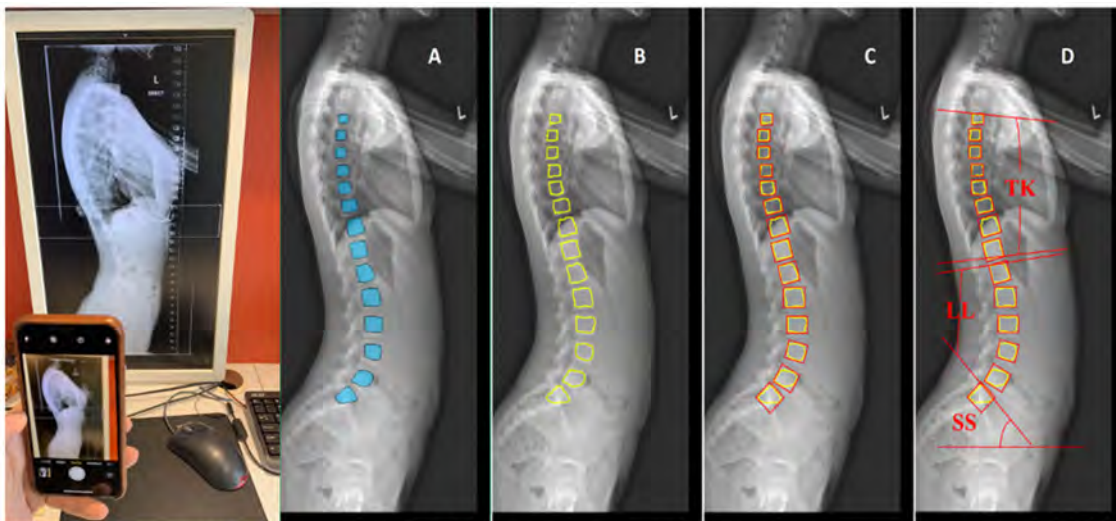
3. Spine Unit, University of New South Wales, Sydney, NSW, Australia

Introduction: Existing automated spine alignment are based on original X-rays that are not applicable for teleradiology for spinal deformities patients. We aim to provide a novel automated vertebral segmentation method enabling accurate sagittal alignment detection, with no restrictions imposed by image quality or pathology type.

Methods: 428 optical images of original sagittal X-rays taken by smartphones or screenshots for consecutive patients attending our spine clinic were prospectively collected. Of these, 300 were randomly selected and their vertebrae were labelled with Labelme. The ground truth were specialists measured sagittal alignment parameters. Pre-trained Mask R-CNN was fine-tuned and trained to predict the vertebra level(s) on the remaining 128 testing cases. The sagittal alignment parameters including the thoracic kyphosis (TK), lumbar lordosis (LL) and sacral slope (SS) were auto-detected, based on the segmented vertebra. Dice Similarity Coefficient (DSC) and mean Intersection over Union (mIoU) were calculated to evaluate the accuracy of the predicted vertebra. The detected sagittal alignments were then quantitatively compared with the ground truth.

Results: The DSC was $84.6 \pm 3.8\%$ and mIoU was $72.1 \pm 4.8\%$ indicating accurate vertebra prediction. The sagittal alignments detected were all strongly correlated with the ground truth ($p < 0.001$). Standard errors of the estimated parameters had a small difference from the specialists' results (3.5° for TK and SS; 3.4° for LL).

Discussion: This is the first study using fine-tuned Mask R-CNN to predict vertebral locations on optical images of X-rays accurately and automatically. We provide a novel alignment detection method that has a significant application on teleradiology aiding out of hospital consultations (Figure 1).



I: Image acquisition. II: Automated vertebral segmentation and alignment measurements.

Figure 1: Mobile image acquisition with automated vertebral segmentation and alignment measurements. The optical images of X-rays were acquired from a stationary PACS (I). The mask of the vertebral body was generated automatically (IIA) and the outline of the mask was obtained (IIB). The smallest circumscribed rectangle was automatically selected to fit each mask (IIC) and the endplates of the specific vertebra (T5, T12, L1, L5, and S1) were detected to calculate the thoracic kyphosis (TK), lumbar lordosis (LL) and sacral slope (SS) shown in image IID.

Proposal for a new scoring system for spinal degeneration: Mo-Fi-Disc**Emel Ozcan-Eksi¹, Murat Eksi², Omer Orhun³, Veli Turgut⁴, M. Necmettin Pamir²***1. Physical Medicine and Rehabilitation, Bahcesehir University School of Medicine, Istanbul, Turkey**2. Neurosurgery, Acibadem Mehmet Ali Aydinlar University School of Medicine, Istanbul, ISTANBUL, Turkey**3. Acibadem University, Istanbul**4. Neurosurgery, Antalya Ataturk State Hospital, Antalya, Turkey***Mo-fi-disc scoring system.**

IVDD grade	Score	End-plate change*	Score	Paraspinal muscle fatty infiltration**	Score
Grade I and II	0	No change	0	Grade 0-1	0
Grade III	1	Type III	1	Grade 2	1
Grade IV and V	2	Type II	2	Grade 3-4	2
		Type I	3		

Abbreviations: IVDD = intervertebral disc degeneration, * = Modic change, ** = Goutallier classification.

Figure 1. Mo-fi-disc scoring system

Introduction: We aimed to develop a new scoring system for spinal degeneration including Modic changes, fatty infiltration (fi) in the paraspinal muscles, and intervertebral disc degeneration (IVDD), briefly Mo-fi-disc, using current radiological classification systems. We also aimed to understand whether Mo-fi-disc could predict patients with more intense low back pain (LBP).

Methods: We conducted a cross-sectional analysis of a retrospective database between March 2018 and July 2020. We evaluated patients in terms of Modic changes, fatty infiltration in the paraspinal muscles, and IVDD at all lumbar levels on lumbar spine MRI. We grouped patients based on their LBP intensity. We scored the MRIs according to our brand new scoring system (Figure 1). Visual analog scale (VAS) scores were used for LBP intensity.

Results: We evaluated 134 patients (female: 66, male: 68; mean age: 35.44 ± 6.5 years). Patients with higher VAS scores had significantly higher 'Mo-disc' scores and higher 'fi' scores compared to those with lower VAS scores (3.54 ± 2.7 vs. 2.55 ± 2.8 , $p = 0.0075$; 6.85 ± 3.2 vs. 5.25 ± 2.9 , $p = 0.0092$). Patients with higher VAS scores had significantly higher 'Mo-fi-disc' scores compared to those with lower VAS scores (10.4 ± 4.2 vs. 7.94 ± 3.8 , $p = 0.0003$). The most significant predictor for patients with higher VAS scores was 'Mo-fi-disc' scoring system with an OR of 1.193 (95 % CI: 1.055-1.349, $p = 0.005$).

Discussion: Patients with more intense LBP had higher 'Mo-fi-disc' scores. This scoring system suggests an easy and objective classification to evaluate the spinal degeneration. It is simple to do in daily routine and gives information regarding discs, vertebral end-plates, and quality of paraspinal muscles. Further validation studies with large sample size, diverse age groups, and spinal pathologies are required to see whether this classification system correctly depicts patients with intense pain and severe spinal degeneration.

Mo-fi-disc scoring system.

IVDD grade	Score	End-plate change*	Score	Paraspinal muscle fatty infiltration**	Score
Grade I and II	0	No change	0	Grade 0-1	0
Grade III	1	Type III	1	Grade 2	1
Grade IV and V	2	Type II	2	Grade 3-4	2
		Type I	3		

Abbreviations: IVDD = intervertebral disc degeneration, * = Modic change, ** = Goutallier classification.

Radiographic Lumbar Spondylosis Evaluated by a Novel Semi-quantitative Method in a Population Based-cohort Study

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INTRODUCTION: Lumbar radiography is a commonly used as basic diagnostic tool for the evaluation of lumbar spondylosis (LS). The Kellgren Lawrence (KL) classification is a widely used semi-quantitative method for evaluating LS. However, it is difficult to evaluate the individual radiographic features of LS because the KL method comprehensively evaluates the extent of LS. We have established a novel semi-quantitative scoring system based on the KL classification that can individually score according to the extent of osteophyte (OP), disc height narrowing (DHN), vertebral sclerosis (VS) and spondylolisthesis (SL). The purpose of this study was 1) to evaluate LS using a novel scoring system of lumbar radiographs and 2) to investigate the relationship between the score of radiographic LS and low back pain (LBP) in a population-based cohort study.

METHODS: 256 inhabitants (74 males and 182 females; mean age: 71.0 y/o) of a typical mountain village who underwent a medical examination in 2019 were subjects of this study. Subjects were divided into two groups as LBP- or LBP+ according to the presence of LBP. Lateral lumbar spine radiographs from L1/2 to L5/S1 of each subject were taken at the medical examination. Radiographic findings of degenerative changes, including OP, DHN, VS and SL were scored and classified into three groups: 0 points- normal; 1 point-mild change; and 2 points-severe change. The sum of scores of degenerative changes at each intervertebral level was designated as 'Total score (TS)'. Lateral lumbar radiographs were also evaluated using the KL classification. Lumbar lordosis (LL) was measured as an indicator of sagittal alignment. All radiographs were evaluated by three certified orthopedic surgeons who were blinded to the information of subjects.

RESULTS: Intra- (inter-) observer reliability (kappa coefficient) of OP, DHN, VS, and SL was 0.83 (0.80), 0.84 (0.72), 0.85 (0.81), 0.92 (0.81), respectively. TS at each disc level and aggregate scores (sum of TS from L1/2 to L5/S1) were significantly correlated with those of KL grade ($R = 0.7 - 0.85$) (Fig. 1). Aggregate scores of OP and TS in males were significantly higher than those in females ($P < 0.01$) (Fig. 2). The percentage of subjects with LBP was not significantly different between males and females. Aggregate scores of OP ($P < 0.01$), DHN ($P < 0.05$), VS ($P < 0.01$) and TS ($P < 0.01$) were significantly higher in the LBP+ group than in the LBP- group (Fig. 3). On the other hand, there was no significant difference in aggregate scores of KL between the LBP- and LBP+ groups. The LL in the LBP- group was significantly higher than that in the LBP+ group ($P < 0.01$). Logistic regression analysis showed that VS was the factor significantly associated with LBP ($P < 0.01$).

DISCUSSION: Lumbar spondylosis scores by semi-quantitative evaluation in the LBP+ group was significantly higher than those in the LBP- group, while the KL classification did not show any significant difference. Therefore, the semi-quantitative evaluation of LS by individually scoring each radiographic feature would more accurately reflect the LBP of the subject than KL classification.

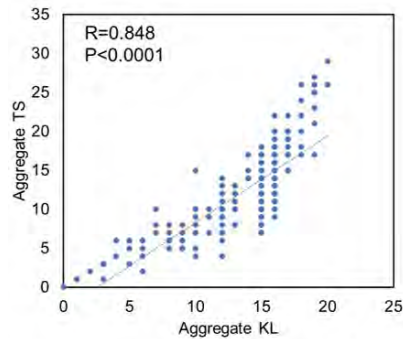


Fig. 1 Correlation between Aggregate TS and KL

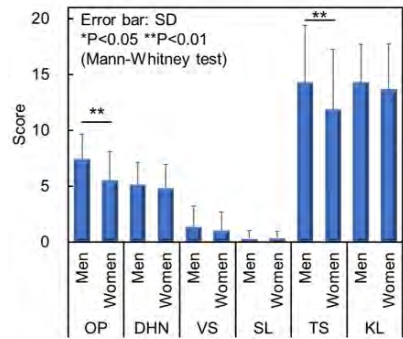


Fig. 2 Scores between men and women

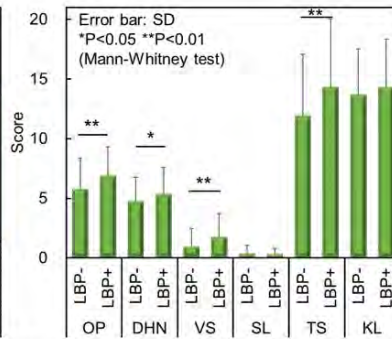


Fig. 3 Scores between the LBP- and LBP+ groups

The longitudinal impact of static intervertebral disc distraction on disc health –magnetic resonance imaging study in a rabbit model

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INTRODUCTION: Intervertebral disc (IVD) degeneration is one of the commonest causes of low back pain. Pharmacological and physical therapy provide only symptomatic relief, while surgical options often predispose to accelerated IVD degeneration at the index or adjacent levels. Potential therapeutic effects of prolonged IVD distraction have yet to be demonstrated.

The aim of this study was to establish an *in vivo*, MRI-compatible rabbit IVD distraction model, to investigate whether this treatment strategy promotes IVD health in a longitudinal study.

METHODS: Seven adult male New Zealand white rabbits were divided into control (n=2), short- (n=2) and long-term (n=3) distraction treatment groups. IVD degeneration was induced by stabbing, and 6 weeks later, treatment group rabbits were implanted with titanium-PEEK IVD distraction devices. IVD hydration and height were evaluated on T2 STIR MRI, and nutrient diffusion was measured on T1 MRI following Gadodiamide injection. MRIs were performed at 7- and 15-weeks post-distraction treatment for the short- and long-term distraction treatment groups respectively. After the last MRI scan, the rabbits were euthanized, and their treated and adjacent spine segments were analyzed via microCT and histology (fast staining). Control group rabbits underwent the same protocol without distraction.

RESULTS: The distraction device was MRI-compatible and generated negligible artefacts. T2-STIR imaging showed that IVD hydration declined faster in the control group than both short term (25.85 ± 10.41 vs 33.26 ± 14.10 ms, $p=0.17$) and long term distraction treatment groups (20.53 ± 6.90 ms vs. 22.09 ± 4.87 ms, $p=0.42$) (**Figure 1A-F**). All stabbed IVDs showed loss of height, which did not improve despite short- or long-term distraction treatment. The disc height loss increase in long term distraction group was slower than control (1.1 ± 0.9 vs 0.85 ± 1.2 mm, $p=0.088$).

Nutrient diffusion was not improved in the short-term distraction group (517 ± 192 vs 727 ± 262 ms, $p=0.23$), but improved in long-term distraction group as compared to the control group (337 ± 151 ms vs. 16.72 ± 796 ms, $p=0.44$). Porosity data on microCT showed that IVD distraction increased vascularity in the long-term distraction group as compared to the control group (30.48 ± 24.93 vs. 23.89 ± 14.09 , $p=0.39$). Histological examination showed that nucleus pulposus (NP) integrity was maintained in both short- and long-term treatment groups (**Figure 1G-I**).

DISCUSSION: The novel MRI-compatible IVD distractor enabled the longitudinal study of IVD health *in vivo* over a 15-week period. Our findings showed that IVD distraction can retard IVD dehydration, improve nutrient diffusion and vascularity, as well as maintain NP integrity in degenerated IVDs. Contrary to a previous study by Kroeber et al. and our control IVD where disc degeneration was induced via disc compression, disc distraction in our current study failed to restore disc height. This difference in findings highlights the integral role of annulus fibrosus integrity in IVD health, and the more severe IVD degeneration induced in this study may explain why distraction failed to restore IVD height. Further studies on the effect of disc distraction on varying grades of disc degeneration should be conducted, in order to further investigate the potential for distraction treatment in improving disc health.

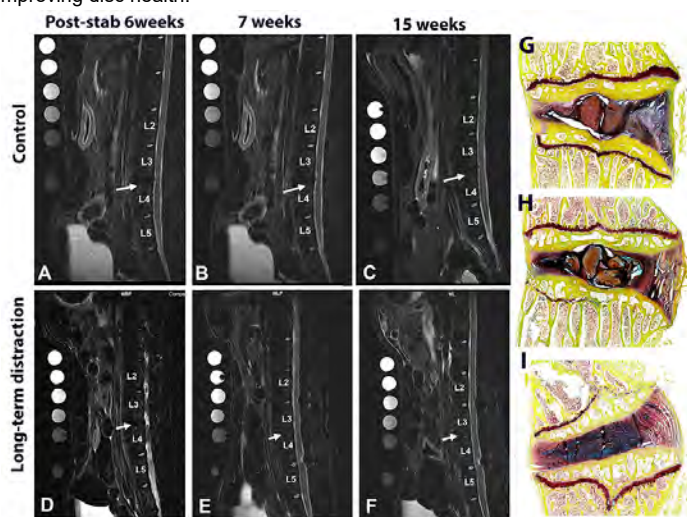


Figure 1A-F T2 Stir MRI image Stabbed IVD was indicated by arrow **G** Control **H** Short-term distraction **I** Long term distraction IVD Histology (Fast staining)
Glycoaminoglycan (Blue), Annulus fibrosus (Red) Bone (Yellowish Green)

Kroeber M, et al. (2005) Effects of controlled dynamic disc distraction on degenerated intervertebral discs: an in vivo study on the rabbit lumbar spine model. Spine (Phila Pa 1976) 30(2):181-187.

SP902

Lactate oxidative phosphorylation by annulus fibrosus cells: Evidence for lactate-dependent metabolic symbiosis in intervertebral discs

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INTRODUCTION: Intervertebral disc degeneration contributes to low back pain. The avascular intervertebral disc consists of a central hypoxic nucleus pulposus (NP) surrounded by the more oxygenated annulus fibrosus (AF). Lactic acid, an abundant end-product of NP glycolysis, has long been viewed as a harmful waste that acidifies disc tissue and decreases cell viability and function. The objective of this study was to determine whether lactic acid or lactate could be used by AF cells as a carbon source rather than being removed from disc tissue as a waste byproduct.

METHODS: Import and conversion of lactate to tricarboxylic acid (TCA) cycle intermediates and amino acids in rabbit AF cells were measured by heavy-isotope (¹³C-lactate) tracing experiments using mass spectrometry. Levels of protein expression of lactate converting enzymes, lactate importer and exporter in NP and AF tissues were quantified by Western blots. Effects of lactate on proteoglycan (³⁵S-sulfate) and collagen (³H-proline) matrix protein synthesis and oxidative phosphorylation (Seahorse XFe96 Extracellular Flux Analyzer) in AF cells were assessed.

RESULTS: Heavy-isotope tracing experiments revealed that AF cells imported and converted lactate into TCA cycle intermediates and amino acids using in vitro cell culture and in vivo models. Addition of exogenous lactate (4 mM) in culture media induced expression of the lactate importer MCT1, and increased oxygen consumption rate by 50%, mitochondrial ATP-linked respiration by 30%, and collagen synthesis by 50% in AF cell cultures grown under physiologic oxygen (5% O₂) and glucose concentration (1 mM). AF tissue highly expresses MCT1, LDH-H, an enzyme that preferentially converts lactate to pyruvate, and PDH, an enzyme that converts pyruvate to acetyl-coA. In contrast, NP tissue highly expresses MCT4, a lactate exporter, and LDH-M, an enzyme that preferentially converts pyruvate to lactate.

DISCUSSION: These findings support disc lactate-dependent metabolic symbiosis in which lactate produced by the hypoxic, glycolytic NP cells is utilized by the more oxygenated AF cells via oxidative phosphorylation for energy and matrix production, thus shifting the current research paradigm of viewing disc lactate as a waste product to considering it as an important biofuel. These scientifically impactful results suggest novel therapeutic targets in disc metabolism and degeneration.

***In-vitro* and *in-vivo* maintenance of rat intervertebral disc homeostasis through Atg5-dependent autophagy**

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INTRODUCTION:

The intervertebral disc is the largest avascular, low nutrient organ. Autophagy is an important cell survival mechanism by self-digestion and recycling damaged components under stress, primarily nutrient deprivation. Our objective is to elucidate the involvement of autophagy in rat disc homeostasis, which has not been uncovered, through the RNA interference (RNAi) technique.

METHODS:

***In-vitro* study:** Disc nucleus pulposus (NP) cells harvested from twelve 12-week-old male Sprague-Dawley rats were used. Small interfering RNA (siRNA) to knockdown an autophagy-essential gene Atg5 was applied by the reverse transfection method. Three different Atg5 siRNA sequences were used to exclude off-target effects. Cells after transfection were cultured in DMEM with or without 10% FBS for 24 h. Expression of an autophagy marker LC3-II and a substrate p62/SQSTM1 as well as Atg5 was measured by Western blotting (WB). Cell viability was assessed by using the Cell Counting Kit-8. Next, cells after transfection were cultured in serum-free DMEM with 10-ng/ml interleukin-1 beta (IL-1 β) for 24 h, and apoptosis and senescence levels were assessed by WB for PARP and caspase-9 cleavage, p16/INK4A, p21/CIP1, and p53.

***In-vivo* study:** Forty-four 12-week-old male Sprague-Dawley rats were used. To confirm *in-vivo* transfection, Atg5 and control siRNAs were injected into respective discs. WB for Atg5, LC3-II, and p62/SQSTM1 was conducted in rat disc NP-tissue protein extracts. To clarify roles of Atg5 in disc homeostasis, a rat tail model of chronic disc degeneration induced by temporary static compression was designed. The Atg5 and control siRNAs were injected into loaded discs as well as unloaded discs. Radiographic, histological, and immunofluorescent assessment was performed for up to 56 d after axial load at 1.3 MPa for 24 h.

RESULTS:

***In-vitro* study:** In rat disc NP cells, Atg5 expression significantly decreased by Atg5 RNAi. The Atg5 RNAi facilitated decreased LC3-II and increased p62/SQSTM1, indicating autophagy inhibition. The Atg5 RNAi significantly decreased cell viability cultured in serum-free DMEM. Pro-inflammatory IL-1 β stimulation induced increases in apoptotic cleaved PARP and caspase-9 and senescent p16/INK4A, p21/CIP1, and p53 expression. Then, Atg5 RNAi developed additional increases in IL-1 β -induced apoptosis and senescence. Atg5 knockdown-dependent reduction in aggrecan and col2 expression was observed.

***In-vivo* study:** WB displayed sustained decreases in Atg5 protein expression at 2, 28, and 56 d. Furthermore, prolonged autophagy suppression by Atg5 RNAi with increased LC3-II and decreased p62/SQSTM1 was observed. In the loaded, Atg5 siRNA-injected disc radiographic disc height significantly decreased compared to unloaded discs and control siRNA-injected discs at 28, and 56 d (28 d, $P=0.006$; 56 d, $P=0.001$). Safranin-O staining showed advanced degeneration the loaded, Atg5 siRNA-injected discs relative to the other conditions. Immunofluorescence showed increases in apoptotic TUNEL-positive cells and senescent p16/INK4a-positive cells of the loaded, Atg5 siRNA-injected discs at 56 d compared to the unloaded, control siRNA-injected discs (TUNEL, $P=0.03$; p16/INK4a, $P=0.02$).

DISCUSSION:

This study demonstrates the involvement of Atg5-dependent autophagy in rat disc NP-cell and NP-tissue homeostasis, which potentially plays protective roles against apoptotic cell death and senescent cell aging. Autophagy is a potent new molecular therapeutic target for intervertebral disc disease.

Involvement of autophagy in human lumbar spine herniated and degenerative disc diseases

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INTRODUCTION: Autophagy is an important cell survival mechanism by self-digestion and recycling damaged components under stress, primarily nutrient deprivation. The intervertebral disc is the largest avascular organ in the body. Resident disc cells may thus utilize autophagy to cope with the harsh low-nutrient environment. However, clinical relevance of disc cellular autophagy is largely unknown. Therefore, an *in-vivo* study was designed. Our objective was to elucidate the involvement of autophagy in human lumbar spine herniated and degenerative disc diseases.

METHODS: Human disc nucleus pulposus (NP) and annulus fibrosus (AF) tissues of 32 patients who underwent lumbar interbody fusion surgery for degenerative disc disease (age, 54.8 ± 19.2 [22–83] yr; male 16, female 16; Pfirrmann degeneration grade, 3.4 ± 0.8 [2–5]) and 12 who underwent micro-endoscopic discectomy for lumbar disc herniation (age, 49.3 ± 19.0 [21–85] yr; male 8, female 4; degeneration grade, 3.1 ± 0.9 [2–4]) were dissected for protein extraction. Western blotting for autophagy marker, LC3-II, autophagy substrate, p62/SQSTM1, and loading control, α -tubulin, was performed. Autophagy-related LC3-II and p62/SQSTM1 expression was analyzed based on the patient age, degeneration grade, and disease type.

RESULTS: First, we assessed autophagy-related protein expression based on the disc degeneration severity. In 12 human disc NP tissues with varying grades 2–5, LC3-II and p62/SQSTM1 levels were both highest in grade-3 and grade-4 discs ($P = 0.049$ in LC3-II between grades 2 versus 4). Next, we analyzed 20 consecutive patient grade-3 and grade-4 disc samples to understand autophagy involvement in human disc aging. Human disc NP tissues in varying ages showed that LC3-II and p62/SQSTM1 levels transiently increased in middle ages of 40–70 but subsequently decreased in older ages of >70 (LC3-II $R^2 = 0.424$, $P < 0.01$; p62/SQSTM1 $R^2 = 0.392$, $P = 0.01$). Human disc AF tissues presented a similar trend (LC3-II $R^2 = 0.546$, $P < 0.01$; p62/SQSTM1 $R^2 = 0.614$, $P < 0.01$). Finally, we compared age-matched and degeneration severity (grades 2–4)-matched 12 patients with degenerative discs requiring fusion surgery and 12 with herniated discs requiring discectomy. Unexpectedly, there were no significant differences in LC3-II and p62/SQSTM1 between degenerative and herniated discs.

DISCUSSION: This is the first study to demonstrate that autophagy is clinically involved in human intervertebral disc degeneration and herniation. Autophagy levels transiently increased in middle-aged and moderately degenerated discs, potentially by stress response. However, autophagy levels subsequently decreased in older-aged and severely degenerated discs, possibly by the reduced stress-response potential. In this study, disc cellular autophagy was dependent on the age and degeneration severity, which would be important in the patient selection for autophagy-modulating molecular therapies. Autophagy modulation could be suitable for treating grade-3 and grade-4 disc disease in middle-aged patients.

Can the COX-2 Inhibitor Celecoxib Influence Discogenic Pain Signals? An In Vitro Study with Inflamed Annulus Fibrosus Cells

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Introduction

The causes of low back pain (LBP) are manifold, while one major cause is the degenerated intervertebral disc (IVD). An inflammatory environment is known to accelerate IVD degeneration. While healthy IVDs are avascular and poorly innervated, increased innervation has been observed in degenerated discs. Nerve endings in the degenerated IVD can be stimulated by the constant inflammation and transmit pain signals to the central nervous system. Thus, counteracting inflammatory responses is a potential therapy for discogenic pain. Inhibition of cyclooxygenase 2 (COX-2) by specific inhibitors like celecoxib has shown promising anti-inflammatory and pain-relieving effects. We hypothesized (1) that inflamed human annulus fibrosus cells (hAFCs) would release factors that sensitize dorsal root ganglion (DRG) cells responsible for the transduction of nociceptive signal, and (2) that celecoxib could inhibit hAFCs-induced DRG sensitization.

Methods

hAFCs were harvested from patients with traumatic disc injury (Pfarrmann grade II-III) with written consent (n=3). Samples (in quadruplicates) were stimulated on day 1 with either TNF- α [10 ng/mL], IL-1 β [10 ng/mL] or a combination of both cytokines [1 ng/mL each] to induce inflammation. On day 2, celecoxib [1 μ M or 10 μ M] was added to the inflamed hAFCs. On day 4, cells were harvested and gene expression levels of matrix metalloproteinases-3 (MMP3), interleukin-6 (IL-6), IL-8, collagen-1 (COL1), COL2, COX-2 and nerve growth factor (NGF) were measured. Unstimulated and untreated cells served as controls. Besides, after 6 day treatment, the conditioned medium from hAFCs was collected and prostaglandin E2 (PGE2), IL-8, IL-6 and NGF concentrations were measured by ELISA. In addition, the conditioned medium was added to DRG cells (rodent cell line, ND7/23). Calcium response to bradykinin (0.5 μ M) in the DRG cells was evaluated using calcium imaging (Fluo-4).

Results

Gene expression levels of IL-6, IL-8, MMP3 and NGF were significantly upregulated after stimulation of hAFCs with TNF- α and/or IL-1 β compared to the control group (p<0.01). Celecoxib treatment at 10 μ M led to an increase in COL2 gene expression in inflamed AFCs; while no significant effect of celecoxib on inflammatory or catabolic genes was observed.

IL-1 β stimulation significantly enhanced the release of PGE2, while this increase was suppressed completely in hAFCs treated with 10 μ M celecoxib (p<0.01). Cytokine treatment of hAFCs also enhanced the release of IL-8 and IL-6, which was reduced by addition of 10 μ M celecoxib (p<0.05).

Bradykinin-induced calcium signal in DRG cells was elevated by conditioned medium of IL-1 β stimulated hAFCs, and was significantly downregulated by 1 μ M or 10 μ M celecoxib treatment (p<0.0001).

Discussion

Celecoxib has a potentially anti-inflammatory effect on prostaglandin and cytokine release of hAFCs in a pro-inflammatory environment *in vitro*. Furthermore, the secretome of IL-1 β stimulated hAFCs induced nerve cell sensitization, which could be counteracted by celecoxib treatment of the hAFCs.

The insights gained from this work are of importance for future studies on local celecoxib application and contribute to a better understanding of the metabolism of inflamed hAFCs and their influence on DRG sensitization and LBP. Translation of the present findings must be confirmed in pre-clinical and ultimately clinical studies.

The pathophysiological duality of Modic Type 1 changes: Transcriptomical differences of infectious and sterile etiology

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Introduction

Modic type 1 changes (MC1) are lumbar signal intensity changes on MRI that highly associate with non-specific low back pain (LBP). An infectious and a sterile etiology of MC1 have been described. In the infectious etiology, the anaerobic aerotolerant *Cutibacterium acnes* (*C. acnes*) invades damaged intervertebral discs (IVDs) resulting in a disc infection and endplate damage, leading to the evocation of an immune response. In the sterile etiology, disc and endplate damage lead to the exposure of normally immune privileged disc cells and matrix to leukocytes, thereby evoking an immune response in the bone marrow.

Different etiologies require different treatment strategies. However, etiology specific pathological processes remain unknown. Additionally, MRI does not allow to distinguish between both etiologies. Hence, there is a strong need to identify etiology specific biomarkers and treatment targets. The aim of this study was to identify etiology specific dysregulated pathways of MC1 serving as base for biomarker and treatment target identification.

Methods

Bone marrow aspirates and IVDs were collected from MC1 patients undergoing lumbar spinal fusion. Presence of *C. acnes* in their IVDs was assessed with bacterial culture and 16S qPCR. In case *C. acnes* was detected, patients were assigned to the infectious etiology, otherwise to the sterile etiology. Aspirates were taken prior screw insertion. From each patient, a MC1 and an intra-patient control (Ctrl) aspirate from an adjacent vertebral body were collected (infectious n=3+3, sterile = 5+5). Bone marrow aspirates were separated with centrifugation into bone marrow plasma and cells. Red blood cells were lysed, RNA was isolated from total bone marrow cells and total bulk RNA sequencing was performed. Genes were considered to be differentially expressed (DEG) if p-value was < 0.01 and log2fc was > ± 0.5.

Results

Comparing MC1 to Ctrl, 204 DEG in the sterile and 444 DEG in the infectious etiology were identified by RNA sequencing (Figure 1a). Sixty-seven genes of both DEGs overlapped (Figure 1b). GO enrichment analysis revealed "T-cell activation" (p = 2.50E-03) in the sterile etiology and "complement activation, classical pathway" (p=1.1E-25) in the infectious etiology as the top enriched upregulated biological process (BP) (Figure 1c). "Adaptive immune response" was among the top dysregulated upregulated GOs in both the sterile (p=3.3E-2) and the infectious (p=7.1E-17) etiology. However, while only B-cell related processes appeared in the infectious etiology, T-cell related processes were dominant in the infectious etiology (Figure 1b). Interestingly, the top 20 upregulated BPs of the infectious etiology included "defense response to bacterium" (p=1.1E-8) (Figure 1c), whereas it was among the top 20 downregulated BPs in the sterile etiology (p=1.6E-2) (not shown).

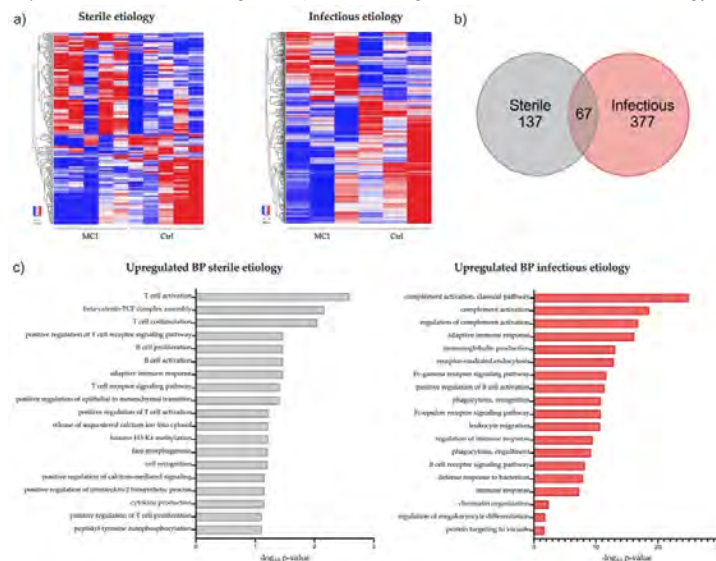


Figure 1: Transcriptomic changes in sterile and infectious MC1 bone marrow. (a) Heatmap of sterile (left) and infectious (right) MC1 compared to intra-patient control. (b) Venn diagram of overlapping DEGs (c) Top enriched upregulated biological processes of sterile (left) and infectious (right) etiology.

Discussion

Sterile and infectious etiologies of MC1 seem to have different pathological mechanisms. This could be explored for diagnostic approaches separating the two MC1 etiologies and supports developing targeted treatment for both etiologies.

Type III collagen is a hallmark of the fibrotic pathomechanism in Modic type 1 changes and is linked to myofibroblast differentiation

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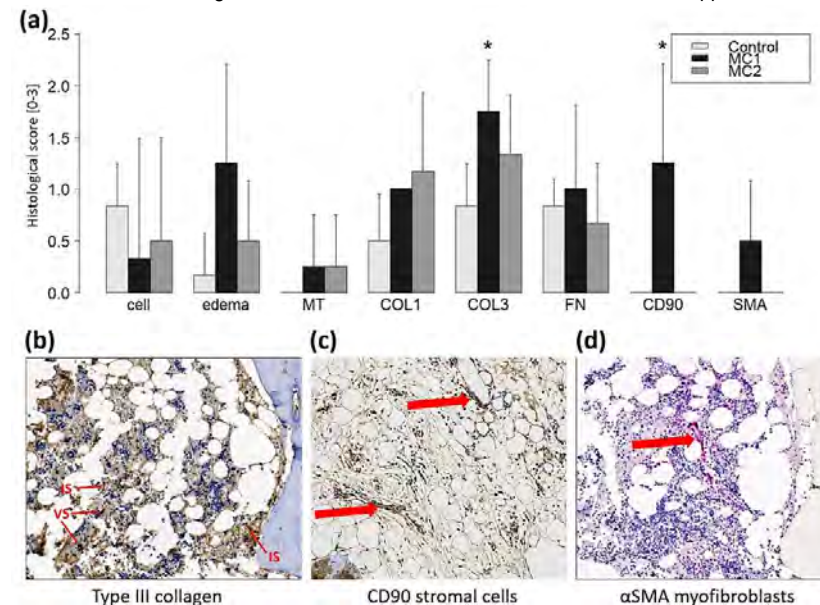
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Introduction: Modic changes (MC) are specific for chronic low back pain. Despite the high prevalence of MC, the histopathology of MC remains poorly understood. There are only two historical studies that describe MC histology based on the analysis of three hematoxylin/eosin stained biopsies (1, 2). They described Modic type 1 changes (MC1) as vascularized fibrous tissue and Modic type 2 changes (MC2) as fibrotic adipose marrow replacement. While fibrosis seems to be important in MC1 and MC2, no molecular data is available that would help to understand the MC pathomechanism. The aim was to characterize MC histopathology with histology and immunohistochemistry (IHC) to better understand MC pathomechanism.

Materials and Methods: From patients undergoing lumbar spondylodesis, vertebral bone marrow biopsies (n=4 MC1, 4 MC2, 6 control) were taken through pedicle screw trajectory before screw insertion. Intraoperative X-ray confirmed correct placement of biopsy needle. MC and degeneration of the adjacent disc were rated by an experienced radiologist based on T1- and T2-weighted MR images. Fixed biopsies were analyzed with histology and IHC. Histology/IHC: sections were stained histologically with eosin/hematoxylin to assess cellularity and edema (seen as interstitial water), and with Masson trichrome to assess connective tissue. IHC staining for type I and type III collagen, and cellular fibronectin was done to assess fibrosis. Bone marrow stromal cells (BMSC) were quantified with CD90 staining and myofibroblasts were quantified with alpha smooth muscle actin (αSMA) staining. Tissue sections were scored (0-3) by an experienced pathologist. Scores were compared between different groups (MC1, MC2, Ctrl) using Kruskal-Wallis test with Holm's p-value adjustment.

Results: There was no difference between groups in mean age 65±14 years (p=0.63) and sex (11/14 male, p=0.99) of the patients. Discs were all strongly degenerated (Pfirman grad 4-5) in all groups (p=0.90). MC1 had more type III collagen (MC1=1.75, Ctrl=0.75, p=0.03), that was located interstitially (IS) and in basement membranes of vascular sinusoids (VS) (Fig. a-b). MC1 also had more CD90-positive stromal cells (MC1=1.25, Ctrl=0, p=0.01) (Fig. a,c) and more αSMA-positive myofibroblasts (MC1=0.5, Ctrl=0, p=0.06) (Fig. a,d). No elongated CD90 or αSMA positive cells were found in Ctrl biopsies. Type I collagen also tended to be more abundant in MC (MC1=1.0, MC2=1.2, Ctrl=0.5, p=0.12). No significant differences were found with the other stains and for all stains in MC2.

Discussion: We found that collagen type III is an important mediator of MC1 bone marrow fibrosis. This may be linked more BMSC and the occurrence of myofibroblasts in MC1. Type III collagen turnover has recently been suggested as biomarker for MC (3). Here, we provide face validity for such serum biomarker. More BMSC and myofibroblast in MC1 indicate BMSC proliferation and their differentiation into pro-fibrotic myofibroblasts. In conclusion, fibrosis is an important pathomechanism in MC1 that should be targeted in biomarker studies and anti-fibrotic treatment approaches targeting BMSC should be considered.



Endplate Volumetric Bone Mineral Density Is a Predictor for Cage Subsidence following Lateral Lumbar Interbody Fusion: A Risk Factor Analysis

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INTRODUCTION:

Lateral lumbar interbody fusion (LLIF) is a common procedure used for various spinal conditions. One of the common complications of this procedure is subsidence, which is the sinking of the interbody device into adjacent vertebrae. Previous work has shown that a decreased BMD as measured by DXA is a risk factor for subsidence, but emerging data suggests a lower endplate volumetric BMD (EP-vBMD) as measured by quantitative computed tomography is a risk factor for subsidence following standalone LLIF. However, it remains unclear if this is the case for LLIF with posterior screws. Additionally, there is interest in the role that patient factors, such as BMI and diabetes status, plays on bone quality. The purpose of this study is to investigate risk factors for subsidence following LLIF.

METHODS:

We reviewed the data of consecutive patients undergoing LLIF from 2014 to 2019 at a single academic institution who had over 5 months of follow-up and radiological imaging between 5 and 14 months after surgery. We excluded levels with previous instrumentation, previous fractures, and poor imaging quality. Cage subsidence was measured using the grading system devised by Marchi et al.¹ As potential contributing factors for cage subsidence, we collected preoperative body mass index (BMI) along with diabetes status. We measured both EP-vBMD and the trabecular volumetric BMD measurement of the vertebral body (VB-vBMD). EP-vBMD was defined as the average of the upper and lower endplate vBMDs measured in cortical and trabecular bone with a 5 mm thickness region of interest beneath the cage contacting surfaces (Figure 1). Univariable analysis and multivariable logistic regression analyses with a generalized mixed model were conducted. For the multivariable analysis, we included BMI, diabetes status, EP-vBMD, VB-vBMD, and all trending ($p < 0.20$) factors in univariable analyses as explanatory variables. The statistical significance level was set at $p < 0.05$.

RESULTS:

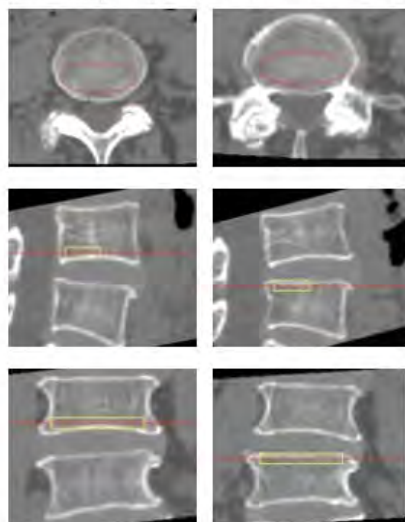
567 levels in 347 patients were included in the final analysis. Mean age (\pm SD) was 61.7 ± 11.1 yrs. 50.3% of the patients were male. 134 (38.7%) patients were overweight, 114 (32.9%) were obese, and 45 (13%) were diabetic. Subsidence with a grade of at least 1 was observed in 160 levels (28.2%). After adjusting for age, American Society of Anesthesiologists Physical Status, Charlson comorbidity index, LLIF level, and VB-vBMD, standalone status ($p = 0.001$) and EP-vBMD ($p = 0.032$) were associated with subsidence. ROC curve analysis demonstrated a cutoff of 211 kg/m^2 for EP-vBMD. Ad hoc analysis demonstrated patients with no risk factors had subsidence at 18.3% of levels, 31.1% of levels with one risk factor, and 44.9% of levels with both risk factors ($p < 0.0001$).

DISCUSSION:

A decreased local EP-vBMD and the absence of posterior screws are risk factors for subsidence following LLIF. When performing LLIF, the preoperative EP-vBMD measurement should be considered, and in patients with a low EP-vBMD, the addition of pedicle screws could be included to limit the risk of subsidence.

FIGURE LEGENDS:

Figure 1. Example endplate volumetric bone mineral density measurement.



Marchi L, Abdala N, Oliveira L, Amaral R, Coutinho E, Pimenta L. Radiographic and clinical evaluation of cage subsidence after stand-alone lateral interbody fusion. *J Neurosurg Spine*. 2013;19(1):110-118. doi:10.3171/2013.4.SPINE12319

Gluteus maximus atrophy affects postoperative deterioration of sagittal alignment after short segment corrective fusion for adult spinal deformity

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Introduction

Previous studies on lumbar degenerative kyphosis reveal that kyphotic patients have significantly smaller lumbar muscle. In addition to muscles located in the lumbar spine region, gluteal muscles may also contribute to maintenance of sagittal alignment especially after multilevel lumbar fusion surgery. The aim of this study is to investigate the association between the cross-sectional area (CSA) of gluteus maximus in magnetic resonance imaging (MRI) and radiographic and clinical assessment of short segment corrective fusion for adult spinal deformity (ASD).

Methods

A total of 34 consecutive patients had undergone posterior corrective fusion for ASD in our hospital. Seventeen patients who could undergo hip MRI after surgery were retrospectively reviewed. They were 2 males and 15 females with a mean age 71 years (range 56–83 years). Surgical procedures were pedicle subtraction osteotomy in 9 patients and transforaminal lumbar inter body fusion with Ponte osteotomy in 8 patients. Length of fusion was 5.5 segments in average (4-7 segments). Radiographic parameters included lumbar lordosis (LL), thoracic kyphosis (TK), pelvic tilt (PT) and sagittal vertical axis (SVA). Clinical outcomes were evaluated by visual analog scale (VAS) of back pain and Roland-Morris Disability Questionnaire (RDQ). We divided the patients into 2 groups: maintenance group (group M) and progression group (group P). Group M included patients with less than 5cm anterior deviation of SVA after surgery and group P included patients with 5cm or more. CSA of gluteus maximus was measured by axial MRI at the center of femoral head level. Gluteus maximus CSA ratio was calculated as muscle CSA normalized by femoral head CSA. We compared gluteus maximus CSA ratio, PT, LL, TK, VAS and RDQ between group M and P. Student's t-test was used for statistical analysis with $P < 0.05$ considered to indicate statistical significance. Mean follow-up period was 56 months.

Results

Anterior deviation of SVA was 12.6cm before surgery, 6.4cm after surgery, and changed to 13.2cm at the final follow-up. Five patients were included in group M and 12 patients were included in group P. Mean gluteus maximus CSA ratio in group P and M were 2.6 and 3.4, respectively ($P < 0.05$). Postoperative individual variations of PT, LL and TK were 3 degrees, -12 degrees and 3 degrees in group P versus 10 degrees, -4 degrees and 5 degrees in group M (PT: $P < 0.05$, LL: $P = 0.078$, TK: $P = 0.701$). VAS of back pain in group P and M improved from 71/100 to 42/100 and 71/100 to 8/100, respectively. RDQ in group P and M improved from 13.4 to 8.6 and 15.6 to 1.2 in group M. The final follow-up VAS and RDQ in group M were significantly lower than group P (VAS: $P < 0.05$, RDQ: $P < 0.05$).

Discussion

The gluteus maximus CSA ratio and the variation of PT in SVA progression group were significantly smaller than SVA maintenance group. These data suggested that atrophic gluteus maximus didn't enable to compensate sagittal malalignment and caused deterioration of SVA. Gluteus maximus may be a key factor for maintenance of sagittal alignment after short segment corrective fusion for ASD.

Does sarcopenia affect short-term clinical outcomes following posterior/transforaminal lumbar interbody fusion?

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[Introduction] According to Asian Working Group for Sarcopenia (AWGS) criteria, sarcopenia should be diagnosed by muscle volume and muscle strength and/or physical performance: height-adjusted appendicular skeletal muscle mass index (ASM) by dual energy X-ray absorptiometry (DXA), handgrip strength and 6 minutes walking test representatively. To our knowledge, there are few studies defining sarcopenia with handgrip strength and DXA, and evaluating sarcopenia patients' clinical outcomes after spinal fusion. The purpose of this study is to clarify the effect of sarcopenia, defined by AWGS2019 protocols, on clinical outcomes of posterior lumbar interbody fusion or transforaminal lumbar interbody fusion (PLIF/TLIF).

[Methods] Patients over 60 years undergoing PLIF/TLIF for lumbar degenerative disease from January to June 2020 were retrospectively analyzed. Patients were separated into sarcopenia or non-sarcopenia cohorts according to AWGS criteria: patients whose ASM were under 7.0kg/m² in men and 5.4kg/m² in women and whose handgrip strength were under 28kg in men and 18kg in women were placed into the sarcopenia cohort. Patient reported clinical outcomes and sagittal spinal alignment were collected. The data were analyzed with the two-tailed Student *t*-test.

[Results] Of the 62 patients, 7 patients (11.3%) were classified as the sarcopenia cohort. Mean follow-up period was 8 months (range 6 -10months). The sarcopenia cohort had significant lower BMI than non-sarcopenia cohort (20.9 vs 24.5, *p* =0.012), whereas there is no significant difference between two groups in age and sex. Comparing the sarcopenia cohort to non-sarcopenia cohort, with regards to the Oswestry disability index (ODI), there was no significant difference preoperatively (59.7 vs 48.1, *p*=0.63) and postoperatively (37.1 vs 32.0, *p*=0.41). Concerning Roland-Morris disability questionnaire (RDQ), there were no significant differences preoperatively (16.0 vs 12.4, *p*=0.17) and postoperatively (6.4 vs 7.4, *p*=0.69). The Japanese orthopedic association (JOA) score showed no significant difference preoperatively (11.3 vs 13.4, *p* = 0.27), postoperatively (22.1 vs 21.8, *p*= 0.81). Visual analogue scale (VAS) of low back pain scores showed also no significant differences preoperatively (56.1 vs 64.2, *p* = 0.53) and postoperatively (11.7 vs 17.8, *p* = 0.40). Anterior deviation of sagittal vertical axis (SVA) is significant larger in the sarcopenia cohort than in non-sarcopenia cohort preoperatively (92.3 vs 52.5, *p*=0.026) and postoperatively (70.2 vs 36.3, *p* =0.019).

[Discussion] There were no significant differences in ODI, RDQ, JOA score or VAS scores between the sarcopenia and non-sarcopenia cohort either preoperatively and postoperatively. Sarcopenia does not affect short-term clinical outcomes following PLIF/TLIF for patients with lumbar degenerative disease.

The prevalence of sarcopenia in our study was 11.3%, which is consistent with the past literature. Majority of earlier studies defined sarcopenia with only DXA or cross-sectional area on CT/MRI of psoas or paraspinal muscle. Only the measurement of muscle mass might not reflect precise sarcopenia prevalence. Due to the definition of AWGS criteria, this study is based on the actual sarcopenia prevalence.

Anterior deviation of SVA was larger in sarcopenia cohort both preoperatively and postoperatively. Sarcopenia patients couldn't improve sagittal malalignment as they had lost trunk muscle mass and strength to maintain optimal standing posture gained by PLIF/TLIF.

Design and Implementation of an Enhanced Recovery After Surgery (ERAS) Protocol in Elective Lumbar Spine Fusion by Posterior Approach: A Retrospective, Comparative Study

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Introduction: Despite wide adoption in other surgical disciplines, ERAS has only been recently implemented in spine surgery. The integrated multidisciplinary approach of ERAS aims to reduce surgical stress to achieve better outcomes. The ERAS movement represents a paradigm shift in the care of surgical patients – from a traditional 'healthcare-centric' approach wherein a patient's surgical journey is broken down into different stages overseen by different teams, to a 'patient-centric' approach with a seamless integration of these stages and a blurring of boundaries between healthcare providers and teams involved in the treatment. The objectives of the study were: i) To design an enhanced recovery after surgery (ERAS) protocol for elective lumbar spine fusion by posterior approach, ii) To compare the results after ERAS implementation in patients undergoing elective lumbar spine fusion with conventional perioperative care.

Methods: Hospital records of adult patients who underwent 1- to 3-level elective lumbar spine fusion by posterior approach at a single centre were retrospectively studied. An ERAS protocol was designed based on the prevalent hospital practices, local resources and supportive evidence from literature. The ERAS protocol was implemented at our institute in December 2016 – dividing patients into pre-ERAS and post-ERAS groups. The outcome measures for comparison were: length of hospital stay (LOS), postoperative complications, 60-day readmission rate, 60-day reoperation rate and patient reported outcome measures (VAS and ODI score) at stipulated time intervals.

Results: A total of 812 patients were included – 496 in the pre-ERAS group and 316 in the post-ERAS group. There was no significant difference between the two groups in baseline demographic, clinical and surgery-related variables. Patients in the post-ERAS group had a significantly shorter LOS (2.94 days v/s 3.68 days). The rate of postoperative complications (13.5% v/s 11.7%), 60-day readmission (1.8% v/s 2.2%) and 60-day reoperation (1.2% v/s 1.3%) did not differ significantly between the pre-ERAS and post-ERAS groups. The VAS and ODI scores, similar at baseline – were significantly lower in the post-ERAS group (VAS: 49.8 ±12.0 v/s 44 ±10.8, ODI: 31.6 ±14.2 v/s 28 ±12.8) at 4 weeks after surgery. This difference however was not significant at intermediate term follow up (6 months and 12 months).

Discussion: The components of the ERAS protocol have differed across studies. However, the theme underlying an ERAS protocol remains the same – mitigating the stress (physiological, psychological, social and economic) placed by the surgery on the patient. Through this study, we highlight the feasibility of applying ERAS to elective lumbar spine fusion surgery in a developing country. We emphasize the importance of team effort, staff training and motivation, use of an evidence-based approach and adapting the ERAS protocol to available resources and local institutional culture. Implementation of an ERAS protocol is feasible for elective lumbar spine fusion, and leads to shorter LOS and improved early pain and functional outcome scores.

SP912

Preoperative MRI-based Vertebral Bone Quality (VBQ) Score Assessment in Patients undergoing Lumbar Spinal Fusion

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Introduction: The importance of bone quality assessment in spine surgery is well recognized. The current gold standard for assessing bone mineral density is dual-energy X-ray absorptiometry (DEXA), however the majority of patients undergoing spinal fusion do not have preoperatively available DEXA data. Furthermore, DEXA has been shown to overestimate BMD in patients with spinal degenerative disease and obesity. Consequently, alternative radiographic measurements using data routinely gathered during preoperative evaluation have been explored for the evaluation of bone quality and fracture risk. Opportunistic quantitative computed tomography (QCT) and more recently the MRI-based vertebral bone quality (VBQ) score both have been shown to correlate with DEXA T-scores and predict osteoporotic fractures. However, to date the correlation between those two modalities has not been studied. The objective of this study was to assess whether the VBQ score can predict the prevalence of QCT based osteopenia/osteoporosis and to evaluate the correlation between those two modalities.

Methods: Patients undergoing lumbar fusion from 2014-2019 at a single, academic institution with available preoperative lumbar CT and T1-weighted MRIs were included. Asynchronous QCT measurements were performed. The average L1-L2 BMD was calculated and patients were categorized as either normal BMD (>120 mg/cm³) or osteopenic/osteoporotic (≤120 mg/cm³). The VBQ score was calculated by dividing the median signal intensity of the L1-L4 vertebral bodies by the signal intensity of the cerebrospinal fluid on midsagittal T1-weighted MRI images. To assess inter-observer reliability of the VBQ measurements, a validation study was performed. Demographic data and the VBQ score were compared between the normal and osteopenic/osteoporotic group. To determine the area-under-curve (AUC) of the VBQ score as a predictor of osteopenia/osteoporosis receiver operating characteristic (ROC) analysis was performed. VBQ scores were compared with QCT BMD using Pearson's correlation.

Results: A total of 198 patients (53% female) were included. The mean age was 62 years and the mean BMI was 28.2 kg/m². The inter-observer reliability of the VBQ measurements was excellent (ICC of 0.90). When comparing the patients with normal QCT BMD to those with osteopenia/osteoporosis, no significant differences existed in terms of sex, race, and BMI. However, the patients with osteopenia/osteoporosis were significantly older compared to the patients with normal BMD (64.9 vs 56.7 years, p<0.0001). The osteopenic/osteoporotic group had significantly higher VBQ scores (2.6 vs 2.2, p<0.0001). ROC analysis revealed that the VBQ score predicts the presence of osteopenia/osteoporosis based on QCT with an accuracy of 71% (p<0.0001). The VBQ score showed a statistically significant moderate correlation with QCT BMD (correlation coefficient = -0.358, p<0.001).

Discussion: This is the first study to correlate MRI VBQ scores with QCT BMD. We found that the VBQ score significantly differentiates patients with normal BMD versus osteopenic/osteoporotic BMD based on QCT. However, the correlation between both modalities was only moderate suggesting that VBQ might not solely be a measurement of bone density, but rather bone quality. Since the two modalities seem to reflect different properties of bone, VBQ may be an interesting adjunct to clinically performed bone density measurements, rather than a substitution.

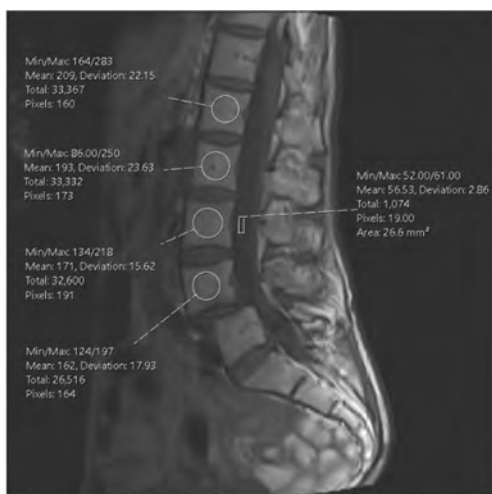


Figure 1: Representative image of a VBQ measurement

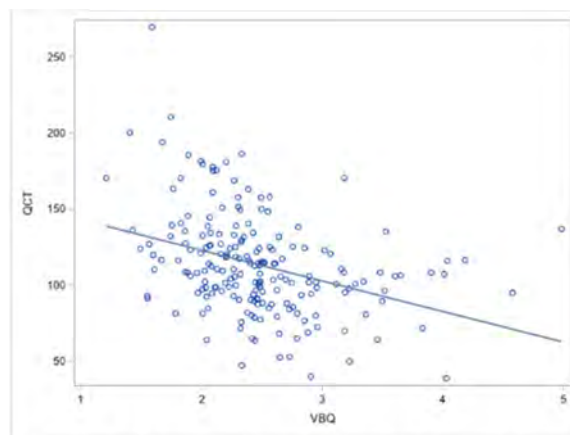


Figure 2 Correlation between VBQ score and BMD measured by QCT

SP913

The Platelet derived from induced pluripotent stem cells accelerates bone union with adequate rigidity in posterolateral lumbar fusion surgery model in rats

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【Background and purpose】 The early and rigid bone union is a major issue in spinal fusion surgery. In our previous studies, we have confirmed that platelet-rich plasma (PRP) has a bone fusion promoting effect. On the other hand, it is difficult to stably procure autologous blood-derived PRP from all patients. In recent years, a method for producing a large amount of artificial platelets characterized by being deficient in human leukocyte antigen (HLA) and suppressing the autoimmune response, has been established by iPS cell technology. The purpose of this study is to confirm the safety and efficacy of universal type artificial platelet preparations based on the fundamental mechanism of bone remodeling by platelets.

【Subjects and methods】 iPS cell-derived megakaryocytes are cultured for 10 days, centrifuged to extract concentrated platelets and megakaryocyte fluid, and then freeze-dried after irradiation to formulate them. Major cytokines (PDGF, TGF- β , VEGF, BMP) were measured by the ELISA method for the purpose of evaluating pharmacological activity. We also evaluated the cell proliferation ability by adding a preparation during osteoblast culture. The bone fusion promoting effect using animals as a safety study, 8-week-old SD rats were used (n = 36), and a lumbar posterior lateral fusion model was created and transplanted between the transverse processes. It was divided into the following three groups according to (1) Artificial bone alone group, (2) Artificial bone + peripheral blood-derived PRP group, (3) Artificial bone + iPS cell-derived platelet preparation group. Bone fusion was evaluated 2, 4 and 6 weeks after surgery. In addition, a histological evaluation (bone formation amount, characteristics of trabecula involved in bone strength) and a mechanical strength test were performed 6 weeks after the operation. We investigated the appearance of adverse events such as tumorigenesis, hyperinflammation, and infection.

【Results】 The iPS cell-derived platelet preparation contained many cytokines, and the BMP content was significantly higher than that of peripheral blood-derived PRP. The proliferative capacity of osteoblasts was clearly increased when the preparation was added during osteoblast culture. In animal experiments, the earliest and highest amount of high-quality bone formation was observed in the artificial bone + iPS cell-derived platelet preparation group. And, no adverse events such as tumorigenesis were observed.

【Discussion】 In this study, various experiments suggested the effect of iPS cell-derived platelet preparation on promoting bone fusion. In the future, by preparing a large amount of preparation from iPS cells and lyophilizing, it will be possible to supply this preparation as a material when needed. It is expected that existing preparations will effectively promote early bone fusion in fractures and spinal surgery without invasion of patients or burden on medical staff.

【Conclusion】 The iPS cell-derived platelet preparation includes many kinds of cytokines and have an effect of promoting early and rigid bone union.

Trunk muscle mass is associated with low back pain, spinal malalignment, and physical function in female patients with lumbar spinal stenosis

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INTRODUCTION: It was recently reported that trunk muscle mass was significantly associated with low back pain, Oswestry Disability Index score, and sagittal vertical axis (SVA) in patients with spinal diseases, and was more strongly related to spinal pathology than appendicular skeletal muscle mass.¹ We also found that muscle mass, and physical performance and physical function as assessed by the 36-item Short-Form Health Survey (SF-36) were lower in patients with lumbar spinal stenosis (LSS) and sarcopenia than in those without sarcopenia. Patients with LSS also reported more severe low back pain.² However, the associations between trunk muscle mass and clinical features of LSS are poorly understood. The purpose of this study was to identify factors associated with trunk muscle mass in patients with LSS.

METHODS: This cross-sectional study was conducted at our institute from September 2017 to December 2018 and included patients presenting with symptoms of neurogenic claudication caused by LSS confirmed by magnetic resonance imaging. Patients with a history of previous spinal surgery or cognitive impairment were excluded. Trunk muscle mass was measured using bioelectrical impedance (InBody S10; BioSpace, Seoul, Korea). We collected data on hand grip strength, 5-m gait speed, numerical rating scale (NRS) of low back pain, leg pain, leg numbness, SF-36 scores, bone mineral density (BMD), and radiographic measurements (SVA, thoracic kyphosis, lumbar lordosis, pelvic tilt, pelvic incidence, sacral slope, percentage slip, and number of vertebral fractures). Spearman correlational analyses were used to identify relationships between trunk muscle mass and physical performance, NRS, SF-36, BMD, and radiographic measurements.

RESULTS: Sixty-four men and 94 women (average ages: 73.5 and 72.9 years, respectively) were enrolled. In men, trunk muscle mass correlated significantly with hand grip strength ($r = -0.710$), and role-physical ($r = 0.388$) and role-emotional ($r = 0.280$) as assessed by the SF-36. In women, trunk muscle mass correlated significantly with hand grip strength ($r = -0.478$), gait speed ($r = -0.478$), physical function ($r = 0.238$), role-physical ($r = -0.248$), bodily pain ($r = 0.231$), general health ($r = 0.264$), and social functioning ($r = 0.236$) as assessed by the SF-36, low back pain as assessed by the NRS ($r = -0.356$), lumbar spine ($r = 0.310$) and femoral neck ($r = 0.353$) BMD, and sacral slope ($r = 0.239$) ($P < 0.05$).

DISCUSSION: In female patients with LSS, lower trunk muscle mass was associated with severe low back pain, spinal malalignment, and poorer physical function. Trunk muscle mass plays an important role in the ability to perform activities of daily living in women with LSS but not in men with LSS.

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2. Matsuo S, Kawakami M, Minetama M, et al. Clinical Features of Sarcopenia in Patients With Lumbar Spinal Stenosis. *Spine.* 2020; 45: E1105-10

SP915

How Effective is Therapeutic Exercise for Back Pain in the Patients with Adult Spinal Deformity?; An analysis focused on minimal clinically important difference

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Introduction

One of the most recommended conservative treatment for patients with adult spinal deformity (ASD) is a therapeutic exercise. Although the benefits of back muscle strengthening exercise have been reported, the effectiveness on QOL and physical functions remains to be clarified. The purposes of the current study were to investigate whether exercise can provide clinically significant improvement in a patient-reported outcome and to determine risk factors predictive of treatment failure.

Methods

This is a retrospective cohort study. Fifty-two ASD patients with back pain were managed with therapeutic exercises. The cases were all female with a mean age of 70.8 years. The ASD was defined based on SRS-Schwab classification. The patients had undergone the exercise on outpatient-basis for more than 3 months. It consisted of a 40-minute exercise every week at the outpatient, accompanied by home-exercise for more than 3 days a week. It aims to improve muscle strength, endurance, and range of motion (ROM) of trunk and lower extremities. The primary outcome measures were the Oswestry Disability Index (ODI), Numeric Pain Rating Scale (NPRS). To determine the treatment effect, minimal clinically important difference (MCID) was used. Based on previous studies, an improvement of at least 10 points in ODI and 20 points in NPRS was considered as a treatment success. Secondary outcome ones included physical function such as muscle strength and ROM of trunk and hip joints. Statistical analysis was conducted using the Wilcoxon signed-rank test to compare the results between pre- and post-treatment. Logistic regression analysis was used to determine the risk factors being predictive of treatment failure. Statistical significance was defined as a p-value of less than 0.05.

Results

Improvement was confirmed in both ODI and NPRS. Twenty-four patients (46.2%) met the MCID for improvement in ODI. The severe sagittal vertical axis (SVA), the restriction of lumbar extension ROM and hip extension ROM were the predictors of treatment failure for ODI. Twenty-seven patients (51.9%) met the MCID for improvement in NPRS. Severe SVA was predictive of treatment failure.

Discussion

The current study demonstrated that therapeutic exercise was effective beyond MCID in terms of QOL and back pain in an approximate 50% patients with ASD. It might be attributed to the improvement of physical function such as muscle strength and ROM. The risk factors for treatment failure included severe SVA, restriction of lumbar extension ROM and hip extension ROM.

AMEC ASD Exercise: Devised by AMEC

ROM ex.

Trunk ext ROM



Trunk muscle strengthening ex.

Trunk ext strength



Hip ext ROM



Trunk flex strength



SP916

Obesity is associated with poor paraspinal muscle quality at upper lumbar levels and degenerated spine at lower lumbar levels: Is this a domino effect?

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Introduction: Vertebral end-plate changes and paraspinal muscles are recently getting much more attention, since they could be associated with intervertebral disc degeneration (IVDD) and low back pain (LBP). Even though obesity is known as a risk factor for LBP, the role of obesity in the process of LBP is still controversial. In this study, we aimed to identify whether increased body mass index (BMI) was associated with IVDD, vertebral end-plate changes and paraspinal muscle quality.

Methods: Consecutive women and men, aged between 20 and 50 years, presented with chronic LBP to the outpatient clinics were included. Patients were evaluated in terms of IVDD, vertebral end-plate changes, fatty infiltration in the paraspinal muscles at all lumbar levels on magnetic resonance imaging.

Results: Severe IVDD was more common in obese patients than in non-obese patients (73.5% vs. 50.4%, $p=0.017$). When we compared the groups level by level, the significant difference for severe IVDD was present only at L4-L5 disc level (50% vs. 27.4%, $p=0.013$). There was a higher trend of harboring Modic change at any lumbar level in obese patients, significantly in women (35.9% vs. 16.4%, $p=0.026$). More severe fatty infiltration in the paraspinal muscles was seen at upper lumbar levels of the obese patients, particularly in the women.

Discussion: Patients with higher BMI and suffering from LBP had more fatty infiltration in their paraspinal muscles at upper lumbar levels, more severe IVDD and Modic changes at lower lumbar levels, particularly in women. The different degeneration patterns in overweight/obese patients might require different prevention and treatment strategies for LBP besides controlled weight loss. Future studies are required to understand the exact mechanism of this pathology in a prospective manner. One last statement would be for paraspinal muscles: Evaluation of the paraspinal muscles should not be limited to only a certain lumbar level, since lumbar spine does not consist of only one level.

Effect of Posture on Lumbopelvic Muscle Morphometry and Geometry in Adult Spinal Deformity Patients from Upright MRI

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INTRODUCTION: Adult spinal deformity (ASD) affects 60% of aging adults in some form. Previously, bone and disc conditions were thought to be the primary cause, however more recent work is starting to highlight the importance of lumbopelvic musculature. Currently though, the upright characteristics of lumbopelvic muscle morphometry are not well understood, and an improved understanding could help inform mitigation and treatment of ASD. Therefore, the aim of this study was to assess the effect of posture on lumbopelvic musculature and geometry in ASD patients using upright magnetic resonance imaging(MRI).

METHODS: Eight pre-operative ASD patients were imaged in a 0.5T upright MRI (MROpen, Paramed) at the lumbopelvic region (sequence parameters and alignment in Table 1). Patients were scanned in 5 postures: standing, standing arms unsupported, standing arms supported, standing 30° flexion and supine. Muscle cross-sectional area (CSA), signal intensity (SI), and position (radius, angle) were measured for the psoas major, multifidus/erector spinae combined, gluteus (maximus, medius, minimus combined) and iliopsoas. SI, representing fatty infiltration, was reported as the average pixel intensity of the muscle normalized by that of the posterior fat. Side-to-side parameters were relative to coronal standing clinical X-ray concavity—concave on apex side, versus convex. Geometry measurements included lumbar vertebra rotation, pelvic tilt (PT), pelvic incidence (PI), sacral slope (SS), and L3-S1 lumbar lordosis (LL). The effect of posture, level, and side was evaluated by ANOVA(p<0.05) and intra-rater repeatability was assessed using intraclass correlation coefficient(ICC(3,1)).

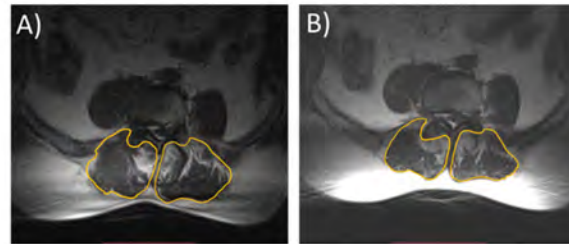
RESULTS: Posture had significant effects and interactions on lumbopelvic parameters. This includes an effect of posture on multifidus/erector spinae CSA and radius. From flexion to other postures, CSA increased up to 11% and radius increased up to 4%(Fig.1). There was also an effect of level on SI, where L3/L4 to L5/S1, SI increased by 21% for the multifidus/erector spinae. For the psoas major, there was a level dependent effect of posture on radius, and an effect of posture on angle. Additionally, for the psoas major there was a level dependent effect of side on CSA where at L3/L4, convex to concave, CSA decreased by 16%. In the pelvis, there was a level dependent effect of posture on gluteus CSA, SI, and radius, and on iliopsoas CSA and radius. At S4/S5, from standing to supine, gluteus CSA increased by 17%. For geometry, posture affected PT, SS, and LL, but not PI. The intra-rater repeatability was 0.52-0.97(CSA) and 0.91-0.97(geometry).

DISCUSSION: This study confirms some findings from previous supine studies and highlights some new postural effects and trends. Previous scoliosis studies demonstrated increased convex multifidus and psoas CSA [1]–[3], which was also observed for the psoas (L3/L4) in this study. Additionally, the increasing multifidus fatty infiltration with decreasing level was similarly observed in previous degenerative kyphosis studies [4], [5]. The added postural results highlight the potential influence of posture when studying ASD lumbopelvic musculature. The generally good repeatability also supports feasibility of upright imaging of lumbopelvic muscle and geometry in tandem.

Table 1: Imaging parameters

Region/Anatomy	Sequence	Alignment	T/RTE (mm)	FOV (mm)	Scan matrix	Slice thickness (mm)	NEA	Scan time (s)
Lumbar Muscle Morphometry & Rotation	T1-weighted Spin Echo	3 axial stacks, aligned to midsagittal plane at L3/L4, L4/L5, L5/S1	300x12	35	224x160	7.07 gap	1	1:11
Lumbar Geometry	T1-weighted Gradient Field Echo	3 Sag. midline spine slices, L3-S1	447	35	192x128	15.7 gap	1	1:14
Pelvic Muscle Morphometry	T1-weighted Spin Echo	Axial stack, L5-concave	537x13	40	224x160	7.07 gap	1	1:14
Pelvic Geometry	T1-weighted Spin Echo	Sagittal stack, femoral head to midline spinal column on right	324x13	34	204x162	10.7 gap	1	1:36

Fig.1: Multifidus/erector spinae L4/L5, CSA decreased 11% standing(A) to flexion(B)



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The natural course of the paravertebral muscles after the onset of osteoporotic vertebral fracture

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Introduction: This study revealed the change in the paravertebral muscles in patients with osteoporotic vertebral fracture. Increased pain is likely to be the driver for reduced activity, reduced activities of daily living, and consequent increase in fat infiltration of the paravertebral muscles, assumed to be secondary to reduced activity level or, conversely, partial immobilization.

Aim: To reveal the time courses and impact of the paravertebral muscles (PVMs) on the healing process of osteoporotic vertebral fractures and risk factors for PVM decrease.

Methods: Consecutive patients with symptomatic osteoporotic vertebral fractures were enrolled in 11 hospitals. At enrollment and 3- and 6-month follow-up, PVMs, including the multifidus and erector spinae, were examined using magnetic resonance imaging (MRI). The PVM cross-sectional area (CSA) and fat signal fraction (FSF) were measured at L3. Low back pain (LBP), activities of daily living (ADLs), and risk factors for PVM decrease at the 6-month follow-up were investigated. PVM decrease was defined as > 1 standard deviation decrease of the CSA or > 1 standard deviation increase of the FSF.

Results: Among 153 patients who completed the 6-month follow-up, 117 (92 women, 79%) had MRI of L3 at enrollment and 3- and 6-month follow-up (mean age at enrollment, 78.5 years). The CSA did not change 6 months from onset (p for trend = 0.634), whereas the FSF significantly increased (p for trend = 0.033). PVM decrease was observed in 30 patients (26%). LBP was more severe, and delayed union was more frequent in patients with PVM decrease ($p = 0.021$ mixed-effect model and $p = 0.029$ chisquare test, respectively). The risk factors for PVM decrease were ADL decline at the 3-month follow-up (adjusted odds ratio = 5.35, $p = 0.026$).

Conclusion: PVM decrease was significantly related to LBP and delayed union after osteoporotic vertebral fracture onset. ADL decline at the 3-month follow-up was a risk factor for PVM decrease. Therefore, restoring ADLs within 3 months after onset is important.

The effectiveness of motor control exercise in improving lumbar multifidus muscles morphology in patients with low back pain - a systematic review

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Introduction: Low back pain (LBP) is the number one cause of disability globally. Given the morphological changes in lumbar multifidus muscles (LMM) among patients with LBP, multiple studies have investigated the effectiveness of motor control exercises in improving LMM morphology and decreasing pain. However, no relevant systematic reviews have summarized these findings. Accordingly, the primary objective of the current review was to summarize the evidence regarding the effectiveness of MCE in improving morphology of LMM [cross-sectional area (CSA), intra-muscular fatty infiltration, resting thickness, contracted thickness, and percentage thickness change during contraction], and decreasing pain among patients with LBP. The secondary objective was to evaluate whether changes in LMM morphology were related to the decrease in LBP or LBP-related disability.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines, six databases: Cumulative Index to Nursing and Allied Health Literature (CINAHL), MEDLINE, Cochrane Central Register of Controlled Trials, the Physiotherapy Evidence Database, EMBASE and SPORTDiscus were searched from inception to September 30, 2020. Two reviewers independently screened abstracts and full-text articles. Studies were included if they were randomized controlled trials (RCTs) related to our objectives. The risk of bias of the included studies was evaluated by the Cochrane Risk of Bias Tool. Grading of Recommendations Assessment, Development and Evaluation was used to evaluate the strength of evidence.

Results: Thirteen RCTs involving 704 participants (663 chronic and 41 acute LBP) were included. The LMM morphology was measured by ultrasonography or computed tomography. Low-quality evidence supported that MCE induced significantly greater increase in LMM CSA than analgesic. There was very low-quality evidence that MCE cause significantly larger increases in LMM CSA of patients with CLBP than no treatment or general physiotherapy. However, only >24 sessions of MCE yielded clinically significant changes in LMM CSA. Very low- to low-quality evidence suggested that MCE was not better than general exercises, high load lifting exercise, McKenzie exercise, general exercise plus physiotherapy, or MCE plus biofeedback in increasing LMM resting thickness. Low-quality evidence suggested that MCE with/without an adjunct treatment significantly increased the contracted LMM thickness although the change was not clinically significant. No included studies investigated the effect of MCE on intramuscular fatty infiltration of LMM. Regarding LBP intensity, very low- to low-quality evidence substantiated that MCE was significantly better than general exercise, McKenzie exercise or no treatment in reducing CLBP although it was not clinically significant. Likewise, MCE with analgesics and non-steroidal anti-inflammatory drugs significantly decreased acute LBP. However, two included studies found no significant correlations between post-treatment changes in LMM morphology and LBP or LBP-related disability.

Discussion: This is the first systematic review to summarize the effectiveness of MCE in improving LMM morphology. While low-quality evidence suggests that MCE is better than no treatment, analgesic, or general physiotherapy in reducing pain in patients with acute/chronic LBP, only very low- to low-quality evidence supports that MCE can improve LMM morphology or decreased pain in LBP patients. It remains unclear whether changes in LMM morphology is correlated with changes in patients' clinical outcomes.

Which Conditions Could Aggravate the Regional and Global Sagittal Balance following Single Level L5-S1 Posterior Lumbar Interbody Fusion?

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Introduction

Although posterior lumbar interbody fusion (PLIF) is a frequently performed surgery in patients with spinal stenosis, its application to L5-S1 is controversial in terms of regional and global sagittal balance. A recent study demonstrated aggravation of sagittal alignment following PLIF at L5-S1 level. However, no further study to evaluate risk factors for the aggravation of the sagittal alignment during PLIF at L5-S1. Thus, this study aimed to reveal the risk factors for aggravation of sagittal alignment following single-level L5-S1 PLIF.

Methods

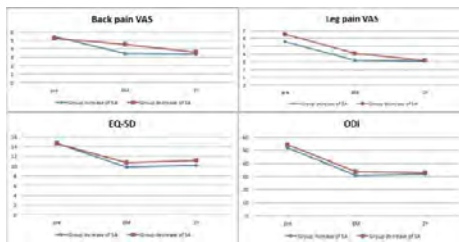
This study included 86 consecutive patients who underwent L5-S1 PLIF for degenerative lumbar disease. The patients were divided into two groups according to postoperative changes in the segmental angle (SA) (Group I: increased; Group D: decreased). Paired t-tests were used to compare pre- and post-operative radiological parameters. Comparisons between two groups were performed in terms of demographic, clinical, and radiologic outcomes. Multivariate logistic regression analyses were used to identify the risk factors for aggravation of regional sagittal alignment.

Results

Eighty-six patients (group I, n=39 and group D, n=47) were included. Demographic and clinical parameters did not differ between the two groups. However, the preoperative SA, LSA, and PDH differed between the two groups. Lordosis of the 4° cage showed a significantly larger ratio in Group D than in Group I. Group D showed postoperative deterioration of local sagittal parameters including lumbar lordosis (LL) (P = 0.034), sacral slope (SS) (P = 0.012), pelvic tilt (PT) (P = 0.003), and thoracic kyphosis (TK) (P < 0.001). In contrast, Group I showed improvement of LL (P = 0.021). However, global C7-S1 sagittal vertical axis (SVA) showed no differences in both groups (P > 0.05). Preoperative large lumbosacral angle (LSA) (odds ratio [OR] 1.287; P = 0.001), large SA (OR 1.448; P < 0.001), and large flexion LSA (OR 1.173; P = 0.011) were independent risk factors for aggravation of SA by multivariate analyses.

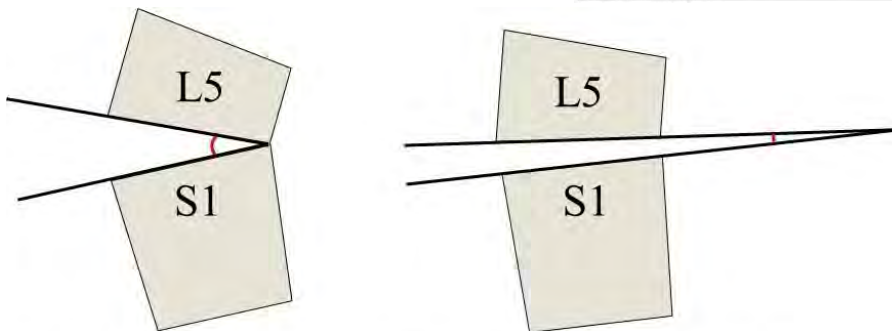
Discussion

Patients with a large SA, large LSA, and large flexion LSA preoperatively were more likely to develop deterioration of regional sagittal alignment following PLIF at L5-S1. In the patients with a large SA and LSA, it might be difficult to maintain a large lordotic angle after posterior fusion surgery. Posterior fusion is reportedly inferior than oblique- or anterior- interbody fusion for the restoration of segmental lordosis. Patients with a small flexion LSA tended to accompany a relatively larger posterior gap. In contrast, patients with a large flexion LSA tended to accompany a tight posterior gap. A large flexion LSA with a small posterior gap resulted in limited distraction of the posterior compartment during surgery. It suggests that patients with these risk factors, surgeons should be cautious of possible aggravation of sagittal balance, and could consider different surgical techniques such as anterior or oblique lumbar interbody fusion.



Factor	Odds Ratio	95% CI	P-value	
Demographic parameters				
PLIF	1.042	0.001 - 0.023	0.993-1.004	0.007*
LL (°)	1.032	0.012 - 0.017	0.980-1.086	0.172
PLIF (%)	1.000	0.000 - 0.014	0.975-1.042	0.046
LSA (°)	1.043	0.061 - 0.034	1.001-1.127	0.033*
SA (°)	1.171	0.101 - 0.011	1.062-1.296	0.001*
Preoperative regional parameters				
ADI (mm)	1.018	0.018 - 0.058	0.988-1.112	0.753
PMI (mm)	0.997	0.100 - 0.117	0.914-1.108	0.541
ADI (PMI) (mm)	1.063	0.065 - 0.069	0.910-1.219	0.539
Dynamic lateral radiograph				
Lordosis (LSA) (°)	1.021	0.021 - 0.033	0.974-1.093	0.547
Flexion LSA (°)	1.150	0.109 - 0.060	1.021-1.291	0.010*
Extension-flexion LSA (°)	0.959	-0.042 - 0.037	0.893-1.011	0.208
Curve profile				
Curve angle (°) (°)	2.270	0.008 - 0.407	0.015-4.362	0.068*
Curve height (mm)	0.760	-0.274 - 0.309	0.422-1.109	0.562

Factor	Odds Ratio	95% CI	P-value	
Demographic parameters				
LSA (°)	1.287	0.251 - 0.074	1.111-1.489	0.001*
SA (°)	1.448	0.570 - 0.101	1.190-1.763	<0.001*
Dynamic lateral radiograph				
Flexion LSA (°)	1.173	0.109 - 0.063	1.039-1.327	0.011*
Curve profile				
Curve angle (°) (°)	1.164	1.178 - 0.487	0.893-1.161	0.014
Curve height (mm)	1.407	1.792		0.007



(A) large flexion LSA with small posterior gap (B) small flexion LSA with large posterior gap

Comparison of Outcomes of Primary and Revision Minimally Invasive Lumbar Microdiscectomy

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Patient-reported Outcome Measures (PROMs)			
	Primary (n=166)	Revision (n=29)	p-value
Oswestry Disability Index (ODI)			
• Pre-operative	46.06 ± 23.67	45.48 ± 15.25	0.977
• Early post-operative	20.69 ± 18.76 (p-value* = <0.0001)	22.48 ± 15.45 (p-value* = <0.0001)	0.788
• Last Follow-up	18.85 ± 17.86 (p-value* = <0.0001)	17.91 ± 12.75 (p-value* = <0.0001)	0.720
VAS Back Pain			
• Pre-operative	5.55 ± 3.12	5.59 ± 2.68	0.929
• Early post-operative	2.20 ± 2.41 (p-value* = <0.0001)	1.98 ± 2.37 (p-value* = <0.0001)	0.961
• Last Follow-up	2.19 ± 2.63 (p-value* = <0.0001)	2.42 ± 2.58 (p-value* = <0.0001)	0.824
VAS Leg Pain			
• Pre-operative	6.33 ± 2.87	6.84 ± 1.88	0.920
• Early post-operative	2.39 ± 2.86 (p-value* = <0.0001)	2.57 ± 2.84 (p-value* = <0.0001)	0.736
• Last Follow-up	2.13 ± 2.79 (p-value* = <0.0001)	2.33 ± 2.86 (p-value* = <0.0001)	0.454
U-12 Physical Health Score			
• Pre-operative	30.87 ± 8.54	32.04 ± 4.45	0.118
• Early post-operative	40.07 ± 10.25 (p-value* = <0.0001)	37.75 ± 8.36 (p-value* = <0.0001)	0.271
• Last Follow-up	41.10 ± 10.48 (p-value* = <0.0001)	39.10 ± 9.47 (p-value* = <0.0001)	0.110
SF-12 Mental Health Score			
• Pre-operative	44.37 ± 12.08	43.60 ± 10.61	0.732
• Early post-operative	51.87 ± 11.04 (p-value* = <0.0001)	53.88 ± 7.55 (p-value* = <0.0001)	0.792
• Last Follow-up	51.61 ± 11.24 (p-value* = <0.0001)	53.60 ± 8.66 (p-value* = <0.0001)	0.704
PROMIS Physical Function			
• Pre-operative	43.20 ± 7.61	45.30 ± 6.70	0.256
• Early post-operative	43.54 ± 8.75 (p-value* = <0.0001)	41.32 ± 8.50 (p-value* = <0.0001)	0.343
• Last Follow-up	45.34 ± 8.61 (p-value* = <0.0001)	43.26 ± 7.95 (p-value* = <0.0001)	0.280

Early postoperative = 2 - 12 weeks. * p-value for change from the pre-operative (baseline).

Introduction:

Although revision surgery carries a higher risk of complications due to dissection through scarred tissue planes, minimally invasive (MIS) techniques are increasingly being utilized to avoid scar tissue from previous approaches. However, it is not currently known whether there is a difference in outcomes between primary and revision MIS lumbar microdiscectomy.

Thus, the purpose of this study was to compare outcomes of primary and revision MIS lumbar microdiscectomy.

Methods:

A retrospective review of prospectively collected data of patients who underwent 1-2 level MIS lumbar microdiscectomy was performed. Patient demographics, operative data, clinical outcomes (length of stay, narcotic consumption, complications and reoperations) and patient-reported outcomes [PROMs— Oswestry Disability Index (ODI), VAS back& leg pain, SF-12 physical (PHS) and mental health (MHS) and PROMIS physical function] of primary and revision surgery were compared.

Chi square test and Fisher's exact test were used to compare categorical variables, and student t-test and Mann Whitney u-test were used to compare normally and non-normally distributed continuous variables respectively. Statistical significance was set at p<0.05.

Results:

195 patients (Primary=166, Revision=29) were included. The revision cohort was younger (42 vs 48yrs for primary, p=0.033), had a lower Charlson Comorbidity Index (0.06 vs 0.36, p=0.006) and shorter operation time (42 vs 48mins, p=0.033). There were no differences in smoking status (p=0.830), insurance type (p=0.689), ASA class (p=0.925), post-operative narcotic consumption (p=0.927) or length of stay (p=0.968). 90% of patients in both cohorts were discharged on the day of surgery.

The only operative complication was 1 Dural tear (0.6%) and the only in-hospital complication was urinary retention (n=3, 1.8%), all in the primary cohort. During the follow-up period, complications managed non-operatively were significantly greater in the revision cohort [n=3(10.3%) vs n=4(2.4%) for primary, p=0.035]. However, there was no difference in reoperations [Primary: n=12(17.2%); Revision: n=3(10.3%); p=0.472]. Reasons for reoperation were- Primary cohort: recurrent disc herniation (n=10), epidural abscess (n=1) and unknown (n=1); Revision cohort: recurrent disc herniation (n=1), epidural abscess (n=1), pseudomeningocele (n=1).

Both groups showed significant improvement in all PROMs at the early follow-up (2-12 weeks) and at last follow-up (p<0.0001). There was no significant difference in the achievement of MCID (Primary vs revision: 2 weeks 50 vs 55.2%, p=0.606; 90 days 62.7 vs 65.5%, p=0.774; last follow-up 68.7 vs 65.5%, p=0.733).

Conclusion:

Patients undergoing revision surgery were younger, had lower comorbidity burden and slightly shorter operative times. There was no difference in narcotic consumption, length of stay, or intra-operative and in-hospital complications. Although the revision cohort had a higher rate of complications managed non-operatively, there was no difference in reoperation rates. Both groups showed significant improvement in PROMs, with no difference between groups. These findings suggest that revision MIS microdiscectomy is a safe and as effective treatment option for patients with recurrent herniation, and can provide outcomes equivalent to primary surgery.

Facet joint opening on CT is a predictor for poor clinical outcomes after less-invasive decompression surgery for lumbar spinal stenosis.

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Introduction: We have performed less-invasive surgery using microscopy or microendoscopy for lumbar spinal stenosis without severe segmental spinal instability by dynamic X-ray. Although spinal fusion surgery is gold standard surgical treatment for case with segmental spinal instability, it has not been clarified what is threshold which can be treated by less-invasive decompression alone surgery. Facet joint opening on CT was reported as an indicator for segmental spinal instability by an experimental study. However, there is no study which investigated the impact of facet joint opening on clinical outcomes after decompression alone surgery.

Aim: The purpose of this study was to investigate association between facet joint opening and clinical outcomes after less-invasive surgery in a long-term cohort study.

Materials and Methods: This study included a total of 296 patients (male 156/ female 140, mean age at surgery 69.1 years, mean follow-up 6.2 years) who underwent less-invasive surgery for lumbar spinal stenosis and have followed up ≥ 5 years in one institution. Facet opening was defined as ≥ 2 mm facet interval on axial images of CT in each lumbar level. Facet joint opening was evaluated at index decompression level (d-FJO) and ≥ 3 levels of facet opening within lumbar segment from L1-2 to L5-S (m-FJO). Clinical outcomes was evaluated by (1) Reoperation: revision surgeries due to progression of degeneration either at index lumbar level or not, and (2)improvement ratio of Japanese Orthopaedic Association (JOA) score, and achievement of minimal clinically important difference (MCID) of visual analogue scale for low back pain or leg pain at 5 years: MCID of low back pain 21, MCID of leg pain 28. Clinical outcomes were compared between patients with and without d-FJO or m-FJO, coupling with factors of patients' demographic, preoperative symptom severity, and radiological findings (plain X-ray and MRI).

Results: There were 129 patients(44%) with d-FJO, and 61 patients (21%) with m-FJO. Preoperative d-FJO was more common in cases with lateralolisthesis (24% vs. 11%, $p<0.01$) and m-FJO was less common in cases with spondylolisthesis of ≥ 6 mm (6% vs. 18%, $p=0.02$). Reoperation was performed in 29 cases (10%): revision at index decompression level 17cases, and revision at other lumbar level 14case. Reoperations were more common in patients with d-FJO (15% vs. 5%). Cox Proportional hazard analysis indicated d-FJO were predictor for revision at index decompression level (hazard ratio[HR] 4.04, $p=0.03$), and m-FJO for revision at other lumbar levels(HR 3.71, $p=0.03$). In addition, patients with m-FJO showed a slightly poorer improvement of JOA score (74% vs. 80%, $p=0.03$) and a lower rate of achieving MCID for low back pain (34% vs. 52%, $p=0.03$).

Conclusion: This study indicated that facet joint openings, not only that at index level but also multi-level facet joint opening, were predictor for poor outcomes. Facet joint opening at index decompression level is useful as a predictor of reoperation at index surgery due to increased instability, while multi-level facet joint opening is useful as a predictor of reoperation at other lumbar levels due to progression of degeneration.

SP923

The relative efficacy of lumbar fusion for low grade isthmic compared with degenerative spondylolisthesis

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INTRODUCTION: Surgical treatment for low grade isthmic spondylolisthesis and degenerative spondylolisthesis of the lumbar spine usually consists of decompression and lumbar fusion. Although the treatment for both is the same, they are two distinct pathologies, and little is known about the relative efficacy of surgery for each. We compared, in a large cohort, patient-rated outcome up to 2 years after single level instrumented lumbar fusion for the two types of spondylolisthesis. We also sought to identify differences in outcome with respect to various patient-specific baseline factors.

METHODS: This was a single-center retrospective analysis of data collected prospectively using the framework of the EUROSPINE Spine Tango Registry, between 2005 and 2017. We included 534 patients (mean age 60±14.6 y; 65% female), divided into four groups of interest based on two variables: type of spondylolisthesis (degenerative vs isthmic) and chief pain complaint (leg pain vs. back pain). Patients completed the multidimensional Core Outcome Measures Index (COMI; 0–10 scale) preoperatively and at 3, 12 and 24 mo follow-up (FU), and rated global treatment outcome (GTO) at the FUs. Regression models (multiple linear regression and random effects panel regression) were used to predict COMI-scores and COMI-pain at 3, 12 and 24 mo, controlling for baseline COMI, age, sex, smoking status, BMI and ASA status.

RESULTS: All patients experienced pronounced reductions in COMI scores with most improvement visible by 3 mo FU. Among the control variables in the regression models, only COMI baseline, smoking status and ASA were retained as being at least borderline significant ($p < 0.1$). The group of patients with degenerative spondylolisthesis and leg pain as chief complaint showed, depending on the exact model, between 5% and 10% greater COMI score reduction relative to the other groups. This appeared to be driven by relatively greater reductions in COMI in patients with high baseline COMI scores. This group also performed best with respect to pain outcomes, showing a 20% greater reduction in 2-year chief pain complaint score than the next best group, while the improvement of the non-predominant pain (back) was greater than in the corresponding isthmic group. These findings were reflected in more positive ratings of GTO in this group: 73% reported that the operation had “helped a lot”, compared with between 56% and 61% in the other groups.

DISCUSSION: Regardless of the type of spondylolisthesis, all groups experienced an improvement in mean COMI score after surgery. While age did not play a role, baseline COMI, ASA and smoking status were influential with respect to outcome. Patients with degenerative spondylolisthesis and leg pain as their chief complaint appear to benefit more from treatment than other types of patients. These results are the first to show that the type of the spondylolisthesis and its chief complaint have an impact on surgical outcome.

Improvement in gait pattern and its relationship with preoperative pelvic compensation after surgery in patients with sagittal plane deformity

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INTRODUCTION. There have been no other studies investigating the influence of preoperative pelvic compensation on surgical outcomes. The purpose of the current study is to investigate the improvement in gait parameters after surgery and whether corrective surgery for sagittal imbalance would be influenced by preoperative pelvic compensation.

METHODS. A total of 32 patients who were scheduled to undergo corrective surgery for sagittal plane deformity were included and were followed-up for 1 year after surgery. Radiological parameters were measured on biplanar full-body imaging. Before surgery and 6 months after surgery, three-dimensional motion analyses were performed to estimate the center of gravity (CoG) deviation from the center of mass (CoM), mean trunk kyphosis (TK) angle, gait deviation index (GDI), and kinematic parameters. Before surgery, the patients were classified into CoG+ and CoG- groups. "+" and "-" representing increases and decreases in the distance of CoG from CoM of the pelvic segment from 1st to 3rd trials, respectively. Oswestry disability index (ODI) and EuroQol-5D (EQ-5D) were measured for 1 year after surgery.

RESULTS. All radiological parameters improved significantly after surgery. For gait parameters, CoG from CoM, mean TK angle, and minimum angle of the hip and knee joints in the stance phase during walking were significantly decreased after surgery, and GDI scores significantly improved after surgery. The mean changes of the CoG distance from the CoG and the mean TK from 1st to 3rd trials of gait analysis significantly decreased postoperatively. There were no significant differences in ODI and EQ-5D scores over a 1-year follow-up assessment between CoG+ and CoG- groups.

DISCUSSION. Preoperative abnormal stooping gait and progressive worsening of sagittal imbalance in patients with sagittal plane deformity improved after corrective surgery. Patients with preoperative dynamic sagittal imbalance could have similar surgical results to those without it after corrective surgery.

Preoperative psychological predictors of satisfaction after lumbar surgery for lumbar spinal stenosis

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INTRODUCTION: Psychological status before surgery is believed to influence the outcome of surgery and patient satisfaction. An association has been demonstrated between depressive symptoms and poorer surgery outcome for patients with lumbar spinal stenosis (LSS).¹ However, the roles of other psychological factors such as pain catastrophizing, and fear-avoidance beliefs are debated. The purpose of this study was to identify preoperative psychological factors associated with patient satisfaction after lumbar surgery for LSS.

METHODS: This study was a retrospective study of prospectively collected clinical data that included 157 patients with LSS who underwent decompression surgery with or without fusion at our hospital. Patients with a history of previous spinal surgery or psychiatric illness were excluded. Clinical outcomes were measured preoperatively and 6 months postoperatively using the Zurich Claudication Questionnaire (ZCQ), a visual analogue scale (VAS) of low back pain, leg pain, and leg numbness, the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ), and the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36). The Hospital Anxiety and Depression Scale (HADS), the Pain Catastrophizing Scale (PCS), and the Pain Anxiety Symptoms Scale were used to evaluate psychological status before surgery. Patients were divided into satisfied and dissatisfied based on a ZCQ satisfaction subscale cutoff score of 2.5. The characteristics of those patients with LSS who achieved satisfactory results with surgery were clarified.

RESULTS: The satisfied and dissatisfied groups contained 128 and 29 patients, respectively. At baseline, there were no significant differences between groups for age, gender, body mass index, duration of symptoms and MRI findings ($P > 0.05$). However, the dissatisfied group had worse baseline scores on the SF-36 subscales for mental health and general health and the HADS subscales for anxiety and depression, with higher scores on the PCS subscales ($P < 0.05$). Six months postoperatively the satisfied group showed significantly greater improvements than the dissatisfied group for all outcome measures except the SF-36 general health subscale ($P < 0.05$). The outcome scores for the dissatisfied group 6 months postoperatively were unchanged or worse (JOABPEQ subscale for lumbar dysfunction) than preoperative scores. Stepwise multivariate logistic regression analysis showed a significant association between dissatisfaction, preoperative low back pain (VAS score over median: odds ratio (OR) 0.27, 95% confidence interval (CI) 0.10–0.74; $P = 0.01$), preoperative mental health (SF-36 score over median: OR 0.26, 95% CI 0.08–0.89; $P = 0.03$), and preoperative anxiety (HADS score over median: OR 3.95, 95% CI 1.16–13.46; $P = 0.03$).

DISCUSSION: Dissatisfied patients showed no improvement in the patient-reported outcome measures of pain, disability, and quality of life 6 months postoperatively. Preoperative less severe low back pain, lower mental health, and higher anxiety, but not depression, pain catastrophizing, and fear-avoidance beliefs are associated with patient dissatisfaction with lumbar surgery. Therefore, the pre- and postoperative psychological status of patients should be carefully assessed and appropriately managed to improve clinical results.

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GP001

Can Small Leucine-Rich Proteoglycans be Ideal Molecular Targets for Regeneration in IVD? - evidence from proteomic signatures of fetal, adult, and degenerative discs

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Introduction: Biological strategies to promote disc regeneration are being explored as therapeutic options in degenerative disc disease (DDD). Fetal disc cells containing notochordal cells have shown preliminary success in regenerating the extracellular matrix (ECM) of nucleus pulposus. Small Leucine-Rich Proteoglycans (SLRPs) form an important constituent of ECM and therefore an in-depth analysis of SLRPs might unravel ideal molecular targets.

Materials and Methods: IVDs of 3 contrasting developmental and health status viz., IVD harvested from 24-week old fetuses (fetal disc, FD), healthy IVD harvested from brain dead alive organ donors (normal lumbar discs, ND), and degenerated discs (DD) harvested from patients undergoing surgery for DDD were subjected to ESI-LC-MS/MS analysis for the identification of proteins after proteolytic digestion. Among the total protein, SLRPs were selectively subjected to gene ontology (GO) analysis, including biological process, molecular function, and cellular component using "cluster Profiler" in R vs. 3.6.1 (2019-07-05) (R Foundation, Vienna, Austria) program. In addition, pathway enrichment analysis was performed by the DAVID database and data visualization tool Cytoscape-ClueGo/CluePedia version 3.7.2 using Reactome databases. The differential expression of SLRPs and their association with Collagen content, and ECM regulators viz, Matrix Metallo Proteinases (MMPs) and their inhibitors (TIMPs) were further analyzed.

Results: A total of 1,029 proteins in FD, 1,785 proteins in ND, and 1,775 proteins in DD were identified. Out of the total 60 proteoglycans reported in the literature, we observed 26 proteoglycans in our data across all the groups which constituted 15 Large proteoglycans and 11 SLRPs. The total number of large leucine-rich proteoglycans (LLRPs) identified were 8 in FD, 7 in ND, and 9 in DD, whereas the total number of SLRPs detected were 11 in FD, 9 in ND, and 10 in DD, respectively. SLRPs such as Fibromodulin (FMOD) and Biglycan (BGN) were upregulated in the FD group. On analyzing the expression of TIMPs and MMPs, DD group showed a higher expression of MMPs when compared to ND group, whereas the FD group did not express MMPs. Statistically significant decrease in abundance was noted in the expression of Lumican (LUM), Decorin (DCN), Chondroadherin (CHAD), and Prolargin (PRELP) in the DD group. The overall decrease in SLRP content of degenerate discs, was associated with decrease in Collagen, LLRP and TIMP expression.

Conclusion: The various SLRPs that we identified are all known to have a beneficial influence on ECM integrity and a negative effect on the degenerative process at different stages in the evolution of degeneration. Biglycan, which is abundantly present in a fetus, may be suitable for regenerative therapy, and the other SLRPs like LUM, PRELP, DCN, and CHAD may serve the same purpose and/or as biomarkers. Our results strongly suggest that there must be an increased focus on the role of SLRPs in the understanding and prevention of DDD.

GP002

SERPIN'S: A potential target for molecular blockade in disc degeneration

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Introduction:

The etiology of disc degeneration(DD) is claimed to be multifactorial. Irrespective of the initiating factor, breakdown of extracellular matrix (ECM) is a critical event in DD. This ECM disassembly is brought about by proteolytic enzymes called proteases that cleave the bond holding the ECM. Serine proteases are a large family of proteases whose activities are kept in check by regulators, Serine protease inhibitors (SERPINS). The role of SERPINS in health and disease of IVD has not been studied in detail so far. In this context, we did a systematic study using high throughput proteomics with appropriate healthy control discs and discuss the inferences here.

Materials and Methods:

After ethical committee approval and consent, twelve intervertebral Nucleus Pulposus tissues each from (1) Normal organ donor volunteers without any sign of low back pain (ND), and patients with (2) herniated discs (DH) and (3) degenerated discs (DD) were harvested under sterile operating conditions and subjected to proteomic analysis. Immunohistochemistry(IHC) was performed to confirm the presence of two SERPINS A1 and E2.

Results:

Mass spectrometry identified a total protein of 2164 in ND, 1734 in DH, and 2394 in DD groups, respectively. We identified 21 SERPINS present in at least one disc sample out of a total of 37 human serpins already reported in the literature. With stringent cut off (>5 PSM and presence in at least in 2 samples per group) to increase the authenticity, we shortlisted 14 SERPINS, 8 in ND, 12 in DH, and 13 in DD group, respectively. 7 SERPINS were common to all three groups that include SERPINA1, SERPINA3, SERPINA5, SERPINA8, SERPINC1, SERPINE2, and SERPING1. SERPINA4, SERPIND1, SERPINF1, SERPINF2, and SERPINH1 were found common to DH and DD groups. SERPINE1 and SERPINB1 were found unique to ND and DD groups, respectively.

SERPINA1, SERPINA5, SERPINE2, and SERPING1 showed higher expression in healthy control NP discs (ND) when compared to diseased discs- DH and DD. SERPINS A1 and E2 are known to play a protective role in maintaining disc homeostasis by inhibiting proteases such as matrix metalloproteinases (MMPs). SERPIN A5, a multifunction protein, inhibits several proteases involved in the coagulation pathway. SERPIN G1 regulates other proteases in the tissue leading to inflammation and has an anti-inflammatory role. SERPIN A3, an acute phase pro-inflammatory protein, was found in abundance in DH. SERPINH1, a procollagen-specific molecular chaperone Hsp47 was found in abundance in DH, the dysregulation of which leads to changes in the expression of ECM proteins such as fibronectin (FN1) and collagen type I. Validation of selected SERPINA1 and E2 IHC staining in the healthy ND and diseased DH and DD IVD confirmed the expression as observed in the proteomics data.

Conclusion:

Our study confirmed the presence of many SERPINS with various functions in the human intervertebral disc. These SERPINS A1 and E2 with inhibitory effect on MMPs could be utilized as a potential target to halt or arrest disc degeneration

Supplemented chondroitin sulfate proteoglycan promotes anabolic turnover in bovine nucleus pulposus cells under *in-vivo*-like physicochemical stresses

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INTRODUCTION: Nucleus pulposus (NP) cells are exposed to high osmotic pressure (OP) due to negatively charged chondroitin sulfate proteoglycan (CS-PG) within the intervertebral disc and exposed to changes in hydrostatic pressure (HP) due to weight bearing and spinal motion. Since the loss of CS-PG is interpreted in the degeneration of NP by MR images, restoration of CS-PG would be a key concept for the regeneration. We hypothesized that NP cells supplemented with CS-PG promoted the anabolic turnover under *in-vivo*-like stresses. We evaluated gene expression of metabolic markers and clarify the involvement of mechanoreceptor of transient receptor potential vanilloid-4 (TRPV4) activation in bNP-cell metabolism.

METHODS: We purchased bovine tails from a local USDA-certified slaughterhouse and harvested caudal NP tissues ($n=6$ repeated experiments). We isolated bNP cells/clusters and enclosed them with or without 2-mg/ml CS-PG extracted from bovine articular cartilage (Sigma-Aldrich) within semi-permeable membrane pouches. The pouches were divided and incubated under 2 different conditions: no HP, in which pouches were placed in the medium with a stirrer, and HP, in which 2-day cyclic HP at 0.2–0.7 MPa, 0.5 Hz followed by 1-day constant HP at 0.3 MPa was repeated 4 times over 12 days. The OP of medium was set at 450 mOsm/kg H₂O supplemented with NaCl. The pouches were harvested at 3 and 12 days. We measured the gene expression of anabolic aggrecan core protein (*Acan*), collagen types I and II (*Col1a1* and *Col2a1*), catabolic matrix metalloproteinase 13 (*Mmp13*), and anti-catabolic tissue inhibitor of metalloproteinases 2 (*Timp2*). We also performed immunohistological staining for keratan sulfate (KS) and TRPV4.

RESULTS: The *Acan* expression was significantly upregulated with CS-PG compared to without CS-PG under no HP at 3 days, and significantly higher under HP than no HP with CS-PG at 12 days ($P=0.03$ and $P<0.01$, respectively). The *Col2a1* expression was significantly upregulated under HP than no HP with CS-PG at 12 days ($P=0.03$). The *Col1a1* expression was significantly downregulated with CS-PG compared to without CS-PG under no HP at 3 days, and significantly higher under HP than no HP with CS-PG at 12 days (both $P<0.01$). The scatter plot demonstrated *Mmp13* suppression under HP compared to no HP both with and without CS-PG, while *Timp2* expression did not show a discrepancy between the culture conditions. Immunohistological staining revealed as much accumulation of KS within NP cells/clusters under HP as no HP and activation of TRPV4 under HP at 3 days.

DISCUSSION: Supplemented CS-PG has the anabolic and anti-fibrotic effects on bNP cells at early phase of the culture period under no HP, furthermore, it showed the synergy with HP to bNP-cell anabolism at later phase. Conversely, repetitive changes in HP downregulated catabolic *Mmp13* and upregulated anti-catabolic *Timp2*. Immunohistology suggested that TRPV4 activation is a possible mechanism of HP on bNP-cell metabolism. CS-PG has a potential to facilitate disc regeneration by reproducing the ECM environment around the NP cells.

Larger Muscle Fibers and Fiber Bundles Manifest Smaller Elastic Modulus in Paraspinal Muscles of Rats and Humans

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INTRODUCTION: Passive elastic modulus of muscles is important for biomechanical functioning of the musculoskeletal system. While most studies assume that muscle fiber bundle size does not influence elastic modulus after normalizing for cross sectional area (CSA), elastic modulus of muscle fibers has been shown to be size-dependent. The objectives of this study were to determine the degree to which this size effect was evident in muscle fiber bundles and to examine the validity of the frequent assumption of a circular cross section of muscle fiber bundles.

METHODS: Muscle fibers and fiber bundles were extracted from lumbar spine multifidus and longissimus of three cohorts: group one (G1) and two (G2) included 13 (330±14g) and 6 (452±28g) Sprague Dawley rats, while Group 3 (G3) comprised 9 human degenerative spine patients. A minimum of six muscle fibers and six muscle fiber bundles from each muscle underwent cumulative stretches, each of 10% strain followed by 4 minutes relaxation. Elastic modulus was calculated as tangent at 30% strain from the resulting stress-strain curve. Linear correlations between the fiber/fiber bundle CSA and elastic moduli in each group were performed. Major and minor axis diameters of fibers and fiber bundles were measured and their ratios were calculated. The results were contrasted against the theoretical median of 1 (for cylindrical shape assumption) using Wilcoxon signed rank test.

RESULTS: The correlations showed that increasing specimen CSA resulted in lower elastic modulus for both rats and humans, muscle fibers and fiber bundles (all $p < 0.05$ except for G2 longissimus bundles with $p = 0.21$, Figures 1-2). The median ratio of major to minor axis exceeded 1.0 for all groups, ranging between 1.15 and 1.29 for fibers and 1.27 and 1.44 for fiber bundles (Figure 3).

DISCUSSION: The lower elastic moduli with increasing size can be explained by relatively less collagenous extracellular matrix in the large fiber bundles (Figure 4). Future studies of passive property measurement should aim for consistent bundle sizes and measuring diameters of two orthogonal axes of the muscle fibers and fiber bundles.

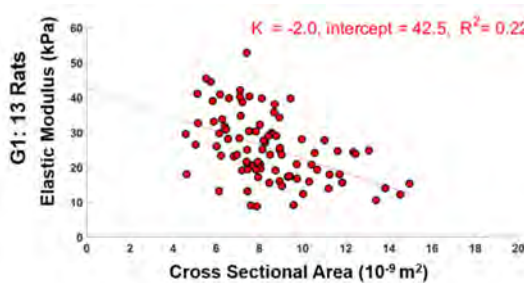


Figure 1. Correlation between elastic modulus and cross sectional area of G1 multifidus single fibers

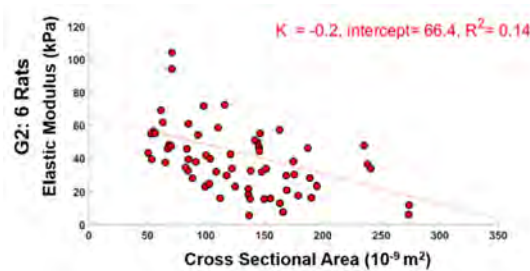


Figure 2. Correlation between elastic modulus and cross sectional area of G2 multifidus fiber bundles

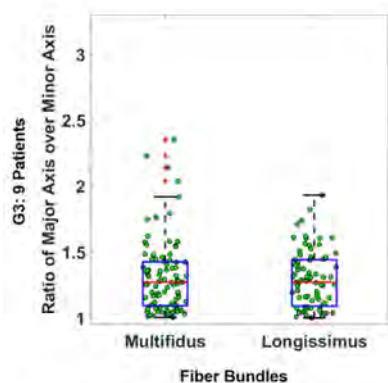


Figure 3. Ratio of major over minor axis diameters of fiber bundles tested in G3

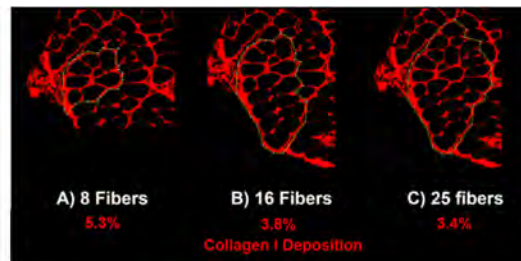


Figure 4. Inverse correlation between collagen I area fraction and size of three bundles of different sizes from multifidus of one rat in G1.

RCAN1.4-calcineurin/NFAT signalling pathway is essential for hypoxic adaption of intervertebral discs

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Introduction: In human adults, IVDs are the largest nonvascular organs. Therefore, the central NP is completely hypoxic and expresses hypoxia-inducible factor 1 and 2 (HIF-1 and HIF-2). HIF-1 α promotes the ECM synthesis in NP and maintains intracellular pH and viability of NP cells. Calcipressin-1, also known as regulator of calcineurin 1 (RCAN1), can specifically bind to and down-regulate the activity of calcineurin at or near the catalytic domain of calcineurin A. RCAN1 plays a critical role in cancer growth, endothelial cells migration and neuronal apoptosis. However, it is still unclear if RCAN1 may affect the hypoxic IVD phenotype through calcineurin/NFAT signalling pathway.

Methods: Firstly, we confirmed degenerative NP characters by H&E, Safranin O/fast green and Alcian blue staining and detected increasing level of RCAN1 in degenerative NP by immunohistochemistry. We then detected the gene and protein expression level of RCAN1.1 and RCAN1.4 in human NP tissues (Pfirrmann Grade I/II, Grade III, Grade IV and Grade V) and analysed its correlation with IVDD. Furthermore, we evaluated the role of RCAN1.4-calcineurin/NFAT signalling pathway in hypoxic NP cells and silenced or overexpressed RCAN1.4 to examine its role in the NP cells phenotype. What's more, we determined that FK506 (a calcineurin inhibitor) repressed hypoxia-induced activation of calcineurin/NFAT signalling pathway in NP cells *in vitro* and in an *ex vivo* model.

Results: Compared with normal NP, protein level of RCAN1.4, rather than RCAN1.1, were significantly increased in NP from degenerative patients, whereas HIF-1 α was sharply decreased. *In vitro*, hypoxia (1%O₂) or overexpression of HIF-1 α both reduced protein level of RCAN1.4 of rat NP cells in a time-dependent manner. We further found that miRNA-124, not degrading pathway (proteasome or lysosome), suppressed the expression of RCAN1.4. As expected, calcineurin of NP cells was activated and primarily promoted nuclear translocation of NFATc1 under hypoxia or RCAN1 siRNA. Furthermore, Sox9, type II collagen and MMP13 was elevated under hypoxia, RCAN1 siRNA or NFATc1 overexpression. FK506 (a calcineurin inhibitor) can reverse NP extracellular matrix synthesis (Sox9, type II collagen) and remodeling (MMP13). Using ChIP and luciferase reporter assay (mutation), we clarified that NFATc1 can specifically bind to Sox9 promotor region (-367~-357), and interaction of HIF-1 α and NFATc1 promoted MMP13 transcription. Finally, we found out that FK506 reversed hypoxia-induced activation of calcineurin/NFAT signalling pathway in NP cells *in vitro* and in an *ex vivo* model.

Discussion: Schemes of disc degeneration classification included sub-scores for major sub-tissues: nucleus pulposus (NP), annulus fibrosus (AF), and cartilaginous endplate (CEP). If any part of these structures is damaged or degenerated, the hypoxic environment of the disc will be destroyed. Understanding the underlying mechanisms that regulates ECM synthesis and remodeling of disc cells under hypoxia is vital for future treatment. In this study, we firstly demonstrated that RCAN1.4 was positively associated with disc degeneration, and hypoxia-induced downregulation of RCAN1.4 activated the calcineurin/NFAT signaling pathway to facilitate the SOX9 and MMP13 expression. RCAN1.4-calcineurin/NFAT signaling pathway under hypoxia was critical for the hypoxic IVD phenotype.

GP006

Nose to back: spheroids derived from human nasal chondrocytes for nucleus pulposus repair

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Introduction. Autologous nasal chondrocytes (NC) could be an excellent source for nucleus pulposus (NP) repair. Indeed, NC possess large cartilage-regenerative capacity (Fulco, Miot et al. 2014, Mumme et al. 2016) and survive in harsh NP microenvironment better than traditionally used MSCs (Gay et al., 2019). To broaden the applicability of NC for IVD repair, we propose a novel scaffold-free approach. We aim this *in vitro* study at analyzing the therapeutic potential of NC spheroids (NCS) namely their capacity for injectability, NP-like extracellular matrix (ECM) accumulation, and integration in conditions simulating degenerative disc disease (DDD).

Methods. Human NC (n=5) were cultured as spheroids with different culture supplements for 1-7 days. Injectability and biosynthetic potential of NCS (biochemical content, gene expression, proliferation, elastic modulus) were evaluated at each time point. Human NP cells (n=3) were cultured as spheroids (NPS) for up to 14 days. DDD-mimicking conditions (inflammation, acidity, low glucose, hypoxia) were introduced and NCS-NPS fusion kinetics was monitored for 4 days (microscopy/image analysis). Anabolic and catabolic responses of NCS vs. NC single-cell suspension were assessed histologically and biochemically using our DDD-mimicking NP microtissue model composed of pooled NPS.

Results. Non-adhesive technology allowed the fabrication of NCS compatible with a common spinal needle (<600 µm). NCS cultured with different supplements for 1-7 days upregulated aggrecan and collagen type II expression and accumulated GAG and total collagen (p<0.05). Furthermore, biomechanical properties of NCS recapitulated native NP tissue (5-30 kPa in unconfined compression). In DDD mimicking conditions, NCS performed superior to NC single-cell suspension in terms of catabolic shift (IL-8 release, p<0.05). The kinetics of NCS-NP fusion was not impaired by the DDD mimicking conditions. Interestingly, "growth" culture supplements facilitated fusion with NP tissue, while "chondrogenic" supplements increased biomechanics properties (p<0.05).

Discussion. Our data indicate that NC cultured as spheroids can produce NP-like matrix, develop biomechanical properties compatible with NP tissue, and possess the capacity to integrate within degenerated NP. Moreover, specific NCS properties are potentially tunable by culture supplements. These results need to be verified in a whole disc organ culture bioreactor, towards demonstration of the functionality of NC for scaffold-free NP repair.

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GP007

Targeted proteomic analysis to explore the anti-inflammatory effects of notochordal cell-derived matrix

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Low back pain due to intervertebral disc (IVD) degeneration is a major health and socioeconomic problem throughout the world. In the young and healthy IVD, large and vacuolated notochordal cells (NCs) are present. These cells are, in some species (e.g. humans and dogs), replaced by chondrocyte-like nucleus pulposus cells (NPCs) during maturation and ageing. In previous studies, porcine NC-derived matrix (NCM), containing matrix and biologic factors secreted by NCs, induced regenerative and anti-inflammatory effects in human, canine and bovine NPCs *in vitro* and degenerated canine IVDs *in vivo*. However, since the precise mechanism behind NCM remains elusive, the aim of this study was to determine the mode of action of NCM in the degenerative IVD environment. For this purpose, canine NPCs were cultured with and without NCM. Afterwards, targeted proteomics was performed with DigiWest technology and results were confirmed in *in vivo* canine IVDs treated with NCM. DigiWest analysis showed that NCM mainly induced changes in the Mitogen-activated protein kinase (MAPK) pathway. The expression of key proteins downstream the MAPK pathway was mostly inhibited by NCM, such as p-ERK1/2, p-JNK/SAPK, and p-PKC, while p-cJun and p-S6 ribosomal protein expression was increased. The expression of proteins that are known to dephosphorylate MAPK key signalling molecules, DUSP5 and DUSP6 was increased, whereas DUSP16 expression was decreased in NCM-treated canine NPCs. Confirming the DigiWest results, *in vivo* canine IVDs treated twice with NCM demonstrated increased DUSP5 protein expression compared with controls. Taken together, these results indicate that NCM exerts its anti-inflammatory effects by increasing DUSP5 expression, which inactivates and dephosphorylates p-ERK1/2 and by directly inactivating p-PKC. This altogether leads to reduced expression of inflammatory cytokines. To further test this hypothesis mechanical inhibitory *in vitro* studies are currently performed.

Regulators of Extracellular Matrix of Intervertebral Discs identified through Proteomic Analysis of Human Fetal Intervertebral Discs

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Introduction: Degeneration of the intervertebral disc is associated with a decrease in Extra-cellular matrix (ECM) content due to imbalance in anabolic and catabolic signaling. In another study, we profiled the core matrisome of fetal NP's and identified various proteins with anabolic potential for regenerative therapies. This study aims to explore ECM regulators, associated proteins and secreted factors of the fetal NP.

Materials and Methods: Proteomic data of 9 fetal and 7 healthy adult (age 22-79) nucleus pulposus (NP) was analysed to understand the expression pattern of ECM regulators. All proteins that were uniquely expressed in fetal NP's, significantly upregulated or >2 fold upregulated if the protein was expressed in <3 fetal NP's, were selected and the respective functions are discussed.

Results: Based on the selection criteria, a total of 45 proteins were identified, of which 15 were uniquely expressed in fetal NP's, 2 showed a significantly higher expression as compared to healthy adult NP's, and 1 protein was >2 fold higher expressed in fetal NP's. Pathway analysis with the 18 abovementioned proteins revealed a significant upregulation of 1 pathway and 3 biological processes, in which 13 proteins were involved. Prolyl 4 hydroxylase (P4HA) 1 and 2, Procollagen-lysine, 2-oxoglutarate 5-dioxygenase (PLOD) 1, 2 and 3, and Heat shock protein 47 (SERPINH1) were involved in 'collagen biosynthesis' pathway. In addition, PLOD 1-3, SERPINH1, Annexin A1 and A4, CD109 and Tetranectin (CLEC3B) were all involved in biological process of 'tissue development'. Furthermore, the second biological process 'regulation of proteolysis' contained CD109, CLEC3B, SERPINH1 and SERPINF1. At last, Annexin A1, A4 and A5, Galectin-3 (LGALS-3) and SERPINF1 featured 'negative regulation of cell death'. When integrating the interaction analysis, ANXA 4 and SERPINH1 interacted directly or indirectly as initiators of all the abovementioned processes.

Conclusion: In addition to core ECM proteome, this study reveals fetal ECM regulators and ECM affiliated proteins of interest to study for regenerative therapies.

Anti-hypertrophic Effect of Adipose Cell Derived Mesenchymal Stem Cells on Mechanically Stressed Ligamentum Flavum Cells

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Introduction

Lumbar spinal canal stenosis (LSCS) in elderly population is a common pathology affecting the quality of life. Nonetheless, the exact pathomechanism of LSCS is still not clearly understood, and effective treatment modalities are lacking so far. In this current study we studied the efficacy of the novel mechanical multi torsional stress inducing device to reproduce the actual stress condition during LFH, and also evaluate the anti-inflammatory effect of ADMSCs on LFH by comparing the cell responses to ADMSCs cultured media under mechanical stress stimulation.

Methods

Human ligamentum flavum (LF) cells were used for the experiments. First, we developed a novel multi-torsional mechanical stress loading cell plate device. 5%, 15% mechanical stress strength load for 24, 48 and 72 hours were done for optimization of the stretch strength.

Subsequently, we inspected the effect of ADMSCs, which have been proposed to have anti-inflammatory effects. Inflammatory markers including interleukin(IL) -6, -8 and vascular endothelial growth factor (VEGF) as well as extracellular matrix (ECM) regulating cytokines such as matrix metalloproteinase (MMP) -1,-3 were evaluated by ELISA.

Results

Under our multi-torsional mechanical stress loading cell plate device, 5% mechanical stretch strength for 24 hours has been discovered to be the optimal strength and duration for LF cells in terms of inflammatory cellular responses.

Ligamentum flavum cells cultured in ADMSC conditioned media under 5% of mechanical stretch expressed significantly reduced amount of IL-6. IL-8 expression was larger under ADMSC conditioned media culture while VEGF expression decreased, suggesting the possible effect of ADMSCs on angiogenesis. In terms of extracellular matrix (ECM) regulation, the expression of MMP-1, -2 were significantly decreased by ADMSC conditioned media culture as well as TIMP-2 indicating the decrease of degeneration related ECM dysregulation.

Discussion

The novel multi-torsional mechanical stress loading in-vitro cell plate device which mimics the mechanical stress that ligamentum flavum encounters. ADMSC conditioned media culture showed anti-hypertrophic effect by modulating the inflammatory response and ECM regulation as well as angiogenic factor expression, indicating the potential possibility as an anti-hypertrophic treatment for LFH in the future

The Effect of Vertebral Level on Biomechanical Properties of the Lumbar Paraspinal Muscles in a Rat Model

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INTRODUCTION: Passive mechanical properties of the paraspinal muscles are important to the biomechanical functioning of the spine. In most computational models, the same biomechanical properties are assumed for each paraspinal muscle group, while cross sectional area or fatty infiltration in these muscles have been reported to differ between the vertebral levels. Two important properties for musculoskeletal modeling are the slack sarcomere length and the tangent modulus. This study aimed to investigate the effect of vertebral level on these biomechanical properties of paraspinal muscles in a rat model.

METHODS: The left paraspinal muscles of 13 Sprague-Dawley rats were exposed under anesthesia. Six muscle biopsies were collected from each rat: three from multifidus (one per each of the L1, L3, and L5 levels) and similarly three from longissimus. Each biopsy was cut into two halves. From one half, two to three single muscle fibers and two to six muscle fiber bundles (14±7 fibers surrounded in their connective tissue) were extracted and mechanically tested in a passive state. From the resulting stress-strain data, tangent modulus was calculated as the slope of the tangent at 30% strain and slack sarcomere length (beyond which passive force starts to develop) was recorded. The other half of each biopsy was snap frozen, sectioned, stained for collagen I and its area fraction was measured. One-way repeated measures ANOVA (p<0.05) was used to evaluate the effect of spinal level on the tangent modulus, slack sarcomere length, and collagen I content of multifidus and longissimus.

RESULTS: In total, 192 fibers and 262 fiber bundles were mechanically tested. For both muscle groups, no significant difference in tangent modulus of the single fibers was detected between the three spinal levels (p=0.92 for multifidus, Figure 1, and p=0.22 for longissimus). Similarly, the tangent modulus values for the fiber bundles were not significantly different between the three spinal levels (p=0.053 for multifidus, Figure 2, and p=0.36 for longissimus). In both muscle groups, the slack sarcomere lengths were not different among the spinal levels except for multifidus fibers (p=0.02, Figure 3). Collagen I area fraction in paraspinal muscles averaged 6.8% for multifidus and 5.3% for longissimus and was not different between the spinal levels.

DISCUSSION: The results of this study highlighted that the tangent modulus, slack sarcomere length, and collagen I content of the lumbar paraspinal muscles appear to be independent of spinal level. This finding provides the basis for the assumption of similar mechanical properties along a paraspinal muscle group.

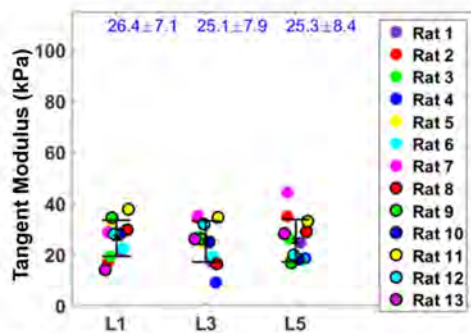


Figure 1. Tangent modulus of multifidus fibers at three different spinal levels

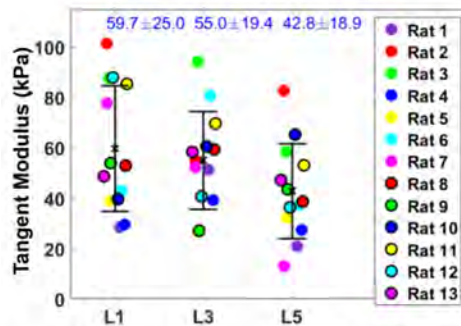


Figure 2. Tangent modulus of multifidus fiber bundles at three different spinal levels

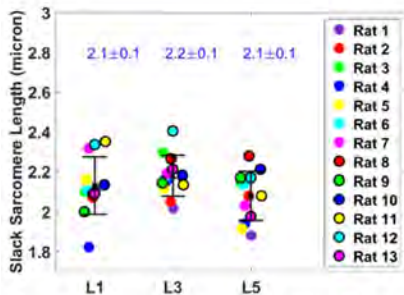


Figure 3. Slack sarcomere length of multifidus fibers at three different spinal levels

Tissue Digestion with Chondroitinase or Papain – a suitable method to create degenerated discs for in vitro experiments?

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Introduction:

Freshly isolated intervertebral discs (IVD) from bovine tails are commonly used in vitro for biomechanical and biological investigations because of a limited availability of native human disc tissue. However, their characteristics correspond to very young human discs rather than to degenerated ones. Chondroitinase ABC (ChABC) and papain have been used to induce matrix degradation in bovine IVDs, thereby simulating disc degeneration in vitro. However, biomechanical changes, such as range of motion (ROM), resulting from enzyme degradation have not been evaluated yet. Hence, the aim of this study was to treat bovine IVD organ cultures with ChABC or papain to create “degeneration” for in vitro experiments and to evaluate ROM, disc height, macroscopic morphology and histology.

Methods:

In total, 18 single motion segments (CY3/4) were prepared from 18 fresh bovine tails and embedded in PMMA. Then, ChABC (0.25 U/ml), papain (65 U/ml), or DPBS as control (n=6 per group) was injected into the nucleus pulposus. Subsequently, specimens were cultured for 7 days under free-swelling condition, hypoxia (6% O₂) and 37°C, with medium exchange at day 3. Afterwards, complex loading as a combination of lateral bending, flexion-extension (both ± 10°) and axial compression (150 N) was applied for 1 hour to mitigate disc swelling during incubation. The ROM and the change in IVD height were determined before and after enzyme treatment and after complex loading. The IVDs were collected and processed for histology with Safranin-O/Fast-Green-Staining. Statistics: Shapiro-Wilk, Mann-Whitney-U, and Friedman test (p≤0.05).

Results:

At day 7, all specimens digested with papain developed a cavity in the IVD space, whereby ChABC specimens macroscopically stayed intact (Fig. 1). During incubation with papain, the disc height decreased whereas it increased for ChABC and control (p≤0.009). Complex loading led to a decrease of the disc height in all groups (p≤0.004). After the 7-day incubation period, the ROM decreased for ChABC and control but not for papain (p=0.002). Complex loading increased the ROM significantly in all groups – strongly for the axial rotation (p≤0.028, Fig. 2). According to the histological staining, both enzymes induced glycosaminoglycan (GAG) loss, but papain showed a more pronounced effect, also influencing the annulus fibrosus.

Discussion:

Cavities and resulting significant biomechanical changes highlight a stronger digestion of the tissue for papain treatment than for ChABC. The increase in ROM and loss in height for the papain specimens indicate a similar behaviour as described for human discs with cavities resulting, for instance, from disc herniation or nucleotomy [1]. The specific digestion of GAG by ChABC led to milder structural defects and biomechanical changes; hence, it more mimics human degeneration occurring without cavities. The latter may reflect more closely the real degenerated disc. ChABC induced milder than expected degeneration, so in future work, higher concentrations will be studied. Overall, these findings enhanced our understanding of the biomechanical impact (especially ROM) of enzyme digestion of IVDs using ChABC and papain, and might enable in future studies the targeted simulation of different disc pathologies in fresh young bovine tail discs for testing purposes. **Acknowledgments:** iPSpine (825925).



Fig. 1: Macroscopic results of 4 exemplary intervertebral discs per group treated with Chondroitinase ABC (ChABC), Papain, or Control for 7 days

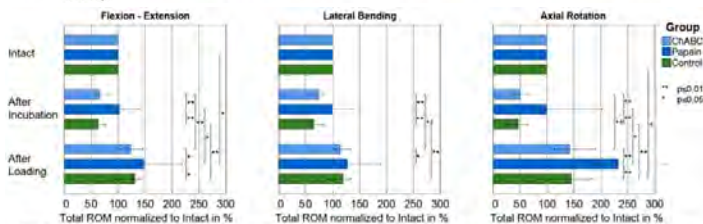


Fig. 2: Range of motion (ROM) of bovine single motion segments after treatment with Chondroitinase ABC (ChABC), Papain, or Control for 7 days in organ culture (After incubation) and subsequently after complex loading (After Loading) normalized to the intact condition (Intact) (** p<0.01, * p<0.05)

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Metformin reduces NF- κ B nuclear translocation under inflammatory stress in rat annulus fibrosus cells

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Introduction: Metformin is the most widely used oral medication for type II diabetes in the US. Recent studies have shown that metformin reduces the intensity of lower back pain in patients.^{1,2} However, it is unclear how metformin produces this effect. Previous cell culture studies in our lab have found that metformin blunts mechanical and inflammatory stress-induced expression of key proinflammatory markers, COX-2, iNOS, and PGE2. Because NF- κ B plays a central role in mediating cell response to inflammatory stress,³ we hypothesized that metformin suppresses inflammation in disc cells by downregulating the NF- κ B signaling pathway. Thus, in this study, our goal was to determine the impact of Metformin treatment on IL1-beta induced NF κ B nuclear translocation using immunofluorescence in rat annulus fibrosus cells.

Methods: Cultures of rat annulus fibrosus cells derived from four individual rats were pre-treated with either 100 mM Metformin HCl (Sigma Aldrich) or F-12 (1% FBS/1% PS) medium for 4hr in a hypoxic incubator. Then, each of the Metformin and medium pretreated cells were further treated with 1nl/mg of IL1-beta (R&D Systems) for 30min, 4hr or 24hr respectively. The cells were stained with Rb anti-p65 subunit of NF- κ B primary antibody (1:200 dilution, Cell Signal) and then treated Cy3 Goat anti-Rb IgG (1:500 dilution, Jackson ImmunoResearch). The cells were finally stained with the nuclear DAPI stain (ThermoFisher) and coverslipped before being imaged at 40x. These images were fed through an in-house quantification software to quantify cytoplasmic and nuclear NF- κ B levels. We then compare the ratio of nuclear to total NF- κ B signal between the IL1-beta treatment group and IL1-beta+metformin treatment groups at each of our time points. Activation of NF- κ B pathway is indicated by its nuclear translocation from the cytoplasm

Results: Metformin treatment of cultured rat annulus fibrosus cells significantly reduced the nuclear translocation of NF κ B after 4hr of IL1-beta treatment from 43.1% in case of IL1 beta treatment down to 26.2% in the case of metformin + IL1 beta treatment. Metformin treatment also reduced nuclear translocation of NF κ B after 30min and 24hr of IL1-beta treatment from 52.1% to 36.76% and from 31.4% to 25.7% respectively, but these results were not statistically significant.

Discussion: Metformin suppresses IL-1-mediated inflammation in rat annulus fibrosus cells by inhibiting the nuclear translocation of the p65 subunit of NF κ B, a key proinflammatory transcriptional factor. Metformin's anti-inflammatory action is mediated at least in part through NF κ B. Thus, metformin could be an important therapeutic agent for treating intervertebral disc degeneration.

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GP013

The effect of anti-RANKL monoclonal antibody on spinal fusion in a mouse spinal fusion model

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Background

Spinal fusion surgery is commonly used to treat unstable spinal condition. The purpose of fusion surgery is to gain a solid union and bony fusion. However, bone fusion sometimes delays or fails and pseudarthrosis is well described complication of fusion surgery. Anti-receptor activator of nuclear factor- κ B ligand (RANKL) monoclonal antibody is widely used for osteoporosis patient. However, the effect of anti-RANKL monoclonal antibody in spinal surgery is unknown. Therefore, we investigated whether anti-RANKL monoclonal antibody accelerate bone fusion in a mouse spinal fusion model.

Methods

A total of twenty-four male, 8-week old, C57BL/6J mice underwent posterior spinal arthrodesis surgery using collagen sponge. The animals were randomly assigned to one of the following groups: saline containing collagen and saline injection (Group1); BMP-2 containing collagen [containing 1.0 μ g in each sponge] and saline injection (Group2); saline containing collagen and anti-mouse RANKL-neutralizing monoclonal antibody injection [OYC1: 5 mg / kg] (Group3); BMP-2 containing collagen and OYC-1 injection (Group4). OYC1 or saline were injected the day after surgery. The quantitative evaluation of bone fusion was performed by direct palpation, computed tomography (CT), and micro-CT.

Results

Newly formed bone were visualized in treated with BMP-2 (Group2 and Group4), whereas no bone formation were observed in treated without BMP-2. Bone fusion was accelerated in Group4 compared to Group2 (Group2: 4 weeks, Group4: 3 weeks). Furthermore, in micro-CT analysis, Group4 showed the superior results than the Group3 [vBMD (151.5 mg/cm³ vs 488.2 mg/cm³), BV/TV (16.8 % v.s. 71.8 %), Trabecular thickness (9.4 μ m v.s. 55.5 μ m), Trabecular separation (51.6 μ m v.s. 19.7 μ m); Group3 v.s. Group4, all p < 0.05].

Conclusion

Postoperative administration of anti-RANKL monoclonal antibody significantly increases fusion rate and improves the quality of newly formed bone. Our result suggest that anti-RANKL monoclonal antibody might be a good option in management of spinal fusion surgery.

Effect of different Cryopreservation Media on Human Nucleus Pulposus Cells' Viability and Trilineage Potential

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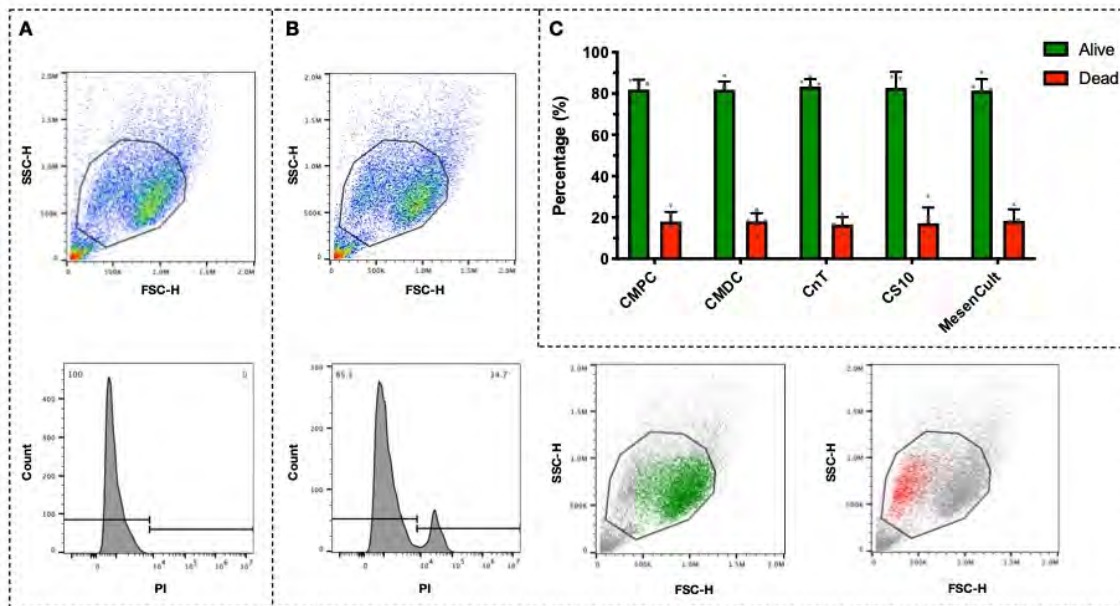
Introduction: Low back pain (LBP) is a significant cause of disability in many countries, affecting more than half a billion people worldwide. In the past, progenitor cells have been found within the nucleus pulposus (NP) of the human intervertebral disc (IVD). However, in the context of cell therapy, little is known about the effect of cryopreservation and expansion on here called “heterogenic” human NP cells (hNPCs).

Our study aimed to analyze whether commercially available cryopreservation media are more efficient than “commonly used” media in terms of cell viability and maintaining the cell’s possible differentiation potential.

Methods: In this study, hNPCs from four trauma patients (age 40.5 ± 14.3 years) and two patients with degenerated IVDs (age 24 and 46 years), undergoing spinal surgery, were collected. Consent, according to the local Human Research Act, was given by all patients. To isolate the cells, the tissue was digested with a mild two-step protocol using pronase and collagenase type 2. After subsequent expansion, hNPCs (passages 2-5) were separated and either differentiated into osteogenic, adipogenic, chondrogenic lineages for 21 days or cryo-preserved for one week at -150°C . Cryopreservation was performed with five different media to compare their effect on the cell’s viability and differentiation potential. Cell viability was determined with flow cytometry using propidium iodide. The trilineage differentiation potential was assessed by quantitative polymerase chain reaction and histological analysis. Cell viability after freezing as well as the cell’s gene expression were analysed as single replicates by two-way ANOVA followed by a Tukey’s multiple comparison test and the histological stains were analysed in technical duplicates by a Kruskal-Wallis test and a Dunn’s multiple comparisons test.

Results: After one week of cryopreservation, the hNPC’s cell viability was comparable for all five conditions, i.e. independent of the cryopreservation medium used ($82.3 \pm 0.8\%$ cell viability). Furthermore, hNPCs showed evidence for osteogenic differentiation, i.e. matrix calcification, adipogenic differentiation, i.e. significant upregulation of adiponectin as well the the production of lipid droplets, and chondrogenic differentiation, i.e. up to 750-fold upregulation of collagen type 2. Moreover, cryopreservation did not affect the cell’s differentiation potential in the majority of the donors tested.

Discussion: To conclude, “commonly used DMSO-based” cryopreservation media seem to perform just as well as commercially available media in terms of cell viability and the overall maintenance of the hNPCs trilineage differentiation potential. However, extensive donor variations were observed throughout our study.



GP015

Effect of Adiponectin receptor agonist AdipoRon on human intervertebral disc cell in a three-dimensional cell culture

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INTRODUCTION:

Intervertebral disc (IVD) degeneration is one of the major causes of low back pain (LBP) and always accompanied by inflammation. Several investigators recently reported that systemic diseases like diabetes mellitus (DM) were involved in LBP. Obesity is also one of the risk factors for LBP. Adiponectin, a hormone secreted by adipocytes, is known to have anti-inflammatory and insulin resistance effects. Previous reports have shown that adiponectin decreased tumor necrosis factor- α (TNF- α) expression in nucleus pulposus (NP) cells, and TNF- α was a pivotal contributor to IVD degeneration. The purpose of the current study was to investigate the therapeutic value and the molecular mechanism of AdipoRon, an orally active adiponectin receptor agonist, on IVD degeneration using a three-dimensional cell culture device.

METHODS:

Human IVD NP cells were obtained from 6 consented patients during the surgical procedure for degenerative disc disease, consisting of 3 males and 3 females with a mean age of 58.5-year-old (range 47-74 year-old). First, cell viability test was performed using Cell Counting Kit-8(CCK-8) to identify the cytotoxicity of AdipoRon to NP cells. After treated with various concentrations of AdipoRon, cell viability was calculated according to the absorbance value. Next, the effects of AdipoRon on inflammation and extracellular matrix (ECM) metabolism in NP cells were investigated. NP cells were pre-cultured in a Tapered Stencil for Cluster Culture (TASCL) device for three-dimensional cell culture. After pre-culture, these cells were assigned to the following four groups: Group C; cells cultured in DMEM without treatment (control group), Group A; cells cultured in DMEM treated with AdipoRon, Group I; cells cultured in DMEM treated with interleukin-1 β (IL-1 β) (10ng/ml), Group A+I; cells cultured in DMEM treated with both AdipoRon and IL-1 β . Relative mRNA expression levels of Aggrecan, type-2 collagen (Col2), interleukin-6 (IL-6), TNF- α , a disintegrin and metalloprotease with thrombospondin motifs-4 (ADAMTS-4) and matrix metalloproteinase-3 (MMP-3) were measured by real-time reverse transcription-PCR (real-time RT-PCR).

RESULTS:

(1) CCK-8 showed that AdipoRon significantly decreased NP-cell viability when the concentration was higher than 2.0 μ M ($p < 0.05$). Therefore, in the subsequent experiments, we selected concentrations of 2.0 μ M, which would not cause significant cell death.

(2) Real-time RT-PCR results showed that mRNA expression levels of TNF- α , IL-6, ADAMTS-4 and MMP-3 were significantly upregulated by IL-1 β treatment ($p < 0.05$). In pro-inflammatory cytokines, Group A+I showed significantly decreased mRNA expression levels of TNF- α and IL-6 compared to Group I ($p < 0.05$). In ECM catabolic factors, Group A+I showed significantly decreased mRNA expression level of ADAMTS-4 compared to Group I ($p < 0.05$). In ECM anabolic factors, mRNA expression levels of both Aggrecan and Col2 were not affected by AdipoRon treatment.

DISCUSSION:

The results of the current study have demonstrated that the AdipoRon treatment under IL-1 β stimulation significantly downregulated mRNA expression level of TNF- α in human IVD NP cells. Moreover, our results have also demonstrated downregulated mRNA expression levels of IL-6 and ADAMTS-4. Our results suggest that AdipoRon might have the potential to protect IVD cells from IVD degeneration by reducing inflammation.

The effects of 3D culture on the expansion and maintenance of nucleus pulposus progenitor cell multipotency.

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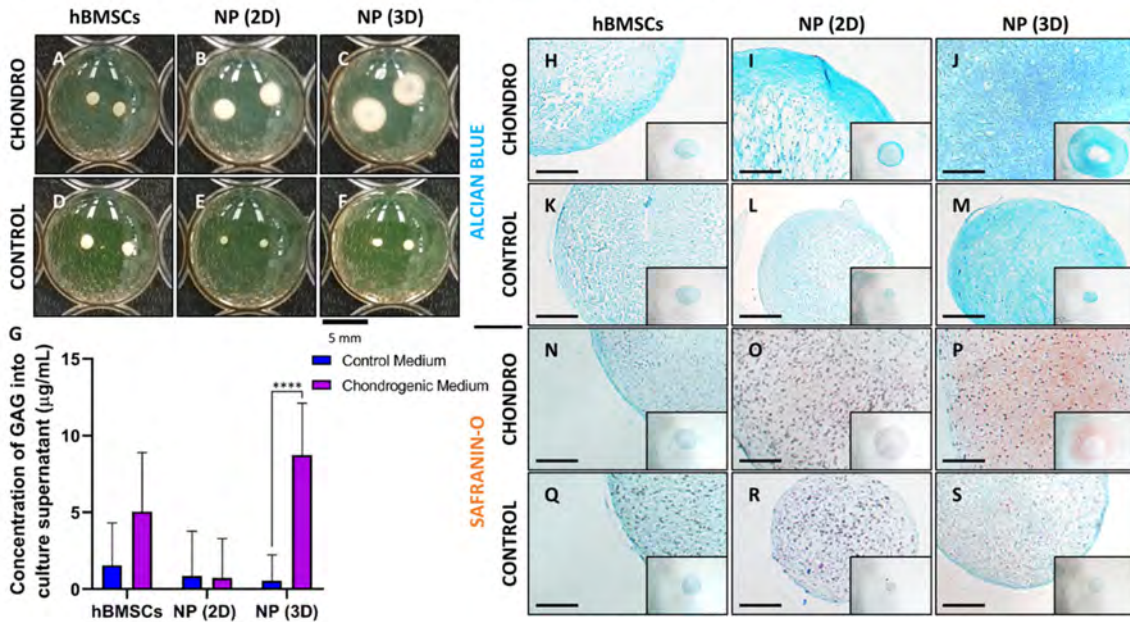
Introduction: Low back pain (LBP) is a global health concern. Increasing evidence implicates intervertebral disc (IVD) degeneration as a major contributor. In this respect, tissue-specific progenitors may play a crucial role in tissue regeneration, as these cells are perfectly adapted to their niche. Recently, a novel progenitor cell population was described in the nucleus pulposus (NP) that is positive for Tie2 marker. These cells have self-renewal capacity and *in vitro* multipotency potential. However, extremely low numbers of the NP progenitors limit the feasibility of cell therapy strategies. Here, we studied the influence of the culture method and of the microenvironment on the proliferation rate and the differentiation potential of human NP progenitors *in vitro*.

Methods: Cells were obtained from human NP tissue from trauma patients. Briefly, the NP tissue cells were cultured in 2D (monolayer) or 3D (alginate beads) conditions. After 1 week, cells from 2D or 3D culture were expanded on fibronectin-coated flasks. Subsequently, expanded NP cells were then characterized by cytometry and tri-lineage differentiation, which was analysed by qPCR and histology. Moreover, experiments using Tie2⁺ and Tie2⁻ NP cells were also performed.

Results: The present study aims to demonstrate that 3D expansion of NP cells better preserves the Tie2⁺ cell populations and increases the chondrogenic (Figure 1) and osteogenic differentiation potential compared to 2D expansion. Moreover, the cell sorting experiments reveal that only Tie2⁺ cells were able to maintain the pluripotent gene expression if cultured in 3D within alginate beads. Therefore, our results highly suggest that the maintenance of the cell's multipotency is mainly, but not exclusively, due to the higher presence of Tie2⁺ cells due to 3D culture.

Discussion: This project not only might have a scientific impact by evaluating the influence of a two-step expansion protocol on the functionality of NP progenitors but it could also lead to an innovative clinical approach.

Chondrogenic Differentiation of NP cells at the end of the 2nd Phase of Expansion



Homocysteine Induces Oxidative Stress and Ferroptosis of Nucleus Pulposus Via Enhancing Methylation of GPX4

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Introduction: Homocysteine (Hcy) is an amino acid involved in gene methylation. Plasma concentration of Hcy is elevated in the pathological condition hyperhomocysteinemia (HHcy), which increases the risk of disorders of the vascular, nervous and musculoskeletal systems, including chondrocyte dysfunction. The present study aimed to explore the role of Hcy in intervertebral disc degeneration (IVDD)

Materials and Methods: Medical history and MRI of 349 volunteers from our medical examination center were retrospectively reviewed. Hcy values were compared between the “non-severe degeneration group” (Pfirrmann grades \leq 3) and the “severe degeneration group” (Pfirrmann grade $>$ 3). We applied Hcy treatment to nucleus pulposus in vitro and HHcy mice models in vivo to explore the mechanism of Hcy in IVDD.

Results: A clinical epidemiological study showed that HHcy is an independent risk factor for human IVDD. Cell culture using rat nucleus pulposus cells showed that Hcy promotes a degenerative cell phenotype (involving increased oxidative stress and cell death by ferroptosis) which is mediated by upregulated methylation of GPX4. An in-vivo mouse ‘puncture’ model of IVDD showed that folic acid (which is used to treat HHcy in humans) reduced the ability of diet-induced HHcy to promote IVDD.

Conclusion: Hcy upregulates oxidative stress and ferroptosis in the nucleus pulposus via enhancing GPX4 methylation, and is a new contributing factor in IVDD. This establishes a new link between hyperhomocysteinemia and intervertebral disc degeneration.

Investigating the effect of culture medium osmolarity on the phenotype and regenerative capacity of canine nucleus pulposus cells

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INTRODUCTION: Intervertebral disc (IVD) degeneration is associated with the loss of healthy extracellular matrix (ECM) within the nucleus pulposus (NP). Delineating physiological stimuli that influence the NP cell (NPC) phenotype and their matrix producing capacity and recapitulating this for cell-based treatment options, represents a promising strategy for treating IVD degeneration. One physiological stimulus that changes during disc degeneration is osmolarity, which decreases during the degenerative process. Recent work demonstrated that increasing the osmolarity during expansion exerted beneficial effects on the regenerative capacity of human NPCs *in vitro*¹. The aim of this study was to investigate the effects of culture medium osmolarity during expansion and subsequent re-differentiation on the identity and regenerative capacity of canine NPCs.

METHODS: NPCs of 6 Beagle donors (mildly degenerated IVDs) were expanded for 2 passages in expansion medium with a standard osmolarity of 300 mOsm/L or adjusted to 400 or 500 mOsm/L by the addition of 5M NaCl and 0.4M KCl. Following expansion, cells from each condition were re-differentiated for 14 days in 3D microaggregates in chondrogenic medium with a standard osmolarity of 300 mOsm/L to mimic the degenerated *in vivo* environment of the disc. Readout parameters during expansion included cell morphology, growth rate constant, and gene expression. And upon re-differentiation, quantitative glycosaminoglycan (GAG) and DNA measurements, immunohistochemistry, and gene expression.

RESULTS: When looking at cell morphology, NPCs expanded in 300 mOsm/L appeared fibroblast-like, stretched out and flattened, whereas NPCs expanded in 400 and 500 mOsm/L were more sphere-shaped with shorter filopodia. Notably, increasing osmolarity up to 500 mOsm/L during expansion resulted in a significant ($p < 0.01$) decrease in the growth rate constant. No significant increase in the expression of NPC/progenitor markers (e.g. *KRT8*, *KR18*, *CA12*, *CD73*) were detected directly after expansion. In contrast, at day 3 of the re-differentiation culture in NP cells expanded at 500 mOsm/L, expression of the osmolarity response gene *NFAT5* and several NPC/progenitor markers (*KRT18*, *CD73*, *CA12*, *FOXF1*, *ACAN*) was significantly increased compared with NPCs expanded at 300 or 400 mOsm/L. Lastly, expansion in 500 mOsm/L resulted in a significantly increased ($p < 0.01$) GAG and DNA content of the NPC micro-aggregates after 14 days of re-differentiation compared with expansion at 400 mOsm/L, but not with expansion at 300 mOsm/L.

DISCUSSION: While increasing the osmolarity during expansion did not affect the NPC phenotype at the level of gene expression, the increased expression of several NPC/progenitor markers when these cells were used in re-differentiation cultures indicates that increasing osmolarity during expansion could generate a specific cell population. To further support this hypothesis, the protein expression levels of these markers are being investigated. However, one notable feature of higher osmolarity during expansion was its negative influence on cell proliferation which would be highly unfavourable when applied for a cell-based treatment strategy. Interestingly, in terms of regenerative capacity (DNA content and healthy ECM production) of the NPCs after re-differentiation, cells expanded at both 300 and 500 mOsm/L showed similar effects. However, the type of osmolyte used in this study might have affected the observed results.

1. Krouwels A et al. (2018), Comparing Hydrogels for Human Nucleus Pulposus Regeneration: Role of Osmolarity During Expansion, *Tissue Eng Part C Methods*.

The Effect of 'Clinical Reporting' on The Perception of Severity and Prognosis of LBP - Results from Blinded Trials in Four Groups of Health Care Professionals

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Introduction: The effect of catastrophization in LBP outcomes is well established. Primary health care professionals and non-spine speciality consultants form the first point of contact with chronic LBP patients. Frequent MRI prescriptions and the over reliance on MRI reports in these health care professionals might influence their perception on the disease pathology, prognostication and initial choice of treatment. In this study we developed and investigated the effects of an alternate 'Clinical reporting' and tested its benefits on LBP perception.

Methods: A google search was performed to secure the online information available to patients on terminologies frequently used in MRI, and those causing concern and anxiety to patients were identified. An alternate method of 'clinical reporting' was evolved, avoiding these terminologies without losing scientific clarity. For MRI of 20 LBP patients, both routine and clinical reporting were developed. Forty health professionals, ten each of Spine surgeons (SS), General Orthopaedic-surgeons (OS), orthopaedic residents (OR), and physiotherapists (PT) involved in spine care went through these reports in a blinded fashion and opined on three factors for each report – 1) their assessment of severity of the spinal condition (scale-0-10); 2) their choice of treatment between conservative therapy, injection and surgery and 3) the probability of requiring surgery (scale-0-10). For the opinions generated by Clinical reporting, a change from surgery to injection/conservative management was considered as a decrease in magnitude of invasiveness. A shift from conservative to injection/surgery was considered as an increase in magnitude.

Results: All three parameters - assessment of severity of the spinal pathology; choice of treatment between conservative, injections and surgery; and the perceived probability of requiring surgery differed considerably between routine and Clinical reporting for the same patient's MRI when the four groups of health care providers studied the reports in a blinded fashion. Clinical reporting significantly reduced the severity assessment of disease in OS (5.68 to 4.99), OR (5.58 to 5.20), and PT (6.07 to 5.39) groups. No significant change was noted among SS (5.05 to 5.23). Following Clinical reporting, the choice of treatment shifted to a decrease in magnitude of invasiveness amongst OS(45%), OR(48%), and PT(44.5%). There was no difference noted with SS(23.5%). The assessment of the requirement of surgery also dropped following Clinical reporting in OS(5.9 to 4.8), OR(5.8 to 4.7), and PT(6.3 to 5.1) with no difference amongst SS (4.9 to 4.6) Overall, the perception of severity, the need for invasive approach, and probability of the disease progressing to surgery showed a significant decrease following Clinical reporting.

Conclusion

Clinical reporting had significant benefits as for the same MRIs, it led to an assessment of lesser severity of the disease, shift to lesser severity of intervention and surgery in all four groups. Our study calls for the need for 'Clinical reporting' rather than 'Image reporting'.

GP020

Relationship between lower extremity muscle tightness and low back pain in elementary school-aged baseball players: a cross-sectional study

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INTRODUCTION

The lower extremity muscle tightness, such as iliopsoas, hamstrings, and quadriceps tightness, has long been debated as physical risk factors for low back pain (LBP) in youth athletes. However, few epidemiological studies examine the relationship between lower extremity muscle tightness and LBP among elementary school-aged athletes. This study aimed to investigate the relationship between lower extremity muscle tightness and LBP in elementary school-aged baseball players.

METHODS

An initial total of 613 players from 47 baseball teams participated in the medical evaluations (a self-completed questionnaire and physical examination). Fifty-seven players who were missing data were excluded, 561 players (121 pitchers, 440 fielders) were included in this study. We investigated the relationship between LBP on the season and the measurements of the flexibility of the lower extremities such as Thomas test (iliopsoas tightness), straight-leg-raising angle (hamstrings tightness), and heel-buttock-distance (quadriceps tightness). We calculated odds ratios and 95% confidence intervals to examine the association between the potential risk factors and the episodes during the seasonal LBP, using univariate and multivariable logistic regression analysis. The following were analyzed as potential risk factors: position (a pitcher), duration of baseball experience, the total amount of practice per week, and the tightness of lower extremity. All tests used were two-sided, and P values of less than 0.05 were considered statistically significant.

RESULTS

A total of 45 of 561 players (8.0%) reported the occurrence of seasonal LBP during the previous year. Iliopsoas tightness (36.5%), hamstrings tightness (18.5%), and quadriceps tightness (24.4%) were confirmed in 205, 104, and 137 players, respectively. Quadriceps tightness (odds ratio 2.22 (1.18-4.18); P=0.018) were associated with the seasonal LBP in univariate analysis. After adjusting for factors associated with LBP using logistic regression modeling, significant associations between quadriceps tightness (odds ratio 2.35 (1.23-4.51); P=0.010) and LBP were found.

DISCUSSION

The quadriceps tightness was identified as a risk factor potentially associated with LBP occurrence in elementary school-aged baseball players. The quadriceps tightness is a modifiable factor that warrants preventative efforts. The findings of our study may guide to the management of LBP in elementary school-aged baseball players.

Low trunk muscle mass impacts on lumbar disability, kyphosis, and quality of life: A multicenter longitudinal study

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Introduction

The trunk muscles are essential supportive components of the spine. We have conducted a large multicenter cross-sectional study indicating that trunk muscle mass (TMM) is significantly associated with spinal disorders and quality of life (QOL)¹. However, these causal relationships have remained unclear, and large-scale longitudinal studies has been needed to elucidate them. The purpose of this study is to investigate the impact of low trunk muscle on spinal pathologies through a longitudinal study.

Methods

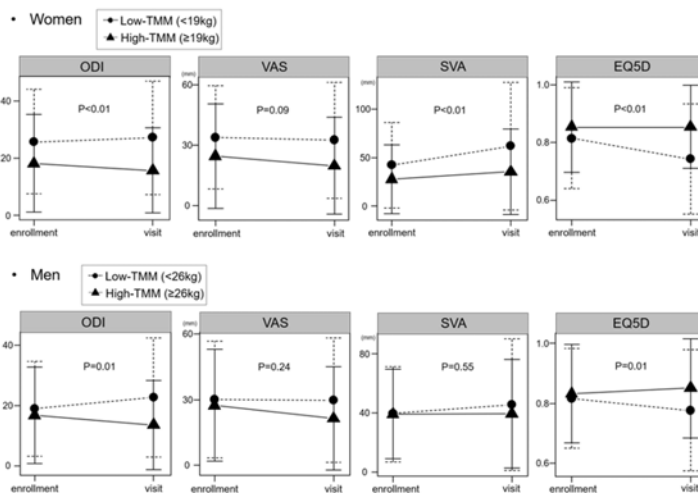
The current study was the multicenter longitudinal study. Patients who visited outpatient clinics for spine or osteoporosis and undertook muscle mass measurements by the bioelectrical impedance analysis (BIA) at two time points (≥ 1 year apart) were included in the study. The exclusion criteria were patients who had undergone lumbar spine surgery between the measurements. TMM, appendicular skeletal muscle mass (ASM), Oswestry Disability Index (ODI), visual analog scale for low back pain (VAS), sagittal vertical axis (SVA), and EuroQOL 5 dimension (EQ5D) were investigated at the measurements. Based on the results of the previous cross-sectional study¹, the low-TMM group was defined as the initial TMM < 19 kg for women and < 26 kg for men. Changes in ODI, VAS, SVA and EQ5D were compared between the low- and high-TMM groups using mixed effect model adjusted for age, body mass index, and ASM.

Results

A total of 654 patients (mean 71.0 years old, 413 females; 241 males, mean interval 2.8 years) were included in this study. Of these, 188 (46%) females and 110 (46%) males were classified into the low-TMM group. In women, ODI, SVA and EQ5D were significantly deteriorated in the low-TMM group ($P < 0.05$). VAS was also deteriorated more in the low-TMM group, without significant difference ($P = 0.09$). In men, ODI and EQ5D were significantly deteriorated in the low-TMM group ($P < 0.05$), whereas no significant difference was observed in VAS and SVA ($P > 0.10$).

Discussion

The current study demonstrated that lumbar disability, QOL, and spinal kyphosis worsened significantly over an average of 2.8 years in the low-TMM group, suggesting that decreased trunk muscle may lead to deterioration in spinal pathologies. The increase in trunk muscle could be effective in overcoming spinal pathologies; it may be necessary to establish efficient interventions for trunk muscles, including physical therapy, medication, and nutrition therapy.



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Central sensitivity is associated with chronic low back pain in the general population

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INTRODUCTION

Central sensitization (CS) is defined as the increased responsiveness of nociceptive neurons in the central nervous system to normal or subthreshold afferent input [1]. Central sensitivity syndrome (CSS) is a group of overlapping conditions that share a common pathophysiological mechanism of CS [2]. Previous studies have shown that CSS is present in patients with several disorders including chronic low back pain [3]. However, the association of CS with chronic low back pain in the general population remains unknown. A Central Sensitization Inventory (CSI) has recently been developed for screening subjects with CS and/or CSS [4]. The purpose of this study was to investigate the association of CS with chronic LBP using the CSI in a population-based cohort of a Japanese mountain village.

METHODS

1. Subjects aged more than fifty years old were recruited from a mountain village in Japan. All subjects provided written informed consent before enrollment in the study. Ethical approval for the study was granted by the Committee for the Ethics of Human Research. 2. Subjects completed an interviewer-administered questionnaire. Anthropometric measurements included body height, body weight and bone mineral density (BMD). All subjects were interviewed by experienced orthopedists regarding the presence of low back pain and were first asked, "Do you have low back pain that lasts more than three months?" Subjects who answered 'Yes' were defined as the chronic low back pain (cLBP) group. Participants completed the following patient-reported outcome measures. CSI was assessed in all participants. LBP intensity was measured on the numerical rating scale (NRS). Health-related QOL was measured using the EuroQol 5-dimension (EQ-5D), EuroQol-visual analogue scales (EQ-VAS), and the Oswestry Disability Index (ODI). The association of CIS and each parameter was statistically evaluated.

RESULTS

1. 272 subjects (average age: 72.1 years-old) were analyzed in this study. 28.3% had chronic low back pain. Average NRS, ODI and CSI were significantly higher in the cLBP group than in the without LBP group. Average EQ-5D and EQ-VAS in the cLBP+ subjects were significantly lower than those without LBP subjects ($P < 0.0001$, respectively). 2. CSI was significantly, but weakly, correlated with NRS ($r = 0.34$, $P < 0.0001$). There was a significant correlation between CSI and ODI ($r = 0.60$, $P < 0.0001$), EQ5D ($r = -0.55$, $P < 0.0001$) and EQ-VAS ($r = -0.52$, $P < 0.0001$) (Figure). A multiple regression analysis identified that ODI (%) ($\beta = 0.43$, $P < 0.0001$), EQ-VAS ($\beta = -0.17$, $P < 0.0001$) and age ($\beta = -0.19$, $P < 0.01$) were factors significantly associated with CSI.

DISCUSSION

The results of this population-based cohort study showed that CSI was significantly higher in the cLBP group than in no cLBP groups. This suggests the possibility that CS would be involved in the pathophysiology of cLBP. The CSI scores of general population and cLBP subjects in this study could be used as essential reference data for future clinical research on LBP.

1. [1] Woolf CJ. Pain. 2011;152(3 Suppl):S2-15, [2] Neblett R, et al. J Pain. 2013;14(5):438-45, [3] Sanzarella I, et al. J Back Musculoskelet Rehabil. 2016;29(4):625-33, [4] Mayer TG et al. Pain Pract. 2012;12(4):276-85.

A Handheld Spine Scanner for Home Monitoring of Scoliosis Patients Can Reduce Clinic Attendance by 60%: A Prospective Longitudinal Study

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Introduction

Early detection of scoliosis by school-screening programs has generated significant burdens on the healthcare system for follow-up. SpineScan3D is a handheld smartphone-based surface profiling tool with a gyroscope and accelerator embedded for the measurement of back shape. One of the output parameters is the “tilt” angle, which represents the rotational prominence, more commonly known as the hump. Initial reliability studies have shown the good correlations of Spinescan3D measurement with the scoliometer and radiographic Cobb measurements. Good consistency has been found between well-trained technicians and newly trained technicians, suggesting its potential for home monitoring by caregivers. This study aims to evaluate the possibility of SpineScan3D for home monitoring of scoliosis subjects.

Methods

Adolescent idiopathic scoliosis (AIS) patients presenting to our scoliosis clinic were recruited. At the initial visit, SpineScan3D measurements were performed at a forward bending posture with Cobb angle noted on spine radiographs. At each subsequent clinic visit, the measurements were repeated. Changes in back shape were measured as a “tilt” angle. Receiver operating characteristics (ROC) curve was used to determine the cut-off values of Cobb angle and tilt angle change.

Results

113 patients were recruited at a mean age of 12 with 86 females and 27 males. Using a cut-off value of 6 degrees in Cobb angle change and 2.4 degrees in tilt angle change, a true-negative rate of 88% was found, representing 60% of the whole sample, while a false-negative rate of 50% was noted, representing 16% of the whole sample (see below Figure).

Discussion

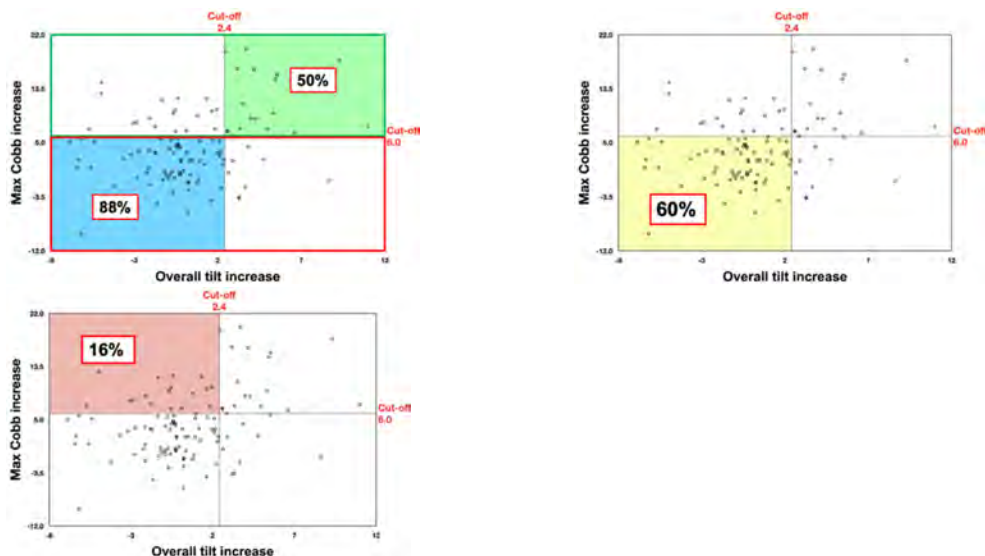
Spinescan3D is a handheld and portable electronic device with a low manufacturing cost and therefore a potential for widespread adoption within the community. In this prospective longitudinal study, we demonstrate its potential to help reduce clinic follow-up for non-progressive curves.

Like all devices that measure surface topography, it cannot replace radiographs. Here we show that by using a relatively conservative cut-off value, therefore accepting a larger false positive value, we can ensure that the majority of those that need follow-up are returned to the clinic. At the same time, the true-negative rate is 88%, this still represents a significant reduction to clinic burden.

However, 16% of the cases may be missed, which is still significant and therefore work is on-going to reduce this rate by examining the value of repeat home scanning and standardized scanning posture.

Conclusions

This is the first study to show that a portable device has the potential to be used at home for follow-up and change the way that we currently manage AIS. In future, non-progressive AIS subjects need not be seen so frequently in clinics, thereby enhancing clinic efficiency, reduce patients' radiation risks and health care costs.



GP024

The profile of the spinal column in subjects with lumbar developmental spinal stenosis

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Introduction

Lumbar developmental spinal stenosis (DSS) is likely a result of genetic disturbance during fetal and postnatal development of the lumbosacral spine. The pre-existing narrowed vertebral canal predisposes patients to a lower threshold of neural compression, in which a milder degree of degenerative changes of the lumbar spine is already sufficient to develop symptoms. However, it is uncertain whether other specific osseous changes of the lumbar spinal column are presented concurrently in patients with a maldeveloped lumbar canal. Changes may be contributed by subjects' height, weight, body mass index (BMI) and vertebral size. Similar changes may also occur through altered development of the spinal column. The study aims to determine the associations of DSS with osseous and soft tissue changes of the spinal column.

Methods

This was a radiological analysis of 2387 subjects who underwent L1-S1 magnetic resonance imaging (MRI). Means and ranges were calculated for their age, gender, body mass index (BMI) and MRI measurements. AP vertebral canal diameters were utilized to differentiate cases of DSS from controls. Other imaging parameters included vertebral body dimensions including midline AP vertebral body diameter, mid-vertebral body width; spinal canal dimensions including midline AP vertebral canal diameter, interpedicular distance, midline AP dural sac diameter, left and right pedicle width, lamina angle; disc herniation, degeneration scores, Modic changes and Schmorl's nodes; and left and right facet joint angle at L1-S1. Mann-Whitney *U* and chi-square tests were conducted to search for measurement differences between cases and controls. To identify possible associations between DSS and MRI parameters, parameters that were statistically significant in the univariate binary logistic regression were included in a multivariate stepwise logistic regression after adjusting for subject demographics.

Results

From 2387 subjects, 7.2% (n=173) was identified to have DSS. Subjects with DSS had shorter axial vertebral canal diameter, interpedicular distance, AP dural sac diameter and vertebral body height at L1-S1. Besides, subjects with DSS had higher disc herniation scores, higher disc degeneration scores and larger right facet joint angulation. No association was observed between DSS and BMI (p=0.195). After adjusting for age, gender and BMI, DSS was associated with narrower interpedicular distance (OR 0.745; p=0.002; 95% CI: 0.618-0.900), smaller AP dural sac diameter (OR 0.506; p<0.001; 95% CI: 0.400-0.641), more obtuse lamina angle (OR 1.127; p=0.002; 95% CI: 1.045-1.214) and right facet joint angulation (OR 0.022; p=0.002; 95% CI: 0.002-0.247). No association was observed between disc parameters and DSS.

Discussion

From this large-scale cohort, the canal size is found to be independent of subject body habitus. Other than spinal canal dimensions, abnormal orientations of lamina angle and facet joint angulation may also be a result of developmental variations, leading to increased likelihood of DSS. Other skeletal parameters are spared. Besides, there is no relationship between DSS and soft tissue changes of the spinal column, which suggested DSS is a unique result of bony maldevelopment.

Association between Low Back Pain in Activities of Daily Living and Quality of Life: A Population-based Cohort Study

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INTRODUCTION: Low back pain (LBP) is a significant worldwide condition with extensive medical expenses, work-related disability and decreased quality of life (QoL) issues. In this study, we have assessed whether the quantification of LBP in each activity of daily living would be useful for evaluating LBP's influence on QoL.

The purpose of this study was to examine (1) the influence of the extent of LBP on the activity of daily living (several situations/positions) on QoL issues and (2) the factors associated with LBP-related QoL in a medical examination of mountain village inhabitants.

METHODS: Institutional Review Board approval was obtained for the study.

Subjects: A medical examination of inhabitants was conducted in a typical mountain village in Japan. 286 inhabitants (79 men, 207 women; mean age: 72.2 years-old) completed an interviewer-administered questionnaire that included the presence of LBP and the evaluation of QoL. To assess the location of LBP and the extent of LBP in several different situations/positions, physical examinations were performed by an orthopedic surgeon. LBP intensity was measured on an 11-point pain intensity numerical rating scale (NRS). The Oswestry Disability Index (ODI), EuroQoL-5D (EQ-5D), and EuroQoL-visual analog scale (EQ-VAS) were measured for LBP and health-related QoL issues. Participants with any of NRS scores more than three were defined as the LBP-positive group.

LBP in several situations/positions: The extent of LBP in the following situations/positions was assessed using an NRS: 1. morning awakening; 2. walking; 3. standing; 4. half-sitting posture; 5. sitting; and 6. lying-down.

Statistics: The association between the presence of LBP and health-related QoL scores was statistically evaluated using the Mann-Whitney U test. Factors associated with LBP-related QoL were identified by multiple regression analysis.

RESULTS: 98 participants (34.2%) were classified as the LBP-positive group. Age, ODI, EQ-5D, and EQ-VAS scores of the LBP-positive group were significantly higher than those of the LBP-negative group ($P < 0.01$).

LBP in several situations/positions: Most of the subjects had LBP in half-sitting posture ($n = 143$, 50.0%), following those in the morning ($n = 50$, 17.4%), and those in the standing ($n = 19$, 17.1%).

Multiple regression analysis: The total NRS score of LBP in several situations/positions, the extent of LBP in standing and those in lying-down were significantly associated with ODI score. The total NRS score of LBP in several situations/positions was significantly associated with EQ-5D scores and EQ-VAS scores.

DISCUSSION: This study showed the relationship between the extent of LBP in an activity of daily living and the influence of the location of LBP on QoL in a medical examination of mountain village inhabitants. The total NRS score of LBP on daily living activity (several situations/positions) was associated with QoL. The results of this population-based study suggest that the clinical evaluation of the extent of LBP in different situations/positions would be of great importance for the treatment of LBP because of their involvement with reduced QoL.

Trends of Spine Surgeries During COVID-19 Pandemic: Survey in Non-epidemic Region in Japan

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Introduction

As a result of the Coronavirus Disease 2019 (COVID-19) pandemic, the importance of triaging surgeries is suggested to reduce burdens on the existing health system and maintaining service. To avoid COVID-19 outbreak in Hokkaido, Japan, the governor declared the state of emergency on February 28th 2020 and lifted on May 25th 2020. In our institution, we didn't triaged spinal surgical candidates because reports of COVID-19 were sporadic in South Hokkaido including our medical region (15 reports among 0.5 million residents). However, there is a potential possibility of increase in patients' requests for cancelling surgery considering stay-at-home request from government. For many spine patients, a significant delay in care may result in a progression of extremity weakness and pain with less predictable improvement after surgery. The aim of this study is to investigate trends of surgical spine pathologies in the non-epidemic region in Japan during COVID-19 pandemic.

Methods

We reviewed surgical spine procedures performed in our institution from March 1st until May 31st between 2017 and 2020. We compared the number of surgical spine procedures and varieties of surgical spine pathologies between 2020 and 2017-2019.

Results

The numbers of surgical spine procedures performed in 2017, 2018, 2019 and 2020 were 136, 115, 112 and 109, respectively (Fig. 1). The percentage of elective surgery was 62.4% (68/109 patients) in 2020 versus 80.2% (291/363 patients) in 2017-2019; the difference was statistically significant ($P < 0.05$ in Chi-square test). The percentage of urgent surgery was 37.6% (41/109 patients) in 2020 versus 19.6% (71/363 patients) in 2017-2019; the difference was statistically significant as well ($P < 0.05$ in Chi-square test). Urgent surgeries were mainly performed for spine trauma, acute worsening of cervical or thoracic myelopathy and cauda equina or severe nerve root compression leading to progressive neurological deterioration or intractable pain. The prevalence of spine trauma was 5.5% (6/109 patients) in 2020 versus 1.4% (5/363 patients) in 2017-2019; there was statistically significant ($P < 0.05$ in Yates' Chi-square test). The prevalence of acute worsening of myelopathy was 5.5% (6/109 patients) in 2020 versus 2.2% (8/363 patients) in 2017-2019; there wasn't statistically significant ($P = 0.144$ in Yates' Chi-square test). The prevalence of cauda equina or severe nerve root compression was 20.2% (22/109 patients) in 2020 versus 12.4% (45/363 patients) in 2017-2019; there was statistically significant ($P < 0.05$ in Chi-square test) (Fig. 2).

Discussion

Compared with 2017-2019, the number of elective surgeries in 2020 decreased by thirty percent, and the number of urgent surgeries in 2020 increased by seventy percent. It is assumed that the main reason of decrease in elective surgeries was increase in cancelling and postponing surgery due to patients' request. In addition, increase in the number of patients with progressive neurological deterioration might be caused by hesitate unduly to visit a hospital in order to accept a government request despite existing severe neurological disorders. The social conditions with COVID-19 pandemic lead to decrease in elective surgeries and increase in urgent surgeries, and may affect progressive neurological deterioration for some spine patients even in a non-epidemic region.

The difference of union rate of early stage spondylolysis among each affected lumbar spinal level in young athletes.

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INTRODUCTION

Virkki (1) reported that there was no significant difference of union rates of spondylolysis between L5 and the other lumbar spinal levels. However, there were very few reports about union rate of early stage spondylolysis of each affected lumbar spinal level, therefore it is not well known about that. The purpose of this prospective study was to clarify the difference of union rate of early stage spondylolysis among each affected lumbar spinal level in young athletes.

MATERIALS AND METHODS

Forty young athletes with early stage lumbar spondylolysis participated in this study. There were 34 male and 6 female. Their mean age was 15 years ranged from 9 to 18 years. All athletes were diagnosed as early stage lumbar spondylolysis by MRI at the first visit. They also underwent computed tomography at the first visit and 3 months later to observe bone union at fractured pars interarticularis. We recommended them to interrupt sports activity and wear a hard orthosis during at least 3 months to treat spondylolysis. Twenty-four athletes (accepted group) accepted and followed our protocol, however 16 athletes (refused group) refused our recommendation because of their competition schedule. Refused group continued sports activities without a hard orthosis depended on the degree of their symptom. Spondylolysis was observed 3 cases in L3, 6 cases in L4 and 15 cases in L5 in accepted group at the first visit. Spondylolysis was observed 1 case in L3, 8 cases in L4 and 7 cases in L5 in refused group at the first visit. Union rates of each affected lumbar spinal level on computed tomogram were calculated in both groups.

RESULTS

Union rates of L3, L4 and L5 was 100%, 83.3% and 80.0%, respectively, in accepted group. Union rates of L3, L4 and L5 were 0%, 75% and 14.3%, respectively, in refused group. There was no statistically significant difference of union rate among affected lumbar spinal levels in accepted group, however, union rate of L5 was significantly lower than that of L4 in refused group (chi-square test $p < 0.0403$).

DISCUSSION

Union rates of early stage spondylolysis of each affected lumbar spinal level were more than 80% and significant difference was not observed among affected lumbar spinal level in accepted group. However, that of L5 was significantly lower than that of L4 in refused group. Tezuka (2) reported variations in arterial supply to the lower lumbar spine. From L1 to L4, each segmental artery was identified bilaterally in more than 90% of subjects, but it was identified in less than 10% of subjects at L5. Smaller amount of blood supply for L5 posterior element may be a factor of lower union rate. Surprisingly, union rate of L4 in refused group was 75% without proper treatment. It suggests that sports doctor may tolerate some athletes with early stage L4 spondylolysis who must participate their competition refusing treatment.

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Do Grit and Self-Control Impact Outcomes following Spine Surgery? A Retrospective Analysis

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Introduction:

The concept of grit, defined as perseverance and passion for long-term goals, was introduced by Duckworth et al as an important predictor for achievement in professional domains. A greater degree of grit has been shown to reliably predict better performance across multiple disciplines.

Another important determinant of achievement is self-control, defined as the capacity to regulate behavioral, emotional, and attentional impulses in the presence of momentarily gratifying temptations or diversions. Previous studies have demonstrated that individuals with greater degrees of self-control were more likely to demonstrate higher academic performance, react with more optimal emotional responses, have better adjustment, and interact with greater interpersonal skills.

Though grit and self-control have been well-explored in their relationship with achieving professional achievement, the association between these traits and outcomes following surgery has not been explored. Thus, the purpose of this study was to assess whether there is an association between grit/self-control and the achievement of minimum clinically important difference (MCID) following elective spine surgery.

Methods: Consecutive patients at a single academic institution who underwent primary elective spine surgery and had at least 1 year follow-up were included. The three surgical cohorts were: 1) ACDF or CDR, 2) Minimally invasive lumbar decompression (MI-D), and 3) Minimally invasive TLIF (MI-TLIF). The 8-Question Short Grit Scale and the 10-Item Self-Scoring Self-Control Scale were used to assess grit and self-control, respectively. Grit and self-control scores were compared between patients who achieved MCID by a certain time-point and those who did not. The time-points were selected based on when the majority of patients in each cohort had achieved MCID. PROMs included NDI for ACDF/CDR patients, and ODI for lumbar patients.

Results: Of the 69 patients included, 17 underwent ACDF/CDR, 28 underwent MI-D, and 24 underwent MI-TLIF (Table 1). In the ACDF/CDR cohort, 64.3% of patients achieved MCID in NDI at 6 months (Table 2). There were no significant differences in grit and self-control scores between patients who achieved MCID in NDI at 6 months post-operatively versus those who did not (Table 3).

In the MI-D cohort, 48% patients achieved MCID in ODI at 2 weeks (Table 2). There were no significant differences in either score between patients who achieved MCID in ODI at 2 weeks post-operatively versus those who did not (Table 3).

In the MI-TLIF cohort, 59.1% of patients achieved MCID in ODI at 12 weeks (Table 2). There were no significant differences in either score between patients who achieved MCID in ODI at 12-weeks versus those who did not (Table 3).

Conclusion: Preliminary results show that grit and self-control scores are not associated with achievement of MCID following spine surgery. A study with a larger sample size will need to be conducted to further evaluate the impact of grit and self-control.

Current status of the oral hygiene in spine surgery patients

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Introduction:

In spine surgery, complications such as surgical site infections and postoperative pneumonia can lead to serious medical conditions, and prevention is extremely important. It has been reported that maintaining a good oral environment is important for the prevention of surgical site infection and postoperative pneumonia. However, there are no reports on the actual status of the perioperative oral environment in patients undergoing spine surgery. In this study, we investigated the oral environment of spine surgery patients who received perioperative oral care, including severe periodontal disease and dental caries.

Material and Methods:

A total of 121 cases of spinal surgery under general anesthesia performed at our hospital between June 2019 and September 2020. A total of 121 cases of spinal surgery under general anesthesia in which perioperative oral care was performed in our dental and oral surgery department were reviewed retrospectively. The oral environment assessment was reviewed by our dentist for the number of remaining teeth, severe periodontitis (periodontal pockets greater than 6 mm), number of caries, and presence or absence of a dental care provider.

Results:

Mean age: 66.1 years, sex: 59 males, 62 females; surgical site: 12 cervical spine, 8 thoracic spine, 101 lumbar spine; disease: 62 lumbar spinal stenosis, 30 lumbar disc herniations, 13 spinal fractures, 11 cervical myelopathy, 3 thoracic myelopathy, 2 others and 89 patients had a dental clinician.

Number of remaining teeth: 12 patients had less than 20 teeth (9.9%), severe periodontitis: 34 patients had periodontal pockets of 6 mm or more (28.1%), caries: 38 patients had one or more caries teeth (31.4%), and 83 patients had a dental care provider (68.6%).

When the age groups aged 70 years and older and those aged under 70 years were compared, the number of remaining teeth tended to be lower in those aged 70 years and older, but there was no significant difference in the number of patients with severe periodontal disease, caries and dental care provider. No significant differences were found between caries and severe periodontal caries when comparing with patients with and without a dentist. Comparing age groups, the incidence of periodontal disease was higher in the 40s, while dental caries was found in all age groups.

Discussion:

Severe periodontitis and caries were found in about 30% of patients undergoing spine surgery. Because periodontal disease was more common in middle age and later, and caries was found in all age groups, perioperative oral care should be provided to all age groups, not just the elderly. Even if a patient is seen in a dental clinic, the oral hygiene environment is not always good in many cases, and all patients need to be closely monitored for perioperative oral environment.

Conclusion:

Severe periodontitis and dental caries were present in 28.1% and 31.4% of the patients, respectively. There was no significant difference in the prevalence of severe periodontitis and dental caries between patients with and without a primary dentist. By age group, periodontal disease was more prevalent after 40 years of age, while caries was found in all age groups.

GP030

Does lumbar spinal stenosis on MRI affect quality of life? -A large scale general population survey-: The Wakayama Spine Study-

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Objective

The relationship between radiographic lumbar spinal stenosis (rLSS) on MRI and clinical symptoms has been sporadically studied in patients. They reported that rLSS prior to LSS surgery had bad effect on walking distance and leg pain. On the other hand, there was one report on rLSS in 21% of 63 healthy volunteers and none of the large-scale studies in the general population have been conducted in the past. The purpose of this study was to determine the relationship between rLSS and quality of life (QOL) in the general Japanese.

Methods

We omitted those who were less than 40 years and had previous lumbar spine surgery. The severity of rLSS was qualitatively graded on the axial images as: no stenosis; mild stenosis - a maximum of 1/3 narrowing; moderate stenosis - narrowing between 1/3 to 2/3, and; severe stenosis as more than 2/3 narrowing. The Oswestry Disability Index (ODI) which includes 10 sections was used to assess QOL and one-way analysis of variance was performed for the relationship between rLSS and ODI as a statistical technique.

Results

Complete data were available for 907 patients (300 men and 607 women; mean age, 67.3±12.4 years) The prevalence of rLSS in severe, moderate, and mild/none was 30% severe, 48% moderate, and 22%. Regarding each rLSS, the mean ODI% was 12.9% in severe, 13.1% in moderate, and 13.1% in mild/none, with no statistically significant difference among these three rLSS groups (P=0.55). In addition, there was no significant difference in each section of ODI among the three rLSS groups. However, severe rLSS was an associated factor for low back pain (LBP) in a logistic analysis adjusted for sex, age and BMI (odds ratio: 1.53, confidence interval: 1.13 - 2.07).

Conclusion.

In the general population study, rLSS was associated with LBP but was not significant difference from QOL.

Effect of Postmenopausal State on Distribution of Bone Mineral Density in the Lumbar Spine

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Introduction:

Hounsfield units (HU), typically measured at L1-L2, have been identified as a surrogate marker for lumbar Bone Mineral Density (BMD). However, concern remains that L1-L2 BMD may not fully capture BMD differences throughout the lumbosacral spine and inadvertently provide inaccurate assessment.

Thus, the purpose of this study was to evaluate the impact of to analyze how conventional HU evaluation relates to local HU at commonly instrumented levels, and to evaluate the impact of age and post-menopausal state on HU in the lumbar spine.

Material and Methods:

Consecutive female patients presenting to a spine clinic who underwent lumbar CT were selected. Previous lumbar surgery, tumor, fracture or infection were excluded. Patients were divided based on whether they were pre- or post-menopausal. Hounsfield Units (HU) were assessed on lumbar CT by placing an elliptical region of interest confined to the medullary space of the vertebral body, and avoiding cortical bone or sclerosis. HU measurements were performed for L1-S1 in 7 regions: Mid-sagittal; Axial plane - Superior, Waist, and Inferior; Axial plane at the waist – Anterior, Middle and Posterior.

HU were compared between the pre- and post-menopausal cohorts using student t-test or Manny-Whitney u-test. The difference between routinely used L1L2 average HU and local HU in each region was calculated and compared between groups. Association of age and menopausal state with HU was assessed using regression analyses.

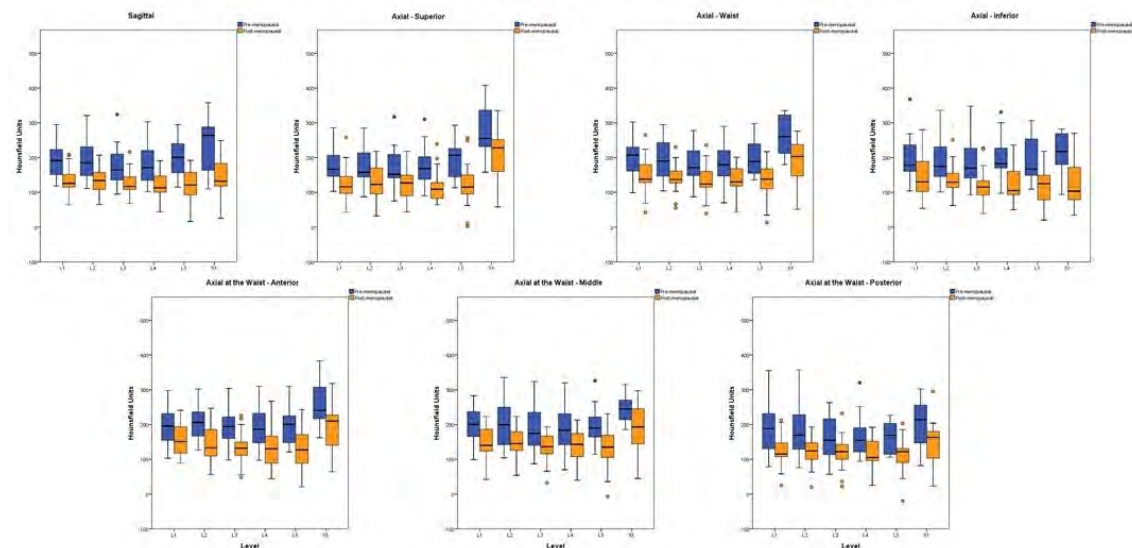
Results:

Forty-eight patients, 18 pre-menopausal and 30 post-menopausal were included. The post-menopausal group was significantly older (67 versus 41 years; $p < 0.0001$). Post-menopausal women had lower HU in all regions at all levels ($p < 0.05$), with the mean difference ranging from 45 to 90 HU. Depending on the region, the L1L2 average was more than 10 units greater than L4 in 30–70% of pre-menopausal and 40–70% of post-menopausal women ($p > 0.05$). L1L2 average was also more than 10 units greater than L5 measurements in 17–78% of pre-menopausal and 40–70% of post-menopausal women ($p > 0.05$, except Sagittal region $p = 0.038$). Age, but not BMI showed a significant negative correlation with HU, which was strong in pre-menopausal and moderate in post-menopausal women. Age and menopausal state account for 35-60% of the variability in HU, except in the Posterior region, where they account for 25-45%.

Conclusion:

Age and post-menopausal state were negatively associated with HU in the lumbosacral spine, and the conventionally used L1L2 average did not adequately capture local HU variations. Local BMD assessment using HU may provide a more accurate assessment of morphometric characteristics and trabecular milieu in the operative region.

Comparison of HU between Pre- and Post-menopausal women



GP032

AGEs are associated with the intensity of back pain symptoms in patients with lumbar spinal stenosis

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Introduction: AGEs affect cell and trigger the generation of free radicals and expression of inflammatory gene mediators in the body and are thought to be one factor in aging. Last year we clarified the association of decreasing muscle mass in men and increasing fat mass in women with increasing AGEs. However, there has been no report of skin AF in patients with low back pain. Autofluorescence (AF) is a proposed marker for accumulation of AGEs in the skin. Skin AF, associated with the content of AGEs, such as pentosidine in skin biopsies, has been reported as a non-invasive method of measuring AGE deposition by emission of a characteristic fluorescence.

In the present study, we measured the relationship between AGEs and intensity of low back pain, lower limb pain and numbness in patients with lumbar spinal canal stenosis (LSS) for clarifying the degeneration to muscle or nerve system.

Method: Among the 160 LSS patients that were treated at our center from September 2017 to May 2019, 44 patients was excluded due to diabetes because diabetes were reported to be associated with AGEs. A total of 116 people were included in this study. LSS was diagnosed by spinal surgeons through examination and MRI. AF was measured by placing the device RQ-AG01J (Sharp Life Science Corporation, Japan) for 30 seconds with the AGEs. Intensity of low back pain, lower limb pain and numbness were measured quantitatively by NRS, and the relationship with AF value was analyzed by Spearman's rank correlation coefficient. Significance level was 5% or less.

Results: The subjects were 46 men (average age 73.9 years) and 70 women (73.6 years). The average AF was 0.51 ± 0.12 and the average NRS was 4.6 ± 2.7 for low back pain, 5.1 ± 2.8 for lower limb pain, and 4.2 ± 3.0 for lower limb numbness. The correlation coefficient between AF and NRS was low back pain and $\rho = 0.20$ ($p < 0.05$), on the other hand, lower limb pain and $\rho = 0.15$ ($p = 0.14$), lower limb numbness and $\rho = 0.07$ ($p = 0.5$).

Discussion: AGEs that accumulate in the body with aging and RAGE which is a receptor for the AGEs, may cause degeneration to muscle or nerve systems. However, in this study, accumulation of AGEs and low back pain were significantly associated with LSS patients, but no significant association with lower limb symptoms was found. Therefore, the accumulation of AGEs may cause degeneration of muscle rather than neurodegeneration.

GP033

Reciprocal relationship between multifidus and psoas at L4-L5 level in women with low back pain

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Introduction: Low back pain (LBP) may originate from different sources such as intervertebral disc degeneration (IVDD), end-plate and paraspinal muscle changes. Our aim is to explore the relevance of paraspinal muscles' fat-infiltration in women with LBP and its association with IVDD and Modic changes.

Methods: Consecutive female patients presenting with chronic LBP to the outpatient clinics were included. Patients were evaluated in terms of IVDD, vertebral end-plate changes, and fatty infiltration in the paraspinal muscles at all lumbar levels on lumbar spine magnetic resonance imaging (MRI). Visual Analogue Scale (VAS) scores were recorded using our prospectively collected database.

Results: Patients with higher VAS scores were significantly more likely to have more fatty infiltration in the multifidus and less fatty infiltration in the psoas at L4-L5 level when compared to those with lower VAS scores (69.1 vs. 31.8%, p50.003). To predict LBP, fatty infiltration in the multifidus and psoas had odds ratio (OR) of 4 (p50.010), and 0.3 (p50.013), respectively; whereas disc degeneration had an OR of 0.5 (p50.028).

Discussion: This study demonstrated that fat-infiltrated multifidus at lower back could be the main source of LBP in younger symptomatic female patients. Besides, it is the first clinical cross-sectional study suggested that women with chronic LBP had less fat-infiltrated psoas to compensate more fat-infiltrated multifidus at L4-L5 disc level. Long-term sick-leaves could be avoided by planning exercises focused on the multifidus at L4-L5 disc level in women with LBP.

Comparing Routine Elective Inpatient Spine Surgery to Orthopedic and Non-Orthopedic Surgery Trends

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Introduction: Comparison of volume, quality, and facility cost trends for inpatient elective spine surgery in the United States (US) relative to other routine inpatient elective orthopedic and non-orthopedic surgical procedures has not been studied.

Methods: Data was extracted from the US National Inpatient Sample dataset.

Results: Routine inpatient elective procedures for comparison to spine surgery included bariatric surgery, coronary artery bypass graft (CABG) surgery, hernia repair, and vascular surgery. Volume significantly increased for spine fusion (+1.2% annually to 436,745) and bariatric surgery (+4.4% annually to 182,915) [$p < 0.05$]. Annual volumes significantly declined for CABG (-2.3%), hernia repair (-3.8%), and vascular surgery (-4.2%). For spine surgery, LOS increased +0.2 days to 3.7 days and mortality rate decreased 0.4% to 2.4% [$p > 0.05$]. Among comparison elective surgeries, bariatrics LOS decreased the most (-0.4 days to 1.8 days) with a reduction in mortality rate from 0.07% to 0.00% while vascular surgery LOS increased the most (+0.6 days to 6.0 days) along with the highest increase in mortality +0.39% to 1.90% [$p < 0.05$]. Spine surgery facility cost grew +\$7,115 to \$31,946; however, this cost grew 2.8% annually on average – lower than US healthcare consumer price index (CPI, 3.2%). Among comparable surgeries, annual costs grew fastest for hernia repair (4.9%) and slowest for bariatrics (0.5%). Net change in cost was greatest for CABG (+\$9,819 to \$43,854).

Conclusion: For 2008-2017, inpatient routine elective spine surgery volume significantly increased. In contrast, only bariatrics volume grew (+47.2%) while other routine elective procedure net volume declined: CABG (-18.8%), hernia repair (-29.6), and (-32.0%). Overall quality of spine surgery has improved in terms of both LOS and mortality rate relative to comparisons. Despite cost to provide routine inpatient spine surgery increasing, the overall annualized growth rate of facility cost was less than US healthcare CPI and average annual growth rate for facility costs of comparable procedures.

Future Activity Goals of Patients Considering Spine Surgery: A Pilot Study

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- Introduction: Regaining capacity for physical activity is a primary predictor for patient satisfaction following treatment for spine morbidity. Patients are more likely to report satisfaction when able to return to physical activities most important to them. An understanding of specific physical activities most important to elective spine surgery patients has not been assessed previously.
- Method: A survey tool was developed to measure patient goals regarding their physical activities, performance levels, difficulty performing these physical activities, and time since the physical activities could be performed at the desired level. This pilot survey was administered during the summer of 2019. Significance at $p < 0.05$.
- Result: During the study, 176 patients were surveyed with 97.7% percent having ≥ 1 reported physical activity goals (213 total goals). Average patient age was 58.9 years ($\sigma = 16.1$, range: 19.0–93.0). Average patient BMI was 27.3 ($\sigma = 5.3$, range: 16.0–47.9). Of all patient activity goals, 28.4% involved active exercise, 27.4% focused on walking exclusively, 15.8% included various recreational activities (non-golf), 11.6% were activities of daily living (ADLs), 9.3% were hobbies, and 7.4% involved golf. Female sex was associated with activity goals focused on both recreational activities ($p = 0.036$) and ADLs ($p < 0.001$). Higher age was associated with activity goals focused on exercise ($p < 0.001$). Higher BMI was associated with activity goals focused on both returning to activities of daily living ($p = 0.011$) and exercise ($p < 0.001$). Activity goals could be performed at a satisfactory level on average 3.2 years prior to screening (range: 0.0–28.0 years) with a longer period associated with higher BMI ($p = 0.040$). Surgeons suggested modification of 11.9% of patient activity goals, generally towards less intensity of activity, most frequently among lumbar spine surgery patients and associated with patients of higher BMI ($p = 0.041$).
- Conclusion: Patient activity goals along with their anticipated likelihood and timing for achievement vary immensely. More than 20 patients from this pilot study cohort were identified to need activity goal modification, reflecting the importance of education and shared decision-making during the pre-surgical assessment and overall care planning processes when treating patients with spine conditions. Follow-up with patients regarding progress with each activity goal is necessary to understand the reasonableness of patient activity goals.

GP036

Construct validity and responsiveness to change of the US English version of the Core Outcome Measures Index (COMI)

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INTRODUCTION: The patient-rated Core Outcome Measures Index (COMI) is a multidimensional tool with one item per key outcome domain, developed for use in patients with spine problems. The individual items of the COMI originated in the English language, but the instrument itself, as an outcome tool, has never been validated in English-speaking patients. The aim of this study was to examine the correlation between COMI and Oswestry Disability Index (ODI; v2.1) scores before and after surgery, and the instruments' respective responsiveness.

METHODS: The data from 171 patients (97 (57%) F, aged 67.6±8.5 years) who were undergoing treatment for lumbar degenerative spondylolisthesis in a tertiary care center in the USA were included. Patients were participating in an "appropriate use of surgery" study and had completed the COMI and the ODI before and 12 months after inclusion in the study. Analyses of known-group validity (scores for surgical vs conservative patients; and for different ASA grade classes), convergent validity (with the ODI as reference questionnaire) and responsiveness to change at 12 months' follow-up (FU) were evaluated.

RESULTS: Surgical patients had a significantly higher COMI score than non-operative patients ($p=0.002$); ODI showed similar group differences ($p=0.013$). COMI and ODI each showed a low but significant correlation with ASA class (each, $Rho=0.35$). There was a moderately strong correlation between COMI scores and ODI scores at baseline ($r=0.61$, $p<0.0001$), and a somewhat higher correlation between the two instruments' 12-month scores and change-scores from baseline to 12months' FU ($r>0.78$; $p<0.0001$). Responsiveness to change was similar in the COMI and the ODI, with standardised response means of 0.90 and 0.91 respectively.

DISCUSSION: The English version of the COMI showed similar construct validity and responsiveness to other COMI language-versions that have evaluated the instrument's performance compared with the ODI. The COMI appears to be a suitable instrument for measuring outcome in English-speaking spine patients.

Total and subscale score patterns of Oswestry disability index and Short-Form 36 based on medical comorbidities, and sagittal and coronal parameters in degenerative scoliosis patient: A prospective study

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Introduction: Previous studies have been inconclusive regarding the correlation of radiographic parameters and clinical parameters in degenerative scoliosis. The medical condition of the patient can affect the clinical results, so it is necessary to analyze them together to reveal the exact relevance. Also, due to the limitations of the analysis using total scores rather than individual items in Oswestry Disability Index (ODI) and Short-Form 36 (SF-36), relevance may not have shown. Therefore, we analyzed the total and subscale scores of ODI and SF36 based on medical comorbidities, and sagittal and coronal parameters in degenerative scoliosis patients.

Methods: In this prospective study, we enrolled 91 consecutive patients with de novo degenerative scoliosis who were referred to a tertiary hospital. The clinical parameters of disability were measured using the visual analog scale (VAS) of the back and legs, the total and subscale scores of ODI and SF-36. Medical comorbidities were analyzed using the Charlson Comorbidity Index (CCI). Sagittal (sagittal vertical axis [SVA]; thoracic kyphosis [TK]; lumbar lordosis [LL]; pelvic tilt [PT]; pelvic incidence [PI]; PI-LL) and coronal (Cobb's angle [CA]; coronal C7 plumb line [Cl]; pelvic obliquity [PO]) parameters were measured on whole spinal radiographs). The correlations between the parameters were evaluated.

Results: CCI scores were not correlated with ODI and SF-36 total scores and subscales. Chronic lung disease was correlated with ODI 9 (social life) and SF-36 physical function (PF), role physical, (RP), body pain (BP), and physical component score (PCS). Dementia was correlated with SF-36 social functioning. Peptic ulcer was correlated with ODI 7 (sleeping). There were no relationships between medical comorbidities and radiographic parameters. Among the radiographic parameters, CA and Cl were correlated with SF-36 PCS and the total ODI score. Back VAS was correlated with Cl and CA. Leg VAS was correlated with Cl. Most ODI subscales correlated with radiographic parameters (1 [pain] with Cl; 2 [personal care] with Cl and CA; 3 [lifting] with Cl; 4 [walking] with Cl, CA, PI, PT, and PI-LL; 5 [sitting] with PO and CA; 6 [standing] with Cl, CA, SVA, LL, PT and PI-LL; 9 [social life] with CA and SVA; 10 [traveling], CA, PI). Some subscales of SF-36 were correlated with radiographic parameters (PF with Cl, CA, and SVA; BP with Cl and CA; vitality with Cl).

Discussion: Medical comorbidities were not correlated with total score of ODI and SF-36 in patients with degenerative scoliosis. Chronic lung disease, dementia, and peptic ulcer were correlated with scores on the ODI and SF-36 subscales. Coronal parameters were only correlated with the total score of ODI and SF-36. Cl, CA, PO, SVA, LL, PT, PI, and PI-LL were correlated with the scores on the ODI and SF-36 subscales.

Which movement and muscular activity biomarkers to discriminate non-specific low back pain patients from an asymptomatic population?

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Introduction: The identification of relevant and valid biomarkers to distinguish patients with non-specific chronic low back pain (NSCLBP) from an asymptomatic population could contribute to a better patient follow-up and to evaluate therapeutic strategies. To date, NSCLBP is often described as a complex disorder where central and peripheral nociceptive processes are influenced by various social, psychological and musculoskeletal factors which interact with each other. It has been proposed that social and psychological factors may play an important role in the pain persistence. However, the role of musculoskeletal factors remains unclear. Several parameters related to movement and/or muscular activity impairments have been proposed in the literature in that respect. In this study, we propose a systematic and comprehensive review of these parameters (potential biomarkers) and related measurement properties.

Methods: This systematic review (PROSPERO registration number: CRD42020144877) was conducted in Medline, Embase, and Web of Knowledge databases until July 2019. In the included studies, all movements or muscular activity parameters having demonstrated at least a moderate level of construct validity were defined as biomarkers, and their measurement properties were assessed.

Results: In total, 92 studies were included. Muscular activity parameters were predominant in the included studies (70%). The tasks related to these parameters were primarily ICF 2nd level category d410 "Changing basic body position" (43%). The variable related to these parameters were primarily spatial/intensity values (82%). These variables were primarily targeted toward the lumbar region (43%). The construct validity of these parameters allowed to identify 121 movement (BMo) and 150 muscular activity (BMu) biomarkers. The measurement properties were mainly assessed by only one study (BMo: 96%, BMu: 85%). Reliability was assessed in only 24% of BMo and 14% of BMu. When considering altogether intra- and inter-observer reliability results, the reported level was generally good (BMo: 73%, BMu: 79%). Criterion validity was never assessed. Content validity was generally good (BMo: 55%, BMu: 53%), but construct validity was mainly moderate (BMo: 48%, BMu: 47%). Interpretability (MDC) was only assessed for 17% of BMo and never assessed for BMu. For a large majority of biomarkers, the clinical applicability, regarding the protocol used in the included studies, was moderate for BMo (83%) and good for BMu (62%). An extensive measurement properties assessment was found only in 31 movement and 14 muscular activity biomarkers.

Discussion: This study highlights that, even if several relevant biomarkers related to movement and muscular activity have been proposed and their measurement properties partially assessed, there is currently a lack of consensus concerning a robust and standardised biomechanical approach to assess low back pain. Prior to such a consensus, it is however crucial to increase the current knowledge on the biomarkers highlighted here (and on any other possible biomarker) to ascertain that all COSMIN domains (reliability, validity, responsiveness, interpretability) have been well explored. For that, future studies should seriously consider reproducing existing protocols and measure parameters in the same conditions than in the original articles, but also in different countries, cultures and pain/disability levels on low back pain populations.

Characteristics of relief and residual low back pain after discectomy in patients with lumbar disc herniation: analysis using a detailed visual analogue scale

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Introduction: Recently, several authors have reported favorable results in low back pain (LBP) for patients with lumbar disc herniation (LDH) treated with discectomy. However, detailed changes over time in the characteristics and location of LBP before and after discectomy for LDH remain unclear. To clarify these points, we conducted an observational study to evaluate the detailed characteristics and location of LBP before and after discectomy for LDH, using detailed and bilateral visual analog scales (VAS).

Methods: Sixty-five patients with LDH treated with discectomy were included in this study. A detailed VAS for LBP was administered under 3 different postural conditions: in-motion, standing, and sitting. Bilateral VAS was also administered (affected versus opposite side) for LBP, lower extremity pain (LEP), and lower extremity numbness (LEN). The Oswestry Disability Index (ODI) was used to quantify clinical status. Changes over time in these VAS and ODI were investigated. Pfirrmann classification and Modic change as seen by magnetic resonance imaging (MRI) were reviewed before and 1 year after discectomy to evaluate disc and endplate condition.

Results: Detailed LBP VAS scores before surgery were 62.8 ± 29.9 in motion, 61.6 ± 31.6 while standing, and 26.6 ± 32.9 while sitting; notably, LBP in motion was significantly higher than LBP while sitting ($p < 0.05$). The heightened LBP seen during motion was significantly improved following discectomy ($p < 0.05$). The detailed LBP VAS at 1 year after surgery was 13.2 ± 19.5 in motion, 13.8 ± 18.9 while standing, and 17.3 ± 22.0 while sitting; notably, the residual LBP while sitting at 1 year after surgery was significantly higher than the LBP during motion and while standing ($p < 0.05$). The bilateral LBP VAS before surgery was 46.9 ± 34.0 on the affected side and 17.4 ± 27.0 on the opposite side. This shows that LBP on the affected side was significantly higher than it was on the opposite side ($p < 0.01$). Bilateral LBP was improved significantly on both sides following surgery, and LBP relief was maintained until the 1-year final follow-up. At 1 year following discectomy, residual LBP while sitting was significantly greater in cases showing larger changes in Pfirrmann grade or Modic type ($p < 0.05$).

Discussion: Improvement of LBP on the affected side while in motion following discectomy suggests that radicular LBP is improved by nerve root decompression. Furthermore, the finding that residual LBP while sitting is reflective of the load and pressure put on the disc and endplate.

Risk factors for low back pain increase in patients with rheumatoid arthritis

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Introduction: Rheumatoid Arthritis (RA) is the most common inflammatory disease with approximately 1% prevalence in the world population. RA sometimes involves to lumbar spine and might cause low back pain (LBP). Although the cause of LBP is multifactorial, recent reports indicated that LBP in patients with RA was common compared with normal population and related to disease activity of RA. However, there is no longitudinal research focused on LBP in RA. Therefore, factors or influences for increase of LBP in RA are not clarified.

Aim: The purpose of this study was to investigate risk factors and impact for increase of LBP in RA by a longitudinal cohort study.

Materials and Methods: This study included a total of 113 patients with RA who were performed secondary survey between 2017 and 2018, out of 201 patients enrolled to the initial survey including lumbar MRI between 2010 and 2011. All patients were followed at out-patients clinic of RA in orthopaedic department. LBP was evaluated by a 100-mm visual analog scale (VAS) score within the previous 4 weeks. Increase of LBP was defined as ≥ 1 standard deviation of mean change in VAS between the baseline and secondary surveys. The impacts of LBP increase on quality of life (QOL) and psychological status were evaluated. Risk factors were determined among patient demographic characteristics, radiological changes, and RA control. RA control was assessed by the disease activity score in 28 joints-C-reactive protein (DAS28-CRP). Poor control of RA was defined as deterioration by ≥ 1 level of disease activity or moderate/high disease activity at the secondary survey, based on the DAS28-CRP.

Results: Mean change in VAS for LBP was -0.8 ± 30.4 during a mean 7-year follow-up. LBP increase was defined as ≥ 30 -mm increase in VAS for LBP, and was observed in 18 patients (16%). Patients with LBP increase showed significantly lower disability (higher RDQ $p < 0.001$, higher mHAQ $p < 0.001$), lower QOL (lower EQ5D $p < 0.001$), and poor psychological status (higher anxiety $p = 0.005$, higher depression $p = 0.007$) than those without LBP increase. Multivariate analysis revealed that one of risk factor for LBP increase was poor control of RA (Odds ratio 9.82, 95% confidence interval 2.52-38.19) other than female and VAS for LBP at baseline.

Conclusion: Patients with poor control of RA were likely to experience LBP increase in the long-term. Control of RA disease activity is important for control of LBP, QOL, and mental status.

Lumbar Spinal Stenosis Stepwise Treatment Pathway: A Delphi Study for International Consensus

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Introduction

People with symptomatic lumbar spinal stenosis (LSS) may suffer from a variety of symptoms that limit their mobility, increasing the risk of other health problems and loss of independence. These typically include neurogenic claudication symptoms, radicular symptoms, or balance and sensory dysfunction. Treatment options commonly used range from watchful waiting, through a wide variety of conservative treatments, to spinal injections and surgical interventions. However, there are currently no clear guidelines to aid clinical decision-making. Treatments offered to people with LSS may not necessarily target their specific symptoms or needs, or optimise the use of healthcare resources. The aim of this study is to develop an agreed treatment algorithm for patients with LSS based on research evidence and expert consensus. Expert opinion is required because of the limited published research evidence currently available.

Methods

The modified Delphi study led by the International Taskforce on Diagnosis and Management of LSS consists of three rounds for the development of a consensus treatment algorithm for people with LSS symptoms. The first and second round surveys aiming for widespread consensus on i) appropriate interventions and ii) stepwise order of interventions for different LSS symptom phenotypes were distributed via international professional and spinal research societies, inviting responses from clinicians and researchers with experience and expertise in the management of LSS. The third round consisting of a face-to-face internal consensus process using the expert knowledge of the study steering group and Taskforce members is being conducted virtually due to Covid-19 restrictions.

RESULTS

There were 323 and 159 participants respectively in Round 1 and Round 2, representing physical therapists, chiropractors, spinal surgeons, osteopaths, physiatrists/ physicians and researchers from Europe, North America, Australia/NewZealand, Asia and Africa. Based on a priori criterion of >70% endorsement, there was consensus from Rounds 1 and 2 to always include Advice/Education and to always include exercise in the treatment pathway for all LSS symptom phenotypes; to include Multimodal care for people with Neurogenic Claudication symptoms; and to select MRI scan when investigations are indicated. Based on <30% endorsement, there was consensus to exclude Complementary Therapies and Physical Modalities for all phenotypes; exclude Lumbar Traction and Spinal Injections for Neurogenic Claudication symptoms; and exclude Walking aids for radicular symptoms. The treatment algorithm will finalised following Round 3 in January 2021.

Discussion

This is the first study to develop international consensus on the management of LSS. If adopted, the algorithm may lead to a more standardised approach to treatment of this common condition globally, reducing confusion for clinicians and patients and potentially leading to better use of healthcare resources through a stepwise approach to treatment. We anticipate regular review and update of the algorithm as new evidence emerges.

The study has been approved by the School of Healthcare Research Ethics Committee, University of Leeds, UK: Ethics Reference Number: HREC 18-007

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Influences of intramuscular fatty degeneration on low back pain and activities of daily living in patients with lumbar spinal canal stenosis

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INTRODUCTION: In recent years, the fatty degeneration of the multifidus muscle (MF) has been reported to be associated with low back pain (LBP). Fatty degeneration seems to be a late stage of muscular degeneration and can be measured in a non-invasive manner using magnetic resonance imaging (MRI). The fatty degeneration of muscles in lumbar spinal canal stenosis (LSCS) for surgical indications has reportedly put patients at risk for postoperative adjacent intervertebral disorders. The fatty degeneration of the MF adjacent to the site of lumbar fusion also reportedly affects postoperative activities of daily living (ADL). Therefore, understanding the extent of fatty degeneration in MF can be important for postoperative physical therapy. However, the impact of fatty degeneration severity of the LSCS MF on LBP and ADL remains unclear.

METHODS: Seventy-seven patients with LSCS who underwent lumbar spinal surgery at our hospital between March 2018 and April 2020 were included in the current study. The patients underwent revision surgery were excluded from this study. Preoperative MRI was used to grade fatty degeneration in MF at the L4-5 (grade 0: <10%, grade 1: 10-50%, grade 2: >50%). Subsequently, they were divided into three groups: the non-fat degeneration (NFD) (grade 0, n=12), low-fat degeneration (LFD) (grade 1, n=45), and high-fat degeneration (HFD) (grade 2, n=20) groups. Age, height, weight, BMI, LBP intensity (Numerical Rating Scale: NRS), ability to perform ADL (Japanese version of Oswestry Disability Index: ODI), and the cross-sectional area (CSA) of the MF and psoas major (PM) at the L4-5 were compared among the three groups. Image J (National Institutes of Health, MD, USA) was used to measure CSA. CSA was used as the value divided by weight. For statistical analysis, one-way analysis of variance, followed by multiple comparisons using the Tukey HSD test, was performed.

RESULTS: There were no significant differences in age, height, weight, and BMI among the three groups. The HFD group had significantly higher NRS values than the NFD and LFD groups (NFD vs. HFD, $p<0.001$; LFD vs. HFD, $p<0.001$). ODI was significantly higher in the HFD group than in the NFD and LFD groups, and the LFD group had higher ODI levels than the NFD group (NFD vs. HFD, $p<0.001$; LFD vs. HFD, $p=0.001$; NFD vs. LFD, $p=0.038$). The HFD group had significantly lower MF and PM CSAs than the NFD and LFD groups (MF: NFD vs. HFD, $p<0.001$; LFD vs. HFD, $p<0.001$; PM: NFD vs. HFD, $p=0.003$; LFD vs. HFD, $p<0.001$).

DISCUSSION: LSCS with HFD in MF may affect LBP, ADL, and CSA. Previous studies have reported a positive correlation between fatty degeneration in MF and LBP. The production of inflammatory cytokines associated with intramuscular fatty degeneration is reportedly involved in LBP. The current study results indicate that intramuscular fatty degeneration on preoperative MRI may possibly be a non-invasive and clinically useful indicator for ADL and LBP assessments in patients with LSCS.

Risk factor analysis for fat infiltration in the lumbar paraspinal muscles in lumbar degenerative disease patients

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INTRODUCTION: Fat infiltration of the lumbar paraspinal muscles is related to the development of low back pain. Identifying risk factors for fat infiltration in the lumbar paraspinal muscles in patients with lumbar degenerative disease can help with postoperative rehabilitation. The aim of this study was to examine the factors related to fat infiltration in patients with lumbar degenerative diseases (spinal stenosis and/or lumbar disc herniation).

METHODS: We studied 205 consecutive patients who underwent posterior spinal surgery for degenerative diseases at our hospital from July 2013 to June 2017. Using preoperative magnetic resonance imaging (MRI), an orthopedic spine surgeon evaluated the presence or absence of fat infiltration at the level of the L4–5 lumbar multifidus muscle using criteria reported by Kjaer et al. We excluded patients who underwent revision surgery. In the evaluation method of Kjaer et al., patients with grade 0 were defined as the group without fat infiltration, and those with grades 1–2 were defined as the group with fat infiltration. Patients were rated as grade 0 for a normal degree of fat infiltration (0–10%), grade 1 for moderate fat infiltration (10–50%), and grade 2 for severe fat infiltration (>50%). Clinical data (age, sex, body mass index, smoking status, diabetes, hemodialysis, chronic steroid or insulin use, and American Society of Anaesthesiologists [ASA] physical status score), preoperative physical function (disease duration of physical symptoms, intermittent claudication, lumbar lordotic angle, lower extremity paralysis, and bladder bowel dysfunction), number of postoperative days to acquire walking ability, muscle dystrophy at each intervertebral disc level, and the number of operated levels were examined retrospectively. Statistical analysis was performed using the χ^2 test and Mann-Whitney U test. The significant variables and the variables that correlated ($p < 0.05$) with factors in univariate analysis were entered into a stepwise multiple logistic regression model.

RESULTS: Of the 205 eligible patients, 151 had fat infiltration and 54 did not. Univariate analysis revealed Logistic regression analysis revealed that two factors—sex (95% confidence interval [CI]: 0.066–0.419) and age (95% CI: 1.045–1.101)—were significantly associated with fat infiltration of the lumbar paraspinal muscles ($p > 0.001$).

DISCUSSION: Fat infiltration is more likely to occur in women and older people, a finding consistent with the results of previous studies. In contrast, we showed that prolonged disease duration and a worsening general condition were also correlated with fat infiltration. Our results suggest that active physical exercise therapy and/or treatment for lumbar neurological symptoms may be necessary to prevent fat infiltration of the lumbar paraspinal muscles from an early stage of lumbar degeneration, especially in elderly women.

The comparison of spinopelvic parameters between normal population and patients with the lumbar degenerative disease at L5-S1.

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Introduction: Several literatures demonstrated that the type of degenerative lumbar diseases are related with spinopelvic parameters. L5-S1 level is the junction between spine and pelvis, which implies that degenerative lumbar disease at L5-S1 may has higher correlation with spinopelvic parameters. There has been no prior study demonstrating the relationship between the degenerative lumbar disease at L5-S1 and spinopelvic parameters. The objective of this study was to identify the relationship between the degenerative lumbar disease at L5-S1 and spinopelvic parameters.

Methods: We retrospectively reviewed 126 cases which include 34 asymptomatic volunteers (control group), 30 patients with the herniation of intervertebral disc at L5-S1 (HNP group), 30 patients with the spinal stenosis at L5-S1 (SS group), and 32 patients with L5 spondylolisthesis (SPL group). We measured spinopelvic parameters including lumbar lordosis (LL; L1-S1), lower lumbar lordosis (LLL; L4-S1), disc angle at L5-S1 (L5S1DA), sacral slope (SS), pelvic tilt (PT), and pelvic incidence (PI) measured on standing radiograph. We compared those parameters between patients with degenerative lumbar disease at L5-S1 and control group using t-test. We also compared parameters between the L5-S1 pathology groups using ANOVA test and post-hoc analysis.

Results: Patients with degenerative lumbar disease at L5-S1 had larger PI-LL ($6.7 \pm 12.5^\circ$ vs. $-4.4 \pm 7.2^\circ$) and PT ($16.5 \pm 8.8^\circ$ vs. $10.0 \pm 4.8^\circ$) and smaller LL ($42.4 \pm 16.3^\circ$ vs. $51.0 \pm 9.8^\circ$), LLL ($29.6 \pm 9.1^\circ$ vs. $37.7 \pm 6.8^\circ$), and SS ($32.5 \pm 11.2^\circ$ vs. $36.0 \pm 7.0^\circ$) than control group (All $P < 0.05$). In SS group, L5S1A ($12.8 \pm 4.6^\circ$ vs. $10.3 \pm 3.9^\circ$, $P = 0.02$) was smaller than normal group. SPL group has larger PI ($57.8 \pm 13.4^\circ$ vs. $46.6 \pm 7.2^\circ$, $P < 0.001$) than normal group. There were no significant differences of LL and LLL between SPL group and normal group. Among L5-S1 degenerative lumbar disease groups, LL, LLL, SS, and PI were significantly different (All $P < 0.05$). In post-hoc analysis, those parameters were significantly larger in SPL group than HNP and SS group, respectively. There was no significant difference between HNP and SS groups.

Discussion: Spinopelvic parameters except PI were significantly different between patients with the degenerative lumbar disease at L5-S1 and the asymptomatic volunteers, which means degenerative lumbar disease at L5-S1 has a great relationship with spinopelvic parameters. LL, LLL, SS, and PI were higher in SPL group than HNP and SS groups, which implies that high shear force by high SS and PI may be one of factors related with the progression of SPL.

Endplate injuries in osteoporotic vertebral fractures were associated with the progression of vertebral collapse

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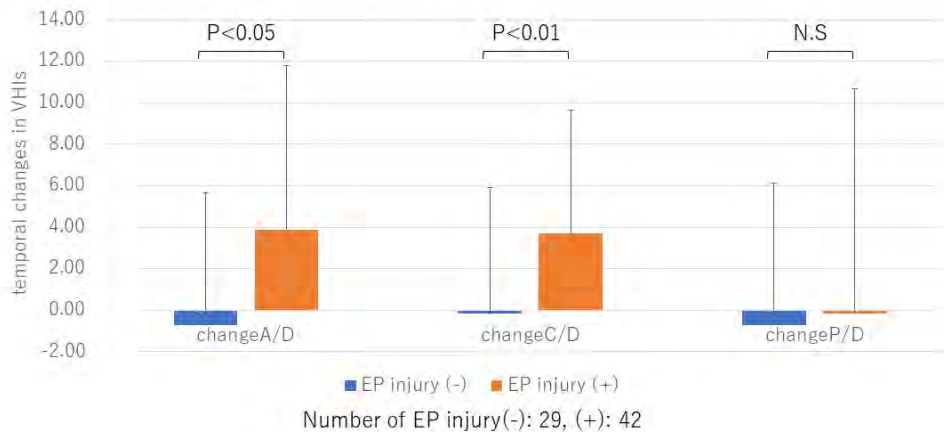
INTRODUCTION: The endplate-intervertebral disc (IVD) complex is closely interrelated with the vertebral body (VB) in the structural integrity of the anterior spinal column, including biomechanical and biological functions. Our previous study has shown that endplate (EP) and intervertebral disc (IVD) injury was frequently (approximately 60%) occurred with osteoporotic vertebral fracture (OVF), and those injuries were not independent risk factor of delayed union at six months after OVF. However, the impact of these injuries on the progression of vertebral collapse remains unknown. The purpose of this study was to elucidate the association of endplate and/or IVD injuries with the progression of vertebral collapse by quantitative evaluation of vertebral height.

METHODS: Endplate and IVD injuries associated with single- and acute-OVFs were retrospectively evaluated using magnetic resonance imaging (MRI). Vertebrae of 71 patients (male: 13, female: 58, average age: 79.6 years) who received conservative treatment for at least six months were included in this study. Using the lateral view of lumbar radiograph, anterior (A), center (C) and posterior (P) vertebral height measured in sitting position. These vertebral height were divided by the anteroposterior diameter of adjacent vertebral endplate (D) and were defined as vertebral body height indexes (VHIs: A/D, C/D and P/D). The vertebral collapse progression was evaluated by the temporal changes in VHIs (VHIs at baseline - VHIs at six months after injury). The factors associated with the progression of vertebral collapse were statistically analyzed.

RESULTS: 1. Endplate/IVD injuries have no significant effect on three VHIs at baseline. 2. Changes in VHIs (A/D, C/D, P/D) were 1.9%, 2.1%, and -0.4%, respectively. Changes in A/D (3.9%) and C/D (3.7%) with EP injuries were significantly higher than those without EP injuries (A/D: -0.7%, C/D: -0.2%). No significant effect of EP injuries was identified on the changes in P/D. 3. IVD injuries and the other patient characteristics (age, gender, level of OVFs and bone mineral density) at the baseline were not significantly associated with the progression of vertebral collapse.

DISCUSSION: The results of this quantitative study revealed that the EP injuries in OVFs were significantly associated with the progression of vertebral collapse. Evaluation of the endplate and/or IVD injuries on OVF's treatment outcome, pain scale and health-related QOL should also be examined in a future study.

Effect of endplate injury on the vertebral collapse progression



Intramuscular circulation of lumbar multifidus in different trunk positions on sitting - Comparison between subjects with and without LBP-

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Introduction A deficiency in lumbar muscle blood circulation is considered to be a major risk factor for nonspecific low back pain. A correlation between lumbar intramuscular pressure and intramuscular circulation was reported in previous researches.

Aim To investigate changes in relative circulation over time on the lumbar multifidus in different positions in sitting between subjects with and without LBP.

Methods Ten subjects (average age 21.0 years) with low back pain (LBP group) for past three months and ten healthy subjects (average age 21.1 years) without low back pain (non-LBP group) for past twelve months were recruited to this study. They received full explanation and all agreed to participate in this study. Near-infrared spectroscopy (NIRS) was used to non-invasively measure total hemoglobin (Total-Hb), oxygenated hemoglobin (Oxy-Hb), and deoxygenated hemoglobin (Deoxy-Hb) of lumbar multifidus at L5-S1 segment. All measurements were obtained in neutral position, 30 degree of trunk flexed position and 20 degree of trunk extended position in sitting. Subjects were asked to move into either flexed or extended position from starting (neutral) position in 3 seconds timed by metronome and to maintain these positions for 30 seconds. The angles of flexed and extended positions were measured with goniometer and self-made devices were used to properly maintain these positions. All participants received education and practice time in order to be able to perform proper body movements and positions prior to assessment. The measurements of Total-Hb, Oxy-Hb and Deoxy-Hb were obtained at -3 seconds (neutral position), 0, 30 and 60 seconds of in each flexed and extended position in sitting and compared between subjects with LBP and non-LBP group.

Results In flexion, significant interactions were observed with the Total-Hb ($p=0.005$) and Deoxy-Hb ($p=0.006$) of lumbar multifidus. There was no significant difference in the changes over time in the LBP group. However, in the non-LBP group, significant decreases were noted at immediately after the flexed position from the neutral position with all measurements. In extension, significant interactions were observed with the Total-Hb ($p=0.04$) and Oxy-Hb ($p=0.02$) of lumbar multifidus. There was no significant difference in the changes over time in the non-LBP group. However, in the LBP group, significant increases were noted at immediately after the extended position from the neutral position with all measurements.

Discussion The results of this study indicate that the intramuscular circulation of lumbar multifidus decreases immediately in non-LBP group once trunk starts moving into flexed position on sitting, but there is no change in LBP group. On the other hand, the intramuscular circulation of lumbar multifidus increases once trunk starts moving into extended position in LBP; however, there is no change in non-LBP group. Therefore, it might be more beneficial for a person to teach to avoid flexed position and move into extended position for therapeutic exercise in order to increase blood circulation of lumbar multifidus in sitting. Yet, these findings have to be more verified in people with different age, gender or spinal deformity groups in clinical practice.

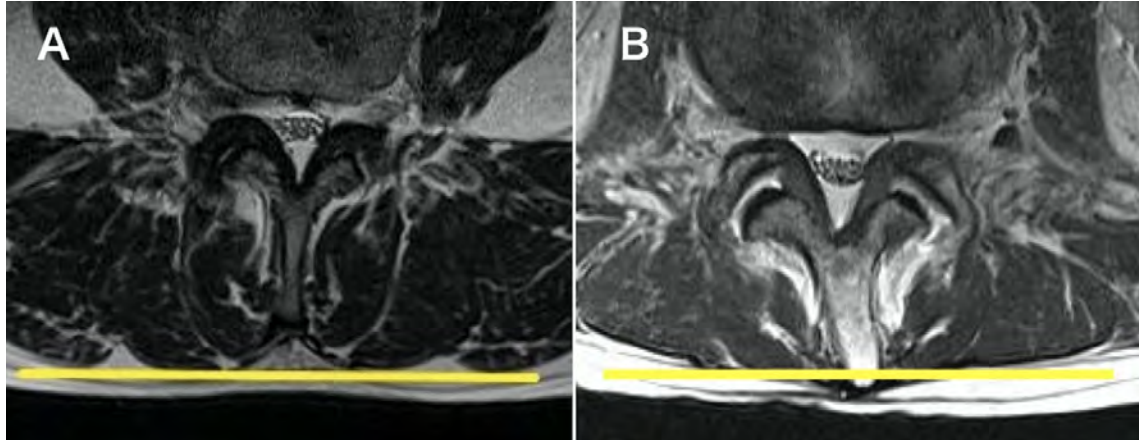
Risk factor analysis of lumbar paraspinal muscle atrophy in patients with lumbar degenerative diseases

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INTRODUCTION: There are several reports of lumbar paraspinal muscle atrophy in patients with low back pain and lumbar degenerative diseases. Regarding factors associated with muscle atrophy, the effects of disuse and segmental innervation have been speculated; nevertheless, definitive data have not been obtained to date. This study aimed to identify the factors associated with muscle atrophy of the lumbar paraspinal muscle in patients with lumbar degenerative diseases.

METHODS: We included 205 consecutive patients who underwent posterior spinal surgeries for degenerative diseases (lumbar spinal canal stenosis and/or lumbar disk hernia) at our hospital from July 2013 to June 2017. Patients who underwent revision surgery were excluded from this study. The evaluation of muscular atrophy of the paraspinal muscles was divided into two groups: the line touching the bilateral dorsal fascia of the paraspinal muscles is located dorsally to the end of the spinous process (patients without paraspinal muscle atrophy: Figure A), and the line is located ventrally to the end of the spinous process (patients with paraspinal muscle atrophy: Figure B). Clinical data (age, sex, body mass index [BMI], smoking history, diabetes mellitus, hemodialysis, insulin, steroids, and American Society of Anesthesiologists score), and preoperative physical data (duration of lumbar neurological symptoms, presence of intermittent claudication, lumbar lordotic angle (LLA), presence of lower motor paralysis, presence of bladder dysfunction, and lumbar osteoporotic vertebral fractures), and degree of fat infiltration at the L4-5 level were investigated retrospectively. Statistical analysis was performed using the χ^2 -test and Mann-Whitney U test, with a significance level of 5%. Statistical analysis was performed using SPSS Statistics version 24 (IBM Corp., Armonk, New York, USA).

RESULTS: Low BMI ($p<0.001$), low degree of LLA ($p<0.001$), and lumbar osteoporotic vertebral fractures ($p=0.026$) were significantly associated with the risk of lumbar paraspinal muscle atrophy in patients with lumbar degenerative diseases. In addition, advanced age ($p=0.07$), female sex ($p=0.07$), and fat infiltration of the paraspinal muscles at the L4-5 level ($p=0.085$) were found to be correlated with lumbar paraspinal muscle atrophy.

DISCUSSION: It has been reported that the mass and strength of the paraspinal muscles are related to low back pain and quality of life, which is considered to be of great significance in preventing muscle atrophy of the paraspinal erector spinae muscles. In our study, muscle atrophy was found to be correlated with lumbar kyphosis, which is generally consistent with the results of previous studies. Paraspinal muscle inactivity due to lumbar kyphosis as well as sarcopenia may be related to paraspinal muscle atrophy. Our results suggest that treatment of osteoporosis and/or lifestyle improvements from an early stage of lumbar degeneration may be necessary to prevent lumbar paraspinal muscle atrophy.

Variation of Bone Mineral Density in the Lumbar Spine

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Introduction:

Hounsfield units (HU), typically measured at L1-L2, have been identified as a surrogate marker for lumbar Bone Mineral Density (BMD). However, concern remains that L1-L2 BMD may not fully capture BMD differences throughout the lumbosacral spine and inadvertently provide inaccurate assessment.

Thus, the purpose of this study was to evaluate the impact of age, gender and BMI on lumbar HU, compare the conventional L1-L2 HU measurements with the common levels of degenerative pathology, compare HU measurements among different vertebral levels and evaluate the distribution of HU within the individual vertebral bodies.

Methods:

Consecutive patients presenting to a spine clinic between Apr'17 and Jan'2019 who underwent lumbar CT were selected. Previous lumbar surgery, tumor, fracture or infection were excluded. HU measurements were performed in 7 regions of each vertebral body: Mid-sagittal; Axial-Superior, Waist, Inferior; Axial at the waist-Anterior, Middle, Posterior. Association with age and BMI was evaluated using Pearson product-moment correlation. The difference between L1-L2 and L4 and L5 HU was assessed. Comparison of HU amongst levels and within each level was performed using ANOVA and paired t-tests.

Results:

100 patients (mean age=56yrs, BMI=26.4 kg/m², 48% males) were included. Age showed a negative correlation with HU in all regions at all levels (p<0.0001). BMI and gender did not show an association with HU. Conventional L1-L2 HU overestimated L4 and L5 HU by at least 10 units in 32-67% of patients, depending on the region.

S1 demonstrated higher HU than L3 (p=0.025) and L4 (p=0.029) in the mid-sagittal plane, and higher HU than all other levels in the Superior (p<0.0001) and Waist [overall (p<0.0001), and anterior (p<0.0001), middle (p<0.0001) and posterior (p<0.0001 to p=0.016)] regions in the axial plane, with no other between-level differences.

From L1 to L4, HU in the Superior region was significantly lower than that in the Inferior region (p<0.0001 to p=0.003). The opposite was seen at S1, with a decrease in HU from Superior to Waist to Inferior (p<0.0001). At all levels, HU was lower in the Posterior region compared to the Anterior and Middle (p<0.001), with no difference between Anterior and Middle (p>0.05).

Conclusion:

Although BMD at L1-L2 is often used as a marker of lumbosacral BMD, it may overestimate BMD of other levels. Furthermore, all levels demonstrated differences among various regions. These findings suggests the need for more detailed BMD estimation, especially in patients undergoing spinal instrumentation in whom variations in local BMD can be used to guide surgical planning and could potentially impact clinical outcomes.

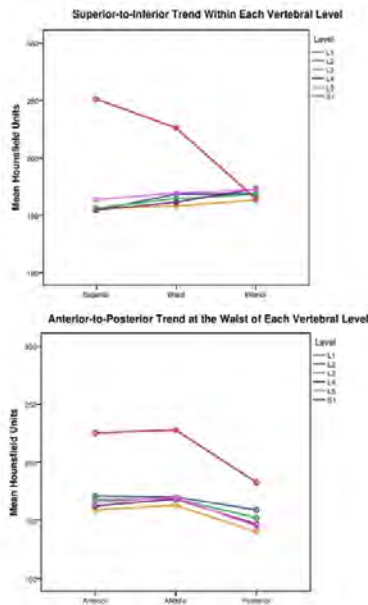


Fig 2. Trends in Hounsfield Units (HU) within each vertebral body

Emerging tetrad issues remodeling treatment strategies for degenerative lumbar spine diseases

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Introduction: Lumbar disc herniation, spinal stenosis, and spondylolisthesis are common phenotypes of degenerative lumbar spine diseases, affecting patients' quality of life greatly. The practice pattern is diverse, with instrumented surgery as the mainstream causing significant expenditure. Therefore, the article aimed at unraveling the cons of surgical intervention for degenerative lumbar spine diseases.

Methods: We performed a literature review and summarized the evidence by subheadings. There are tetrad critical issues pertaining to surgical treatment of degenerative lumbar spine diseases, i.e., favorable natural history, insufficient evidence in recommendation of fusion surgery for patients with spinal stenosis/ spondylolisthesis, metallosis, and hardware removal.

Results: Firstly, accumulating evidence reveals immune privilege and auto-immunity hallmarks of human lumbar discs within the closed niche. Progenitor cells within human discs further expand the capacity with the endogenous repair. Clinical watchful follow-up studies with repeated diagnostic imaging reveal spontaneous resolution for lumbar disc herniation, even calcified tissues. Secondly, emerging evidence indicates long-term complications of lumbar fusion, such as adjacent segment disease, with undefined surgical indications and procedures in spinal stenosis or spondylolisthesis. Thirdly, systemic and local reactions (metallosis) for metal instrumentation have been noted with long-term health concerns and toxicity. Fourthly, the indications and timing for spinal implant removal have not reached an agreement. Other challenging issues are postoperative lumbar stiffness, et al.

Discussion: Collectively, the emerging underlying evidence questions the benefits of traditional surgery for patients with degenerative lumbar spine diseases. The awareness of these insights needs further enhancement among surgeons, ultimately shedding light on the change of treatment pathways for patients.

Association between vertebral endplate structural defects and back pain: A systematic review and meta-analysis

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Introduction: Despite physiological evidence suggesting a role for the endplate in pain generation, the association between endplate defects and back pain remains unclear with conflicting results. To clarify the current state of knowledge, we reviewed and synthesized the available scientific literature on the association of endplate structural defects and back pain, and where possible pooled data for meta-analysis.

Methods: Five databases (PubMed, Scopus, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Google Scholar and EMBASE) were searched for studies reporting on the association between endplate structural defects and back pain. Covidence and Comprehensive Meta-analysis software were used for article screening and selection, and pooling of the extracted data. GRADE was used to rate the quality of evidence. Our a priori hypothesis was that differences in associations are primarily based on the type of vertebral endplate structural defect, back pain definition, and population studied. The study was prospectively registered in Prospero (CRD42020170835).

Results: 26 studies comprised of 11,095 subjects from 3 continents were identified and included. Cross-sectional studies (n=15) and MRI (n=17) were the most common study design and imaging modality used. Schmorl's nodes (n= 16) were the most frequently studied endplate defect phenotype, followed by other general or global phenotypes (e.g., endplate defects or lesions). Back pain definitions varied considerably, related to severity, duration, frequency and associated disability. The majority (59%) of studies did not adjust for confounders in the study design or analysis, which was the most common source of study bias. When confounding was considered, age (n=9) and BMI (n=6) were the most commonly adjusted variables. There was no evidence of publication bias (Eggers Test: p = 0.82). The presence of moderate heterogeneity ($I^2=67\%$; $p=0.001$) prevented the pooling of estimates across all the studies. However, studies of specific phenotypes of endplate defects, such as erosion (OR: 2.28; 95%CI: 1.84–2.81) and sclerosis (OR: 1.97; 95%CI: 1.48–2.58), were pooled ($I^2 = 0.0\%$, $p = 0.483$ and $I^2 = 0.0\%$, $p = 0.424$, respectively) and yielded significant associations with back pain. Schmorl's nodes were also associated with all back pain phenotypes (OR: 1.04-1326, $I^2 = 0\%-16\%$) and back pain overall (OR: 1.76, 95%CI: 1.20-2.58, $I^2=26\%$) in general population samples. The pooling of data from all studies of specific back pain phenotypes, such as back pain incidence (OR: 1.63; 95%CI:1.32–2.0), lifetime history of back pain (1.5; 95%CI:1.2–1.79), frequent back pain (OR: 2.83; 95%CI:1.77–4.52) and severe back pain (OR: 18.88; 95%CI:5.23–68.11) each yielded significant associations with endplate structural defects in general, and was supported by low I^2 values ranging from 0% to 7.5%.

Discussion: Overall, there is moderate evidence of an association between endplate structural defects and back pain, with strong evidence indicating a dose-response relationship with back pain severity. Pooled estimates of an association were explained by endplate defect phenotype, back pain definition, and population studied. However, the heterogeneity of the pooled data was not explained by differences between adjusted and unadjusted estimates, which may be in part due to a lack of uniformity in variables adjusted across studies.

CHARACTERISTICS OF ACUTE LUMBAR VERTEBRAL FRACTURES ASSOCIATED WITH OSTEOPOROSIS

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INTRODUCTION

Vertebral fractures are the most common type of osteoporotic fracture and are associated with substantial morbidity and decreased survival. Vertebral fractures mostly occur at the thoracolumbar spine. In contrast, the mobile lumbar spine is a less common site of fracture.

The aim of this study is to investigate characteristics and risk factors of acute osteoporosis-related fractures of the lumbar vertebra compared to those of the thoracolumbar spine.

METHODS

Retrospective clinical data was obtained from 65 consecutive patients (male, 10; female, 55) with acute thoracolumbar (T10-L2) fractures and lumbar (L3-5) fractures. The mean age was 78.4 years old (range, 58-102). Magnetic resonance imaging (MRI) was performed to detect acute vertebral fractures in all patients. All patients exhibited osteoporosis and back pain, regardless of history of trauma or fall. Multilevel thoracolumbar-lumbar vertebral fractures and burst fractures were excluded from this study. The vertebral fracture sites included 60 thoracolumbar vertebrae in 48 patients and 19 lumbar vertebrae in 17 patients. Medical records were examined for age, sex, body mass index (BMI), osteoporosis medication, steroid therapy, history of diabetes mellitus, previous vertebral fractures, lumbar bone mineral density (BMD), and femoral neck BMD. Patients were classified into those with thoracolumbar fractures and those with lumbar fractures. Risk factors were assessed and compared between these two groups using univariate analysis.

RESULTS

Lumbar vertebral fracture occurred at the level of L3 in 9 vertebrae, L4 in 8, and L5 in 2. In terms of age, sex, BMI, osteoporosis medication, steroid therapy, history of diabetes mellitus, lumbar BMD, and femoral neck BMD, there were no significant differences between patients with thoracolumbar fractures and those with lumbar fractures. Mann-Whitney's U test revealed that previous vertebral fractures were a significant risk factor associated with lumbar vertebral fractures ($p < 0.05$).

DISCUSSION

This study was based on accurate acute fracture data collected from MRI to detect vertebral fractures. MRI is useful to determine fresh vertebral fractures when a fracture is presented with a less marked collapse and when there is no history of trauma or fall. The incidence of acute lumbar vertebral fracture was approximately one third of acute thoracolumbar fractures, and was common at the level of L3. Previous vertebral fractures were a significant risk factor associated with lumbar vertebral fracture compared with thoracolumbar fracture. Therefore, a strong and effective treatment for osteoporosis should be considered in patients with osteoporotic lumbar vertebral fracture.

L3-L4 Level in Limbo: Does it belong to the Upper or the Lower Lumbar Spine?

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Introduction: We aimed to compare the degenerative findings at L3-L4 level with those at other lumbar levels in young adults with LBP. We also aimed to identify whether L3-L4 level belonged to the upper or the lower lumbar spine.

Methods: We conducted a cross-sectional analysis of a retrospective database collected between March 2018 and August 2020 in patients aged between 20-50 years. We divided patients into two groups as the elder (aged ≥ 35 years= 327) and the younger (aged < 35 years= 200). All patients were evaluated in terms of intervertebral disc degeneration (IVDD) and vertebral end-plate changes using Pfirrmann grading and Modic classification on lumbar spine MRIs, respectively. Lumbar lordosis (LL) angles were measured. Visual analog scale (VAS) scores and body mass index (BMI) were recorded, if applicable.

Results: We evaluated 527 patients (female: 285 and male: 242; mean age: 36.33 ± 6.9 years; mean BMI: 27.01 ± 4.3 kg/m²; mean VAS: 7.27 ± 1.6 points). In all patients, 44.2% and 25% had severe IVDD and Modic changes at any lumbar level, respectively. The elder and younger groups were similar in gender, VAS, and LL. The elder group had higher BMI (27.82 ± 4.0 kg/m² vs. 25.82 ± 4.5 kg/m², $p=0.008$). Age had a predictive value for the severity of IVDD and presence of Modic changes at L3- L4, L4-L5 and L5-S1.

Discussion: It has been controversial whether L3-L4 belonged to the upper or the lower lumbar spine. Thus, L3-L4 level has been in limbo. We observed that L3-L4 level was similar to the lower lumbar levels in terms of not only disc herniation pattern but also IVDD and Modic changes patterns. Our results showed that L3-L4 level belonged to the lower lumbar spine in terms of spinal degeneration pattern.

Effectiveness of amino-acid supplementation after decompression surgery for lumbar spinal stenosis: a randomized controlled trial

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INTRODUCTION: Protein nutrition in combination with exercise is considered important to maintain muscle function in older adults.¹ Essential amino-acid treatment was reported to attenuate muscle atrophy and accelerate the return of functional mobility in older adults following total knee arthroplasty.² However, it is unknown whether amino-acid treatment is beneficial in older adults following decompression surgery for lumbar spinal stenosis (LSS). The purpose of this study was to evaluate whether amino-acid supplementation could attenuate muscle atrophy and improve physical performance and clinical outcomes after decompression surgery for LSS.

METHODS: This was a single-center, randomized, open-label, controlled trial that included patients who underwent decompression surgery (more than 3 levels) without fusion or decompression surgery with fusion for LSS from January 2018 to March 2020. Patients were randomly assigned to the amino-acid (100 kcal, 10 g amino acids) or nonprotein (100 kcal, no amino acids) supplement group. Patients ingested the supplement twice daily at breakfast and lunch for 3 weeks and received two hours of postoperative inpatient rehabilitation for approximately 3 weeks. Clinical outcomes were measured using a body composition meter (InBody S10; BioSpace, Seoul, Korea), a Biodex dynamometer (System 4, Biodex Medical Systems, Inc., Shirley, NY, USA), a timed up-and-go test (TUG), and controlling the nutritional status (CONUT) score preoperatively and at 2 weeks and 3 months postoperatively. The patient-reported outcomes (PROs) were assessed preoperatively and 3 months postoperatively using the Zurich Claudication Questionnaire, a numerical rating scale of low back pain, leg pain, and leg numbness, and the Japanese Orthopaedic Association Back Pain Evaluation Questionnaire. Scores and mean changes after 2 weeks and 3 months were compared between the groups. A *P*-value <0.05 was considered significant.

RESULTS: Thirty-three patients (17 men and 16 women, average age 70.6 years) were randomly allocated to the amino-acid group and 33 patients (16 men and 17 women, 71.4 years) to the nonprotein group. At baseline, there were no significant differences between groups for demographic data, appendicular and trunk muscle mass, knee muscle strength, TUG, CONUT score, and PROs (*P*>0.05). At 2 weeks postoperatively, the nonprotein group showed significant deterioration compared with the amino acids group for strengths of right and left knee extensor and knee flexor (*P*<0.05). At 3 months postoperatively, the amino-acid group showed significant improvements in right and left knee extensor strength and knee flexor strength compared with the nonprotein group (*P*<0.05). However, there were no significant differences in the PROs for the two groups.

DISCUSSION: Amino-acid supplementation attenuated the loss of muscle strength, and promoted to increase muscle strength, but did not improve muscle mass and clinical outcomes after decompression surgery for LSS. Amino-acid intake combined with exercise might promote postoperative rehabilitation in older adults following decompression surgery for LSS.

1. Deutz N.E., Bauer J.M., Barazzoni R., et al. Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. *Clin Nutr.* 2014; 33: 929–36.
2. Dreyer HC, Strycker LA, Senesac HA, et al. Essential amino acid supplementation in patients following total knee arthroplasty. *J Clin Invest.* 2013; 123(11): 4654–66.

Is there a place for surgical repair in adults with spondylolysis or grade I spondylolisthesis? – A systematic review and treatment algorithm

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Introduction

Surgical repair is less explored than fusion in adults with spondylolysis/low-grade isthmic spondylolisthesis, due to associated disc-degeneration with increasing age. However, there may be a place for lysis-repair in adults with:(1)spondylolysis/grade-I isthmic spondylolisthesis, (2)no progressive radiological disc-changes, and (3)pars-defect as the only source of pain. There are no systematic reviews, exploring direct pars-repair in adults. Hence, we conducted a systematic review to: (1)describe the characteristics of adults suitable for pars-repair, and (2)evaluate the effectiveness and safety of various pars-repair techniques.

Methods

This review is in accordance with PRISMA-P guidelines and registered with PROSPERO(CRD42020189208). Studies in English, including patients≥18-years with spondylolysis/grade-I spondylolisthesis treated with standard pars-repair techniques, were considered eligible. A systematic search was performed in June 2020 in PubMed, Embase, Scopus and Web of Science databases. The MeSH terms for search were “spondylolysis” and “spondylolisthesis”, while free-text words included “pars interarticularis”, “pars defects”, “repair”, “pars repair”, “surgical repair”, “Buck*”, “Scott*”, “Scott wiring”, “modified Scott”, “Morscher*”, “pedicle”, “screw”, “pedicle–screw–rod system”, “pedicle–screw–hook system”, “minimally invasive”, “minimal access”, “endoscopic”, “percutaneous”, “navigation”, “image-guided”, and “robot*”. Search strings were developed by combining the MeSH and free-text words using Boolean operators. A two-staged screening process was used. The articles identified in four data bases were screened initially by three independent reviewers by reading title/abstracts and applying eligibility criteria. Full-text of shortlisted articles after removal of duplicates were further screened for eligibility by three independent reviewers. Any conflict in article selection was discussed and resolved. Quality assessment was done using Joanna Briggs Institute critical appraisal checklist for selection of final articles. Data was extracted from finalised articles into a data-extraction template and narrative synthesis was conducted.

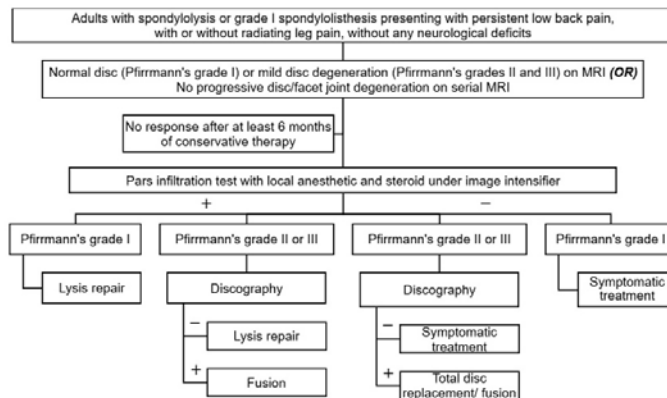
Results

A total of 5813-articles were retrieved. Initial screening resulted in identification of 289-articles. Of these, 111-articles (PubMed,n=34; Embase,n=51; Scopus,n=20; Web of Science,n=6) were available for full-text review after removal of duplicates. Further screening resulted in exclusion of 64-articles. A final 47-articles were available for data extraction after quality assessment. The total number of adults across 47-studies was 590. A high proportion of patients were young adults(18–35-years)(93%). Male:female ratio was 4.4:1. Commonest presentation was persistent low-back-pain. The lysis defect was primarily bilateral(96.4%) with L5 being the most involved vertebral level(68.5%). Majority had no disc degeneration(84%). Spondylolysis was the primary diagnosis in 86%. Diagnostic pars-infiltration test was conducted in 22-studies. Conservative-therapy prior to pars repair ranged from 3–72 months. Buck’s-repair was the commonest technique(27-studies,n=372), and pedicle screw-rod method was the least explored. Successful repair was reported in 86% treated with Buck’s and ≥90% treated with Scott, Morscher and pedicle-screw-based techniques. Improvement in pain/functional outcomes, union rate and rate-of-return to sports was high and comparable across all techniques. Positive long-term(≥2 years) outcomes were noted in >80% of patients. The complication-rate was 11.9%, with implant loosening accounting for majority of cases.

Discussion

We have established the feasibility, success, safety, and long-term effectiveness of pars-repair in selected adults with spondylolysis/grade-I spondylolisthesis. We propose the following parameters for optimising selection of adults:(1)age:18–45-years, (2)no/minimal disc/facet-degeneration, (3)no progressive disc-changes on serial-MRI, (4)normal discography, and (5)positive pars-infiltration test. We present a treatment algorithm for adults(Figure 1) and conclude that all standard techniques have comparable clinical outcomes/complications.

Figure 1. Algorithm for optimizing the selection of adults with spondylolysis or grade-I spondylolisthesis and associated disc degeneration for pars repair.



MRI: Magnetic resonance imaging.

Characteristics of Patients With Short-Term Versus Long-Term Readmission-Free Survival After Metastatic Spine Tumor Surgery

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Introduction

Unplanned hospital readmissions (UHR) after metastatic spine tumor surgery (MSTS) are important indicators of the poor general condition of the patient, aggressive disease, and inappropriateness of treatment approach. Increase in UHR reduces the quality of life of the patient and increases resource utilization. The incidence of UHR is considerably high after MSTS. Hence, survival free from UHR or readmission-free survival (ReAFS) defined as 'time duration between discharge after index-operation and first UHR/death', may serve as a new outcome indicator and a "true integrated index" in these patients. The aim of our study was to identify the characteristics of patients with ReAFS up to 3 months (short-term) versus up to 1 year (long-term) after index-MSTS.

Methods

We retrospectively reviewed the medical records of 266 consecutive adult patients who underwent MSTS between 2005–2016 with follow-up until 2 years or demise, whichever was earlier. Institutional Review Board approval was obtained prior to initiation of the study. Demographic, oncological, procedural, and postoperative details of the patients were collected. The characteristics of patients with short and long-term ReAFS were evaluated using multivariate logistic regression analysis.

Results

Final analysis included 209 patients. Mean age was 60±12 years; 50.7% were males. Majority had lung primaries (25.8%) followed by breast (18.7%). Overall, 110 and 57 patients had ReAFS up to 3 months and up to 1 year of index-MSTS, respectively. Both univariate and multivariate analysis revealed that ECOG 0–2 [multivariate adjusted odds ratio (confidence interval)= 0.286 (0.110–0.747), p=0.011], preoperative-hemoglobin >12 g/dL [0.444 (0.244–0.807), p=0.008], number of comorbidities <4 [0.474 (0.223–1.008), p=0.052], index length of stay ≤10 days [0.359 (0.170–0.760), p=0.007] and no neurologic/hematologic complications during index stay [0.132 (0.028–0.620), p=0.010] were significantly associated with ReAFS up to 3 months after MSTS. Univariate and multivariate analysis for long-term ReAFS revealed the following characteristics to be significantly associated with ReAFS up to 1 year after index MSTS: ECOG 0–2 [0.254 (0.054–1.202), p=0.084], preoperative hemoglobin >12 g/dL [0.350 (0.173–0.706), p=0.003], and breast [3.885 (1.349–11.190), p=0.012], prostate [7.990 (1.931–33.058), p=0.004], hematologic [4.680 (1.547 – 14.160), p=0.006] and renal/thyroid primaries [3.890 (1.080–14.008), p=0.038]. Having lung and gastrointestinal primaries was associated with significantly higher UHR/death when compared to other primaries, both on univariate and multivariate analysis.

Discussion

Our study revealed that the general condition of the patient at the time of index surgery (ECOG and preoperative hemoglobin status) may significantly influence both short and long-term ReAFS after MSTS. Short-term ReAFS may also be influenced by the number of comorbidities and quality of postoperative recovery (length of index stay and postoperative complications during index stay), while long-term ReAFS may be influenced by the primary tumor type. Knowledge of factors influencing short-term ReAFS can allow oncologists and surgeons to optimize the treatment approach, quality of cancer care, and patient surveillance to prolong the ReAFS. Additionally, understanding factors affecting long-term ReAFS can help clinicians counsel their patients, set expectations, and enhance patient surveillance to improve their QoL in the long-term.

Analysis of unplanned hospital readmissions up to two-years after metastatic spine tumour surgery

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Introduction

Unplanned hospital readmissions (UHR) after discharge following metastatic spine tumour surgery (MSTS) adversely affect quality of life of these patients. Majority of studies on UHR focus on assessment of readmissions within 30days following index-discharge. The aim of this study was to investigate rates, causes, and risk factors of UHR within 30days, 90days, 1year and 2years after MSTS to augment multi-disciplinary treatment planning and improve patient education.

Methods

We retrospectively reviewed 272-patients (age \geq 18years) who underwent MSTS between 2005–2016 with a follow-up for minimum two-years or until their demise, whichever was earlier. Institutional review board approval was obtained prior to commencement of study. Hospital records were utilised to obtain demographics, oncological and procedural details, and postoperative outcomes. All UHR within 2years were reviewed. UHR were defined as unscheduled hospitalisations after index-discharge and did not include planned follow-up/readmissions for radiotherapy/chemotherapy. Primary outcomes were rates and causes of UHR. Four-time frames were considered with regards to UHR: (i) <30days, (ii) 30–90days, (iii) 90days–1year, and (iv) 1–2years. UHR rate was calculated as number of patients being readmitted divided by total number of surviving patients within each timeframe. Risk factors for UHR were evaluated using multivariate logistic regression analysis.

Results

A total of 204-patients were included in the final analysis. The mean age was 60+12 years; 49% were females. An Eastern Cooperative Oncology Group Performance Status (ECOG-PS) score of 0–2 was noted in 88% of patients. Median Charlson Comorbidity Index (CCI) and Tokuhashi scores were 7 and 8, respectively. Most common primary tumour type was lung (24.5%), followed by breast (19.1%). Majority underwent open surgery (72.1%). Overall, perioperative complication rate was 46%. A total of 425-UHR occurred across all four studied timeframes in 151-patients. Thirty-day, 90-day, 1year, and 2year UHR-rates after MSTS were 17.2%, 31.1%, 46.2%, and 52.7%, respectively. Majority of patients had their first UHR between 30–90days (32.5%). The highest number of readmission-events occurred after one year from discharge (n=153/425). Lung cancer primaries had the highest UHR-events (24.7%) whilst renal/thyroid displayed the least (6.6%). Disease-related causes (16.2%) were the most common reason for readmissions across all timeframes, followed by respiratory (13.7%) and progression of metastatic spine disease (12.7%). Urological conditions accounted for majority of readmissions within 30days (25%); disease-related causes (27.9%), symptomatic spinal metastases (16.7%), and respiratory conditions (19.6%) represented the most common causes at 30–90days, 90days–1year, and 1–2years, respectively. An ECOG >1 (p=0.057), CCI >7 (p=0.01), and primary lung tumour (p=0.02) significantly increased UHR-risk on multivariate analysis.

Discussion

Our study findings offer useful insights into UHR during the overlooked timeframe of beyond 90days. Overall, 74% of patients had at least one UHR within 2years of MSTS and majority were secondary to disease-related causes. Majority of first UHR occurred between 30–90days after surgery. Local disease progression and overall disease progression accounted for the highest UHR-events at 90days–1year and 1–2year timeframes, respectively. This information allows clinicians to anticipate causes of UHR within specific timeframes, thereby enabling better surveillance and prevention of MSTS-related morbidity.

Characteristics of patients with poor short-term outcomes after symptomatic postoperative lumbar spinal epidural hematoma

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Introduction. Symptomatic postoperative lumbar spinal epidural hematoma (PLEH) is a potentially serious complication of lumbar spine surgery, and evacuation surgery of the hematoma is required in cases with severe symptoms. However, postoperative clinical outcomes after evacuation of PLEH which may impact the recovery after lumbar spine surgery are still unclear. The aim of this study is to verify the short-term clinical outcomes in the cases of evacuation of PLEH and to clarify the clinical characteristics of cases with poor postoperative outcomes.

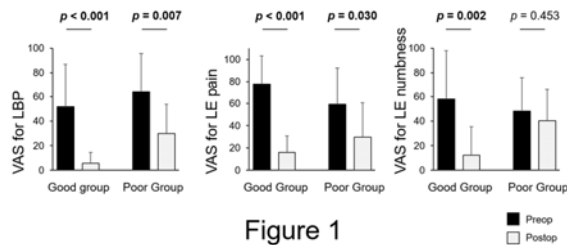
Methods. Of 5,598 patients who underwent lumbar spine surgeries from January 2007 to June 2020, 25 patients (average age; 70.4 years, 13 males, 12 females, incidence; 0.4%) underwent evacuation surgeries of PLEH after spine surgery for lumbar degenerative disorder. The mean follow-up period was 12 months (range 3–37 months). We retrospectively reviewed the medical records including pre- and postoperative the Japanese Orthopedic Association (JOA) scores, visual analog scale (VAS) for low back pain (LBP), VAS for lower extremity (LE) pain, VAS for LE numbness, duration from primary surgery to PLEH onset, duration from the onset to evacuation, and grade of the manual muscle test (MMT) of tibialis anterior (TA) at the onset. Narrowest dural sac area was measured with an axial view of magnetic resonance imaging (MRI) of the most compressed level by PLEH. Patients whose JOA recovery rate were 50% or more were classified as a good group, while patients whose JOA recovery rate were less than 50% were classified as a poor group.

Results. Of 25 patients who underwent evacuation for PLEH, 12 were divided into the good group and 13 were divided into the poor group. The rate of the patients who underwent hematoma evacuation after 24 hours or more from onset was significantly higher in the poor group (69%, 9/13 cases) than in the good group (25%, 3/12 cases, $p=0.027$). The narrowest dural sac area was significantly lower in the poor group (43.9 mm^2) than in the good group (57.6 mm^2 , $p = 0.032$) (Table1). In the good group, all of VAS for LBP, LE pain, and LE numbness was significantly improved postoperatively. On the other hand, in the poor group, VAS for LBP and LE pain were significantly improved postoperatively, but there was not significant difference in pre- and postoperative VAS for LE numbness (Figure 1).

Discussion. Our data showed that PLEH with a narrower dural sac area or delayed hematoma evacuation can lead to poor short-term clinical outcomes after spine surgery for lumbar degenerative disorder. Especially, patients of the poor group remained LE numbness postoperatively. These mean that patients of PLEH with a narrower dural sac area should undergo early evacuation of hematoma to avoid poor clinical outcomes and remains of LE numbness postoperatively.

Table 1. Comparison of perioperative factors between the 2 groups

	Good Group (n=12)	Poor Group (n=13)	p Value
Delayed onset	3	1	0.238
Duration to evacuation > 24h	3	9	0.027
MMT of TA < 2	3	6	0.271
Narrowest dural sac area (mm ²)	57.6 ± 15.8	43.9 ± 14.2	0.032
Previous spinal surgery	2	4	0.410
Dural tear	2	2	0.930
Osteoporosis	5	4	0.571
Hypertension	6	7	0.848
Diabetes mellitus	1	2	0.588
Cerebrovascular disease	0	2	0.157
Steroid	1	0	0.288
Anticoagulation therapy	3	2	0.548
platelet (10 ⁹ /L)	23.6 ± 6.0	21.3 ± 8.4	0.443
PT-INR	1.05 ± 0.06	1.03 ± 0.07	0.586



Does instability occur after transforaminal full-endoscopic ventral facetectomy?

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【Introduction】

We have performed transforaminal full-endoscopic ventral facetectomy (FEVF) for unilateral nerve root-type lateral recess stenosis.

In this operation, the superior articular process (SAP) is completely resected, and a part of the inferior articular process (IAP) is resected to decompress the lateral recess. Postoperative instability is feared by damaging part of the facet joint by excision of the SAP. Therefore, the purpose of this study was to investigate whether dynamic instability occurs after FEVF.

【Material and Methods】

The residual rate of facet joints was investigated using sagittal plane images of computed tomography (CT) in 74 patients who underwent FEVF from June 2016 to October 2019 and had CT images taken before and after surgery.

For 34 patients (11 males and 23 females) who had lumbar spine function imaging before and 6 months after surgery, disc height in the middle position, slippage during flexion-extension, local vertebral body angle and Cobb angle in the A-P view were measured and compared before and after surgery. The Cobb angle is + on the convex side.

【result】

The residual rate of facet joints was $61.0 \pm 15.9\%$.

The average age of 34 patients with confirmed functional imaging was 72.1 ± 9.2 years, and the average follow-up period was 16.7 ± 8.7 months.

The disc height was significantly reduced, anterior (9.4 ± 2.6 mm before surgery / 7.4 ± 3.8 mm after surgery, $P < 0.01$) and posterior (6.0 ± 2.1 mm before surgery / 4.4 ± 2.0 mm after surgery, $P < 0.01$).

There was no difference in the slippage during flexion-extension (preoperative 0.8 ± 1.1 mm / postoperative 1.0 ± 1.4 mm, $P = 0.21$), local vertebral body angle (preoperative $5.6^\circ \pm 4.8^\circ$ / postoperative $4.1^\circ \pm 5.7^\circ$, $P = 0.13$) and Cobb angle (preoperative $1.5^\circ \pm 2.9^\circ$ / postoperative $-1.2^\circ \pm 3.6^\circ$, $P = 0.32$) over 6 months after surgery.

【Discussion】

From this result, it was clarified that dynamic instability did not occur after FEVF. In addition, we did not find any cases in this study in which postoperative instability increased and additional fusion surgery was required.

The disc height was significantly reduced in this result. It was considered that the cause was the addition of discectomy in the case of lateral recess stenosis with disc bulge. It is considered that long-term follow-up is necessary because the decrease in intervertebral disc height may cause foraminal stenosis.

Transforaminal full-endoscopic discectomy for the patients with down-migrated lumbar disc herniation

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Introduction: The application of transforaminal full-endoscopic discectomy (TELD) for down-migrated lumbar disc herniation (DM-LDH) is difficult because of interference with surrounding anatomical bony structures. Therefore, in general, interlaminar full-endoscopic discectomy is conducted.

Materials and Methods: Between January 2014 and March 2020, among 203 patients who underwent TELD in our institution, 169 patients who have excluded the cases of recurred LDH, lateral-type LDH, and multiply operated back were included in this study. All patients underwent TELD under local anesthesia. The definition of DM-LDH was that the top of LDH was below the cranial endplate line of the caudal vertebra (E line) on the sagittal MRI T2 weighted image. We retrospectively evaluated pre-op/post-op MRIs and clinical results. The distance of the tip of DM-LDH below the E-line was measured on pre-op MRIs, and removal of DM-LDH was checked on post-op MRIs. Clinical results on follow-up visits were evaluated by MacNab's criteria.

Results: Twenty-nine patients (21 male, 8 female) had DM-LDH, and their mean age was 39.2 years old. Preoperative MRI showed that the average distance of DM-LDH was 8.1 mm (range: 4.2 mm to 15.0 mm). On the lateral view of the lumbar radiograph, tips of DM-LDH in 6 patients were far from the midline of pedicle line (highly DM-LDH). Postoperative MRI revealed that 10 patients achieved complete removal of DM-LDH, 17 cases did the partial reduction of DM-LDH, and 2 patients remained DM-LDH. Among 29 patients, 16 patients were excellent, 11 patients were good, and 2 patients were fair on MacNab's criteria.

Discussion: Present study revealed satisfactory clinical results on MacNab's criteria for the patients who had DM-LDH and underwent TELD under local anesthesia. There were 2 patients who were not achieved satisfactory results in TELD. One remained DM-LDH on postoperative MRI, and the other had highly DM-LDH. However, among 6 patients who had highly DM-LDH, 4 patients achieved excellent clinical results. Foraminoplasty is the procedure of widening the intervertebral foramen using a high-speed drill which removes the ventral side of the supra-articular process and the cranial side of the pedicle. TELD with foraminoplasty could visualize the lateral part of DM-LDH and help easier resection.

Clinical results of transforaminal full-endoscopic ventral facetectomy for lateral recess stenosis.

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【Introduction】

We have performed transforaminal full-endoscopic ventral facetectomy (FEVF) for unilateral nerve root-type lateral recess stenosis under local anesthesia.

The aim of this study was to examine the postoperative results of transforaminal full-endoscopic ventral facetectomy (TF-FEVF) for lateral recess stenosis (LRS) and to elucidate the factors associated with a poor outcome of FEVF.

【Material and method】

A total of 85 patients who underwent FEVF for lateral recess stenosis from September 2016 to October 2019 were enrolled in this study. The mean age was 71 years old, and there were 47 males and 38 females.

We evaluated age, gender, diagnosis, previous history of spine surgery, follow-up period, surgical level and image evaluation items such as intervertebral angulation, vertebral body translation, disc height, Cobb angle, thickening of the ligamentum flavum, and bone stenosis.

We defined a positive value of cobb angle is convex side. We use Macnab criteria as a clinical evaluation.

We compared and analyzed excellent/good group and fair/poor group on Macnab criteria.

【Results】

Diagnosis is 43cases of lateral recess stenosis and 42cases of combined stenosis. Surgical level is 3cases of L2/3, 12cases of L3/4, 64cases of L4/5, and 6cases of L5/S1. Clinical outcome is 39cases of excellent, 21cases of good, 13cases of fair, 12cases of poor on Macnab criteria.

In the comparison between the excellent/good group and the fair/poor group, there was no significant difference in age(70 years old vs 73 years old, $P=0.21$), gender(male: 60% vs 60% $P=0.23$), previous history of spine surgery(4.3% vs 8.1% $P=0.59$), follow-up period(15months vs 15months $P=0.73$) between the two groups.

In the image evaluation, there were significant differences in the intervertebral angulation (4.3° vs 8.1° $P<0.05$), vertebral body translation (0.7mm vs 1.6mm $P<0.05$), and cobb angle(-0.5° vs -1.9° $P<0.05$) between the two groups, and there was no significant difference between the two groups in intervertebral disc height, yellow ligament thickening, and bone stenosis

【Conclusion】

Mid-term results of FEVF were generally good. poor performance factors of FEVF were cases of large intervertebral angulation on the flexion-extension radiograph, cases of large vertebral body translation, and concave side of scoliosis.

Risk factors for deep surgical site infection following posterior instrumented surgery for spinal trauma: A multicenter study with registry of 623 consecutive adult cases

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INTRODUCTION: Surgical site infection (SSI) is a dire complication in spinal surgeries, resulting in reoperation, prolonged hospitalization, and increased expenses. Patients with traumatized spine have been reported as having a high risk of postoperative SSI. Accurate identification of risk factors associated with SSI can be helpful in its prevention. However, only a few studies have previously investigated the risk factors of SSI after posterior instrumented fusion for traumatized spine. The aim of this study was to determine the precise independent risk factors in adult patients for deep SSI after posterior instrumented fusion surgery for spinal trauma. In this study, we have retrospectively reviewed prospectively collected multicenter observational research data of 623 registered cases.

METHODS: From July 2010 to June 2015, we conducted an observational study on deep SSI following posterior instrumented fusion surgery for spinal trauma in adult patients at 10 research hospitals. Detailed clinical data were prospectively collected using a standardized data collection chart. The prospectively obtained preoperative patient characteristics included age at the time of surgery, sex, height, and weight. Preoperative patient-related risk factors of SSI included smoking, diabetes mellitus, body mass index, American Society of Anesthesiologists (ASA) score, and preoperative chronic steroid use. Additionally, data pertaining to surgery-related factors including operation duration, intraoperative blood loss, anatomical location of the surgical site (cervical, thoracic, and/or lumbosacral), emergency surgery, dural tear, use of intraoperative fluoroscopy, use of a bio-clean room, prophylactic intravenous administration of cefazolin, intrawound administration of powdered vancomycin, and types (academic or non-academic) of institutions considered as possible risk factors for SSI, were collected and analyzed. SSI was diagnosed based on the definition by the Centers for Disease Control and Prevention.

RESULTS: From July 2010 to June 2015, a total of 623 consecutive adult patients (292 women and 331 men; mean age, 63.0 years; age range, 18-97 years); of these, 20 (3.2%) developed deep SSI. According to multivariate regression analysis, surgery at academic institutions (odds ratio, 4.13; 95% confidence interval, 1.58–10.85; $P=0.004$) and an ASA score ≥ 3 (odds ratio, 3.10; 95% confidence interval, 1.22–7.88; $P=0.017$) were independent risk predictors of deep SSI following posterior instrumented fusion surgery for spinal trauma.

DISCUSSION: We identified that surgery at academic hospitals and ASA score ≥ 3 were significantly and independently associated with the occurrence of deep SSI after posterior instrumented fusion surgery for spinal trauma in adult patients. A definitive explanation for the increased risk of SSI at academic hospitals may be difficult to deduce from our data alone; however, the complexity of patients and resident involvement in surgeries may be greater at academic hospitals than nonacademic hospitals, and these factors may correlate with an increased risk of wound infection. ASA score can be a comprehensive and accessible tool for surgeons to preoperatively gauge the potential risk of SSI in patients suffering spinal trauma, a complex clinical entity. The result of this study can provide clinicians with improved risk perception when managing patients undergoing posterior fusion for spinal trauma.

Hand grip strength can predict clinical outcomes and risk of falls after decompression and instrumented posterolateral fusion for lumbar spinal stenosis

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Introduction : There has been limited research on the association between hand grip strength (HGS) as one of the diagnostic criteria for sarcopenia and surgical outcomes of lumbar spinal stenosis (LSS). We aimed to determine the effect of HGS on surgical outcomes and risk of fall in patients with LSS.

Methods : This is a retrospective observational study. We included 200 patients who underwent spinal surgery for LSS. We recorded clinical outcome parameters, including Oswestry Disability Index (ODI), Euro-QOL (EQ-5D), and visual analog scale (VAS) scores for back or leg pain. To assess the risk of fall we used HGS and four functional mobility tests (alternative step test, six-meter walk test, timed up and go test, sit-to-stand test). ODI, EQ-5D, and VAS scores for back and leg pain were assessed preoperatively and 1 year after surgery. The four functional mobility tests were assessed at each time point during the 1-year follow-up period to assess the risk of fall in patients with LSS. We divided the patient cohort according to sex and allocated them into two different groups based on HGS: high HGS (≥ 26 kg for men, $n=26$; ≥ 18 kg for women, $n=35$), and low HGS (< 26 kg for men, $n=48$; < 18 kg for women, $n=91$). The pre- and postoperative ODI, EQ-5D, and VAS scores for back and leg pain, as well as the functional mobility test results, and demographic data were compared between the two groups using independent t tests. Correlations between HGS and clinical outcome parameters were analyzed using Pearson correlation.

Results : In women and men, HGS correlated with the preoperative/postoperative ODI ($r_1=0.217/r_2=0.345$ in women, and $r_1=0.384/r_2=0.411$ in men) and EQ-5D scores ($r_1=0.190/r_2=0.309$ in women, and $r_1=0.373/r_2=0.467$ in men). HGS also correlated with the four postoperative results for the functional mobility tests: alternative step test ($r=0.238$ in women, $r=0.431$ in men), six-meter walk test ($r=0.232$ in women, $r=0.282$ in men), timed up and go test ($r=0.285$ in women, $r=0.359$ in men), and sit-to-stand test ($r=0.238$ in women, $r=0.251$ in men). The preoperative and postoperative ODI and EQ-5D scores in the high HGS group were superior to those in the low HGS group. Among the four functional mobility tests, preoperative and postoperative six-meter walk test results showed improvements in the high HGS group.

Discussion : Considering the multifactorial nature of falls, HGS may be a useful surrogate marker for predicting the risk of falls and clinical outcomes in patients with LSS.

Incidence & Risk Factors of Postoperative Delirium After Spinal Surgery in Older Patients

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Introduction: Postoperative delirium is a common complication in the elderly after surgery but few papers have reported after spinal surgery. Therefore, the risk factors for postoperative delirium following spinal surgery have not been fully clarified. The objective of this study was to analyze various perioperative risk factors for delirium after spine surgery in elderly patients.

Methods: Between March 2016 and July 2017, 138 patients over 65 years of age were reviewed retrospectively. The patients were divided into two groups : Group A with delirium and Group B without delirium. For preoperative assessment, cognitive function was investigated with the MMSE-K (Mini-Mental State Examination - Korean), K-DRS 98 (Korean version of the Delirium Rating Scale-Revised-98). Various preoperative assessments included age(65-69/70-74/75-79/≥80years-old), gender, admission type (acute/elective), reason for surgery (fracture/degenerative), laboratory findings (level of Hemoglobin), VAS score (Visual Assessment Score) and ODI score (Oswestry Disability Index). Intraoperative assessments included type of surgery, blood loss and duration of surgery, and postoperative assessments included type of immediate postoperative pain controller (Opioid/Non-opioid). We analyzed the risk factors for delirium with each odds ratio using univariate and multivariate regression analysis.

Results: Postoperative delirium developed in 25 patients (Group A). The preoperative scores for the MMSE-K, in Group A was 28.12 ± 1.24 and these was significantly lower than those of Group B 29.65 ± 0.87 ($p < 0.05$). The scores for the K-DRS 98 also shows significantly higher result, in Group A was 1.92 ± 1.35 and Group B 0.35 ± 1.02 ($p < 0.05$). And odds ratio of MMSE-K was 0.337 ($p < 0.0001$), K-DRS 98 was 2.315 ($p < 0.0001$). The duration of surgery, in Group A was 185.8 ± 106.8 and these was longer than those of Group B 147.7 ± 83.29 ($p = 0.0517$). And its odds ratio was 1.004 ($p = 0.0592$). On multivariate regression analysis, 75-79 years-old patients had higher risk than 65-69 years-old (odds ratio 3.207 ($p = 0.0013$)) but lower risk than ≥80 years-old patients (odds ratio 0.002 ($p = 0.0001$)). The odds ratios of MMSE-K and K-DRS 98 were 0.351 ($p = 0.0094$) and 2.941 ($p = 0.0071$). The other factor was no significant difference or did not increase risk of postoperative delirium.

Discussion: The elder age and low level of preoperative cognitive function (e.g. lower MMSE-K, higher K-DRS 98) are most important risk factor of postoperative delirium after spine surgery. Also, long duration of surgery can affect the postoperative delirium. Therefore, surgeons have to keep in mind about this factor.

The advantages of revisional transforaminal full-endoscopic spine surgery for patients underwent posterior spine surgery

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Introduction

Revisional lumbar spinal surgery by posterior approach is more challenging than primary surgery due to epidural or perineural scar tissue. It demands to further removal of posterior structure to confirm intact bony landmarks and could cause operation-related instability, so fusion surgery was often selected. However, adjacent segment disease after fusion surgery could be a problem and further exposure of posterior muscles could cause multiple operated back syndrome. To resolve these problems, we have performed transforaminal full-endoscopic spine surgery (TF-FES) for patients underwent posterior lumbar surgery. Several studies published many advantages of TF-FES such as possible under local anesthesia and minimally invasiveness to posterior structures. The purpose of this study is to evaluate clinical outcomes of revisional TF-FES and describe the advantages.

Method

Forty-eight consecutive patients (60 levels) underwent revisional TF-FES for under local anesthesia. Revisional surgery was defined as the surgery after ipsilateral partial laminectomy in the same intervertebral level and/or lumbar fusion surgery in the adjacent level. Intraoperative blood loss, operation time, and the rate of complication were evaluated. Postoperative clinical outcomes were assessed by Modified Macnab Criteria Outcome and Visual Analog Scales (VAS) for leg pain, back pain, and leg numbness. In addition, we compared the outcome of revisional FES cases and primary FES cases matched for age, sex, level, and procedure of FES by software EZR[®].

Result

The mean operation time was 70.5±14.4 (52-106) minutes, and blood loss was unmeasurable. The clinical outcomes were rated as follows: Excellent in 16 levels (26.7%), Good in 28 levels (46.7%), Fair in 10 levels (16.7%), Poor in 6 levels (10.0%). The mean preoperative VAS for back pain was 6.0±2.6, for leg pain was 6.8±2.4, and for leg numbness was 6.3±2.8. At the last follow up, the mean postoperative VAS for back pain was 4.3±2.5, for leg pain was 3.8±2.6, and for leg numbness was 4.6±3.2. VAS score was significantly improved ($p<0.05$). In addition, no significant difference was observed in the operation time, blood loss, and complication rate between revisional FES and primary FES.

Discussion

Clinical outcomes of revisional TF-FES for patients with a history of posterior lumbar spine surgery was good. We consider the advantages of revisional TF-FES are avoiding effect of adhesion due to another route and preserving posterior structures. It could provide only decompression without fusion due to avoiding operation-related instability. In addition, it can be performed in an awake and aware state under local anesthesia and direct decompression for foraminal and lateral recess stenosis can be done. TF-FES could be an effective procedure for patients underwent posterior lumbar spine.

Uniportal-bichannel foraminoplasty for percutaneous endoscopic transforaminal discectomy: a technical note

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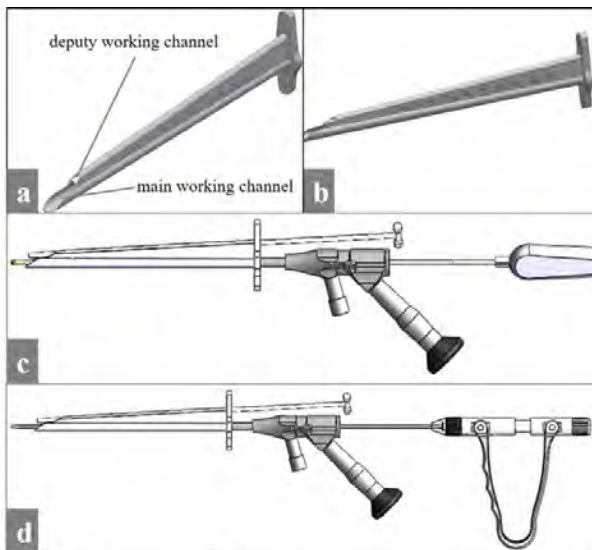
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Introduction: Lumbar foraminoplasty could enlarge the foramen to get an extensive surgical view in some L5/S1 lumbar disc herniation (LDH) cases with high iliac crest or hypertrophic transverse process. Lumbar foraminoplasty is commonly considered as a crucial and challenged procedure in percutaneous endoscopic transforaminal discectomy (PETD). The traditional strategy uses trephines and reamers to perform foraminoplasty, which is difficult to control the direction and may cause unexpected consequences including neural injury, bleeding and massive bone-cutting that may cause iatrogenic lumbar instability. Even though many solutions were proposed to assist foraminoplasty like lases, they couldn't realize a full-time and real-time visualization of foraminoplasty. We hereby introduced an uniportal-bichannel endoscopic foraminoplasty for PETD.

Methods: We conducted PETD via uniportal-bichannel endoscopic foraminoplasty on 11 patients confirmed as L5/S1 disc herniation. The duration of working cannula placement, decompression time, radiation exposure time were recorded. All patients underwent MRI and CT after surgery. The visual analogy scale (VAS) of leg, Oswestry Disability Index (ODI), modified MacNab criteria and radiologic performances were evaluated.

Results: Uniportal-bichannel endoscopic foraminoplasty was successfully performed in all cases. There was a significant difference between preoperative VAS of leg and postoperative VAS of leg (6 months) ($p < 0.05$). The postoperative ODI (6 months) was significantly improved ($p < 0.05$). The recorded duration of working cannula placement and radiation exposure time were shorter than many other previous studies. 90.90% patients received an excellent or good recovery and no poor result was reported. Uniportal-bichannel endoscopic foraminoplasty could significantly enlarge the foramen and sufficiently decompress the nerve. No postoperative spinal instability or other surgical complications were observed during 6 months follow-up.

Discussion: Uniportal-bichannel endoscopic foraminoplasty could effectively and safely enlarge the foramen and was a promising technique in PETD. Furthermore, randomized controlled trials should be conducted to explore the clinical value of Uniportal-bichannel Spinal Endoscopic System (UBiSES).



Uniportal-bichannel spinal endoscopic system. a-b The schematic diagram of the original designed bichannel cannula. The wedge-shaped bichannel cannula consists of main working channel and deputy working channel. c-d Uniportal-bichannel cannula could accommodate surgical instruments and spinal endoscopic system simultaneously to realize full-time and real-time visualization.

Percutaneous endoscopic transforaminal lumbar interbody fusion (PE-TLIF) with a Uniportal Bichannel Spinal Endoscopic System (UBiSES): technical note

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Introduction: There are some disadvantages of current percutaneous endoscopic transforaminal lumbar interbody fusion (PE-TLIF) such as limited working space, difficulty in monitoring, complications like paresthesias. We hereby introduce a novel surgical system named Uniportal Bichannel Spinal Endoscopic System (UBiSES) that could perform PE-TLIF with smaller incision under real-time and full-time visualization.

Methods: UBiSES is consisted by bichannel cannula, expandable cages and associated devices. One incision could satisfy UBiSES and expandable cages make implantation feasible in one small incision. The entry point was identified at L5 superior articular process (SAP) level and about 5 cm right from the midline. The puncture trajectory was designed from the entry point to the right L5 SAP. After the bichannel cannula was placed, reamer rather than drill was introduced through the main channel to resect part of right L5 SAP. Next, discectomy was completed by 6.3 mm endoscopic system. After the endplate preparation, an expandable cage was inserted, and the resected bone tissue was grafted around the cage. We used 2.7 mm endoscopic system through the deputy channel to monitor bone resection and cage insertion.

Results: Without internal fixation, PE-TLIF with UBiSES cost about 70 minutes in this cadaveric case. We could clearly visualize all surgical process under extensive endoscopic view. No sign of neural structure damage was observed. The fluoroscopy confirmed that the inserted cage could be fully expanded in the interbody space.

Discussion: UBiSES can complete PE-TLIF conveniently with just one incision and provide full-time and real-time visualization of the procedures.



UBiSES instruments. a. Bichannel cannula has two working channels, the main channel and deputy channel. b. An obturator can be inserted into the main channel during the introduction of bichannel cannula. c. A self-designed suction device can be used through the main channel. d. Reamer can be used through the main channel. e. Expandable cage can be inserted through the main channel by using a cage holder. f and g. Normal and flexible curette can be used through the main channel. h. The general view of expandable scraper. i. The general view of cage holder.

Sacral Insufficiency Fracture after Instrumented Lumbosacral Fusion: Focusing Pelvic Deformation -A Retrospective Case Series-

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Introduction: Sacral insufficiency fractures (SIF) after instrumented lumbosacral fusion (ILSF) is a rare complication but can induce prolonged pain and disability. Moreover, diagnosis is so difficult that it is often delayed. Conservative management can bring favorable outcomes, however surgical treatment is needed in limited cases. Still, there is no guideline reporting for appropriate treatment for SIF after ISLF. The objective of this study was to report the characteristics of SIFs after instrumented lumbosacral fusion (ILSF) and discuss its management focusing on pelvic deformation

Methods: We retrospectively reviewed all consecutive patients who underwent ILSF for degenerative disc diseases during the period between 2000 and 2017 and were diagnosed as SIF at our institute. The clinical and radiographic data were reviewed on their medical charts. Treatment outcomes for SIF were also investigated.

Results: Eight patients (all females) were identified as SIF after ILSF. Mean age at SIF diagnosis was 72 years, and the mean follow-up period was 3.8 years (range 1-7 years). SIF developed average 7.5 years (range 1 month - 17 years) after the index ILSF. Fracture patterns were unilateral vertical in 4 patients, bilateral vertical in 3 patients, and horizontal in 1 patient. Unlike patients with unilateral vertical SIF, patients with bilateral vertical or horizontal SIF showed a marked increase of pelvic incidence (PI) by mean $17.0^{\circ} \pm 5.0^{\circ}$ and sagittal vertical axis (SVA) by mean 4.5 ± 2.2 cm, compared to the respective values before the onset of abrupt pain. All patients with unilateral vertical SIF were treated favorably by conservative management, however sacropelvic fixation was inevitable in patients with bilateral vertical or horizontal SIF.

Conclusion: SIFs after ILSF had several fracture patterns. Bilateral vertical or horizontal SIF showed marked changes on sagittal radiographic parameters including PI and SVA. Although unilateral vertical SIF has benign courses that responded well to conservative management, bilateral vertical or horizontal SIF is likely to need surgical treatment. Treatment plan should be determined depending on fracture pattern and pelvic deformation.

Ten-year results of lumbar spinal stenosis with degenerative spondylolisthesis treated with decompression alone

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INTRODUCTION

In spine surgery, it is still controversial whether fusion is necessary for lumbar spinal stenosis (LSS) with degenerative spondylolisthesis. In our institution, LSS patients with neurogenic intermittent claudication always received decompression alone even if they have degenerative spondylolisthesis. The purpose of this study was to clarify the long-term result of decompression alone for LSS with degenerative spondylolisthesis.

METHODS

This study was a retrospective cohort study. Ninety-one patients with LSS who received surgery for L4/5 stenosis from 2002 to 2009 were included. All surgeries were decompression alone without fusion despite spondylolisthesis. The patients with cervical and thoracic spinal disease, rheumatoid arthritis, destructive spondyloarthropathy, or history of lumbar surgery were excluded. The primary outcome was revision surgery for the L4/5 level. Secondary outcomes were the numerical rating scale (NRS) scores for low back pain, leg pain, and leg numbness, and the Roland Morris Disability Questionnaire (RDQ). The presence of residual symptoms of operating level and continuous treatment were also investigated. Subjects were divided into two groups according to preoperative radiological findings with or without spondylolisthesis (grade I or more) and compared to each other. Statistical analysis was performed by the Chi-square test and the Wilcoxon test. A p-value of less than 0.05 was considered significant.

RESULTS

Preoperatively, 46 patients had degenerative spondylolisthesis (DS group), and 45 patients showed only spondylosis (Sp group). There were no significant differences in preoperative NRS of low back pain, leg pain, and leg numbness, and RDQ between the two groups. Ten years after surgery, 45 cases (50%) completed follow-up. There were 6 cases (13%) needed revision surgery for L4/5 level (2 cases in the DS group and 4 cases in the Sp group), and no significant difference in revision rate between them. There were also no significant differences in NRS scores of symptoms, RDQ, residual symptoms, and continuous treatment. The surgical outcome of decompression surgery was not affected by the presence of preoperative degenerative spondylolisthesis.

DISCUSSION

This study showed that preoperative spondylolisthesis did not influence the 10-year outcomes of decompression surgery for LSS patients. Decompression surgery was considered suitable to treat LSS patients even if the degenerative spondylolisthesis was found in preoperative radiological examination.

Trends and measures against postoperative wound dehiscence after surgery for spinal metastasis

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Introduction

Palliative surgery for spinal metastasis plays an essential role in improving and maintaining the activity of daily living (ADL) and quality of life (QOL). Wound dehiscence is one of the severe complications after surgery for spinal metastasis. In the current study, the authors investigated trends and measures against postoperative wound dehiscence.

Patient and Method

Two hundred twenty patients with symptomatic spinal metastasis who underwent spine surgery were enrolled in the current study. Every patient received radiation therapy and was treated by chemotherapy if indicated. Wound dehiscence was defined postoperative complication needs skin flap surgery because of large skin defects.

The multivariable analysis was performed to identify the risk factor of postoperative wound dehiscence. The candidate of risk factor was age, gender, original cancer, surgery, radiation therapy, ADL, PS, and chemotherapy, including the bone modified agent (BMA). Besides, the authors performed the curved skin incision when spine surgery for spinal metastasis was done.

Results

Four patients (1.8%) had the postoperative wound dehiscence at the mean of 5.5±10.7 months after surgery. Every patient underwent negative pressure wound therapy (NPWT) and skin flap surgery. The duration until a cure was the mean 6.0±4.0 months. Original cancer was renal cell carcinoma in two patients, colon cancer and hepatic cell cancer in each one patient. The multivariate analysis could not reveal the significant risk factor of postoperative wound dehiscence.

On the other hand, the curved skin incision was performed for 16 patients with spinal metastasis to escape the skin received radiation therapy. After skin incision, the authors exposed over the fascia toward the spinal process. After this kind of surgery with the curved skin incision was enrolled, no postoperative wound dehiscence has occurred.

Discussion

Postoperative wound dehiscence is the most severe complication. The multivariate analysis did not identify the significant negative factor. The curved skin incision might be able to prevent postoperative wound dehiscence.

GP070

Risk assessment of abdominal and retroperitoneal organ injuries performing transforaminal full-endoscopic spine surgery

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Introduction

Transforaminal full-endoscopic spine surgery (TF-FES) is a minimally invasive procedure for the surgical treatment of lumbar hernia and degenerative disease and has several advantages for the patients. Severe complications such as abdominal and retroperitoneal injuries have never been reported. However, the biggest pitfall of minimally invasive spine surgery is that we cannot visualize the anatomical structures during approaching the affected surgical site. TF-FES has risks of abdominal and retroperitoneal organs injuries due to taking the insertion point outside. The purpose of this study is to investigate organs that could exist in the trajectory of TF-FES.

Method

We evaluated whether organs (liver, ascending and descending colon, kidney, spleen) and bones (rib, iliac crest) appear in the trajectory of TF-FES using preoperative lumbar spine computed tomography image taken in the prone position. Fifty cases (33 males and 17 females) were evaluated at each L1/2-L5/S1 disc level. The mean age was 52.0 (17-91). We assumed the medial interpedicular line as the cannula installation position. The maximum tilt angle of the trajectory inserted without interfering with organs (liver, ascending and descending colon, kidney, spleen) and bones (rib, iliac crest) was measured.

Result

The organs/bones (number of cases; right/left) interfered with the trajectory when tilted up to 90 ° were kidney (19/18), rib (21/20), spleen (-/1), and colon (0/1) at L1/2. Similarly, kidney (11/14), rib (1/3), and colon (3/2) at L2/3, kidney (1/1) and colon (6/7) at L3/4, colon (1/0) and iliac crest (23/20) at L4/5, and iliac crest (50/50) at L5/S1, respectively. When interfered with any bones/organs, the mean±SD tilt angle (right / left) was 74.7±8.6 / 74.1±9.6 ° at L1/2, 77.8±9.0 / 79.3±7.7 ° at L2/3, and 82.8±7.0 / 84.0±4.2 ° at L3/4, 70.5±9.5 / 70.0±7.7 ° at L4/5, and 50.1±6.4 / 50.4±7.0 ° at L5/S1, respectively.

Discussion

Abdominal and retroperitoneal organs could appear backward than the tangent line of the posterior edge of the disc in the upper lumbar intervertebral disc level. It is risky to approach from far-lateral point horizontally, in particular in the upper lumbar level. It is important to assess the possible risk to avoid the severe complication in FES.

Assessing Changes in Cervical Epidural Pressure During Biportal Endoscopic Lumbar Discectomy

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Introduction: Endoscopic spinal surgery is becoming an increasingly frequent procedure. It is known that intracranial pressure is increased due to the massive irrigation fluid used during the uniportal endoscopic lumbar discectomy, and it is associated with developing posterior neck pain and seizure during surgery. Biportal endoscopic spinal surgery has been performed for several years, and its effectiveness have been well known, but no studies on its safety and about intracranial pressure have been conducted. By monitoring cervical epidural pressure (CEP) changes throughout the procedure, we intended to discover the safety and effect on intracranial pressure of biportal endoscopic lumbar discectomy.

Methods: Twenty patients who undergoing single-level biportal endoscopic lumbar discectomy were enrolled in this study. In all patients, a cervical epidural catheter was placed at the C6-7 level before the procedure and was connected to a pressure transducer. CEPs were monitored throughout the procedure (Phase 1 – make surgical portal and working space; Phase 2 – perform decompression and discectomy; Phase 3 – dismiss from fluid irrigation system). After discectomy was completed, we evaluated CEP changes as the irrigation pump pressure changes (Phase 4 – increasing pump pressure with outflow open; Phase 5 – increasing pump pressure with outflow closed).

Results: Of 20 patients, change in CEP during surgery were in similar way. The baseline CEP was measured 17 mmHg. In phase 1, the mean CEP was 17.75 mmHg and no significantly different with baseline CEP. In phase 2, mean CEP abruptly increased up to 38 mmHg when epidural space was first communicated with working space, then, CEP stabilized in 32.6 mmHg. In phase 4 and phase 5, CEP increased with linear correlation as the inflow pressure increased. There were no patients with neurologic complications. In the independent factor analysis, total irrigation time was not correlated to change of CEP.

Discussion: Biportal endoscopic lumbar discectomy which allows continuous irrigation with separate portal for outflow is safe procedure, and CEP has not increased beyond the physiologic range.

Analysis of medium long-term effect of microendoscopic assisted mis-TLIF on lumbar instability and spondylolisthesis

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Introduction: To investigate the medium long-term effect of endoscopic decompression and lumbar interbody fusion (minimally invasive transforaminal lumbar interbody fusion, MIS-TLIF) with percutaneous pedicle screw fixation for lumbar instability and spondylolisthesis.

Methods: From 2005.05 to 2018.05, 935 patients of lumbar spondylolisthesis and lumbar spondylolisthesis were mis-TLIF treated by microendoscopy. There were 574 males and 361 females. Age 36-82, mean age 61.7. single segment 816 patients. double segment 119 patients. L4-5 677 patients, L5-S1 219 patients, L3-4 33 patients. Postoperative 3,6,9 months, 1,2,5 and 8 years follow-up, Preoperative and postoperative assessments were performed about VAS and ODI score; Anterior and lateral lumbar examination was performed after 3,6,9 months of operation. the lumbar flexion and extension of the dynamic position and CT 3D reconstruction examination was performed after 1,2,5 and 8 years of operation. Fusion was evaluated by SUK, BSF criteria. data analysis using SPASS25.0 system software.

Results: In 935 patients, the operative time of single segment decompression fusion with percutaneous fixation (4 nails, 2 rods, 1 cage) was 62.34±7.29 min, Double-segmental operation time :98.55±4.47 min; Intraoperative bleeding: single segment :74.06±17.22 ml; Double segment :97.11±8.46 ml. Length of incision: screw incision :1.0 cm; fusion incision :2.2±0.5cm; incision design: skin incision: consistent with the skin lines, deep fascia and muscle: fascia incision consistent with muscle fiber lines, with blunt separation of muscle space. a single segment fusion surgical incision, operative time, and bleeding volume compared with traditional surgery^[1], the difference was statistically significant ($P<0.05$, table-1). time of getting out of bed:6.00±1.00 days, according to the VAS、ODI evaluation of the recent and mid-term recovery (Table-3), In six months, microendoscopy assisted mis-TLIF recovery was better than traditional surgery^[2], the difference was statistically significant ($P<0.05$). intermediate and long-term outcomes were similar, and there was no statistical difference ($P>0.05$). while the fusion rate was assessed according to SUK and BSF (table-3). Bridwell criteria were used to judge the intervertebral fusion after surgery. the fusion rate was 92% after microscopes assisted mis-TLIF and 85.7% after traditional surgery. there was no statistical difference ($P>0.05$). **Discussion:** The treatment of lumbar instability and lumbar spondylolisthesis(<II degree) with mis-TLIF of microscopically assisted endoscope can obtain similar curative effect and fusion rate compared with traditional operation, The field of vision is clear under the endoscope, and Concentric circle was expanded step by step, and effective limited fenestration decompression was performed, and muscle and medial dorsal spinal branch of spinal nerve got less injury, so the incidence of psoas weakness syndrome is lower after operation, but better than open operation.

Lumbar and Anterior Cervical Spine Fusion Results using an Injectable Bioactive Glass Microfiber-Based Material for Bone Grafting

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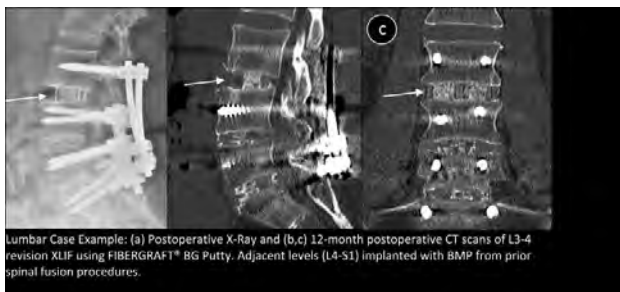
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Introduction: Bioactive glass (45S5) is a well-known osteoconductive material that forms a bone-like hydroxyapatite (HA) surface under *in vivo* conditions, and has been shown to develop a crystallized HA surface within 24 hours *in vitro*¹. Microscopic fibers composed of bioactive glass can be used to form resorbable bone void fillers that are moldable and injectable when placed in an appropriate carrier. This clinical study evaluated the fusion rates of a novel, resorbable bioactive glass putty material, made from bioactive glass fibers in a bioactive carrier, when used in lumbar and cervical fusions.

Methods: A retrospective chart review of subjects treated with the study device (FIBERGRAFT® BG Putty) for either anterior cervical fusion (ACDF) or lumbar fusion (posterolateral (PLF) and/or interbody) was performed under IRB approval at 4 US centers. Subjects were excluded if treatment was for trauma, if other synthetic bone grafts were included, or if at least 6 months postop images were not available for fusion analysis. Standard of care post-operative imaging (X-Ray and/or CT scan) was utilized to assess fusion and provide real world evidence of fusion outcomes. Fusion was defined as bridging bone between vertebral body endplates or transverse processes. Fusion failure was defined as the absence of bridging bone or confirmed pseudoarthrosis. Due to the retrospective nature of this study, the latest timepoint for study evaluations varied with institution standard of care. Available clinical outcomes and complications were also evaluated.

Results: There were 102 patients included in the study (58 men and 44 women; mean age 59.1 ± 12.2 years), including 57 lumbar subjects and 45 cervical subjects. Autograft supplement was used in 52% of the PLF cases, 33% of the lumbar interbody cases, and 73% of the ACDF cases. The number of levels treated ranged from 1-4 (167 levels total). For the lumbar spine group, 93.0% (53/57) of the subjects were successfully fused (average 11.4 ± 9.4 months postop). In the cervical spine group, 95.6% (43/45) were successfully fused (average 8.4 ± 6.5 months postop). Clinical outcomes trended to improvement over time in both cervical and lumbar groups. There were no complications or adverse events attributable to the study device.

Discussion: These results compare favorably to those reported in the literature, including a meta-analysis² of six published studies pertaining to lumbar fusion where the fusion rates ranged from 46%-95%. In another meta-analysis of cervical fusions³, the overall fusion rate was 89.5% (n = 2682) with single level fusion rates of 92.1% for ACDF (n=1231). Overall, patients treated with this resorbable bioactive glass putty in lumbar and cervical spine fusion procedures achieved a successful fusion outcome as well as a trend toward decreased patient reported pain and disability.



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Postoperative endplate injury after minimally invasive lateral lumbar interbody fusion: Risk factor analysis

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Introduction: Immediate endplate injury (Epl) after minimally-invasive lateral lumbar interbody fusion (MIS-LLIF) is quite common and can lead subsequent cage subsidence and deterioration of surgical outcomes. The purpose of this study was to identify risk factors for immediate Epl after MIS-LLIF.

Materials and Methods: One hundred eighty-six patients underwent MIS-LLIF and posterior instrumentation for degenerative lumbar diseases with one-staged or two-staged manner between 2012 and 2017. All surgeries were performed with the same manner by a single surgeon. Age, sex, BMI, and BMD were recorded. On preoperative standing X-ray, coronal disc angle, and each sagittal disc angle in neutral, flexed, extended positions were measured. Also, anterior and posterior disc heights were measured on lateral neutral X-ray. Other radiographic parameters including osteophyte formation, Kellgren-Lawrence grading, facet degeneration grading, endplate sclerosis were assessed. Epl was defined as compromise of bony endplate with more than 1mm. recorded on immediate postoperative X-ray. All parameters were analyzed statistically regarding endplate injury at each disc level.

Results: Three hundreds seventy-two discs underwent MIS-LLIF in 186 patients and 76 levels (20.4%) showed Epl. Among them, 67 had single-side injury and 9 had both-side injury. One case with two adjacent Epl showed vertebral body fracture leading to early revision. The incidences were similar for each level. When periodic analysis was performed for each 100 levels, the incidences were steady from the first period to the last one. BMD of vertebrae with Epl was not different from BMD of vertebrae without Epl. The differences between cage height and disc height were also not different according to Epl. Multivariate regression analysis demonstrated that sagittal disc angle in extension, gender, and endplate sclerosis were correlated with Epl. Bone mineral density was not correlated with Epl.

Conclusion: The incidence of Epl was 20.4% and showed steady tendency. The smaller sagittal disc angle in extension, female gender, and endplate sclerosis was correlated with Epl. The development of Epl is correlated with various factors: surgeon-related, patient-related, and implant-related. In this study, there was no learning curve and no significant correlation between Epl and implant dimensions. Immediate postoperative Epl seemed not to be procedure-related, but to be patient-related. At the beginning of this study, authors had expected that bone mineral density might be correlated with Epl, however, no significance was noted. When performing MIS-LLIF, spine surgeons should check X-ray thoroughly and pay more attention to female patients with smaller sagittal disc angle in extension.

GP075

The Feasibility of 3D Intraoperative Navigation in Lateral Lumbar Interbody Fusion: Perioperative Outcomes, Accuracy of Cage Placement and Radiation Exposure

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Introduction: Intraoperative navigation (ION) has been widely used in posterior spine surgery. However, few studies have reported the use of ION in lateral lumbar interbody fusion (LLIF) and, to our knowledge, there are no comparative cohort studies on it. Thus, the safety remains unclear. The objective of this study was to evaluate perioperative outcomes, accuracy of cage placement and radiation exposure in LLIF using ION, compared to conventional 2D fluoroscopy only.

Methods: Patients who underwent LLIF for degenerative pathology for by a single surgeon at a single academic institution were included in this study. The perioperative outcomes and accuracy of cage placement were examined in all patients who underwent LLIF using ION (ION group) or fluoroscopy only (non-ION group) for degenerative pathology. Cage placement was graded as previously described, dividing the disc space into quarters with Quarter 1 representing the anterior 25% of the disc space and Quarter 4 representing the posterior 25%. The radiation exposure was examined in patients who underwent stand-alone LLIF.

Results: A total of 87 patients with 154 levels (ION 49 patients with 79 levels/ non-ION 38 patients with 75 levels) were included in this study. Demographics are shown in Table 1. The mean number of surgical levels was 1.61 in the ION group and 1.97 in the non-ION group (p=0.102). There were no significant differences in perioperative outcomes including operative time, time from induction end to surgery start, estimated blood loss, perioperative complications and length of stay (Table 2). The accuracy of cage placement was comparable (Table 3). ION did not significantly increase total radiation dose and tended to reduce radiation dose during the procedure (Table 4).

Conclusion: The perioperative outcomes, accuracy of cage placement and radiation exposure in LLIF using ION were comparable to those using fluoroscopy only. The use of ION in LLIF was feasible, safe and accurate and may reduce radiation dose to the surgeon and surgical team.

	ION group (49 pts, 79 levels)	Non-ION group (38 pts, 75 levels)	p value
Age (years)	61.7 ± 8.9	60.4 ± 9.5	0.781
Gender			0.050
Male	32 (65.3%)	16 (42.1%)	
Female	17 (34.7%)	22 (57.9%)	
BMI (kg/m ²)	27.5 ± 4.2	27.3 ± 5.4	0.515
Smoking			0.200
Current smoker	5 (10.2%)	0 (0.0%)	
Former smoker	15 (30.6%)	13 (34.2%)	
Never	29 (59.2%)	25 (65.8%)	
CCI			0.271
0	37 (75.5%)	23 (60.5%)	
1	7 (14.3%)	7 (18.4%)	
≥2	5 (10.2%)	8 (21.1%)	
Diagnosis			0.788
Stenosis	17 (34.7%)	11 (28.9%)	
Spondylolisthosis	17 (34.7%)	11 (28.9%)	
Disk herniation	7 (14.3%)	5 (13.2%)	
Degenerative	6 (12.2%)	8 (21.1%)	
Other	2 (4.1%)	3 (7.9%)	
History of previous lumbar surgery			0.388
Primary	23 (46.9%)	22 (57.9%)	
Revision	26 (53.1%)	16 (42.1%)	
The number of levels of LLIF	1.61 ± 0.84	1.87 ± 1.05	0.102
The level of LLIF			0.205
T12/L1	1 (2.0%)	0 (0.0%)	
L1/L2	6 (12.2%)	4 (10.5%)	
L2/L3	19 (38.8%)	16 (42.1%)	
L3/L4	33 (67.3%)	33 (86.8%)	
L4/L5	20 (40.8%)	21 (55.3%)	
L5/S1	0 (0.0%)	1 (2.6%)	
Posterior instrumentation			0.127
Yes (with pedicle screw)	25 (51.0%)	26 (68.4%)	
No (stand-alone)	24 (49.0%)	12 (31.6%)	
Assistant in surgery			0.027
Fellow	46 (93.3%)	29 (76.3%)	
Others	3 (6.1%)	9 (23.7%)	

	ION group (49 pts, 78 levels)	Non-ION group (38 pts, 75 levels)	p value
1-2	12 (15.4%)	10 (13.3%)	0.279
2-3	13 (16.7%)	17 (22.7%)	
3-4	4 (5.1%)	0 (0.0%)	
1-3	18 (23.1%)	23 (30.7%)	
2-4	24 (30.8%)	21 (28.0%)	
1-4	7 (9.0%)	4 (5.3%)	

	ION group (49 pts, 79 levels)	Non-ION group (38 pts, 75 levels)	p value
Operative time (min)	143.5 (72.8-226.0)	126.0 (62.5-195.0)	0.406
Time from induction end to surgery start (min)	31.0 (27.0-38.0)	31.0 (28.0-39.5)	0.761
EBL (ml)	37.5 (25.0-112.5)	50.0 (25.0-150.0)	0.351
Perioperative complications	8 (16.3%)	3 (7.9%)	0.335
New onset neurological deficits	4 (8.2%)	2 (5.3%)	
Wound			
Wound infection	0 (0.0%)	1 (2.6%)	
Subcutaneous hematoma	2 (4.1%)	0 (0.0%)	
Other			
Ileus	1 (2.0%)	0 (0.0%)	
Cholecystitis	1 (2.0%)	0 (0.0%)	
Length of stay (hours)	50.6 (27.4-93.0)	41.7 (28.1-78.3)	0.841

	ION group (24 pts, 35 levels)	Non-ION group (12 pts, 16 levels)	p value
Fluoroscopy Time (sec)			
Surgical Procedure	24.0 (17.0-31.0)	29.5 (17.0-36.8)	0.668
Navigation spin	9.0 (9.0-9.0)	-	<0.001
Total	33.5 (26.3-45.0)	29.5 (17.0-26.8)	0.128
Radiation Dose (mGy)			
Surgical Procedure	32.2 (20.3-57.4)	47.4 (13.4-57.6)	0.932
Navigation spin	10.6 (6.9-20.7)	-	<0.001
Total	51.0 (29.3-75.5)	47.4 (13.4-57.6)	0.237

An Active Hybrid Model of the Human Lumbosacral Spine: Simple and Robust Modeling of Facet Joints

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INTRODUCTION

The pronounced influence of facet joints on the mechanical responses of human lumbosacral functional spinal units (FSU) have been shown in a large number of studies. Also chronic lower back pain is directly associate with facet joints. However, modeling of facet joints still remains a great challenge, amongst others due to complex anatomy. In computationally efficient musculoskeletal (MS) whole-body models, facet joints are mostly neglected or considered subordinately by means of limited joint formulations of the intervertebral joint. Detailed investigation of motion couplings, travelling instantaneous axes of rotation, and load sharing are almost exclusively driven by passive finite element (FE) models. Therefore, the aim of the following study is to evaluate and discuss a simple and robust approach in facet joint modeling for using it in an active hybrid model of the lumbosacral spine (LSS).

METHODS

A physiological hybrid model of the ligamentous LSS is built in ArtiSynth (www.artisynth.org) – an open source java-based toolkit combining methods of dynamic MS and FE models. For the passive part of the hybrid model, we segment and post-process the lumbar vertebrae and sacrum from the CT data of the male NIH Visible Human Project. Hyperelastic intervertebral discs represented by FE connect the rigid bones. We use multi-point springs with customized non-linear materials to model all intervertebral ligaments, including capsular ligaments, and reinforce the discs with collagen fibers. By comparing our anatomical data with morphological records and average in vitro map angles, the general cylindrical joint shapes according to functional descriptions are created (figure 1). Additional rigid contact bodies for the superior articular processes are derived and merged with the vertebrae. For soft frictionless contacts the inferior articular facets are implemented as elastic FE bodies (Neo-Hookean $E=35\text{MPa}$, $\nu=0.4$) and are arranged concentrically with initial facet gaps of 0.5mm. A calibration of the modeling parameters and validation are performed under various combined loading modes, based on prior published studies.

RESULTS

Mechanical responses like poses of instantaneous rotational axes correlate well with published data. Non-linear load-displacement curves, especially in axial rotation, demonstrate typical motion coupling effects. Depending on the pre-load amplitude, applied by a path optimized follower load, the facet joint surfaces start touching at varying moments, except for flexion. Intervertebral rotations increase inferiorly by up to 31% at extension. The maximum force is at L5/S1. In lateral bending, the maximum rotation lies at FSU L2/3. In both cases, the facet joint contact forces increase inferiorly.

DISCUSSION

By means of hybrid simulation tools and coupled models, the inherent limitations of conventional FE and MS models are constantly reduced. First results of our new hybrid LSS model confirm this through procedures already established in FE models integrated in a multi-segmental MS model. However, simplified facet joints can be a drawback, when evaluating detailed aspects of the complex surface curvatures and physiologically non-ideal contacts. On the other hand, the straightforward modeling approach chosen here enables geometric parameterizations and meets the requirements for use in a hybrid model of the LSS with active muscles.

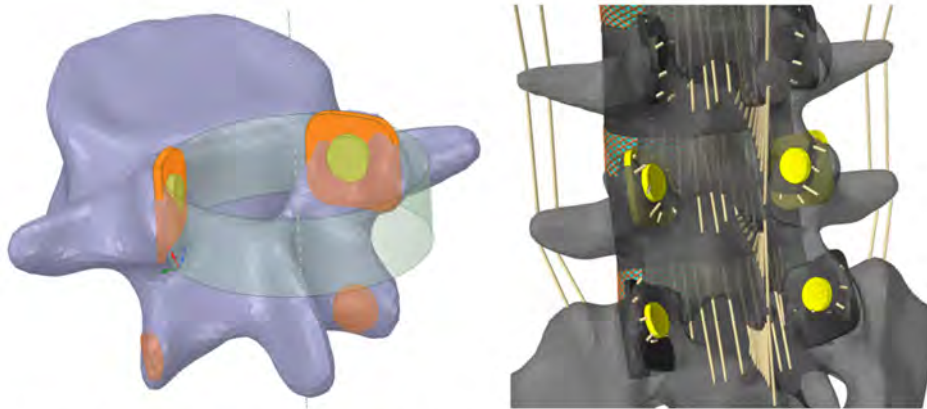


Figure 1. General setup of additional collision bodies for simple facet joints by the example of vertebra L5 (left). Implementation of final facet joints in passive hybrid model of the lumbosacral spine (right).

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Lumbar Posterolateral Fusion using a Bioactive Fiber-Based Bone Graft Substitute: A Multi-Center Clinical Evaluation

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Introduction: Posterolateral fusion (PLF) is a common procedure performed in the lumbar spine to treat a range of degenerative conditions. Effective bone grafting and the ensuing bony fusion is an important component of the healing process that may influence long-term results. New synthetic materials have been developed as a bone graft alternative option. Specifically designed as a resorbable, porous bone graft material made from 45S5 bioactive glass fibers, this material creates an ultra-porous granular structure embedded in a collagen matrix.¹ The purpose of this clinical evaluation was to assess bony fusion in PLF procedures in which this novel, resorbable bioactive glass matrix was used.

Methods: A retrospective chart review of subjects treated with the study device was performed at 4 US centers under IRB approval. All subjects underwent PLF with the study device (FIBERGRAFT® BG Matrix), with or without interbody fusion, at 1-4 levels. This was a consecutive series with limited exclusion criteria (excluded trauma, use of BMP) to reflect real world use of the device. A total of 54 patients were included in the final dataset. Fusion was defined as bridging bone between transverse processes and absence of pseudoarthrosis, and was assessed using all available post-operative imaging (X-Ray, CT scan). Due to the retrospective nature of this study, the latest timepoint for study evaluations varied with institution standard of care. The average time of last subject evaluation was 11.0 ± 4.4 months postop.

Results: Of the 54 subjects included, there were 33 men and 21 women (average age 64.8 ± 11.7 years). In the majority of cases (92.6%) bone marrow aspirate was added to the study device prior to implantation and supplemental autograft was added in 66.7% of cases. Half the subjects (50.0%) concurrently underwent interbody fusion at the level(s) treated. The majority of cases were 1-2 levels (87.0%) with 9.3% prior non-unions. Posterior hardware was used with the exception of 3 cases (5.6%). CT scan and X-ray analysis indicated that the overall fusion rate at last follow-up was 96.3%, with successful fusion in 52/54 subjects. There were no complications or adverse events related to the study device.

Discussion: In a systematic review of notable literature by Lee et al.², the fusion rate for PLF (with or without interbody) using autogenous bone graft (local or ICBG) varied widely from 14% to 95%, likely dependent on several factors including quality of the bone graft used, bone graft volume, and other patient-specific factors. Patients treated with this resorbable bioactive glass matrix achieved a successful outcome with an average fusion rate of 96.3% and a trend toward decreased patient reported pain and disability, with no safety concerns. These outcomes are favorable and comparable to other published studies.

Fusion Results	Subjects (N=54)
Fusion Success for All Lumbar PLF Cases	96.3% (52/54) Confidence Interval: (88.8%, 99.3%)
The confidence interval (CI) is one-sided 95% CI, estimated using the Clopper-Pearson (exact) approach.	

- 1. Bondre S, Bagga C (2018). Soc for Biomaterials Annual Meeting, April 11-14, Atlanta, GA
- 2. Lee CS, Hwang CJ, Lee DH, Kim YT, Lee, HS (2011). Clinics in Orthopedic Surgery, 3(1), 39-47.

Minimally Invasive Spinal Fusion Surgery Using Percutaneous Pedicle Screwing Can Provide Better Lumbar Function in Early Stage than Conventional Methods in the Treatment of Degenerative Lumbar Spinal Diseases; A minimum of one-year follow-up study

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INTRODUCTION: The real effectiveness of minimally invasive spinal fusion (MISF) surgery has not been adequately clarified for the treatment of degenerative lumbar spinal diseases. The purpose of this study was to investigate whether the MISF can provide the better outcome than conventional fusion surgery in the treatment of degenerative lumbar spinal diseases.

METHODS: One hundred and twenty-five patients who had undergone single-level fusion surgery for degenerative lumbar spinal diseases were examined with a minimum of one-year follow-up (mean period of 28 months). There were 61 men and 64 women with a median age of 70s ranging 47-88. The main pathology was unstable degenerative spondylolisthesis in 94 patients and foraminal stenosis in 31. The following 3-types of fusion surgery were performed; minimally invasive transforaminal interbody fusion after microscopic decompression through a unilateral approach with percutaneous pedicle screwing (PTLIF), transforaminal interbody fusion after microscopic decompression through a unilateral approach (TLIF), and posterior lumbar interbody fusion with posterolateral fusion after open decompression through a bilateral approach (PLIF). PTLIF was performed using percutaneous pedicle screwing with a guidance of CT-based navigation system. In TLIF group, pedicle screws were inserted through the open method for approach side and the subcutaneous-transfascial method for the opposite side under X-ray fluoroscopic control. PLIF was performed by the posterior lumbar interbody fusion combined with posterolateral fusion after open decompression through a bilateral approach. All screws were inserted with a freehand method in PLIF group. Two board-certified spine surgeons operated all patients. One junior surgeon performed PTLIF in 46 patients and TLIF in 34 patients. The other senior surgeon performed PLIF in 43 patients. There were no statistically significant differences among 3 groups in terms of age, gender, preoperative severity, and follow-up period. Outcome measures were as follows; Visual analogue pain scale (VAS) for low back pain, lower limb pain and numbness, Roland-Morris Disability Questionnaire (RDQ), and Japanese Orthopaedic Association Back Pain Evaluation Questionnaire (JOABPEQ). Kruskal-Wallis test was used for statistical analyses. Statistical significance was defined as a p-value of less than 0.05.

RESULTS: There were no statistically significant differences among 3 groups in terms of VAS scores, RDQ scores, and all of the domains in the JOABPEQ scores at the baseline before the surgery. There were no statistically significant differences in terms of scores of all the outcome measures among 3 groups at the final follow-up. The score of pain related disorders in JOABPEQ at 6 months after surgery was statistically significant higher in PTLIF group than the other 2 groups (P=0.023). There were no statistically significant differences in the scores of the other outcome measures among 3 groups in whole follow-up period.

DISCUSSION: The current study demonstrated that there were no statistically differences of VAS and health related QOL among 3 groups with different surgical invasiveness at the final follow-up. However, pain related disorders at 6 months after surgery was significantly better in PTLIF group. The results strongly indicate that PTLIF can remarkably improve disorders due to pain in early stage after surgery.

Incidence rate of adjacent-segment disorder after oblique lateral interbody fusion at more than two levels: Data from the Chiba Spine Surgery Registry database

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Background: Adjacent-segment disorder (ASD) is an important complication of spinal fusion, but the detailed incidence of ASD has not been fully reported. We investigated the incidence of ASD after oblique lateral interbody fusion (OLIF) at multiple levels that were performed in different centers and registered in the Chiba Spine Surgery Registry database.

Methods: We collected cases of OLIF at >2 levels that were performed for lumbar degenerative disease and followed up for at least 1 year. We defined radiological ASD as follows: >3-mm decrease in intervertebral disk height from that before surgery or >5% spondylolisthesis in the lateral view of the whole spine on radiography. Furthermore, we extracted cases of worsening intervertebral disk degeneration as compared with that before surgery according to the Pfirrmann classification of cranial and caudal adjacent intervertebral disks on magnetic resonance imaging. In addition to the image diagnosis, as a clinical diagnosis, we defined the occurrence of new-onset clinical symptoms at the surgery site as symptomatic ASD.

Result: We identified 42 patients (21 men and 21 women) with a mean age of 69.6 ± 9.6 years. The mean number of fused intervertebral levels was 4.2 ± 3.2 , and the mean observation period was 1.4 ± 0.9 years. Of the 42 ASD cases, 10 were radiological ASDs by image diagnosis. Six cases showed loss of cranial adjacent intervertebral disk height, 8 cases showed loss of caudal adjacent intervertebral disk height, and none of the cases had spondylolisthesis. Twelve (28.6%) and 2 cases (4.8%) had progression at the cranial and caudal adjacent intervertebral disks, respectively, according to the Pfirrmann classification. As for symptomatic ASD, we found 4 cases, all of which were at the caudal adjacent segments (L5/S). Three patients needed follow-up surgery after 2 years (mean).

Discussion: According to previous reports, the incidence rates of ASD 3 years after posterior or transforaminal lumbar interbody fusion at multiple levels ranged from 11.7% to 29%. The reoperation rate ranged from 5.6% to 10%, and cranial ASD was significantly more prevalent than caudal ASD. In this study, we found that the incidence of ASD diagnosed using imaging modalities after multiple OLIF was similar to that of ASD after posterior lumbar spinal fusion. In clinical ASD after OLIF, this result suggests that the caudal adjacent segment is more vulnerable.

Comparison of the facet fusion rates between percutaneous pedicle screw and cortical bone trajectory screw fixation for degenerative lumbar spondylolisthesis

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Introduction: Previous studies have reported that cortical bone trajectory (CBT) screws have higher pullout strength and insertional torque than pedicle screws (PSs). In our previous study, facet fusion (FF) using a percutaneous pedicle screw (PPS) system (PPS-FF) for degenerative lumbar spondylolisthesis (DLS) as a minimally invasive evolution of posterolateral fusion yielded good clinical outcomes. Furthermore, we have been performing FF using CBT screws (CBT-FF), a much less invasive FF technique, since 2013. This study aimed to compare the FF rates between PPS and CBT screw fixation for DLS.

Methods: The indications for lumbar fusion were: 1) sagittal translation $\geq 8\%$ on a flexion–extension lateral radiograph or 2) anterior wedging $\geq 5^\circ$ on a flexion radiograph and disc range of motion $\geq 10^\circ$. A total of 139 patients (77 women, 62 men; mean age = 68.5 years; mean follow-up = 78.1 months) who underwent PPS-FF and 57 patients (34 women, 23 men; mean age = 70.8 years; mean follow-up = 45.8 months) who underwent CBT-FF for single-level DLS were retrospectively reviewed after a minimum follow-up of 1 year. The surgical method involved making a 5-cm skin incision, bilateral laminar fenestration, and FF with autologous bone harvested from the spinous process. PPSs or CBT screws were then inserted. The PPS diameter was determined by the minimum endosteal diameter of the pedicle on the axial plane seen on preoperative computed tomography (CT) (maximum = 7.5 mm). The CBT screw diameter was uniformly 5.5 mm for the first 14 patients. Thereafter, a screw diameter of 6.5 mm was used for visibly thick pedicles. From the 24th patient, CBT screws with a 1 mm smaller diameter than the endosteal diameter of the pedicle were used (maximum = 7.5 mm). In the first 10 patients who underwent CBT-FF, a probe was directed toward the posterocranial edge of the vertebra on the lateral view, engaging only the cortical bone in the pedicle without involvement of the vertebral body trabecular space. In the subsequent 47 patients, a probe was inserted toward the midpoint of the cranial endplate. FF was defined as bony continuity on a facet joint seen on CT. Subsequently, the FF rate was evaluated.

Results: The FF rate at the 1-year follow-up was 78.1% and 82.5% for PPS-FF and CBT-FF, respectively. On the final follow-up, the rates were 89.9% and 89.5%, respectively. There was no significant difference between the two groups.

Discussion: Although biomechanical studies have reported that CBT screws have higher pullout strength and insertional torque than PSs, one study concluded that PS fixation was stiffer than CBT screw fixation. There was no significant difference in the FF rates between PS and CBT screw fixation. This finding is consistent with that reported in previous studies for other fusion techniques, such as posterior lumbar interbody fusion and transforaminal lumbar interbody fusion.

Polyethylene tapes at the proximal end in long spinal fusions reduce the revision rate due to Proximal Junctional Kyphosis

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INTRODUCTION: Recently, long spinal fusions for adult spinal deformity (ASD) have been markedly increasing in the aging society. However, they have high complication rate because the patients often have severe osteoporosis and other medical problems. Therefore, revision surgery due to proximal junctional kyphosis (PJK) is a serious issue in the populations. Because PJK is multifactorial, the preventive measures against PJK and consequent revision surgery have not been established. The purpose of this study was to elucidate the preventive effects of different proximal end fixation methods, hooks alone and polyethylene tapes with or without hooks, on PJK as well as revision surgeries.

METHODS: Seventy-six adult patients with spinal deformity who underwent corrective long spinal fusion with S2AI screws as distal anchors and followed up at least for 12 months were enrolled. As the proximal end of fusion constructs, hooks (group H) or two-level polyethylene tapes with or without hooks (group T) were used. The PJK was defined as the progression of kyphosis over 10 degrees at the proximal end of fusion. In addition, revision surgery due to PJK was defined as proximal junctional failure (PJF). We evaluated age, gender, operation time, estimated blood loss, pre and postoperative sagittal parameters (SS, PI, and PT), sagittal vertical axis (SVA), and the incidence of PJK and PJF in the two groups within 12 months after surgery.

RESULTS: Twenty patients were involved in group H (age, 72.3 ± 9.6 years) and 56 in group T (age, 74.4 ± 7.5 years). Mean operation time was 452 minutes and 436 minutes, respectively. Mean estimated blood loss was 1272 ml and 1128 ml, respectively. There was no significant difference in age, gender, operation time, estimated blood loss, and pre and postoperative sagittal parameters between the two groups. Group H had 11 PJK (55.0%), while group T had 14 (24.1%), indicating that PJK was significantly prevented in group T ($P=0.014$). Moreover, group H had 7 PJF (35.0%) and group T had 6 (10.3%), indicating that PJF was also significantly prevented in group T ($P=0.013$). No clinical problems related to S2AI screws were found, regardless of the presence or absence of screw loosening.

DISCUSSION: It was suggested that PJK and PJF were suppressed by using polyethylene tapes at the proximal end of fusion constructs within postoperative 12 months and the S2AI screw would be a reliable distal anchor with minimal clinical problems.

Bilateral double iliac screw fixation for traumatic sacral fracture

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【Introduction】

Denis classification zone 1 injuries are the most frequent sacral fractures, constituting approximately 50% of all sacral fractures. Several surgical options are available for their treatment. We herein report the use of bilateral double iliac screw fixation for the treatment of traumatic Zone 1 sacral fractures.

【Methods】

Five patients with an acute, unstable zone 1 sacral fracture underwent a mini-open procedure using bilateral iliac screws for stabilization. Two paramedian incisions were made over the iliac crest, and 8 mm iliac screws were bilaterally placed with minimal fluoroscopic guidance. Titanium rods were inserted into the subcutaneous layer between the incisions and affixed to the screw heads

【Results】

All the patients underwent follow-up for more than 12 months. The average follow-up period was 20 months. The average operation time was 107 minutes, and the average amount of intraoperative blood loss was 180 ml. No intraoperative complications occurred, and all the patients achieved rapid relief from postoperative pain and were ambulatory at an early stage.

【Discussion】

The double iliac screw fixation method for traumatic zone 1 sacral fractures is minimally invasive and involves minimal radiation exposure. This method is therefore a good surgical option for the treatment of sacral fractures.

Evolution of Image Guidance in Minimally Invasive Transforaminal Lumbar Interbody Fusion (MI-TLIF): Comparing the Learning Curves of Fluoroscopy, Navigation, and Robotics

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Introduction:

Intra-operative image-guidance has undergone tremendous advancements in recent years, evolving from two-dimensional imaging modalities such as 2D fluoroscopy or serial radiography to 3-dimensional computer assisted navigation, and more recently robotics. Despite these advances, concern regarding the learning curve of new technologies remains a deterrent to greater adoption.

Thus, the purpose of this study was to **evaluate the learning curve of fluoroscopy, intraoperative navigation (ION) and robotic navigation for minimally invasive TLIF (MI-TLIF).**

Methods:

A retrospective review of prospectively collected data on consecutive patients who underwent single-level MI-TLIF by a single surgeon using fluoroscopy, intra-operative navigation or a robot was performed. Outcomes of interest were operative time, estimated blood loss (EBL), intra-operative complications, radiation exposure, length of stay (LoS) and reoperations. Chronologic case number for each modality was plotted against each outcome of interest. The derivative of a nonlinear association or dissociation curve fit to the dataset was solved for the point at which the slope of the curve equaled the linear slope. At this point, average rate of change equals the instantaneous rate of change on the nonlinear curve. Therefore, rate of change after this case will be less than the average rate of change, suggesting a plateau in learning had occurred.

Results:

Of the 225 patients included, 109 underwent MIS-TLIF using fluoroscopy, 77 using ION and 39 using robotic navigation. There was no learning curve for estimated blood loss, length of stay or operative complications in any cohort.

Fluoroscopy

Median operative time was 112minutes, fluoroscopy time 144seconds and radiation dose was 62.7mGy. There were no intra-operative complications; 11(10.0%) patients required reoperation (2 epidural hematoma, 2 failed hardware, 2 pseudoarthrosis, 2 recurrent stenosis, 3 ASD).

-Operative time: Proficiency: 38 cases (Before vs after proficiency=137 vs 104mins, $p<0.0001$).

-Fluoroscopy time: Proficiency: 51 cases (Before vs after proficiency=168 vs 126secs, $p<0.0001$).

-Radiation dose: Proficiency: 51 cases (Before vs after proficiency=72.05 vs 53.95mGy, $p=0.008$).

-Reoperations: Proficiency: 43 cases. (Before vs after proficiency=18 vs 5%; $p=0.023$).

Intra-operative 3D Navigation

Median operative time was 88minutes, fluoroscopy time 25seconds and radiation dose 47mGy. There were no intra-operative complications; 5(6.5%) patients required a repeat spin intra-operatively and 7(9.1%) underwent a reoperation (1 each - SSI, screw repositioning, cage displacement, superficial hematoma, ASD, recurrent stenosis, pseudoarthrosis with painful hardware).

-Operative time: Proficiency: 31 cases (Before vs after proficiency=95 vs 80mins, $p<0.0001$)

-Fluoroscopy time, radiation dose, repeat spin and reoperations: No learning curve.

Robotic Navigation

Median operative time was 103minutes, fluoroscopy time 18seconds and radiation dose 38.1mGy. There were no intra-operative complications; the first patient required intra-operative manual repositioning of one screw (2.6%), and 1 (2.6%) required a revision surgery for residual stenosis.

-Operative time, fluoroscopy time and radiation dose: No learning curve.

-Intra-operative screw repositioning and reoperations: Could not be assessed due to low incidence.

Conclusion:

Our results suggest that newer intra-operative image-guidance modalities have the potential to reduce or even eliminate the learning curve for minimally invasive procedures and may thus allow for greater adoption of these techniques.

The influence of ethnicity/race and sex on lumbar spinal fusion outcomes

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Introduction: Fusion for the lumbar spine is among the most common orthopaedic procedures performed. While substantial data exists on factors that influence surgical outcomes, there are few studies that investigate the impact of demographics on postoperative complication rates. The aim of the current study was to assess if there are differences in outcomes following lumbar spinal fusion between sexes and various races.

Methods: A retrospective cohort study was conducted using the National Inpatient Sample (NIS) 2016 database, which contained 35,967 patients who underwent lumbar spinal fusion surgery as their primary procedure. Statistical analysis was conducted in R. One-way ANOVA followed by Tukey's multiple comparison was performed to analyze differences in complication rates between races. Odds ratios and Fisher's exact test were used to assess complication differences between sexes. Complications assessed included death, prolonged length of stay (LOS) > 4 days, surgical site infection, urinary tract infection (UTI), urinary retention, pneumonia, deep vein thrombosis/thrombophlebitis, pulmonary embolism, renal insufficiency/failure, cardiac arrest, neurologic injury, and posthemorrhagic anemia. Additionally, comorbidities will be controlled for using the Charlson Comorbidity Index.

Results: There was a significant difference in inpatient postoperative mortality between male and female sex following lumbar spinal fusion, with females having a significantly lower chance of death (OR: 0.339, 95% CI: 0.170, 0.635, $p < 0.001$). Females also had lower chance of urinary retention (OR: 0.511, 95% CI: 0.463, 0.564, $p < 0.001$), surgical site infection (OR: 0.747, 95% CI: 0.583, 0.957, $p < 0.01$), renal insufficiency/failure (OR: 0.638, 95% CI: 0.450, 0.900, $p < 0.01$), and cardiac arrest (OR: 0.385, 95% CI: 0.341, 0.434, $p < 0.001$). However, females were found to have a higher risk of prolonged LOS (OR: 1.108, 95% CI: 1.053, 1.166, $p < 0.0001$), UTI (OR: 2.189, 95% CI: 1.856, 2.593, $p < 0.001$), neurologic injury (OR: 1.092, 95% CI: 1.033, 1.155, $p < 0.01$), and posthemorrhagic anemia (OR: 1.477, 95% CI: 1.388, 1.572, $p < 0.001$). No differences were found in cardiac arrest, pulmonary embolism, UTI, or death rates following lumbar fusion between races. Compared to black, Asian, and Hispanic patients, white patients were less likely to have a prolonged LOS ($p < 0.05$). White patients were also significantly less likely to have infections than black patients ($p < 0.001$) and less likely to have renal complications than blacks or Asians ($p < 0.01$). Posthemorrhagic anemia was significantly higher in Asians compared to Hispanics and whites ($p < 0.05$).

Conclusion: There are multiple significant differences in complication rates following lumbar spinal fusion between different sexes and races. These demographic factors should not be overlooked during preoperative assessments and should be taken into consideration when educating patients on surgical risks.

Three-dimensional analysis for pedicle screw deviation in thoracolumbar spinal fusion

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Introduction: A lot of studies have examined about incidence of pedicle screw (PS) deviation in various maneuvers. However, most previous studies evaluated using simple reconstructed CT images. Three-dimensional (3D) reconstructed images enable more detailed analysis in terms of screw setting. The purpose of this study was to compare between the preoperative planning and postoperative screw position using 3D planning software, and to investigate factors for screw deviation among setting error, methods of screw setting, or patients' factors.

Methods: Twenty-four patients who underwent thoracolumbar fusion between April 2019 and March 2020 were included in this study. A total of 201 screws were analyzed. The maneuver of PS setting was 115 percutaneous technique using fluoroscopy and 86 conventional open technique using lateral fluoroscopic images. One hundred and twenty-four screws were set by the skilled surgeon (experienced ≥ 10 years) and 77 screws by the inexperienced surgeon (experienced < 10 years). All screws were planned preoperatively for diameter/length/trajectory in a 3D analysis software (ZedSpine, LEXI, Tokyo, Japan). Differences between a preoperatively planned screw and postoperative screw position were evaluated by 3D image matching to measure errors in insertion point distance and screw trajectory angle in 3D, axial or sagittal plane. Deviation of PS was assessed from postoperative CT (Grade 0: no deviation/ 1: < 2 mm deviation/ 2: ≥ 2 mm of deviation without complications/ 3: ≥ 2 mm with complications). Differences between deviated PS (\geq grade 1) and non-deviated PS were investigated among screw setting error, methods of screw setting, Cobb angle, vertebrae tilt angle and vertebrae rotation angle. Multiple logistic regression analysis was performed to assess related factors for PS deviation adjusting for age, gender, and parameters with $p < 0.10$ in univariate analysis. The cut-off value to predict deviation was set by ROC curve analysis.

Results: There were 13 PS deviations (6.4%): Grade 1, 2, and 3 deviations were 8, 4, and 1, respectively. Errors of the distance of insertion point in the 3D and axial plane were significantly greater in the deviated PS than non-deviated PS (7.5 mm vs. 5.2 mm $p = 0.015$, 7.1 mm vs. 4.1 mm, $p < 0.01$, respectively). There was no difference in deviated PS in methods of screw setting, surgeon experience, or patients' factors. In multivariate analysis, factors associated with deviated PS was the error of insertion point distance in the axial plane (odds ratio 1.41, 95% confidence interval 1.13-1.77). The ROC curve showed that the area under the curve for deviated PS was 0.725 in the error of insertion point distance in the axial plane, and the optimal cutoff value for predicting PS deviation was ≥ 6.5 mm (sensitivity, 79.3%; specificity, 81.5%).

Conclusions: The risk of PS deviation increases when the insertion point was far from the planning in the axial plane as the result of well-planned methods using 3D analysis software. These results suggest that the surgeon should take care of the insertion point, especially medial-lateral direction to avoid screw deviation.

Discrepancies in nosocomial urinary tract infection rates between patients receiving single-level and multi-level lumbar fusion

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Introduction: One of the most common complications during inpatient admission is nosocomial urinary tract infection (NUTI). Procedures resulting in longer inpatient lengths of stay and placement of urinary catheters have been linked to increased rates of NUTI. Multi-level lumbar fusion procedures typically require longer time than single-level fusions and thus require urinary catheter placement more frequently. The aim of the current study was to assess whether the incidence of NUTI differs between patients receiving one-level and multi-level lumbar fusion.

Methods: The 2016 National Inpatient Sample (NIS) database to conduct a retrospective cohort analysis of 27,522 patients who received single-level (N=17,905) or multi-level (2 or more joints, N=9,617) lumbar fusion as their primary procedure. ICD10 diagnosis and procedure codes were used to identify patients and evaluate complications. Inpatient urinary retention was used to identify individuals with urinary catheter placement. Statistical analysis was conducted in R, and odds ratios and Fisher's Exact Test were used to compare NUTI rates in groups receiving different levels of spinal fusion surgery.

Results: Average inpatient length of stay after lumbar fusion was found to be 3.77 ± 3.32 days. Within all patients, the rate of NUTI during post-fusion inpatient stay was found to be 2.09%. The rate of NUTI in patients receiving single-level lumbar fusion was found to be 1.74% and the rate in those receiving multi-level fusion was 2.75%. The length of stay (LOS) for single-level lumbar fusion was 3.36 ± 2.77 days and the LOS for multi-level lumbar fusion was found to be 4.53 ± 4.06 . Urinary retention requiring potential catheter placement was identified in 796 patients after single-level lumbar fusion (4.45%) and 667 patients after multi-level fusion (6.95%). The odds ratio for developing a NUTI during inpatient stay after single-level lumbar fusion compared to multi-level fusion was 0.787 (95% CI: 0.677, 0.914, $p = 0.00184$).

Conclusion: Multi-level lumbar fusion is associated with a significantly increased rate of postsurgical NUTI when compared to single-level lumbar fusion. This difference in NUTI rates may be due to the increased average operating time and rate of urinary catheterization in multi-level lumbar fusion. Further investigation is necessary to precisely identify the factors that contribute towards discrepancies in post-fusion NUTI so that steps can be taken to address this epidemiological concern.

GP087

Bilateral Lumbar Erector Spinae Plane Blocks Reduce Postoperative Pain and Opioid Requirements in Minimally Invasive Transforaminal Lumbar Interbody Fusion (MI-TLIF)

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Introduction:

Erector Spinae Plane (ESP) block is a relatively new fascial plane block that has been described for the management of chronic neuropathic pain and postoperative pain in abdominal and thoracic procedures, and hip surgery. However, the current literature on ESP blocks in spine surgery is limited.

Thus, the purpose of this study was to evaluate the impact of ESP blocks on postoperative pain, opioid requirements and perioperative outcomes in MI-TLIF.

Material and Methods:

Patients undergoing MI-TLIF by a single surgeon and single anesthesiologist from Feb'19–Nov'19 who received bilateral Lumbar ESP blocks were selected (22 patients, Group E). Revision surgeries and patients with chronic opioid use were excluded. From a historic cohort of MI-TLIF patients (Apr'17–Nov'18), an age and gender matched control group that did not receive an ESP block was selected (Group NE). Postoperative pain, opioid consumption (oral morphine milligram equivalents – MME and need for intravenous patient controlled analgesia – IV-PCA), complications and length of stay (LoS) were compared. Chi square test and Fisher's exact test were used to compare categorical variables, and student t-test and Mann Whitney u-test were used to compare normally and non-normally distributed continuous variables respectively. Statistical significance was set at p<0.05.

Block Technique: All patients received a standardized anesthetic with multimodal analgesia. All ESP blocks were performed by the same Anesthesiologist (30ml of 0.375% bupivacaine with 2mg preservative free dexamethasone per side). In addition, all patients received local anesthetic infiltration (30ml of 0.5% bupivacaine with epinephrine) at the end of surgery.

Results:

Forty-four patients, 22 in group E and 22 in Group NE were included. There were no significant differences in demographics, operative factors or in-hospital complications. There were no intraoperative complications in either cohort.

Group E had lower 24hr opioid consumption (median=22.5 MME vs 57.5 in NE, p<0.0001), primarily due to lower opioid consumption in the 0-6 hrs post-operative period (p=0.034) and less need for IV-PCA (0 vs 22.7% in NE, p=0.048). Intraoperative opioid requirements were lower in Group E (median=40 MME vs 75 in NE, p<0.0001). Highest pain score within 3hrs of surgery was median of 7 and 8 in Group E and NE, respectively (p=0.140). However, Group E reported significantly lower average pain (median NRS=3.3 vs 5.1 in NE, p=0.034).

Group E also reported no opioid-related side effects versus rates of 4.5%, 4.5% and 9.1% for nausea/vomiting, ileus and urinary retention, respectively in Group NE; however, this difference was not statistically significant.

There was no difference in LoS (Group E: median=24hrs vs NE: 26; p=0.250), with about 70% of patients in both groups being discharged on post-operative day 1 (p=0.388).

Conclusion:

Our results show that ESP blocks resulted in a clinically significant reduction in opioid consumption in the perioperative period and average NRS pain score on POD 0, with no difference in complications or length of stay. Larger randomized studies are required to validate these findings and confirm the benefit of ESP blocks in spine surgery.

	ESP Block (n=22)	No ESP Block (n=22)	p-value
Post-operative Pain (NRS 0-10)			
• First pain score recorded after procedure end	0 [0-0]	0 [0-0]	0.713
• Highest pain score within 3 hours of procedure end	7 [4-8]	8 [6-9]	0.340
• Average POC (µg/hr)	2 [1.2-3.0]	3.1 [1.6-6.0]	0.039
• Average MME	40 [30-40]	75 [40-200]	<0.0001
Opioid Consumption up to 24 hours post surgery			
• Need for IV PCA	0 (0.0%)	5 (22.7%)	0.048
• Time to need for IV PCA (minutes)	-	77 [66-346]	
• Total MME	22.5 [10-57.5]	61.5 [40-116.0]	0.006
NRS by hour post surgery			
• 0-1	1.2 [0-8.0]	16.25 [20-39.7]	0.084
• 1-6	0.0 [0-2.5]	6.25 [0-15]	0.094
• 6-9	0.0 [0-10]	0.0 [0-10.4]	0.479
• 9-12	0.0 [0-1.1]	0.0 [0-1.0]	0.760
• 12-15	0.0 [0-1.0]	8.75 [0-11]	0.042
• 15-18	0.0 [0-0]	0.0 [0-0]	0.933
• 18-21	0.0 [0-0]	6.75 [0-11]	0.068
• 21-24	0.0 [0-0]	0.0 [0-7.5]	0.370
In-hospital complications			
• Urinary retention requiring catheterization	2 (9.1%)	4 (18.2%)	0.694
• Nausea/vomiting requiring antiemetic	0 (0.0%)	1 (4.5%)	0.468
• Ileus	0 (0.0%)	1 (4.5%)	1.000
• Respiratory depression	0 (0.0%)	1 (4.5%)	1.000
• New onset neurological deficit	1 (4.5%)	0 (0.0%)	1.000
• New onset septic arthritis	1 (4.5%)	0 (0.0%)	1.000
Post-surgical length of stay (Hours)	24.04 [22.83-41.51]	26.18 [24.67-44.95]	0.250

The Role of Hounsfield Unit in Intraoperative Endplate Violation and Delayed Cage Subsidence with Oblique Lateral Interbody Fusion

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Introduction: Oblique Lumbar interbody fusion (OLIF) is an established surgical procedure to treat various spinal pathologies. One of the major complications of OLIF is cage subsidence as it may lead to compromised clinical results. As a bone density assessment, Hounsfield units (HU) of the endplate are measured from routine computerized tomography (CT) scans that are readily available as a part of the preoperative assessments. The HU of the epiphyseal ring and the central endplate can provide detailed information regarding bone quality across the endplates, potentially assisting surgical planning. Despite an increasing body of clinical evidence about the potential risk factors for cage subsidence, the role of HU values at the endplate remains unclear. The objective of this study was to investigate the role of HU values, as well as other risk factors, in intraoperative endplate violations and delayed cage subsidence after oblique lateral interbody fusion (OLIF) surgery.

Methods: Participants included 61 consecutive patients (aged 65.1 ± 9.5 years; 107 segments) who underwent OLIF with or without posterior instrumentation from May 2015 to April 2019. Intraoperative endplate violation was defined as more than 2mm collapse of the cage into the endplate of adjacent vertebral body on sagittal reconstructed CT images immediate postoperatively. Delayed cage subsidence was evaluated using lateral radiographs and defined as more than 2mm migration of the cage into the adjacent vertebral endplate at 1-month follow-up or later. As potential contributors, bone mineral density, number of surgical levels, preoperative and postoperative disc height and HU at different regions of the endplate were obtained along with other demographic factors to be analyzed in univariate and multivariate logistic regression.

Results: Total postoperative cage subsidence was identified in 45 surgical levels (42.0%) in 26 patients (42.6%) up till postoperative 1-year follow-up. These consisted of 25 intraoperative endplate violation segments (23.4%) and 20 levels (18.7%) with delayed cage subsidence. Low HU value at the ipsilateral epiphyseal ring was an independent risk factor for intraoperative endplate violation ($p=0.01$) with a cut-off value of 326.21 HUs (sensitivity 79.0%, specificity 77.3%). Low HU values at the central endplate had a significant correlation with delayed cage subsidence in stand-alone cases ($p=0.01$) with a cut-off value of 296.42 HUs (sensitivity 76.9%, specificity 76.6%).

Discussion: Our study revealed that endplates with lower HU at the ipsilateral epiphyseal ring are more likely to suffer from intraoperative endplate injury. In the process of distraction during an OLIF surgery, the ipsilateral side of the epiphyseal ring is in the most frequent contact with the metal trial and withstands the largest impact. On the other hand, HU of the central endplate was the only parameter that showed a significant association with delayed subsidence in stand-alone patients. HU of the central endplate is a good addition to BMD as a predictor for cage subsidence since it can represent the regional bone density of the endplate in contact with the implant. Measures may be taken preoperatively to maximize the HU to reduce the risk of surgical complications related to endplate violation and cage subsidence.

GP089

LUMBAR PLIF RECONSTRUCTION WITHOUT INPATIENT ADMISSION. RESULTS OF A STANDARDIZED CARE PROTOCOL IN OVER 100 SELECTED PATIENTS TREATED OVER A FIVE-YEAR PERIOD.

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Introduction

Resource limitations in health care argue for a continued evolution of "doing more with less". The author's hospital has set policy allowing for only one admitted scheduled care spine surgery case per day that has potential to impact adversely on wait times and care. A standard care path used in decompression surgery was adapted to accommodate more invasive mono- and bi-segmental reconstructions starting in 2015 and has been followed forward comprehensively with a view to determining the success rate in managing these cases with only an overnight stay in the Recovery Room.

Method

Qualifying cases were 1- and 2-level reconstructions in ambulatory patients with supportive households to which they could be discharged. These were not MIS surgeries but classical open PLIFs which can be considered as LISS procedures because dissection is limited to within the facets and so the long paraspinal musculature is not violated. The authors prospective surgical practice logs were reviewed to collect all cases treated and the success rate of next-morning discharge determined.

Results

Of 114 qualifying cases reviewed, 110 were primarily discharged. Two were admitted to ward beds simply because there were no Overnight Stay beds available. One patient who initially refused discharge was successfully supported home by a physiotherapy visit to the Recovery Room. Two more failed discharge and required admission, both for just 48 hours. There was one early visit to clinic for pain control in a patient who had refused to take prescribed postop narcotics, one readmission at two weeks for a CSF leak, and one later readmission for DVT. There were no infections.

Conclusions

Short open PLIF reconstruction can be accomplished safely and consistently on a semi-ambulatory basis not requiring inpatient beds in Canada.

GP090

The Outcome Of Epidural Injections In Sciatica Is Not Dependent On The Presence Of Disc Herniation On MRI: Assessment Of Short-term And Long-term Efficacy

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Introduction: Sciatica is a condition with major physical, social and economic consequences. Despite its favourable prognosis the burden can be significant for the patient. Transforaminal epidural injections (TEI) with steroid are a minimally invasive treatment that can create a more bearable situation to await natural recovery. However, before patients can receive TEI they have to undergo routine MRI examination after referral by the neurologist prolonging the time until treatment. In this study, we aimed to determine the value of routine MRI before TEI on the short and long-term efficacy of TEI in patients with sciatica secondary to lumbar disc herniation (LDH) and other causes (non-LDH).

Methods: 1824 patients with sciatica that visited the outpatient neurology clinic were retrospectively reviewed for their radiological diagnosis based on MRI. For patients that were referred for treatment with TEI, response after 8 weeks (short term) and 16 weeks (long term), number of injections received, subsequent surgery and eventual patient outcome were evaluated. Treatment response was assessed by patient-reported symptom relief and NRS pain scores.

Results: 66% of 1824 MRI examinations demonstrated a clinically relevant LDH. 486 out of 1824 patients were referred for TEI of which one-third did not demonstrate LDH. 70% of patients reported a short-term effect with significant pain reduction after 6-8 weeks and 44% reported long-term effect at 16 weeks. No significant differences were observed between LDH and non-LDH groups. 59% of patients required multiple injections, and eventually reported similar efficacy compared to patients treated with a single injection. More patients in the LDH group eventually underwent neurosurgical intervention, but were satisfied at the end of treatment.

Conclusions: A considerable part of routine MRI examinations in sciatica patients does not demonstrate a clinically relevant LDH. Independent of the radiological diagnosis the vast majority of patients treated with TEI benefits on both short and long term after a single or multiple injections regime. Subsequent injections are advisable if the effect from the first injection is unsatisfactory or deteriorates. Since the effect of TEI is independent of the radiological diagnosis, routine MRI examination before TEI therapy may be redundant for TEI which could allow for expedition of this treatment.

Chronic low back pain and self-efficacy in the community

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【Introduction】 It is widely known that chronic low back pain (CLBP) is difficult to treat and has a great impact on society and individuals. Recently, the concept that CLBP should be considered as part of the chronic widespread musculoskeletal pain (CWMP) has been widely accepted. Cognitive-behavioral therapy approaches have been shown to be effective in treating CLBP in clinical setting. Self-efficacy is a concept that expresses the degree of confidence that you can deal with various things. However, the relationship between CLBP, CWMP and self-efficacy in local residents is unknown. The purpose of this study was to clarify the relationship between CLBP, CWMP and self-efficacy in the community.

【Participants and methods】 Subjects were 2182 local residents aged 40 and over (965men, 1217 women, and most age group 70s) who agreed in writing to participate in this study. The presence or absence of low back pain lasting 3 months or longer (CLBP), the general self-efficacy scale (GSES) and the self-efficacy for pain (pain self-efficacy scale questionnaire, PSEQ) were assessed by a questionnaire. In this study, chronic musculoskeletal pain was assessed at eight musculoskeletal locations: neck, low back, shoulder, elbow, hand or wrist, hip, knee, and ankle or feet by a questionnaire. Criteria for CWMP were pain above and below the waist and axial skeletal pain (back or neck pain).

【Results】 1. Five-hundred fifty-eight (25.6%) showed CLBP. Of the subjects with CLBP, 28.5% were determined to be CWMP and 1.2% of subjects without CLBP were determined to be CWMP. There was a statistically significant difference of the prevalence of CWMP between the subjects with and without CLBP ($p < 0.0001$).

2.No interaction was observed between CLBP and CWMP for GSES standardized score and PSEQ score by ANOVA. In multiple comparison test, the presence of CLBP or CWMP negatively influenced on the difference of GSES standardized score and PSEQ score.

3.According to logistic regression analysis, when the standardized GSES score or PSEQ score increase by 1 point, the odds ratio for the absence of CLBP was 1.015 and 1.020, respectively. Similarly, the relative risk for the absence of CLBP in the absence of CWMP was 13.2 to 32.8.

【Discussion】 In this study, no interaction with self-efficacy was observed between CLBP and CWMP. This indicates that patients with CLBP, whether CWMP or not, need to take an approach that enhances self-efficacy. However, in clinical setting, treating CLBP in CWMP patients is often difficult. Therefore, in patients with CLBP with CWMP, treatment with CWMP as well as CLBP may improve the outcome of treatment with CLBP.

Determining Low Back Pain Specific Targets for Physical Activity Interventions

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Introduction: It remains unclear if physical inactivity is a cause or a consequence of low back pain (LBP). While current physical activity guidelines for the general population focus on the quantity of moderate and vigorous physical activity, it is unclear if these are appropriate targets for the LBP population. In this study, we aim to objectively quantify and characterize the real-life physical activity of people with LBP compared to healthy controls, and to identify **LBP-specific physical activity thresholds** to use as targets in future physical activity interventions for LBP.

Methods: Real-life accelerometry data from 177 individuals were analyzed in this study, including 22 LBP participants enrolled at our center and 155 age and gender matched healthy controls without LBP extracted from the National Health and Nutrition Examination Survey (NHANES). All subjects wore the same research-grade accelerometer on the right hip for 7-consecutive days and passed a wear-time validation that confirmed valid accelerometry data for analysis. Features from the accelerometry data were extracted based on signal intensity and duration using the standard intervals described by Freedson (sedentary, light, moderate and vigorous activity) and by Smuck (physical performance thresholds for pain research). A Random Forest classifier was trained to classify LBP status using a standard data split and a cross-validation procedure. A recently proposed machine learning feature interpretation algorithm, the SHapley Additive exPlanations (SHAP) algorithm was applied to rank feature importance and to establish LBP-specific physical activity profiles.

Results: The random forest classifier achieved 88.1% accuracy for LBP classification. All of the top-ranked features derived from the sedentary and light activity intervals (count per min 0-99; 100-189; 190-349; 350-799). Moderate and vigorous activity (count per min >1952) was not found to be a discriminative factor between LBP and healthy controls. Compared to healthy controls, LBP participants spent more time being inactive and fewer minutes doing activity in the light range. The following **LBP-specific physical activity thresholds** describe the details that reliably differentiate LBP participants from healthy controls (daily sedentary time > 452 min combined with < 157 min of light activity).

Conclusion: Increased sedentary time and reduced time spent in light activity (instead of moderate or vigorous physical activity) were identified as the key discriminative features that distinguish between LBP participants from healthy controls. The cause and effect relationship between physical inactivity and LBP can be examined in future studies by using the **LBP-specific physical activity thresholds** described here as targets for LBP treatment and prevention.

COMPARATIVE EFFECTIVENESS OF FOUR MAJOR DRUGS PRESCRIBED FOR CHRONIC LOW BACK PAIN IN JAPAN

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INTRODUCTION: The economic burden induced by chronic low back pain (CLBP) is a worldwide problem. Although pharmacological treatment plays an important role, limited data exist regarding the drugs suitable to treat CLBP. We conducted a prospective nationwide multicenter study to compare the effectiveness of four major drugs commonly used for CLBP in Japan.

METHODS: Four hundred seventy-one subjects aged 20 to 85 years with CLBP persistent for at least 3 months were enrolled. Patients with a Brief Scale for Psychiatric Problems in Orthopaedic Patients (BS-POP) score <10 (physician version) or <15 (patient version) were excluded. Patients were treated with either celecoxib, loxoprofen, acetaminophen, or tramadol/acetaminophen (TA) combination tablets, four major drugs used for CLBP in Japan. Prescription allocation was at the discretion of each prescribing physician. The mean daily prescribed dose for each group at baseline was 208 mg, 2.3 tablets, 1,122 mg, and 2.7 tablets, respectively. The visual analog scale score for LBP, Japanese Orthopaedic Association (JOA) score, JOA Back Pain Evaluation Questionnaire (JOABPEQ), Roland-Morris Disability Questionnaire (RDQ), EuroQol (EQ)-5D, and Short Form (SF)-8 were evaluated at the time of enrollment and once monthly for 6 months, and the treatment effect evaluated by the change from baseline, was compared among the 4 groups. We conducted a multivariable linear regression analysis; this included the change from baseline for each outcome at each time point as a dependent variable. Independent variables were those indicating that the medicine was prescribed continuously from baseline, the observation period, and the cross-product terms. These models were adjusted for baseline covariates of age, sex, body mass index (BMI), smoking status, disease duration, history of cancer, osteoporosis, spine surgery, spine disease, medicine, Center for Epidemiologic Studies Depression scale (CES-D) score, exercise status, work, hobbies, number of family members, and number of comorbidities. Statistical hypotheses were tested 1 and 6 months after drug allocation, using a two-sided 5% significance level.

RESULTS: A significant difference was observed in the treatment effect on the mental health subscale of the JOABPEQ at 1 month and in the JOA score at 6 months, and acetaminophen was the most effective drug. Although there was no significant difference among drugs in the other treatment measures, a treatment effect was confirmed in all four groups, except on the SF-8 mental component summary, which tended to decrease over 6 months.

DISCUSSION: Although acetaminophen showed significant effectiveness for CLBP on one outcome measure at each time point of 1 and 6 months, at a relatively low dose of less than 1,200 mg, no significant difference among the four drugs was found on most of the outcome measures. Although we excluded patients with psychological factors by the BS-POP, our results suggest that symptoms related to mental health were not improved by analgesics alone. Since the 6-month trend of each drug showed a different course depending on the treatment measure, a comprehensive evaluation using multiple outcome measures is warranted to measure treatment effectiveness for CLBP.

Improved sagittal spinal alignment and balance by a “locomotion training” rehabilitation program in patients with “locomotive syndrome”

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INTRODUCTION: “Locomotive syndrome” is a degenerative condition of reduced mobility due to the impaired musculoskeletal system, which has gained increasing attention as a Japan’s health policy target. The Japanese Orthopaedic Association (JOA) recommends “locomotion training” exercises (basically squatting and single-leg standing) to be effective in preventing “locomotive syndrome”. However, the extent to which “locomotion training” affects body function is unknown. Therefore, a cohort study was designed. Our objective was to clarify effects of a “locomotion training”-based rehabilitation program on the sagittal spinal alignment and balance.

METHODS: Patients who fulfilled the JOA criteria for “locomotive syndrome” were enrolled and prospectively followed in our outpatient clinic ($n = 106$: age, 76.1 ± 5.9 years; male:female = 12:94). While 44 patients accepted and completed our “locomotion training”-based rehabilitation program once per week for 6 months (20-min stretching and self-exercise achievement evaluation), 41 patients denied the exercise participation but received medicinal treatment (NSAIDs, pregabalin, duloxetine, and/or tramadol). Standing whole-spine radiographs for the spine-pelvis-lower extremity axis, ODI and SF-36 questionnaires for QOL, and piezoelectric force-plate measurement for postural stability were taken at baseline and >6 months.

RESULTS: [Exercise-intervention analysis] While there were no obvious differences in baseline sagittal vertical axis (SVA), >6-month changes were significantly different (exercise, -5.5 ± 20.0 ; control, $+5.2 \pm 22.6$ mm: $P = 0.02$). In other radiographic parameters, >6-month changes were more remarkable in the lumbar lordosis (LL) (exercise, $+1.5 \pm 8.1^\circ$; control, $-1.3 \pm 9.1^\circ$: $P = 0.14$), thoracic kyphosis between T5 and T12 (TK) (exercise, $-0.05 \pm 5.5^\circ$; control, $+1.8 \pm 6.0^\circ$: $P = 0.13$), and T1 slope (exercise, $-0.4 \pm 6.3^\circ$; control, $+1.6 \pm 5.8^\circ$: $P = 0.14$). No obvious differences in ODI and SF-36 were observed. However, in force-plate examination, the center-of-pressure area (exercise, -0.4 ± 1.8 ; control, $+0.2 \pm 1.6$ cm²: $P = 0.07$), speed (exercise, -0.1 ± 0.4 ; +0.1 \pm 0.4 cm/s: $P = 0.03$), and distance (exercise, -5.1 ± 24.3 ; control, $+6.5 \pm 23.3$ cm: $P = 0.03$) decreased after >6-month rehabilitation. [SVA analysis] Of 40 patients with baseline SVA ≥ 40 mm, endpoint SVA improvement to <40 mm was observed in 12 (30.0%). In the comparison between 12 patients with and 28 without improved SVA, baseline SVA ($+51.6 \pm 10.2$; $+79.5 \pm 34.0$ mm: $P < 0.01$), C2–C7 angle ($+10.9 \pm 6.0^\circ$; $+19.6 \pm 13.0^\circ$: $P = 0.03$), and hip-flexion angle ($+8.1 \pm 2.4^\circ$; $+11.2 \pm 4.0^\circ$: $P = 0.02$) were significantly different. Then, >6-month changes were relatively obvious in LL ($+4.6 \pm 9.0^\circ$; $-0.6 \pm 8.1^\circ$: $P = 0.08$). In force-plate examination, >6-month changes were marked in the area (-1.6 ± 5.3 cm²; $+0.2 \pm 1.7$ cm²: $P < 0.01$).

DISCUSSION: This is the first study to demonstrate that “locomotion training” protects against “locomotive syndrome”-associated positive SVA shift and improves the standing spinal balance. However, rehabilitation-induced SVA improvement is limited in patients with advanced baseline SVA positive shift, C2–C7 hyperlordosis, and hip contracture.

Plaster cast fixation for patients with osteoporotic vertebral compression fractures: Part 2 Comparison of reduction in standing position and suspension in supine position

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Introduction: Vertebroplasty or kyphoplasty as forms of percutaneous vertebral augmentation (PVA) are recommended for patients with osteoporotic vertebral compression fracture (OVCF) who experience persistent severe back pain. However, PVA is reportedly associated with higher risks of refracture at both adjacent vertebrae and any segment. Therefore, for early conservative treatment with OVCF, we recommend conventional plaster cast fixation (PCF) treatments. As reduction methods for PCF of OVCF, reduction in a standing posture (STP) and suspension reduction in a supine position (SUP) can be used. We reported at the 45th ISSLS annual meeting that SUP showed better efficacy of reduction than STP. The present study compared 3-month outcomes of PCF using STP and SUP in terms of examined collapse rate and local kyphosis angle.

Material and Methods: Subjects in this study were the same 49 patients with OVCF reported on at the 45th ISSLS annual meeting. Follow-up was continued for >3 months after discharge in all cases. In PCF, STP was performed by pulling on the head along the center of gravity line in a standing position, while SUP was performed by the dorsal suspension method with the patient supine on the cast table. In conservative management of OVCF, subjects used a rigid brace for 12 weeks after PCF for 8 weeks. The STP group comprised 22 patients (4 men, 18 women; mean age, 78.4 years), and the SUP group comprised 27 patients (5 men, 22 women; mean age, 76.0 years). After PCF, we confirmed the efficacy of the reduction of the OVCF on standing-position X-rays. Radiographic parameters were anterior and posterior heights of vertebrae, collapse rate, and local kyphosis angle, with comparisons between before and 3 months after PCF.

Result: Mean collapse rate before PCF tended to be higher in SUP (30.6%) than in STP (24.5%) ($P=0.23$). At 3 months after PCF, collapse rate was significantly worse in STP (44.6%) than in SUP (38.5%; $p<0.019$). Amount of change in both anterior and posterior vertebral heights between before and 3 months after PCF was significantly worse for STP than for SUP (anterior: $p<0.001$; posterior: $p<0.015$). Local kyphosis angle deteriorated significantly more with STP (from 14.1° to 21.5°) than with SUP (from 15.2° to 18.3°; $p<0.036$).

Conclusion: At the 45th ISSLS annual meeting, we reported that the period to pain reduction and the duration of hospitalization were significantly shorter with SUP than with STP. However, 3-month outcomes for PCF suggested shape of the injured vertebral body as a cause for concern regarding development of vertebral deformity and subsequent kyphosis. Brace therapy is used as general conservative therapy, but does not seem to achieve rigid external fixation. Kim et al. (2014) compared rigid and soft-brace treatments, reporting no differences in improvement of back pain, radiographic anterior body compression ratio, or patient satisfaction rates among treatment groups during the 3-month follow-up after OVCF. We therefore suggest that conservative PCF is initially warranted. Based on the present results, we recommend applying SUP for rigid external fixation of OVCF.

Gabapentinoids associated with lower explantation rate in 203 patients with Spinal Cord Stimulation for Failed Back Surgery Syndrome

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Introduction

Spinal cord stimulation (SCS) is an effective treatment in failed back surgery syndrome (FBSS).¹ We studied the effect of gabapentinoid use on SCS outcomes measured by trial success, explantation rate and opioid dose reduction during a two-year follow-up.

Methods and Materials

The study cohort included 203 consecutive FBSS patients who underwent SCS in a single tertiary center during January 1997–March 2014. Purchase data of gabapentinoids, opioids, tricyclic antidepressants, and benzodiazepines during January 1995–March 2016 were retrieved from national registries.

Results

In multivariate Cox regression analysis, patients using gabapentinoids had significantly fewer explantations during the two-year follow-up (HR 0.3, CI 95% 0.094–0.96, $p = .04$). In contrast, patients with strong or intermediate opioid use before implantation had significantly more explantations (HR 3.6, CI 95% 1.3–9.4, $p = .011$). In bivariate logistic regression analysis adjusted for gender, age, number of previous operations, location and duration of pain, status of instrumented lumbar fusion, use of anxiolytic medication, use of strong or intermediate opioids, and use of tricyclic antidepressants, patients using gabapentinoids significantly more often experienced over 20% reduction of their total opioid dose (OR 3.6, CI 95% 1.1–12, $p = 0.042$) during the two-year follow-up. Gabapentinoid use was not associated with success of the preimplantation trial.

Discussion

This is the first study to analyze the effect of continuous gabapentinoid use on explantation rate. Prabhala et al.² studied gabapentinoids and duloxetine with SCS treatment. Gabapentinoids did not significantly affect any pain outcomes positively, but they significantly increased the perception of pain. Maher et al.³ studied neuropathic pain medication and its effect on pain reduction or opioid dose reduction. Neither the use of opioids nor neuropathic pain medications were associated with changes in the odds of a successful SCS trial or a 50% pain reduction.

In our study, patients using gabapentinoids were able to reduce their opioid dose significantly more often than nonusers. In a study by Jang et al.⁴, quality of life was assessed after SCS with a combination of opioid and gabapentinoid therapy against opioid therapy alone. They showed a similar trend in opioid dose reduction with gabapentinoid as in our regression model.

The use of gabapentinoids was associated with a lower spinal cord stimulator explantation rate and a higher chance of over 20% opioid reduction. This indicates that patients with SCS could benefit from the concomitant use of gabapentinoids. Prospective randomized trials would be warranted to verify this hypothesis.

Acknowledgements

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Novel Inflammation-Preserving Treatment for Symptomatic Lumbar Disc Herniation: a Prospective Imaging and Clinical Outcomes Study

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Introduction: Acute lumbar disc herniation is one of the leading causes of back pain and radicular symptoms. Initial treatment is often conservative, whereby some patients will improve, owing to the natural inflammatory response of the body, leading to disc resorption and potential relief of symptoms. Interestingly, however, many established guidelines dictate that oral steroids and other anti-inflammatory agent (NSAIDs) should be prescribed; however, this mode of treatment may disrupt the natural macrophage-driven disc resorption, and potentially increase the duration of symptoms. The concept of an “inflammation-preserving” treatment for lumbar disc herniation in humans has yet to be explored. The following prospective study addressed a novel inflammation-preserving treatment (i.e. no NSAID drug use etc) for symptomatic lumbar disc herniation patients to promote natural healing, facilitate disc resorption and provide pain relief.

Methods: A prospective study of patients with MRI-proven lumbar disc herniation and acute radiculopathy was performed. All patients received sufficient Gabapentin to relieve their leg pain and 12 sessions of acupuncture and were instructed to avoid anti-inflammatory agents. Repeat MRI was performed after 12 sessions of treatment continued for those without improvement. Disc herniation dimensions were measured on sagittal T2 MRI sequences.

Results: A total of 101 patients (51% females) met inclusion criteria, with a mean age of 47.9 years. Mean size of disc herniation was 115 mm² and the mean VAS-leg score was 6.1 at initial presentation. A total of 26 patients improved at the time of the repeat MRI. Baseline disc herniation was smaller in the fast recovery group versus the prolonged recovery group (105 versus 166 mm²). LDH size was directly associated with both the length of recovery and the degree of leg pain at baseline. The amount of Gabapentin needed to reduce leg pain was a mean of 4.4 IU per day in the first 12 weeks; followed by a mean 1.3 IU per day after that time. Surgery was avoided in all cases.

Discussion: This is the “first” study to note that the inflammation-preserving treatment of Gabapentin and acupuncture, without anti-inflammatory medications, was safe and effective for patients with an acute lumbar disc herniation, and surgery was avoided in all cases. The present proof of concept study raises awareness of a potential novel therapeutic modality that would allow for natural resorption of the LDH with sustained pain relief while also avoiding the pitfalls and side-effect profiles associated with anti-inflammatory medication. Future comparative studies with control subjects are critical, which as a result of this study are currently underway.

SpineTrak: The First Randomized Control Trial Using the Apple Watch to Objectively Track Spine Surgical Patients

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Introduction

Early mobilization after surgery reduces complications and is associated with improved survival, decreased length of hospitalization, and improved psychological well-being [1]. However, current methods for evaluating the mobility and outcomes of spine surgery patients are limited and rely on patient-reported outcome measures (PROMs) that are subjective and may be influenced by psychiatric comorbidities and chronic pain.

There are numerous commercially available wearable activity monitors, including the Apple Watch, that allow for real-time tracking of objective measures that may allow patients and surgeons to better monitor post-operative mobility and outcomes.

Here we present the study design and early results of the first randomized controlled trial utilizing the Apple Watch to objectively monitor patients before and after elective spine surgery.

Methods

Our study is enrolling English-speaking adult patients undergoing elective spine surgery by six neurosurgery attending physicians at Stanford University Hospital. Patients are randomized to either the interventional or control groups. Interventional patients receive an Apple Watch, which they are required to wear for 2-6 weeks pre-operatively and 1 year post-operatively. They are also asked to download an application developed for this study, NeuroCoach. This is a HIPPA-compliant app that is available on the Apple app store and collects the following activity measures: daily steps, distance traveled, flights climbed, calories, heart rate, and heart rate variability. Objective progress reports are provided to the intervention patients and their surgeons at each follow-up visit (see Figures 1,2).

Both intervention and control patients receive surgery and follow-up visits per the attending surgeon's standard of care. They respond to the following well-validated quality of life surveys pre-operatively and at 4-6 weeks, 3 months, 6 months, and 1 year post-operatively: Oswestry Disability Index (ODI), Neck Disability Index (NDI), Visual Analog Scale (VAS), EuroQOL-5 Dimensional Questionnaire (EQ-5D), 36-Item Short Form Survey (SF-36) and Patient-Reported Outcome Measurement Information System (PROMIS). All patients also complete a study-specific questionnaire about their satisfaction with their surgery and understanding of their surgical recovery.

Our study is approved by the Stanford IRB and actively enrolling as of Sep 1, 2020. Further details are available at <spinetrak.stanford.edu> and <clinicaltrials.gov/ct2/show/NCT04379921>. Target enrollment is 100 intervention and 100 control patients, which is powered at alpha 0.05 and power 80% to detect a 15% difference in ODI.

Results

To date, we have enrolled 6 patients (n=3 intervention; n=3 control) in SpineTrak. On average, intervention participants have worn their Apple Watch 83.3% (+/-37.5%) of the days since enrollment and for 12.6 hours (+/-4.9) per day. Figure 1 shows the objective and subjective progress report of the first SpineTrak participant, before and after undergoing L4-pelvis fusion for high grade spondylolisthesis.

Discussion

To the best of our knowledge, this is the first randomized control trial to assess feasibility of using a commercially available activity monitor in spine patients before and after spine surgery. Here, we present preliminary results of early participants. Our ultimate goal is to determine whether objective measures correlate with subjective PROMs and to develop a novel combined metric to better track spine surgical patients in real-time.

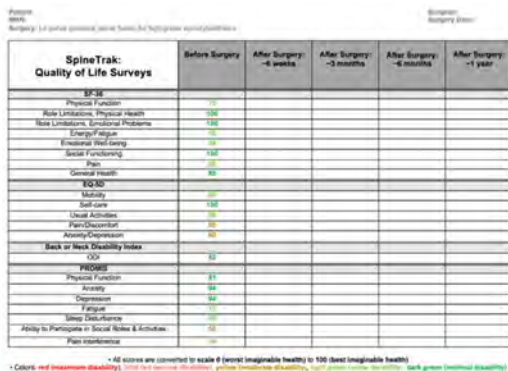


Figure 1: Progress report demonstrating survey results for 1st SpineTrak study patient before and after L4-pelvis fusion for high grade spondylolisthesis.

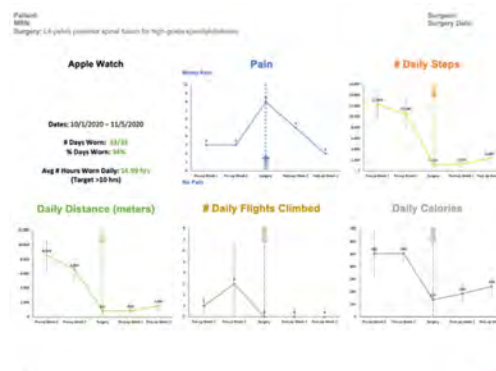


Figure 2: Progress report demonstrating objective data report for 1st SpineTrak study patient.

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Foot tapping test as a predictor of postoperative gait disorder in lumbar spinal stenosis

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(Background) Lumbar spinal stenosis (LSS) causes gait disorder, which is caused by intermittent claudication and palsy such as drop foot. However, it is thought that mild lower extremity motor dysfunction, which does not extend to the drop foot, may also be involved in the actual gait disorder. We have previously reported that the Foot tapping test (FTT, Tominaga et al., 1991) is useful for the quantitative assessment of lower limb motor function in LSS as well as cervical myelopathy. The purpose of this study is to screen for mild motor dysfunction in the lower extremities using the FTT and to investigate whether it can predict postoperative gait disorder.

(Material and Methods) One hundred sixty-five patients (mean age 63.7 years, 88 males and 77 females) with intermittent claudication due to LSS and who underwent surgery at our hospital were included in the study. Drop foot (paralysis of the lower extremity MMT3 or less) and reoperation were excluded. Preoperatively, the cutoff value was set at less than 23 times, and the patients were classified into two groups: one with lower extremity motor dysfunction and the other without dysfunction. The JOABPEQ gait disturbance scores at preoperative, 3 months, and 1 year postoperatively were used to compare between the two groups. The Wilcoxon rank-sum test was used for statistical examination (significance level: $p < 0.05$).

(Results) The median scores at preoperative, 3 months, and 1 year postoperatively were 28.6, 64.3, and 42.9 in the impaired group and 21.4, 67.9, and 75.0 in the non-impaired group, respectively. Both groups showed a significant improvement in scores at 3 months postoperatively compared to preoperatively, with no significant difference between the groups. On the other hand, at one year postoperatively, the scores of the impaired group were significantly lower than those of the non-impaired group.

(Conclusion) In LSS with mild motor dysfunction that can be screened by FTT preoperatively, gait impairment improves partly with improvement in intermittent claudication in the early postoperative period. Thereafter, however, the improvement is poor, and the improvement is poorer than in cases where there is no loss of motor function. FTT could be used to predict the course of postoperative gait disorder in LSS.

Extending the Straight Leg Raise Test for Improved Clinical Evaluation of Sciatica: Reliability of Hip Rotation and Ankle Dorsiflexion

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Introduction: The straight leg raise (SLR) is the most commonly applied physical tests on patients with sciatica, but the sensitivity and specificity ratings for disc hernia and neural compression leave areas for improvement. The SLR moves the sciatic nerve up to the nerve roots and a positive test may arise from problems anywhere along this course – thigh, buttock, and spine. With published data on neural movement during the SLR (with or without pathology), and the fact that sciatic symptoms can be caused variously, we modified the SLR to address these issues. Hip internal rotation tensions the lumbosacral nerve roots and ankle dorsiflexion tensions the sciatic nerve along its course. We added these movements to the SLR (extended SLR=ESLR) as structural differentiators and tested interrater reliability in patients with LBP, with and without sciatica.

Methods: Forty subjects were recruited to the study by the study controller (SC), 20 in the sciatic group and in the control group. Two independent examiners (E1&E2) performed the ESLR and did not communicate to the subjects other than needed to determine the outcome of the ESLR. First, SLR was performed traditionally until first responses were evoked. At this hip flexion angle, a location-specific structural differentiation (hip internal rotation for distal symptoms and ankle dorsiflexion for proximal symptoms) was performed to confirm whether the emerged responses were of neural origin. Two aspects were required for a 'positive' ESLR test: i) reproduction of the subject's clinical symptoms during the leg raise, and ii) increase of those symptoms with structural differentiation. Cohen's Kappa (CK) and Fleiss Kappa (FK) for interrater reliability were calculated, and sensitivity and specificity to detect sciatic patients were calculated.

Results: The interrater agreement between the testers for the result of the ESLT was found to be almost perfect as measured by Cohen's Kappa and Fleiss Kappa scores: CK between E1 and E2 was 0.85. CK between SC/E1 was 0.90, and 0.95 between SC/E2. FK between E1/E2/SC was 0.90. Sensitivity and specificity to detect sciatic patients were 0.95 and 0.98, respectively.

Discussion: Many mechanisms and pathologies can relate to radicular pain and the SLR: Not only lumbar disc herniation but also mechanosensitivity and impairment of neural movement for whatever the cause may be the reason behind the SLR-provoked symptoms. The SLR as a test is indirect because it tests physical mechanisms such as mechanical function (excursion) and sensitivity, not pathology or anatomical changes. We found out that SLR with the addition of location-specific structural differentiation is a reliable and repeatable tool in discerning neural symptoms from musculoskeletal in patients with radiating low back pain. We recommend adding these movements to the standard SLR with aim of improving diagnostic efficacy.

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Correlation between preoperative CT measurement/evaluation of lumbar paraspinous muscle and postoperative ambulatory status in patients with femoral neck fractures

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Introduction

Lumbar paraspinous muscle evaluation has been reported to be related to low back pain and lumbar degeneration. Sarcopenia and frailty have been related to mortality in elderly people, however the relationship between postoperative ambulatory status improvements and sarcopenia/frailty are still unknown. That motivated us to evaluate the relationship between the paraspinous/psoas muscles evaluation and the postoperative ambulatory status in patients with femoral neck fractures, as a typical geriatric trauma requiring surgical treatment.

Method

Ninety-eight consecutive patients with femoral neck fractures who underwent bipolar hip arthroplasty were included and retrospectively assessed. The cross-sectional area and degeneration of muscles were measured/evaluated using preoperative CT scans, and an axial slice of superior end of L5 vertebra was used to evaluate paraspinous and psoas muscles. The degeneration of the muscles were evaluated according to the Goutallier classification. Ambulatory status was assessed at 1 and 2 weeks after surgery, at the point of discharge from our hospital, and at the final follow-up. Ambulatory status was classified into six levels as follows: level 1, independent walking on surface; level 2, walk with crutches without assistance; level 3, use of regular front or reverse walker; level 4, need continuous support from one person who helps carrying weight and with balance; level 5, wheelchair; level 6, bedridden. Ambulatory status before injury was self-reported by patients and families. Pearson correlation coefficient was used for statistical analysis, and $p < 0.05$ was considered significant.

Results

Ambulatory status before injury was significantly correlated with cross-sectional area of the paraspinous muscle ($r=0.20$), and degeneration of the paraspinous muscle ($r=0.37$). The improvement of ambulatory status from the time of 1 week after surgery to discharge was significantly correlated with the cross-sectional area of the paraspinous muscle ($r=0.21$). Among 57 patients who were followed-up for more than 30 days after discharge, ambulatory status at the time of the last follow-up was significantly correlated with the cross-sectional area of the paraspinous muscle ($r=0.27$).

Conclusion

The measurement/evaluation of cross-sectional area and degeneration of the paraspinous muscle using preoperative CT might be useful for predicting ambulatory status improvement after bipolar hip arthroplasty.

Assessing nonspecific effects of osteopathic manipulative treatment for low back pain

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Introduction: Therapeutic outcomes consist of specific and nonspecific effects¹. Specific effects are the outcomes that result from theoretically-derived mechanisms of an intervention. Nonspecific effects are all other outcomes that do not arise according to an intended mechanism of an intervention (e.g., regression to the mean, placebo, etc.). Understanding both effects are important in order to individualize treatment and maximize the outcomes. Osteopathic manipulative treatment (OMT) has been shown to be an effective intervention for low back pain (LBP)², though the specific mechanisms are unknown. It is also difficult to assess the nonspecific effects of OMT in clinical trials because the perfect sham treatment and double blinding are not possible. Thus, debate exists as to the relative size of specific and nonspecific effects. The purpose of this study was to assess the magnitude of nonspecific effects of OMT for LBP using the Credibility and Expectancy questionnaire (CEQ)³ and Healing Encounters and Attitudes Lists (HEAL)⁴.

Methods: As a part of a larger randomized clinical trial, 46 (17 males) LBP patients (age=44±13 years, BMI=27.2±3.6 kg/m², average pain (NPRS)=5.3±1.9 points, disability (ODI)=33±19%) received 4 OMT treatments (2 patients received 3 OMT treatments) delivered over 4-6 weeks. Treatment consisted of a mandatory high-velocity, low-amplitude spinal manipulation and any number of the following techniques: soft tissue, muscle energy, myofascial, and articular. NPRS and ODI measures were obtained at baseline and the end of the study. CEQ and HEAL questionnaires were administered at baseline and after the treatment period, respectively. Changes in NPRS and ODI scores were evaluated with the 1-sample t-test and were correlated with CEQ and HEAL metrics using Pearson's r. Significantly correlated CEQ and HEAL metrics (p<0.05), patients' demographics, and baseline outcome values were entered into a stepwise multiple regression model to assess how much of the variance in outcomes following OMT can be explained by nonspecific effects.

Results: NPRS and ODI improved significantly (p<0.05) following OMT by 1.3±2.2 points (range: -4, 7) and 3±9% (range: -14%, 36%), respectively. NPRS change significantly correlated with Spirituality (r=-0.33) and Expectancy (r=-0.37) scores. ODI change significantly correlated with Spirituality (r=-0.35) and Patient-Provider Connection (r=-0.34) scores. Aside from the baseline NPRS score, the regression model did not reveal additional metrics of nonspecific effect to be predictive of NPRS change (R²=0.21). The regression model for ODI change returned baseline ODI, Spirituality, and Patient-Provider Connection as predictors (R²=0.36).

Discussion: The magnitude of the treatment effects in this study was consistent with the literature⁵. The strongest predictors of these treatment effects were the baseline outcome measures confirming that higher levels of pain and disability at baseline are associated with larger treatment effects. Greater Spirituality and better Patient-Provider Connection were also associated with better disability outcomes. Together, the nonspecific factors measured in this study accounted for 21% and 36% of the variance in pain and disability outcomes, respectively. These results warrant further investigation into how nonspecific effects influence outcomes in LBP patients.

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Cervical Spine Steroid Injections for Delay of Surgery for Cervical Spondylotic Myelopathy

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- Introduction: Cervical spine steroid injections are increasingly being used for diagnosis and treatment of degenerative pathology. For cervical spondylotic myelopathy, traditionally treated with surgery, there has been little investigation of possible therapeutic or preventative effects of targeted injections. As injections may be targeted to the epidural space, the transforaminal region, or the zygapophyseal joints, differing injection modalities may also have variable therapeutic effects.
- Method: All patients with a new diagnosis of cervical spondylotic myelopathy, without previous cervical spine surgery or steroid injection treatment, were identified in a large insurance database. Administration of steroid injections and surgical treatment timing was determined based on Current Procedural Terminology (CPT) codes. Multivariate logistic regression was used to determine the association of steroid injection administration with surgical treatment at various time points after initial diagnosis. Significance at $P < 0.01$.
- Result: A total of 686 surgically managed CSM patients were retrospectively identified in the PearlDiver database. A total of 244 patients underwent pre-surgical spinal steroid injection therapy to manage CSM symptoms. Of these, 185 patients (75.8%) underwent epidural steroid injections, 35 (14.3%) underwent zygapophyseal injections, and 24 (9.8%) underwent transforaminal steroid injections. Median time from initial CSM diagnosis to surgery was 75.5 days ($\mu = 351.6$ days; $\sigma = 544.9$ days). In multivariate analysis, both transforaminal injections ($OR = 0.40$, $P = 0.20$) and zygapophyseal injections ($OR = 0.33$, $P = 0.02$) were insignificantly associated with decreased odds of surgery within 1 month of diagnosis, while epidural injections were not associated with decreased odds of surgery ($OR = 1.17$, $P = 0.35$). Interestingly, epidural and transforaminal injections were both associated with increased odds of surgery after six months post-diagnosis ($P < 0.01$). Only zygapophyseal injections had consistently reduced odds of surgery (without significance).
- Conclusion: The practice of steroid injection, regardless of approach (epidural, transforaminal, or zygapophyseal), does not prevent treatment of CSM via a surgical modality over the long term. While symptomatic relief may lead to short-term benefits from steroid injection, specifically with transforaminal and zygapophyseal injections, it appears that this short-term benefit only delays definitive surgical treatment. Assessment of diagnostic and treatment decision-making workflow may enable identification of other aspects of CSM management that lead to delays in diagnosis and definitive treatment as well as additional cost burden.

GP104

Exploring the Core matrisome Profile of Fetal Intervertebral Discs in search of Molecular targets of therapeutic Potential

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Introduction: Intervertebral disc degeneration is accompanied by a loss of Extra-cellular matrix (ECM) content due to an imbalance in anabolic and catabolic pathways. Identifying ECM proteins with anabolic and/or regenerative potential could be the key to developing regenerative therapies. Since human fetal discs grow and develop very rapidly, studying these discs may provide valuable insights on proteins with regenerative potential. The primary aim of this study was to explore fetal intervertebral disc and identify molecules with regenerative potential

Materials and Methods: LC-MS/MC analysis of 9 fetal and 7 healthy adults (age 22-79) nucleus pulposus (NP) was performed to profile the core matrisome. Protein expression was compared between the two groups and pathway analysis was performed with all proteins that were uniquely expressed or significantly upregulated in fetus, or >2 fold upregulated if the protein was expressed in <3 samples fetus samples. Relevant pathways for ECM assembly were selected and the respective proteins were discussed.

Results: Of the 64-expressed core matrisomal proteins in fetus, 22 were unique in > 1 sample, 7 were significantly higher expressed compared to healthy adult NP's, and 4 proteins >2 fold higher. Pathway analysis with these 33 proteins revealed that 20 proteins were integrated in ECM assembly and growth pathways: Fibromodulin, Biglycan, Heparan Sulfate Proteoglycan 2, Chondroitin Sulfate Proteoglycan 4 were involved in Glycosaminoglycan metabolism. In addition, Fibromodulin, Biglycan, procollagen C-endopeptidase enhancer (PCOLCE) and Collagen- type 1a1, 1a2, 6a1,6a3,11a1,11a2, 12a1, 14a1 and 15a1 were involved in Collagen fibril formation, biosynthesis and organization. Regarding the growth pathways: Thrombospondin 1,2,3 and 4, Tenascin C and Collagen- type 1a1, 1a2, 6a1,6a3,11a1,11a2 were involved in 'PIK3-Akt signaling' and Matrilin-3 and tenascin C in 'IGF transport and uptake'.

Conclusion: The consistency of the human fetal NP differs greatly from that of a healthy adult. The Core-matrisome of human fetal discs is of great potential for developing future regenerative therapies.

GP105

Validity of Scoliotic discs as controls in Inter vertebral disc research

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Introduction

Despite being a highly researched subject, the studies on etio-pathogenesis have been inconclusive. One of the primary reasons for elusiveness being, lack of appropriate controls for making a precise comparison with degenerated discs. Discs from scoliosis surgery is a common control used in molecular studies of disc disorders. This study aims to compare the validity of scoliotic discs as controls by comparing it against MRI normal discs from voluntary organ donors and establish 'True Controls' that can be utilized for future Intervertebral disc (IVD) research.

Materials and Methods

After appropriate ethical clearance and consent, nucleus pulposus of Eight MRI normal discs from eight brain dead voluntary organ donors (ND) and eight scoliotic discs (SD) from three patients who underwent anterior surgery for adolescent idiopathic scoliosis were harvested under sterile precautions. After protein extraction, prefractionation and in-gel tryptic digestion, the extracted peptides were subjected to tandem mass spectrometry. The raw data were subjected to further bioinformatic analysis to understand the patho-mechanisms involved.

Results

Mass spectrometry identified a total of 235 proteins in ND and 438 proteins in the SD group and 157 proteins common to both group. About 78 (15.31%) proteins were found only in the ND group, and 281 (54.45%) were found only in the SD group. Proteins involved in Extracellular matrix integrity (Versican, Keratins KRT6A, KRT14, KRT5 and KRT 13A1, A-kinase anchor protein 13, Coagulation factor XIII A chain, Proteoglycan 4) and proteins involved in transcription and DNA repair (Von Willebrand factor A domain-containing 3B, Eukaryotic initiation factor 2B, Histone H4, Leukocyte Cell-Derived Chemotaxin 2) were found to be down-regulated in SD. Inflammatory proteins (C3, C1S), and oxidative stress response proteins (Peroxiredoxin-2,6, Catalase, Myeloperoxidase, Apolipoprotein E) were found to be up-regulated in SD. These changes were reflected at the pathway level also.

Conclusion

Our study found that scoliotic discs have an abundance of inflammatory, oxidative stress response proteins. Whereas, these proteins were either absent or downregulated in the MRI normal discs from voluntary organ indicating a more biologically inert state. These findings establish MRI normal discs from voluntary organ donors as the 'true' control for molecular studies in IVD research and recommend it for future studies.

GP106

Exploring the influence of Modic Changes and spinal level on macrophage differentiation in disc herniations.

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INTRODUCTION

Cervical- and lumbosacral radiculopathy symptoms due to disc herniation are likely to be not solely caused by mechanical compression of the nerve root, but also by pain inducing elements from inflammatory processes caused by local neovascularization and macrophage infiltration. The present pilot study was conducted to assess the efficacy of immunohistological methods to discern pro-inflammatory M1- and anti-inflammatory M2 macrophage differentiation patterns in herniated intervertebral disc tissue and to evaluate the influence of Modic changes (MC) on this differentiation process.

METHODS

Herniated disc samples were collected from 38 patients with 12 or more weeks of radicular pain symptoms, undergoing surgery for cervical- or lumbosacral radiculopathy. Samples were processed for immunohistochemistry and stained for the presence of T-cells (CD3), neutrophils (CD15) and macrophages: CD68 (macrophage marker), CD163 (M2), CD40 (M1), Arg1 (M2) and iNos (M1). Slides were evaluated and counted by two independent researchers. Counting was performed using an automated algorithm designed for imageJ.

RESULTS

Inflammatory cells were present in 29 of 38 samples. An interobserver correlation coefficient of >0.8 was found for all markers at all times. Expression levels were highest for CD68, followed by CD15 and CD3. Expression levels with CD68 were slightly higher in lumbar than cervical patients (p=0.18). CD68+ cells were dominantly CD163 positive (>20%) rather than CD40, iNOS or Arg1 positive (<5%). Presence of MC was associated with higher levels of CD68 (OR=6.0, p=0.023) and with lower relative expression of CD163 (OR=0.123, p=0.02). Lumbar samples had higher levels of CD15 positive neutrophil infiltration as compared to cervical samples (OR=12.6, p=0.038).

DISCUSSION

M2 macrophages are abundantly present in symptomatic disc herniations, both at lumbar and cervical level. The relative high expression of CD163 (M2 marker) indicates abundance of an anti-inflammatory macrophage presence. The dominance in patients without MC suggests that these patients have a quicker recovery rate after surgery. This has to be verified in a follow up study.

Table 3: overview of inflammatory marker expression in subgroups for spinal level and MC status

The values are medians for CD68, CD3 and CD15, and percentages of CD163, Arg1, CD40 and iNOS are relative expressions compared to CD68+ cells.

Subgroups	CD68/cm2	CD3/cm2	CD15/cm2	CD163 %	Arg1 %	CD40 %	iNOS %
Cerv_MC+	40	0	2	21%	0%	0%	0%
Cerv_MC-	16	0	0	59%	0%	2%	0%
Lumb_MC+	231	0	3	8%	2%	0%	4%
Lumb_MC-	223	0	3	26%	0%	0%	6%

Increased risk of delamination following rapid pressurization of the intervertebral disc

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INTRODUCTION: Vertebral endplate fracture is generally accepted to occur as a result of excessive, typically rapid, pressure developed within the intervertebral disc in response to external axial compression. Clinical evidence of disc disorders later in life following endplate fracture suggests that the disc may also be impacted by the fracture event. There is an abundance of evidence to indicate that loss of disc pressure at the time of fracture alters annulus fibrosus loading which could impact disc health long-term. However, little is known regarding the isolated impact of the rapid pressurization which precedes the fracture event. The purpose of this in vitro study was to determine if rapid disc pressurization with and without resulting fracture impacts the mechanical properties of the annulus.

METHODS: Intervertebral discs of porcine cervical functional spine units (FSU) at the level of C3/4 and C5/6 were pressurized via rapid injection of hydraulic fluid (motor oil) using a standard inflation needle. Average rate of pressurization was 118.3 MPa/sec (± 29.5) and average peak pressure was 6.6 MPa (± 1.2). FSUs (total = 32) were subsequently grouped according to whether the pressurization resulted in endplate fracture ('fracture'; n=9) or not ('non-fracture'; n=13); Figure 1. Annular tensile properties (via bilayer mechanical testing at a rate of 1% strain/sec; Figure 2A) and lamellar adhesion strength (via peel test mechanical testing at a rate of 0.5mm/sec; Figure 2B) were quantified for both fractured and non-fractured samples. Annular mechanical properties from a third control group where FSUs did not undergo the pressurization protocol ('control'; n=10) were also determined. Differences in annulus properties were assessed with a one-way ANOVA.

RESULTS: Neither peak pressure nor rate of pressurization were found to be statistically different between the non-fractured and fractured FSUs ($P=0.127$ and 0.163 , respectively). Further, annular tensile properties were not found to be statistically different between fractured, non-fractured, and control FSUs ($p>0.05$). Lamellar adhesion strength, in contrast, was found to be, on average, 53% lower in specimens which were pressurized compared to control, non-pressurized samples ($p=0.03$). In addition, no statistical difference in adhesion strength was found between fractured and non-fractured pressurized samples ($p=0.990$) indicating that rapid pressurization, and not the presence of an endplate fracture, impacted the adhesion properties of the annulus.

DISCUSSION: Adhesion strength between the layers of the annulus in pressurized discs, regardless of the presence of an endplate fracture, was found to be lower than in non-pressurized control discs. This finding suggests that rapid pressurization, and not the presence of an endplate fracture, negatively impacts the mechanical adhesive properties of the annulus. Such decreased lamellar adhesion increases risk of delamination which has been linked to disc disorders.

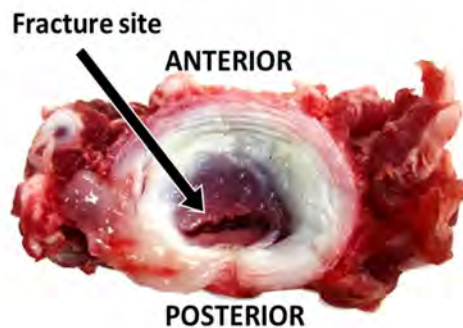


Figure 1. Example of a fractured specimen. Note the location of the fracture in the endplate. All fractured specimens sustained fractures in the inferior endplate of the superior vertebra.

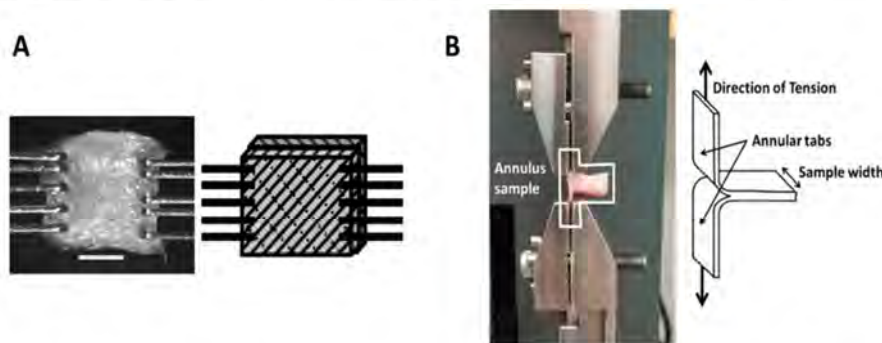


Figure 2. A) Mounted bilayer sample for the annular tensile test. Five-prong rakes were used to secure the sample. Size bar is 2 mm. B) Mounted annular peel test sample in 180° configuration;

Is the lumbar disc degeneration profile on imaging interconnected with the degenerative status of its adjacent or non-adjacent segments ?

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Introduction:

Lumbar disc degeneration is one of the most clinically relevant findings which can be extracted from plain radiographs, characterized by the presence of radiographic degenerative phenotypes such as osteophytes, disc space narrowing and endplate sclerosis. A greater understanding of the association between disc degeneration of each level to that of its immediate adjacent (cranial or caudal) and distant non-adjacent segments would be important for both basic and clinical research, but has not been documented in detail in the scientific literature to date.

Methods:

Lateral lumbar radiographs of 279 consecutive patients from a single university hospital (n=160 males, n=119 females) with a mean age of 49.3 years (range: 20-95) were retrospective evaluated. Subjects were excluded if they had a history of previous surgery or evidence of congenital abnormalities, fractures, tumor, infection or inflammatory arthritis. The presence and severity of osteophytes, disc space narrowing and endplate sclerosis from L1/L2 to L5/S1 (1,395 intervertebral discs) were assessed using a validated grading system (score 0-3). The cumulative degenerative score (CDS) for each disc level was defined as the sum of the scores for osteophytes, disc space narrowing and endplate sclerosis, and CDS for each patient was calculated as the sum of the degenerative scores. Univariate and multivariate analyses were performed, further adjusting for age and gender, with a main focus on examining the associations between each lumbar disc degeneration with the degenerative status of its adjacent or non-adjacent segments. All radiographs were evaluated by the same observer and good to excellent intra-observer reliability was noted.

Results:

Overall, 84.2% (235/279) of the subjects had radiographic degenerative changes and there was no difference between males and females (83.1% vs. 85.7%, p=0.557). The mean CDS was not significantly different in males and females (7.6± 10.5 vs. 6.5± 7.4, p=0.518). Age was positively correlated with the CDS at all disc levels in males and females (p<0.001). Multivariate linear regression analyses adjusted for age and gender showed that disc degeneration of each lumbar level was significantly correlated with the degeneration profiles of their respective cranial or caudal adjacent disc segments (p<0.01). Moreover, the cranial or caudal adjacent segments disc degeneration had greater influence than non-adjacent levels, irrespective if the index degenerative level was in the upper, mid or lower lumbar spine. For example, the CDS of L4/L5 was highly correlated with more degeneration (larger β coefficient) between its cranial adjacent level at L3/L4 (β coefficient = 0.40) than that between L4/L5 and non-adjacent level at L2/L3 (β coefficient = 0.20) (Table 1).

Discussion:

Our study noted that the degeneration profiles of lumbar motion segments, irrespective if the index disc level was in the upper, mid or lower lumbar spine, were interconnected to their adjacent segments, providing evidence that degeneration occurs contiguously and implicates a mechanical etiology. Our findings suggest that knowledge of a lumbar motion segments degenerative profile may predict the degenerative course of its adjacent segment, but prospective studies are further needed to validate this position and to further account for modifiable and non-modifiable risk factors.

Table 1. The association between each lumbar disc degeneration with the degenerative status of its adjacent or non-adjacent segments after adjustment for age and gender by multivariable linear regression.

Dependent Variable	Independent variables							Adjusted R ²
	Age	Gender	Adjacent and non-adjacent lumbar spine segments disc degeneration					
	β coefficient	β coefficient	L1/L2 CDS	L2/L3 CDS	L3/L4 CDS	L4/L5 CDS	L5/S1 CDS	
L1/L2 CDS	0.13 (P = 0.015)	-0.06 (P = 0.164)	N.A	0.45 (P < 0.001)	0.24 (P < 0.001)	-0.09 (P = 0.157)	0.17 (P = 0.001)	0.57
L2/L3 CDS	0.15 (P = 0.004)	-0.01 (P = 0.770)	0.44 (P < 0.001)	N.A	0.17 (P = 0.007)	0.19 (P = 0.001)	-0.06 (P = 0.283)	0.59
L3/L4 CDS	0.16 (P = 0.002)	-0.02 (P = 0.691)	0.21 (P < 0.001)	0.16 (P = 0.007)	N.A	0.35 (P < 0.001)	0.09 (P = 0.053)	0.62
L4/L5 CDS	0.13 (P = 0.020)	-0.09 (P = 0.020)	-0.09 (P = 0.157)	0.20 (P = 0.001)	0.40 (P < 0.001)	N.A	0.27 (P < 0.001)	0.57
L5/S1 CDS	0.08 (P = 0.191)	0.43 (P = 0.370)	0.23 (P = 0.001)	-0.08 (P = 0.283)	0.15 (P = 0.053)	0.37 (P < 0.001)	N.A	0.40

CDS: Cumulative Degenerative Scores.
 All statistical analyses were performed using IBM SPSS software version 27.0.
 The level of significance was set at p value less than 0.05.
 N.A not applicable.

The Residual Strain State of the Intervertebral Disc

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INTRODUCTION:

The intervertebral disc exists in a state of residual stress and strain due to both osmotic swelling and inherent (generational) fiber strain. The generational fiber strain likely originates in early disc development, when angled actin stress fibers establish the orientation of the annulus fibrosus (AF) collagen fibers [1]. As the disc grows, the aligned fibers are stretched, which results in AF residual strain. We recently developed and validated two finite element models of the disc to investigate the role of tissue-scale residual strain on disc-scale mechanics: one (“swelling-only model”) with osmotic swelling and the other (“multigeneration model”) with both osmotic swelling and a generational fiber strain [4]. The first objective of this study was to quantify the fiber residual strain contribution in these models. Residual strain in the disc has been previously investigated in caudal bovine discs by Michalek, who released the disc’s residual strain with a radial cut (Fig 2A), causing the disc to open [2,3]. The resulting opening gap is a measure of residual strain. The second objective of this study was to calculate a corresponding opening gap using our finite element models and verify it against the experimental outcomes.

METHODS:

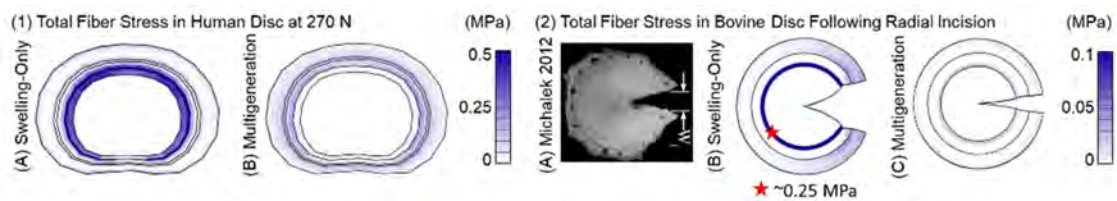
For details regarding the human disc model geometry and test protocols refer to [4]. An axial 270 N preload was applied to represent physiologic axial pressurization and the fiber stress and strain were calculated for the first objective. To replicate the observed bovine disc opening gap outcome [3], we modeled the bovine disc as a cylinder. The radial cut in the residual strain experiment was simulated by the release of a boundary condition used to hold the disc midsection to the central plane. The opening gap after the radial cut (W_i) was compared with the experimental data [3].

RESULTS:

The fiber stress distribution in the human disc at preload for the swelling-only model was concentrated in the inner AF (Fig 1A) while the fiber stress in the multigeneration model was distributed and uniform throughout the AF (Fig 1B). Following radial incision, the swelling-only model overestimated the opening gap (11.5 mm, Fig 2B) compared to the experimental range (4.3±1.8 mm, Fig 2A) [3]; while, the multigeneration model replicated the experimental opening gap well (4.5 mm, Fig 2C).

DISCUSSION:

This study successfully evaluated disc residual strain and outcomes demonstrated that the two primary mechanisms of residual strain in the disc are osmotic swelling and generational AF fiber strain. The more uniform distribution of fiber strain that we observed for the multigeneration model is more likely to represent physiological condition and likely contributes to the multigeneration model’s superior ability to fit experimental data [4]. Replication of the disc’s residual strain state in a finite element model is essential when using finite element models to study the functional efficacy of therapeutics for disc disorders.



- [1] Hayes+ Dev Dyn 1999, [2] Duclos+ JMBBM 2017, [3] Michalek+ J Biomech 2012, [4] Newman+ BMES 2020

Anatomical localization of type 1 Modic change

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[Introduction] It has been reported that Modic change (MC) are present in more than 80% of the elderly. Among them, Type 1 MC, which are considered to be inflammation in the vertebrae, have been suggested to be associated with low back pain. The cause is thought to be mechanical stress due to lumbar instability. The aim of this study is to investigate the localization of MC and examine its association with mechanical dysfunction.

[Method] 727 patients were investigated in which lumbar spine MRI was performed from July 2019 to July 2020. Of the 727 cases, those with type 1 MC and who were undergoing dynamic radiography were investigated. As the evaluation of mechanical dysfunction, we investigated spondylolisthesis, segmental kyphosis at flexion, and segmental scoliosis (segmental Cobb angle of 5 ° or more). The relationships between these and the localization of MC were examined. Localization was evaluated by dividing the vertebral body into four parts, anterior, posterior, left and right, using by MRI.

[Results] There were 161 patients (22%) with type 1 MC. Of these, 141 vertebral bodies 86 patients (mean age 71.3 years (30-88 years), 43 males, 43 females) who had lumbar dynamic radiography were investigated. There were 109 vertebral bodies had both MC and mechanical dysfunction. Of these, 34 vertebral bodies (24%) in 21 patients had spondylolisthesis. There was no uneven distribution of MC. The segmental kyphosis group had 37 patients and 60 vertebral bodies (43%); 36 vertebral bodies (60%) Localization tended to be in anterior. The local scoliosis group had 34 patients and 56 vertebral bodies (40%); 48 vertebral bodies (86%) were found on the concave side. On the other hand, in 24 patients and 44 vertebral bodies (31%) without mechanical dysfunction, there were no localization bias.

[Discussion] In 77% of cases, type 1 MC was found in the site considered to be mechanically dysfunctional. And, in particular, local scoliosis was significantly localized in the concave side. Furthermore, the posterior opening group also tended to be localized anteriorly. That is, as previously reported, the involvement of mechanical dysfunctions between affected vertebrae was suggested as the basis of type 1 MC. However, MC also occurred in the group without mechanical dysfunctions. we need to clarify the pathophysiology of non-mechanically occurring MC.

[Conclusion] The anatomical localization of Type 1 Modic change was investigated. It was shown to be strongly associated with mechanical dysfunctions such as local scoliosis and segmental kyphosis. However, MC has occurred even without mechanical dysfunctions, and in the future, we need to clarify these pathologies.

Spinal kinematics of Type 1 Modic change

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[Introduction] It has been reported that Modic change (MC) are present in more than 80% of the elderly. Among them, Type 1 MC, which are considered to be inflammation in the vertebrae, have been suggested to be associated with low back pain. The cause is thought to be mechanical stress due to lumbar instability. The aim of this study is to clarify the kinematics in MC.

[Method] 727 patients were investigated in which lumbar spine MRI was performed from July 2019 to July 2020. As the evaluation of mechanical dysfunction, we investigated spondylolisthesis, segmental kyphosis at flexion, and segmental scoliosis (segmental Cobb angle of 5° or more). Those who had at least one of these mechanical dysfunctions were designated as Mechanical group (M group), and those who did not have any of these mechanical dysfunctions were designated as Non-mechanical group (N group). The intervertebral disc degeneration was evaluated by Pfirrmann classification on MRI, and the M group and N group were compared.

[Results] Type 1 MC was found in 161 patients (22%). Of these, 86 patients (mean age 71.3 years (30-88 years), 43 males, 43 females) who were performed dynamic images of the lumbar spine were investigated. There were 63 patients (73%) in the M group and 23 patients (27%) in the N group. In the M group, grade IV or V disc degenerations, which are strong degenerations, were accounted for 38 patients (60%). However, in the N group, grade IV or V disc degenerations were as low as 8 patients (35%) ($p < 0.01$), 40 patients (46%) had no disc degeneration.

[Discussion] 73% were in group M. As previously reported, mechanical dysfunctions between affected intervertebral discs suggested to be the base of type 1 MC. However, in the remaining 27%, even without these mechanical dysfunctions, it was confirmed that type 1 MC occurred. In addition, disc degeneration was milder in group N than in group M, and it was possible that type 1 MC occurred due to causes other than mechanical. Some surgical specimens and some animal experiments reported the association between type 1 MC and *Acne bacterium*. In 27% of the N group, we consider *P. acnes* infection to be a cause other than mechanical dysfunctions.

[Conclusion] We examined the kinematics of Type 1 MC. It was shown that there are two types, mechanical MC, which is highly involved in mechanical dysfunctions, and non-mechanical MC, which is not related to mechanical dysfunctions.

Efficacy of growth differentiation factor-6 on three-dimensionally cultured human intervertebral disc cells and a rat tail puncture model

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INTRODUCTION:

Several studies have suggested that growth differentiation factors (GDFs) regulate intervertebral disc (IVD) homeostasis. In addition, cells cultured on atelocollagen gel (AC) show higher levels of matrix synthesis than those cultured on monolayers. Therefore, we hypothesized that GDFs and AC cultures might have an advantage in the extracellular substrate synthesis capacity of nucleus pulposus (NP) cells in vivo. In this study, we investigated effects of GDF6 on human disc NP cells using three-dimensional (3D) culturing system in vitro and on the structural integrity of AC using a rat tail puncture model in vivo.

METHODS:

In vitro: Human disc NP tissues (n = 12) were collected during surgery. GDF6 expression was measured by Western blotting according to age and the Pfirrmann degeneration grading system (grades II, III, and IV). Disc NP cells were first cultured in a 3D culturing system for 48 h and then treated with GDF6 (group G, 100 ng/mL), interleukin (IL)-1 β (group I, 10 ng/mL) as an inflammatory stimulus, or both (group G+I). Following 48-h cultures, levels of extracellular matrix components (aggrecan and type-II collagen) and pro-inflammatory cytokines (IL-6, MMP-3, TNF- α , and ADAMTS4) were assessed by immunofluorescence and reverse transcription-polymerase chain reaction (RT-PCR) in groups C (control), G, I, and G+I.

In vivo: An established rat tail annular puncture model of IVD degeneration was used. Four continuous disc heights in the rat tail (Co5-8, random order) were compared across four experimental groups: control (group C), punctured using a 20G needle (group P), injected with 2 μ L of AC after puncture (group AC), and injected with AC and 20 μ g of GDF6 after puncture (group G+AC). The IVD height was expressed as the disc height index (DHI) as shown by Masuda K et al.

RESULTS:

In vitro, Western blotting showed that GDF6 expression of disc NP cells decreased with the severity of disc degeneration. Immunofluorescence revealed increased expression of extracellular components in group G compared with that in group C cells in Pfirrmann grade-II and grade-III discs. RT-PCR demonstrated increased expression levels of extracellular components in group G compared with those in group C in the Pfirrmann grade-II and grade-III discs and decreased expression levels of pro-inflammatory cytokines in group G+I compared with those in group I in grade-II and grade-III discs. In vivo, groups P (P = 0.001) and AC (P = 0.003) showed a significant decrease in DHI at 28-d post-puncture compared with that of group C. In contrast, the DHI decrease was significantly reduced in group G+AC compared with that in groups P (P = 0.009) and AC (P = 0.048) at 28-d post-puncture.

DISCUSSION:

GDF6 expression in IVDs decreased with age and degeneration severity. Exogenous GDF6 administration to young and middle-aged, up to moderately degenerated disc cells in a 3D-culturing-system increased the expression of extracellular components and decreased the expression of pro-inflammatory cytokines. Furthermore, intradiscal injection of GDF6 prevented decreases in IVD height in the rat tail. Therefore, effects of GDF6 on disc NP cells might contribute to the prevention of IVD degeneration.

Intervertebral Disc Degeneration at Lower Lumbar Levels is Associated with More Coronally Aligned L1-L2 and Misaligned L5-S1 Facet Joints

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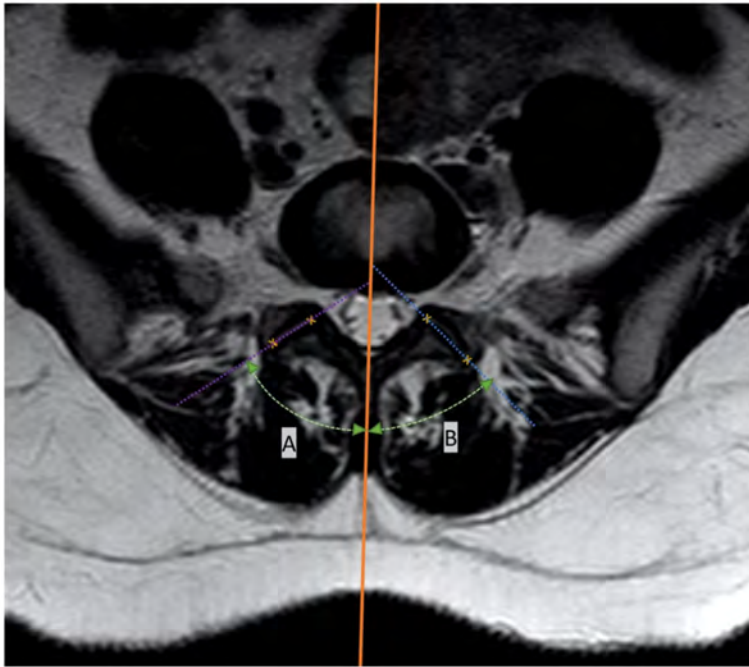


Figure 1. Facet joint orientation is the angle between 2 lines drawn; one passing through center of the disc and the center of the spinous process, and one passing through the anteromedial and posterolateral edges of superior articular processes of facet joints.

Introduction: The aim of this study was to understand how facet joint orientation (FJO) and facet joint tropism (FJT) affected severe intervertebral disc degeneration (IVDD) process at lower lumbar levels in patients with LBP.

Methods: This study is a cross-sectional analysis of a retrospective database. Patients were evaluated in terms of IVDD, FJO, and FJT at all lumbar levels on magnetic resonance imaging. Right- and left-sided FJO angles were measured side-by-side and averaged for each lumbar level. This average value was used as FJO angle throughout the text. The difference between right- and left- sided FJOs was described as FJT

Results: In this study (n: 123) facet joints were aligned more coronally in men than in women at upper lumbar levels. Men had less FJT compared to women, significantly at L2-L3 and L3-L4 levels. Patients with severe IVDD at L4-L5 level had greater FJO angles at L1-L2 level ($29.6 \pm 9.3^\circ$ vs. $22.9 \pm 7.7^\circ$, $p < 0.001$), and increased FJT at L5-S1 level ($10.5 \pm 8.2^\circ$ vs. $7.2 \pm 5.4^\circ$, $p = 0.029$). Patients with severe IVDD at L5-S1 level had greater FJO angles at L1-L2 level ($27.1 \pm 8^\circ$ vs. $23.6 \pm 8.9^\circ$, $p = 0.044$). When significance of associations between IVDD, FJO and FJT were analyzed; patients with severe IVDD at L4-L5 level had ORs of 1.114 ($p < 0.001$) for FJO at L1-L2 level, and 1.086 ($p = 0.023$) for FJT at L5-S1 level. Patients with severe IVDD at L5-S1 level had an OR of 1.049 ($p = 0.047$) for FJO at L1-L2 level.

Discussion: Patients had more coronal facet joints and increased FJT at lower lumbar levels. Men had more coronally aligned facet joints at upper lumbar levels (L1-L2 and L2-L3) when compared to women. Men also had less FJT at mid-lumbar levels (L2-L3 and L3-L4). Severe IVDD at lower lumbar levels (L4-L5 and L5-S1) was associated with more coronally aligned facet joints at L1-L2 level. Besides, severe IVDD at L4-L5 was also affected by a 3° of FJT at L5-S1 level. Facet joint orientation and FJT do not affect the disc at only the corresponding level; the lumbar spine should be evaluated as a whole.

GP114

End-plate defects could start the inflammatory process in the bone marrow and cause Modic changes

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Introduction: We aimed to evaluate serum white blood cell (WBC) counts, C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), and neutrophil-to-lymphocyte ratios in patients with chronic low back pain (LBP). We also aimed to identify whether severe intervertebral disc degeneration (IVDD) and Modic changes were associated with elevated blood cell counts and serum inflammatory markers.

Methods: Lumbar IVDD and vertebral end-plate changes were evaluated using Pfirrmann grading and Modic classification on lumbar spine MRI. Serum WBC counts, CRP levels, and ESRs were recorded from patients' charts. A comparative analysis was made between serum biomarkers and radiology findings.

Results: We included 218 patients. Severe IVDD and Modic changes were detected at any lumbar level in 39% and 20.6% of the patients, respectively. Patients with Modic changes at any lumbar level had significantly higher WBC and neutrophil counts and higher serum CRP levels compared to those without Modic changes ($7.71 \pm 1.95 \times 10^3/\mu\text{L}$ vs. $6.89 \pm 2.08 \times 10^3/\mu\text{L}$, $p=0.026$; $4.56 \pm 1.58 \times 10^3/\mu\text{L}$ vs. $3.95 \pm 1.54 \times 10^3/\mu\text{L}$, $p=0.028$; 0.31 ± 0.23 mg/dL vs. 0.22 ± 0.31 mg/dL, $p=0.014$). White blood cell and neutrophil counts had ORs of 1.192 (95% CI: 1.018-1.396, $p=0.03$) and 1.260 (95% CI: 1.021-1.555, $p=0.031$) to predict Modic changes at any lumbar level in subjects with chronic LBP.

Discussion: Serum WBC, neutrophil counts and CRP levels were higher in patients with Modic changes. Serum WBC and neutrophil counts were predictive for Modic changes in patients with LBP.

GP115

Mole Holes in the Spine: Schmorl's Nodes Could be Associated with Intervertebral Disc Degeneration at Upper Lumbar Levels and End-plate Disease at Lower Lumbar Level

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Introduction: Schmorl's nodes (SNs) have increasingly been recognized on vertebral end-plates using advanced imaging techniques. Even though vertebral end-plates are the closest structures to discs, their pathologies are underestimated in the etiology of low back pain (LBP). We aimed to detect the prevalence of SNs in patients with LBP and to understand whether SNs were associated with LBP and/or spinal degeneration.

Methods: Patients were evaluated in terms of SNs, intervertebral disc degeneration (IVDD), and vertebral end-plate changes (Modic changes) at all lumbar levels on lumbar spine magnetic resonance imaging (MRI).

Results: Schmorl's nodes were seen in 33.1% of patients. Higher Pfirrmann scores (OR: **2.696**) and higher SN scores (OR: **8.076**) were significantly associated with Modic changes at L4-L5 disc level. Patients with higher SN scores at L1-L2 or L2-L3 levels had approximately 7-fold increased risk of severe IVDD at the corresponding levels. The most significant factor associated with presence of SNs was body weight of the patients (OR: **1.417**). The most significant factor associated with intensity of LBP was severe IVDD at L5-S1 level (OR: **3.670**)

Discussion: SNs were detected in 33.1% of the patients with LBP. Body weight was the most significant factor associated with SNs. SNs had no direct association with LBP. The most significant factor associated with LBP was severe IVDD at L5-S1 level. Presence of SNs at upper (L1-L2 and L2-L3) and lower (L4-L5) lumbar levels was closely associated with IVDD and Modic changes at corresponding levels, respectively.

GP116

Is the distribution pattern of Modic changes in vertebral end-plates associated with the severity of intervertebral disc degeneration?: A cross-sectional analysis of 527 Caucasians

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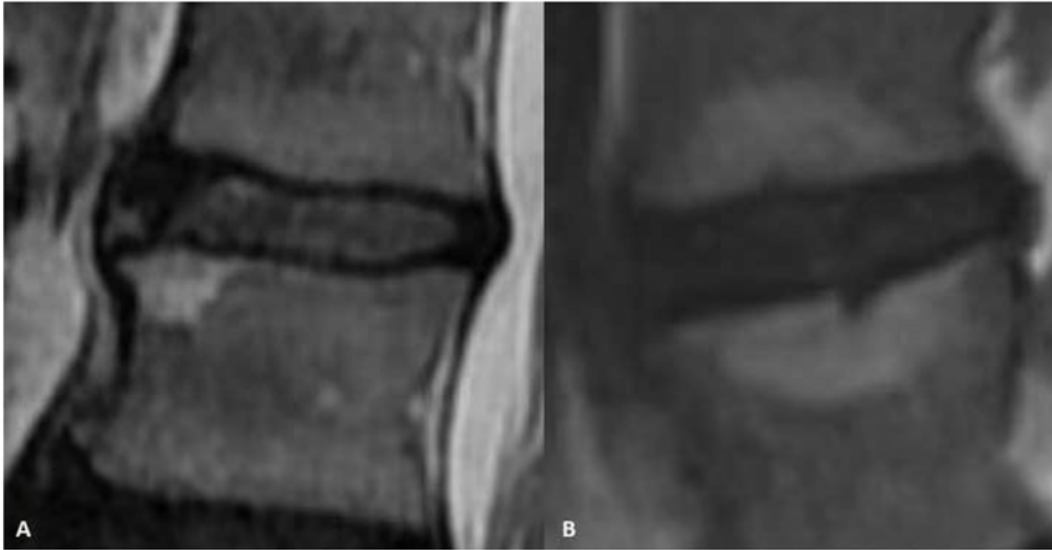


Figure 1. A patient with Modic changes at the edge of the vertebral end-plate (a), and a patient with Modic changes through the whole surface of the vertebral end-plate (b).

Introduction: Low back pain (LBP) is one of the most common disorders with many possible causes including intervertebral disc degeneration (IVDD) and Modic changes. In this study we aimed to analyze whether the distribution pattern of Modic changes in the vertebral end-plates was associated with the severity of IVDD.

Methods: We conducted a cross-sectional analysis of a retrospective database. Patients with constant LBP were evaluated in terms of IVDD and Modic changes on lumbar spine MRIs. Modic changes have been categorized as the ones at the edge of the end-plates (Figure 1a) and the ones presenting through whole end plate (Figure 1b). Statistical analyses were specifically performed for the lower lumbar levels.

Results: We evaluated 527 patients. Modic changes were detected in 25% of the patients. At any lumbar level, severe IVDD was significantly more common in patients with Modic changes (whole end-plate 86.2%, edge of end-plate 42.3%, no Modic change 9.7%; $p < 0.001$). Severe IVDD was detected in 90% and 88% of patients with Modic changes through the whole end-plates at L4-L5 and L5-S1 levels, respectively. Patients with Modic changes at lower lumbar spine were significantly older. Patients with Modic changes at L5-S1 level had significantly higher BMI values and lower lumbar lordosis (LL). The most significant predictive factors for Modic changes at L4-L5 and L5-S1 levels were severe IVDD at the corresponding levels (OR: 2.577 for L4-L5, OR: 2.355 for L5-S1; $p < 0.001$).

Discussion: Modic changes were more commonly located through the whole surface of the vertebral end-plates than only at the edge of the vertebral end-plates at lower lumbar levels. The most significant predictive factors for distribution pattern of Modic changes at L4-L5 and L5-S1 levels were severe IVDD at the L4-L5 and L5-S1 levels, respectively. Severe IVDD was significantly more common in patients with Modic changes through the whole end-plate and in those with Modic type I changes. Further large sample-sized, multicenter imaging studies are required to analyze these results comprehensively.

Physiological method to provoke lumbar disc herniations

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Introduction: An intervertebral disc prolapse can lead to a compression of nerve roots causing pain, numbness or even paralysis. Complex, superphysiological loading conditions might facilitate disc prolapses. The biomechanical mechanism and the risk of herniations during daily-life activities and due to initial annulus damage are not completely understood yet.






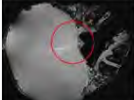


The aim of this study was to investigate, during which physiologic activity a prolapse may happen and how it is influenced by distinct annular defect sizes.

Methods: A new in vitro test method was developed to simulate typical in vivo activities with complex movements and loading conditions using 6 cadaveric human lumbar motion segments (L2-3, L3-4, L4-5, age: 24 – 33 years) with low disc degeneration (Pfirrman 1 - 2). In vivo movements [1] and intradiscal pressures [2] were replicated in a dynamic spine loading machine to simulate standing, tying shoes, complex bending, lifting boxes (20 kg) and complex lifting boxes (20 kg) for 6 cycles at 0.1 Hz, each. During another run of existing test standards (ISO 1819-1, ASTM F2423-11 and a common dynamic test method [3]), intradiscal pressure was monitored and compared with in vivo data. Daily activities were simulated again after setting distinct defects (vertical scalpel cut, 1.0 x 5.5 mm, 1.2 x 6.5 mm) in the posterolateral annulus. Disc height, range of motion and intradiscal pressure were evaluated between all test steps and analysed statistically using a Friedman-Test with Bonferroni Post-Hoc correction ($\alpha \leq 0.05$).

Results: A prolapse could be provoked in 5 of 6 specimens but only after setting a defect (Tab. 1). After herniation, disc height significantly decreased by 1.5 mm, intradiscal pressure by 2 MPa and range of motion increased by 1°. A physiological pressure could be achieved by the new physiological test method as well as with the standards suggested for implant testing (Tab. 2).

Discussion: This new test method replicates physiological activities and can be recommended for further biomechanical investigations concerning the therapy and treatment of disc herniations under physiological loading conditions. In order to simulate a high number of worst-case scenarios for implant testings like disc replacements, the ISO standard should be favoured. The long-term dynamic test method³ can also be used to examine implant loosening.

Tab. 1: Overview about herniations with view of the posterior annulus with endoscopic camera and ultra-high field MRI (11.7 T)

Herniation	Cases	Posterior annulus	MRI (11,7 T)
... in intact state	n = 0		
...after scalpel cut	n = 1		
...after defect (1.0 x 5.5 mm)	n = 2		
...after defect (1.2 x 6.5 mm)	n = 2		

Tab. 2: Comparison of in vivo and in vitro intradiscal pressure values during different daily-life activities

Activity	Standing	Tying shoes	Complex bending	Lifting (20 kg)	Complex Lifting (20 kg)
In vivo motion	Neutral position	Maximal flexion	Maximal flexion, Lateral bending left, Axial rotation left	Maximal flexion	Maximal flexion, Lateral bending left, Axial rotation left
In vivo intradiscal pressure in MPa	0.5	1.1	n/a	2.3	n/a
In vitro intradiscal pressure of physiological method in MPa	0.5	1.7	1.9	3.0	2.8
In vitro intradiscal pressure of equivalent standards in MPa	Dynamic longterm test protocol 0.3 MPa (0.2 MPa - 0.4 MPa)	ASTM F2423-11 1.2 MPa (0.7 MPa - 1.7 MPa)	ISO 1819-1 2.0 MPa (1.6 MPa - 2.8 MPa)	ISO 1819-1 2.0 MPa (1.6 MPa - 2.8 MPa)	ASTM F2423-11 alt. 2.9 MPa (1.9 MPa - 4.0 MPa)

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Kettler A., Schmoelz W., Shezifi Y., Ohana N., Ben-Arye A., Claes L., Wilke H.J. Biomechanical performance of the new BeadEx implant in the treatment of osteoporotic vertebral body compression fractures. Clin Biomech 2006; 21; 676-682

Clinical Outcome of Anterior Lumbar Interbody Fusion Using a Stand-alone Cage for the Treatment of Symptomatic Disc Degeneration

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Introduction: Lumbar discogenic pain remains a challenging condition to treat after failure of non-operative care. The primary treatment involves removal of the disc tissue and performing an interbody fusion. In the 1990s, the addition of supplemental posterior fixation to provide stability to the operated segment was commonly done. With innovations in fusion cage design and material as well as graft options, the need for posterior fixation has been questioned, unless specifically indicated. The purpose of this study was to evaluate the clinical outcome of ALIF using a stand-alone fusion cage with integrated screws.

Methods: The study was based on the consecutive series of 92 patients beginning with the first case experience undergoing anterior lumbar interbody fusion (ALIF) using a STALIF cage (Centinel Spine). Patients were treated for symptomatic disc degeneration. Stand-alone ALIF is not recommended for patients with greater than Grade I spondylolisthesis or severe stenosis requiring direct decompression. All patients were at least 24-months post-operative, with the longest follow-up duration being 100 months. Clinic charts were reviewed to collect general demographic data, clinical outcome measures including the Oswestry Disability Index (ODI), visual analog scales (VAS) separately assessing back and leg pain, surgical procedure details including level(s) operated, and blood loss. Any re-operations in the series were also recorded. For patients not recently seen in clinic, mailings and phone calls were conducted to collect current ODI, VAS, and re-operation data.

Results: Stand-alone ALIF was performed in 100 levels in 92 patients. Hybrid surgery was performed in 37 of the cases with total disc replacement performed at the level adjacent to the ALIF level. 42.4% of patients had previously undergone lumbar spine surgery, most often discectomy. The mean estimated blood loss was 66.5 ml. There was statistically significant improvement in the mean ODI scores from 42.3 pre-operative to 23.9 post-operative ($p < 0.01$). The mean VAS back pain score improved significantly from 6.2 to 2.8 and VAS leg pain scores also improved significantly from 4.3 to 1.8 (both $p < 0.01$). The re-operation rate in the series was 10.8%. Reasons for re-operation were: Foraminal stenosis at the index level ($n=1$, decompression performed), metal allergy reaction ($n=2$, one patient underwent device removal and replacement with allograft, in the other case posterior fusion was performed); adjacent segment degeneration ($n=1$, fusion performed); progressive cage subsidence ($n=1$, instrumented posterior fusion performed); pseudoarthrosis ($n=3$, instrumented posterior fusion performed); ongoing pain ($n=1$, pseudoarthrosis not described, instrumented posterior fusion at index and adjacent segments), and ongoing pain with scar/fibrosis ($n=1$, spinal cord stimulator implantation). There were no cases of fusion cage failure, vertebral body fracture, or screws backing out.

Discussion: Stand-alone ALIF was associated with statistically significant improvements in ODI scores, back pain, and leg pain. The re-operation rate for frank pseudoarthrosis or cage subsidence was 4.3%. These results support that stand-alone ALIF produces good outcomes in patients treated for symptomatic disc degeneration while avoiding the use of posterior fixation and its associated complication risk and cost.

A computerised analysis of the aetiology of Modic Changes associated with intervertebral disc degeneration

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Introduction: The aetiology of Modic changes is multifactorial. We aim to investigate the underlying biomechanical mechanism of intervertebral disc (IVD) degenerative characteristics (morphological and biomechanical) and Modic Changes (MCs) patterns detected using magnetic resonance imaging (MRI).

Methods: Through a finite-element (FE) modelling of L4/5 combined with various high bio-fidelity IVD degenerative features. Models with various IVD degenerative features included 1) nucleus shrinkage, 2) annulus fibrosis (AF) ossification and 3) the combination of both under vertical compressive loading. The MR images of patients with MCs were identified with associated IVD degenerative features. Biomechanical simulations of the endplates stress distributions were conducted under vertical loading.

Results: Stress concentrations on endplates were observed for the models with simulated IVD degenerative features. Nucleus shrinkage (Figure 1) and AF ossification both led to an increased von Mises stress on the endplate (2.579MPa and 7.388MPa) in comparison with the stress associated with the normal IVD simulations (1.476MPa). The max focal stress was significantly increased for the IVD with combined nucleus shrinkage and AF ossification (9.933MPa). The stress along the thickness direction of the endplate also revealed an increased max compressive stress for IVD with degenerations (normal: -0.2077MPa; nucleus shrinkage: -0.3274MPa; AF ossification: -3.983MPa; combined: -5.369MPa).

Discussion: MCs were associated with nucleus shrinkage and increased regional AF stiffness. IVD degeneration produces stress concentrations on the adjacent endplates under loading in comparison with healthy IVD, which provides further insight into the relationship between IVD degeneration and MCs.

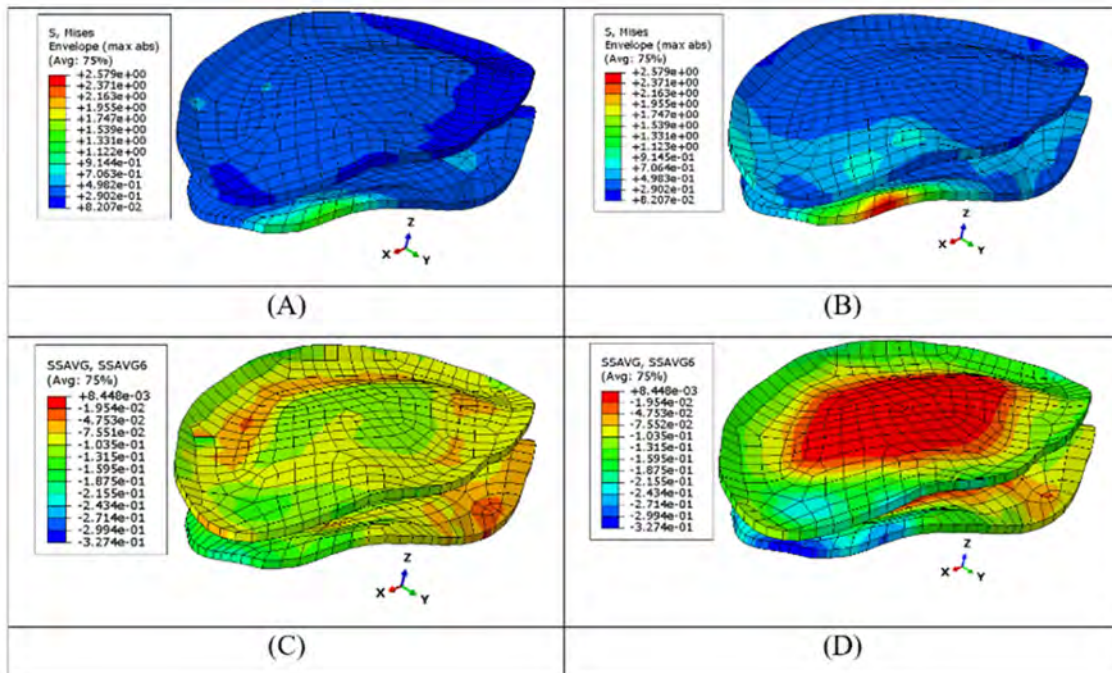


Figure 1: Endplate stress distributions for nucleus shrinkage. (A) and (B) are the von Mises stress for the model with and without nucleus, respectively. (C) and (D) are the average thickness stress (SSAVG) for the model with and without nucleus, respectively. The compressive stress is defined as positive and the tensile force is defined as negative.

Lumbar disc extrusions reduce faster than bulging disc due to an active role of macrophages in sciatica

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INTRODUCTION:

This retrospective observational histological study aims to associate the size and type of disc herniation with the degree of macrophage infiltration in disc material retrieved during disc surgery in patients with sciatica.

METHODS:

Disc tissue of 119 sciatica patients was embedded in paraffin and stained with haematoxylin and CD68. Tissue samples were categorized as mild (0-10/cm²), moderate (10-100/cm²), and considerable (>100/cm²) macrophage infiltration. All 119 patients received an MRI at baseline, and 108 received a follow-up MRI at one-year. MRIs were reviewed for the size and type of the disc herniations, and for Modic Changes in the vertebral end plates.

RESULTS:

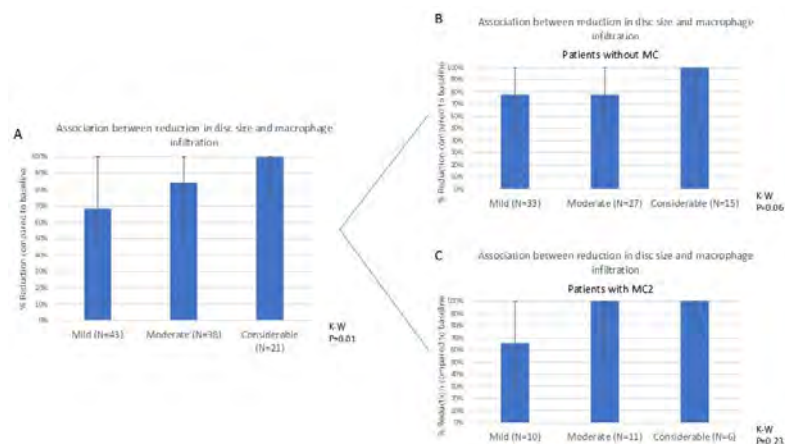
Baseline characteristics and duration of symptoms before surgery were comparable in all macrophage infiltration groups. The degree of macrophage infiltration was not associated with herniation size at baseline, but significantly associated with reduction of size of the herniated disc at one-year post surgery. Moreover, the degree of macrophage infiltration was higher in extrusion in comparison to bulging (protrusion) of the disc. Results were comparable in patients with and without Modic changes.

DISCUSSION:

macrophage infiltration was positively associated with an extruded type of disc herniation as well as the extent of reduction of the herniated disc during one-year follow-up in patients with sciatica. This is an indication that the macrophages play an active role in reducing herniated discs. An extruded disc herniation has a larger surface for the macrophages to adhere to, which leads to more size reduction.

Figure 4

Association between the degree of macrophage infiltration and the percentage surface reduction of the HNP between baseline and one-year follow-up on MRI. Macrophage infiltration groups are shown on the X axis, values on the Y axis are median percentages of axial surface reduction compared to baseline, error bars are interquartile ranges. and p values for the Kruskal Wallis test are provided. 2A displays this comparison for the whole population, 2B for patients without MC and 2C for patients with MC.



Djuric, N., Yang, X., El Barzouhi, A., Ostelo, R., van Duinen, S. G., Lycklama à Nijeholt, G. J., van der Kallen, B., Peul, W. C., & Vleggeert-Lankamp, C. (2020). Lumbar disc extrusions reduce faster than bulging discs due to an active role of macrophages in sciatica. *Acta neurochirurgica*, 162(1), 79–85. <https://doi.org/10.1007/s00701-019-04117-7>

Is Intradiscal Vacuum Phenomenon Associated with Intervertebral Disc Degeneration and Modic Changes?

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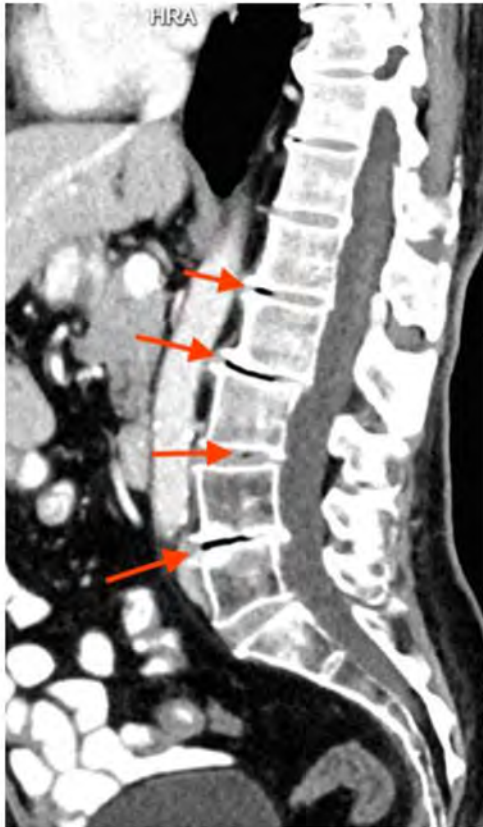


Figure 1.

Intradiscal vacuum phenomena are observed at multiple lumbar intervertebral disc levels (red arrows).

Introduction: Intradiscal vacuum phenomenon (IVP) is the radiographic appearance of gas collection in intervertebral discs or vertebra. Since it has been considered as an insignificant and incidental finding, its association with spinal degeneration remained unclear. We aimed to analyze the prevalence of IVP in adults with LBP and its association with intervertebral disc degeneration (IVDD) and Modic changes.

Methods: Consecutive patients, who admitted to outpatient clinics between March 2017 and March 2020 and had both lumbar spine magnetic resonance imaging (MRI) and abdominal computed tomography (CT) scans, were retrospectively reviewed. We excluded patients with history of malignancy, metabolic disease, spine infection, traumatic or osteoporotic spine fractures, and spine surgery.

Results: We evaluated 330 lumbar intervertebral disc spaces in 66 patients (mean age: 51.33 years). Severe IVDD was more prevalent at lower lumbar levels, whereas Modic changes were common at mid-lumbar levels. IVP was present in 24% of the patients. IVP was significantly more prevalent at the intervertebral discs with severe degeneration (27.8% vs. 3.1%, $p < 0.001$), and at those with Modic changes (25% vs. 5.4%, $p < 0.001$) at the corresponding disc levels. Severe IVDD and Modic changes together had an OR of 9.74 (95% CI= 3.74-25.38; $p < 0.0001$) to predict IVP at the corresponding disc level.

Discussion: Intradiscal vacuum phenomenon is an old entity that attracted little attention in the field of spine research. IVP could convey a good ecosystem for *P. acnes* and other possible pathogens residing in vertebral end-plates. The present study proved us that IVP is closely associated with severe IVDD and Modic changes. Further large sample-sized prospective clinical and laboratory studies are required to understand the exact association between those entities and to establish better management strategies in patients with LBP.

Neutrophils in Modic type I changes are in an activated (pro-inflammatory) state

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Introduction

Modic type 1 changes (MC1) are vertebral bone marrow lesions associated with non-specific low back pain (LBP). Sparse histological data is available and show vascularized granulation tissue at the disc-bone junction in MC1 biopsies. Granulation tissue is a sign of inflammation and characterized by deposition of loose extracellular matrix and infiltration of myeloid cells. We have shown dysregulated neutrophil maturation in MC1 bone marrow, underscoring the importance of neutrophils in MC1 pathophysiology. However, the molecular mechanism of neutrophil activation in MC1 remains unknown. The aim of this study was to identify dysregulated pathways and transcriptomic changes in MC1 neutrophils for the sterile etiology.

Methods

Bone marrow aspirates were obtained from LBP patients with MC1 undergoing lumbar spinal fusion. Aspirates were taken prior screw insertion through pedicle screw trajectory. From each patient, a MC1 and an intra-patient control (Ctrl) aspirate from an adjacent vertebral body without Modic changes were collected (n = 5+5). CD45+CD66b+ neutrophils were sorted with fluorescent-activated cell sorting, RNA was isolated and bulk RNA sequencing was performed. Reads were mapped to the reference genome, counted and statistical analysis was performed with EdgeR. Genes were considered to be differentially expressed (DEG) if p-value was < 0.01 and log2fc was > ± 0.5. Gene ontology (GO) enrichment was performed in R studio (GOseq) and gene set enrichment analysis (GSEA) was carried out with the GSEA software.

Results

By RNA sequencing, we identified 185 DEGs between MC1 and Ctrl neutrophils (Figure 1a). GO analysis revealed “immune response” (p=6.32E-07) and “inflammatory response” (p=2.5E-4) (Figure 1b) as the top upregulated biological processes in MC1 neutrophils. The upregulated biological processes “neutrophil chemotaxis” (p=3.3E-3), “neutrophil degranulation” (p=3.6E-3), “type I interferon signaling” (p=9.2E-3), “positive regulation of cytosolic calcium ion concentration” (p=8.2E-3) and “calcium-mediated signaling” (p=2.4E-2) give evidence that neutrophils in MC1 are activated. This was further confirmed by the enriched gene sets “inflammatory response” (p=0.001, NES=1.6) and “interferon alpha response” (p=0.0, NES=2.2) in MC1 neutrophils (Figure 1c). Moreover, calcium influx is required for the formation of neutrophil extracellular traps (NET), an important defense mechanism of neutrophils. Upregulated calcium-signaling in MC1 neutrophils gives indications for NET formation, a further sign of a pro-inflammatory phenotype. Finally, GO analysis (p=4.1E-3) and GSEA (p=0.0, NES=1.9) revealed enriched “interferon gamma response” in MC1 neutrophils. IFN-γ delays neutrophil apoptosis and primes respiratory burst, processes which are both associated with neutrophil activation and inflammation.

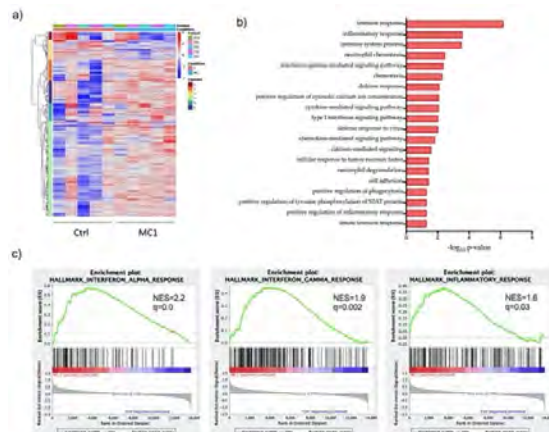


Figure 1: Transcriptomic changes of MC1 neutrophils. (a) Heatmap of 185 DEGs, (b) GO enrichment of upregulated BP in MC1, (c) GSEA showing enriched gene sets in MC1 neutrophils.

Discussion

Exaggerated neutrophil activation, resistance to apoptosis and the formation of neutrophil extracellular traps (NETs) are associated with inflammation and autoimmunity. Transcriptomic analysis points towards activated pro-inflammatory neutrophils in MC1. Neutrophils seem to be important contributors to MC1 pathobiology and might represent relevant treatment targets.

Intradiscal pressure at L4L5 level in adolescent idiopathic scoliosis: A computational study based on musculoskeletal modelling approach

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Introduction: Adolescent idiopathic scoliosis (AIS) is a three-dimensional deformity of the spine occurring in the general population with prevalence between 2 and 3%, the aetiology and pathogenesis of which are poorly understood¹. Investigating the relationship between scoliosis and biomechanical measures such as intradiscal pressure (IDP) would provide valuable information for the understanding of the pathomechanics of the AIS spine. Unfortunately, this measure cannot be obtained *in vivo* due to the invasiveness of the measurement procedure. An alternative strategy is represented by computational simulation based on musculoskeletal modelling approach, which allows calculating the biomechanical loads in assigned postures by the means of inverse static analysis. In this regard, a thoracolumbar model with articulated ribcage, developed in AnyBody software (AnyBody Technology, Denmark) and validated for the computation of IDP at L4L5 level^{2,3}, has been recently adapted to replicate the spine alignment in AIS. The present study exploits the available model to replicate the subject-specific spine alignment in orthostatic position in a dataset of 92 AIS subjects with scoliotic curve (Cobb angle >10°) with apex in the thoracolumbar/lumbar region. IDP calculated at L4L5 level is put in relation with curve severity and type of scoliosis (according to Lenke classification). Specifically, type 3, 5 and 6 were available.

Methods: The exploited dataset was acquired by our group in a previous clinical study⁴. The subjects underwent radiological examination in orthostatic position by EOS system (EOS Imaging, France), providing the simultaneous acquisition of the frontal and lateral plane images (Fig.1a,b). The 3D vertebral orientations (from T1 to L5, and the pelvis), weight and height were available. The spine alignment was replicated in the musculoskeletal model (Fig.1c,d) and scaling by subject's weight and height was performed. The intervertebral force (F) at L4L5 level was computed, and IDP was calculated as the ratio between the compression component of F and the upper endplate area of L5 (manually measured on the radiographic images), multiplied by a correction factor obtained from experimental studies⁵ (Fig.1). The relation between IDP and scoliosis severity was evaluated by Pearson correlation coefficient (ranging from 0 to ±1) and differentiated by Lenke type. The mean IDP in mild (Cobb angle 10-25°) and moderate (25-45°) cases was compared.

Results: IDP ranged from 0.5 to 1.4 MPa (Fig.2). The correlation with scoliosis severity was weak overall (0.29) and in each Lenke type (from 0.27 to 0.35). The mean value was significantly larger in the moderate cases compared to the mild ones (0.93 and 0.83, respectively).

Discussion: The results pointed out that the range of IDP calculated at L4L5 level in AIS is generally comparable to that observed in literature for adult healthy subjects⁶ (ranging from 0.4 to 1 MPa). The larger values found in AIS (>1 MPa) are not dependent on scoliosis severity (Fig.2). Scoliosis at thoracolumbar/lumbar level demonstrated to have a weak impact on IDP, independently on the type of deformity. Accordingly, although the mean value was observed as significantly larger in the moderate cases, the difference compared to mild ones was rather small (0.1 MPa).

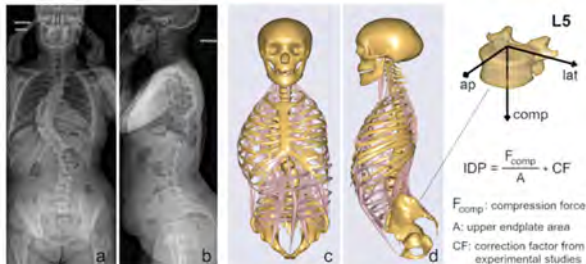


Figure 1. Frontal and lateral radiographic images of one subject (a,b) and corresponding musculoskeletal model in AnyBody software (c,d). Right panel: intradiscal pressure (IDP) as obtained at L4L5 level, with CF (equal to 1.54) from Lee et al., *Ergonomics*, 2013;56(5):832-41.

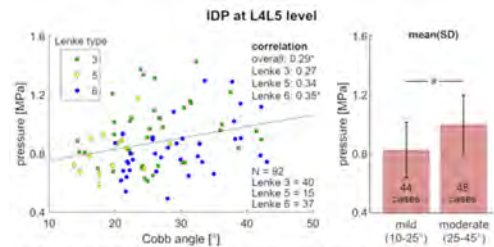


Figure 2. Left panel: scatter plot depicting the intradiscal pressure (IDP) at L4L5 level depending on the Cobb angle of the thoracolumbar/lumbar curve and differentiated by Lenke type. The overall regression line with the 95th percentile confidence interval are reported, as well as the correlation coefficients (r), indicating significant difference from zero with $p < 0.05$. Right panel: mean(SD) value for mild and moderate cases (*, significant difference between groups, with $p < 0.05$).

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Validity and responsiveness of the Core Outcome Measures Index (COMI) in patients with adolescent idiopathic scoliosis

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INTRODUCTION: The Core Outcome Measures Index is a brief 7-item instrument used for the routine assessment of the main outcomes of importance to patients with back problems (pain, function, symptom-specific well-being, quality of life, disability). When evaluating patients with specific pathologies, it might be expected to perform less well compared with a disease-specific instrument. In the present study, we sought to examine the correlation between scores on the COMI and on the widely accepted SRS-22 questionnaire in patients with adolescent idiopathic scoliosis (AIS).

METHODS: Data were evaluated from 40 patients (31 F, aged 16.1±5.1 years) with AIS, presenting for surgery in a tertiary care spine unit. The majority of patients underwent posterior spinal fusion. Patients completed the SRS-22 and the COMI at baseline and at 12 months' FU. Correlations between the COMI and SRS-22, and their respective subdomains, were evaluated. Responsiveness was assessed by the standardised response mean (SRM; mean of the individual change scores from preoperative to 12months postoperative / standard deviation of those change scores).

RESULTS: Baseline COMI correlated strongly with SRS-22 ($r=-0.86$), and with the individual SRS-22 domains (with pain, $r=-0.85$; function, -0.71 ; self-image, -0.68 ; mental health, -0.59). For the individual domains, COMI-pain correlated with SRS-pain (-0.86); COMI-disability, with SRS-function (-0.79); COMI-function, with SRS-function (-0.60); COMI-quality of life, with SRS-mental health (-0.61); COMI-symptom-specific well-being, with SRS-self-image (-0.67). The SRM for the COMI (1.03), was slightly lower than that of the SRS-22 (1.34), but was still a "large" effect size.

DISCUSSION: For routine spine outcome assessment within large spine units, the ability to use a "one size fits all" questionnaire considerably eases the administrative burden compared with using a condition-specific instrument for each separate pathology. The availability and ease of administration of simple, brief instruments can be expected to encourage participation in surgical registries. The COMI is able to detect meaningful change in the status of patients with AIS after surgery.

Altered proprioception on balance control, repositioning, and evoked potential in adolescent idiopathic scoliosis: A systematic review

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Introduction

Adolescent idiopathic scoliosis (AIS) is a three-dimensional spine deformity developed during the adolescence rapid growth period. Due to the nature of multifactorial causes, the definite aetiopathogenesis of AIS remains unknown. Recent genetic studies (i.e. Ptk7 mutated zebrafish, Runx3 knockout mice and Poc5 mutation in humans) have suggested that AIS may be considered as a neuromuscular disease which characterizes by proprioceptive defects. Since the appearance of abnormal curvature did not damage the spinal structure, the underlying causes of AIS may be attributed to the regulatory mechanism of proprioception that maintains the spinal alignment/balance. Therefore, the present review aimed to identify the proprioceptive deficits in patients with AIS with reference to non-AIS controls.

Methods

The present review was conducted according to the PRISMA guidelines. The inclusion criteria were all English articles related to: (I) AIS; (II) proprioceptive measure; and (III) human trial. In contrast, papers were excluded if they were: (1); case report (2) commentary; (3) review; (4) conference proceeding; or (5) study protocol. Database search including AMED, CINAHL, CENTRAL, EMBASE, MEDLINE, PubMed, and WOS was conducted from inception to May 2020. Newcastle-Ottawa Scale (NOS) was used as the risk of bias assessment.

Results

From 601 identified citations, 10 case-control studies comprising 840 participants were included. The mean NOS score was 5.3 points out of 9. Year of publication among studies were between 1981 and 2018. Among the proprioceptive measurements, four studies adopted balance control tests, two employed repositioning tests, two utilized evoked potential tests, as well as one on vibratory detection test. Compared to non-scoliotic controls, scoliotic adolescents demonstrated significantly moderate to high effect sizes on increased energy consumption and proprioceptive weighting in static standing, lower somatosensory ratio in sensory organization test, greater reposition errors in neck and lower extremity, slower nerve conduction velocity, and higher latency of somatosensory-evoked potential.

Discussion

As for the clinical implication, several studies have hypothesized that the proprioceptive defect is a cause of AIS. In case of proprioceptive deficit is a secondary symptom to the development of AIS, the magnitude of curve and its progression rate should be negatively correlated to the proprioceptive performance yet the current findings reject this hypothesis. Therefore, the proprioceptive deficits could possibly be considered as a potential initiation factor of AIS. Following this hypothesis, the proprioception test could be proposed to determine the populations at risk of developing AIS for those with negative testing results. Those patients might be beneficial by certain rehabilitation exercises targeting the correction of proprioceptive sense, for instance the dynamic proprioceptive stimulations. In conclusion, defective static and dynamic proprioception has been evidenced among patients with AIS. Future investigation on establishing the proprioceptive defect as a significant risk factor for AIS was able to identify those with high risk for curve development and/or progression, as well as may result in its potential use as a screening test for early detection and management.

The effect of curve location on the prediction rate of the severity index for adolescent idiopathic scoliosis

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Introduction

Early treatment of adolescent idiopathic scoliosis (AIS) is more effective than late; this requires determining early which patients will progress. A severity index was recently proposed to detect progressive AIS at the first exam. In the present work, a larger cohort was included to determine the effects of curve location on the severity index.

Methods

AIS patients were included from six clinical centers in four countries, both retrospectively and prospectively. Inclusion criteria were: Cobb angle between 10° and 25°, age > 10 years and Risser sign < 3. Patients underwent biplanar radiography and 3D reconstruction of the spine, which allowed to compute the severity index. The index was also weighted according to the patient's European Risser sign, to account for the lower risk of progression at more advance skeletal growth; a multiplicative factor of 1, 0.8 or 0.7 was applied to the index of patients with Risser 0, 1 or 2, respectively. An index < 0.4 suggests a stable curve, while > 0.6 a progressive one; values in-between are undetermined. Patients were then followed until decision of treatment ("progressive" patients) or until they reached skeletal maturity without progression ("stable patients", with Risser ≥ 3, Cobb angle ≤ 25°). Patients were grouped by major curve location: thoracic (T, apex above T12), thoracolumbar (TL, apex in T12 or L1) or lumbar (L, apex below L2).

Results

191 patients were included (159 girls, 12±1 years old, 114 Risser sign 0, 39 Risser 1 and 38 Risser 2). 82% of these patients were correctly classified as stable or progressive (Table 1). Sixteen patients (9%) were undetermined (severity index between 0.4 and 0.6). Table 1 reports the result by curve type. The rate of correctly classified patients was not affected by curve type. Sensitivity was higher in T and L curves, while specificity was slightly higher in TL curves.

Discussion

The severity index for AIS was able to correctly classify 82% of patients as progressive or stable. This is a promising result for the early detection of progressive scoliosis, which allows for an early treatment. The effects of major curve location on the severity index showed a modest impact on overall correct classifications, although TL curves showed lower sensitivity and higher specificity than T and L curves.

The main strength of the present work is the multicenter and international character of the data collection and processing. Inclusion of patients is ongoing to further test the severity index on a still larger cohort for a full validation allowing its use in clinical routine. However, the severity index is now robust with small influence from curve topology.

Table 1. Severity index results according to curve topology. 95% confidence intervals are reported between brackets.

	All	Thoracic	Thoracolumbar	Lumbar
N	191	79	50	62
Stable patients	102	41	27	34
Progressives patients	89	38	23	28
Correctly classified (%)	82	83	80	81
Sensitivity (%)	87 [80-94]	95 [87-100]	71 [52-91]	89 [77-100]
Specificity (%)	77 [68-86]	71 [56-86]	88 [74-100]	75 [60-90]

Relationship between radiological parameters of the lumbar spine and low back pain in the community

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【Introduction】

Degenerative change in the lumbar spine increase with aging. Up to now, a lot of radiological parameters of the progression of adult spinal deformity have been presented. However, the relationship between radiological parameters and symptoms is still unclear. The purpose of this study was to assess the relationship between radiological parameters and low back pain (LBP).

【Participants and Methods】

This was a cross-sectional study. Five hundred fourteen participants in the residents (170 males and 344 females, mean age were 65.1 years) were eligible for X-ray photography of the lumbar spine on the standing AP and lateral view. Cobb angle and lumbar vertebral tilt angles (L3, L4) from the AP view. The L1 axis-sacral vertebral distance (LASD), T11-L1 angle, L1-S1 angle, L4-S1 angle, and sacral slope (SS) angle were measured from the lateral view. The presence of LBP and the Roland-Morris Disability Questionnaire (RDQ) were also assessed. RDQ score was defined as a norm-based score, and less than 50 points were as low QOL compared to the national norm. The chi-square test and Kruskal-Wallis test were used for statistical examination, and a p-value of less than 5% was used as statistical significance in this study.

【Results】

1. Coronal view: Participants were classified into three groups based on Cobb angle (0-9.9 degrees, 10-19.9 degrees, and ≥ 20 degrees). There was no significant difference in the prevalence of LBP and norm-based RDQ scores among the three groups. Lumbar tilt angles of L3 and L4 were classified into three groups (0-4.9 degrees, 5-9.9 degrees, and 10 degrees or more), respectively. The prevalence of LBP was 13.2%, 10.8%, and 28.6% in each group for the L3 tilt angle, whereas 13.2%, 12.9%, and 25.8% for the L4 tilt angle. There was a significant difference in the LBP prevalence only for the L3 tilt angle ($p=0.029$). There was no significant difference in norm-based RDQ scores among three groups of L3 and L4 tilt angles.
1. Sagittal view: SS angle was categorized into three quartiles (low, middle, and high groups). The prevalence of LBP decreased with increasing SS angle (19.2% vs. 12.0% vs. 10.4%, $p=0.020$). The prevalence of low norm-based RDQ score decreased with increasing SS angle (35.5% vs. 26.5% vs. 22.6%, $p=0.013$). On the other hand, there was no significant association of LBP or norm-based RDQ with LASD, T11-L1 angle, L1-S1 angle, and L4-S1 angle.

【Discussion】

In this study, the L3 tilt angle in the coronal view and SS angle in the sagittal view had the possibility to associate with LBP. It is widely known that there are various factors other than the items evaluated by X-ray photography as the cause of low back pain. Further study should be needed to verify the results of this study.

Dynamic Lumbopelvic-hip Alignment in the Patients with Degenerative Lumbar Spinal Canal Stenosis is Closely Correlated with Lower Limb Pain intensity during Walking; Three-dimensional motion analysis

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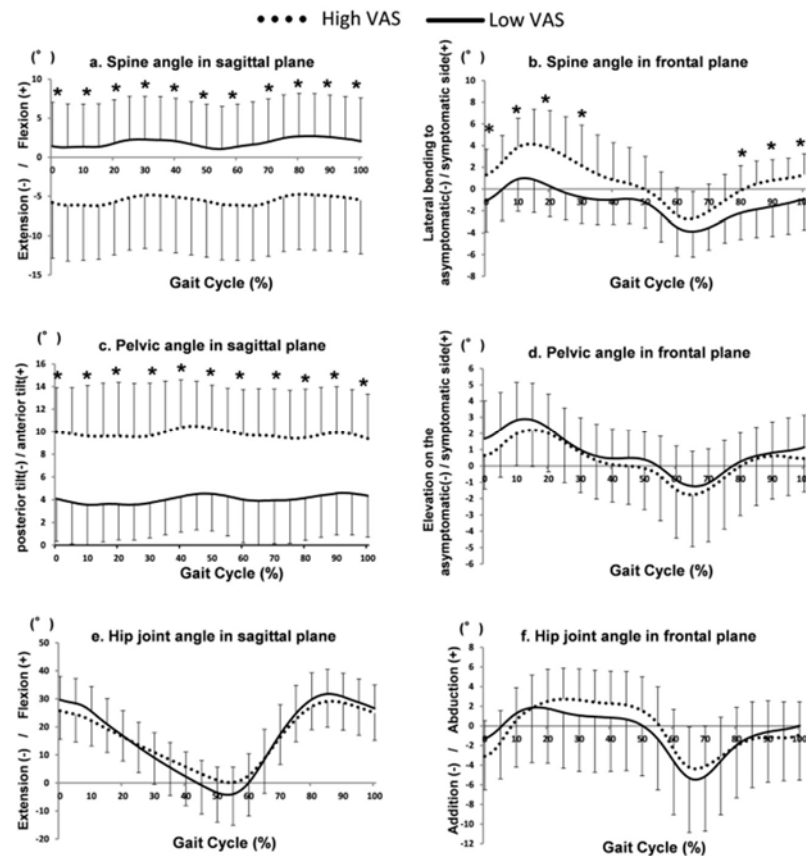
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INTRODUCTION: Lower limb pain with intermittent claudication is common symptom in the patients with degenerative lumbar spinal canal stenosis (LSS). Although lumbopelvic-hip alignment may contribute to leg pain in LSS patients, it remains to be clarified on the real pathomechanism behind it. The purpose of the current study was to investigate whether dynamic alignment of the spine, pelvis and hip joint in the patients with LSS affects the intensity of lower limb pain during walking.

METHODS: Twenty-three LSS patients (13 males and 10 females; Mean age 68.0 y.o.) were participated in this study. All the diagnosis was confirmed with MRI. Leg pain was assessed using visual analogue scale (VAS). The mean value of VAS in all subjects was calculated. Then subjects with higher values than the mean were assigned to the High-VAS (H) group, and those with less were assigned to the Low-VAS (L) group. The dynamic alignment of spine, pelvis and hip joint during one gait cycle was measured using a 3-D motion analysis system (VICON with 8-cameras and 2-force plates). For statistical analysis, the angle of spine (flexion/ extension, lateral bending to symptomatic/ asymptomatic side), pelvis (anterior/ posterior tilt, elevation on symptomatic/ asymptomatic side) and hip joint (flexion / extension, abduction / adduction) were compared between two groups (H vs. L) every 10 % in gait cycle using unpaired t-test. Statistical significance was set at the $p < 0.05$.

RESULTS: Regarding the spine angle, the H group was significantly extended (in entire interval) and bent to the symptomatic side (0-30% and 80 to 100% in one gait cycle) compared with the L group (Figure a,b). Regarding the pelvic angle, the H group was significantly tilted forward (in entire interval in one gait cycle) compared with the L group (Figure c). There were no significant differences in hip joint angles between two groups.

DISCUSSION: This is the first study to investigate how closely the dynamic alignment of the spine, pelvis and hip joint during walking is correlated with lower limb pain intensity using time series data. Our results suggested that LSS patients with severe leg pain walk with improper spinal alignment on a daily basis. Rehabilitative approach to maintain an appropriate walking posture might be needed to alleviate lower limb pain in the LSS patients.



Correction of apical vertical translation may prevent unfused lumbar intervertebral disc degeneration after posterior spinal fusion for adolescent idiopathic scoliosis

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Introduction: Although numerous studies have examined unfused lumbar intervertebral disc degeneration (IVDD) after posterior spinal fusion for adolescent idiopathic scoliosis (AIS), risk factors of uninstrumented IVDD after surgery is not fully elucidated. The aim of this study was to investigate longitudinal clinical and imaging results focusing on the uninstrumented lumbar spine after posterior spinal fusion for AIS in adulthood, and to clarify whether successful correction surgery for AIS was associated with reduced progression of the caudal unfused IVDD in adulthood.

Methods: Thirty-two AIS patients (6 male, 26 female, mean age 31.5 years) who underwent posterior collection surgery when their age was over twenty and were followed more than 5 years were included. We evaluated lumbar MRI and standing X-ray at preoperatively and 5 years postoperatively. Unfused lumbar disc was assessed by one radiologist and one spine surgeon using modified Pfirrmann classification. We divided the patients into two groups depends on the progression of IVDD on MRI, that is degenerated group (group D) consisted of patients with deteriorated IVDD, and non-degenerated group (group ND) consisted of those without. Demographic data, radiographic parameters, and clinical evaluation using SRS-22 was performed between the two groups.

Results: A total of 130 discs were evaluated. Of nine patients in group D, deteriorated IVDD was observed in 15 discs (11.5%) consisting of at L2-3 in 1 disc, L3-4 in two discs, L4-5 in six, and L5-S1 in six. No significant differences were observed between the groups in age, sex, BMI ($P=0.71$, 0.65 , 0.10 , respectively). In radiographic analysis, there were no significances in curve type ($P=0.64$), Cobb angle of the main curve ($P=0.65$), flexibility of the main curvature ($P=0.51$), number of fusion ($P=0.46$), correction rate of the main curvature ($P=0.38$), level of lowest instrumented vertebra (LIV) ($P=0.06$), LIV tilt ($P=0.68$), LIV inclination ($P=0.90$). The correction rate of the apical vertical translation of the main curvature was significantly greater in group ND than that in group D (69.7% vs 56.8%, $P=0.03$). The SRS-22 scores was equal between the two groups.

Discussion: Horizontalization of LIV did not have influence on the postoperative IVDD. Correction rate of apical vertical translation of the main curvature was significantly greater in patients without degenerated lumbar discs than those with, suggesting that unfused lumbar IVDD could be prevented by maximum correction of apical translation of the main curvature.

Computed Tomography Study of the Relationship Between Pelvic Incidence and Osseous Contribution to Lumbar Lordosis in Children

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INTRODUCTION

Although the relationship between pelvic incidence (PI) and segmental lordosis in the adult population is well described there is a distinct lack of data from the paediatric population. The aim of this study was to define the contributions to segmental lordosis by the vertebral bodies and relate this contribution to the PI in skeletally immature patients.

METHODS

CT scans obtained for assessment of non-spinal pathology were reviewed in children aged <16 years. Segmental lordosis (SL) was measured for each vertebrae L1-L5 inclusive; a positive value indicates lordosis while a negative indicated kyphosis. Global lordosis (GL) was calculated by the sum of L1-L5 inclusive. PI, sacral table angle (STA) and sacral kyphosis (SK) were additionally measured. Children were grouped into three age groups: (1) 0-60 months; (2) 61-120 months; (3) 121-196 months. Data was analyzed using Pearson correlation co-efficient and one-way ANOVA.

RESULTS

150 scans were analyzed: mean age 90.7 months (s.d. 46.4); 94 (62.7%) male. The mean PI was 40.4 (s.d. 8.4; range 19.3 – 64.7). There were 40 in group 1, 63 in group 2 and 37 in group 3. Age was significantly different between each of the age groups; gender proportion was not different between age groups with a similar proportion of males in each.

Statistically significant differences were detected between the age groups for PI, STA, vertebral segmental lordosis at L1, L3, L4 and L5, distal lordosis and global lordosis. Pairwise comparisons showed significant differences: for PI between age groups 2 and 3, and; for STA between groups 1 and 2 and between groups 1 and 3.

In the proximal spine (L1-L3), significant differences in the vertebral segmental lordosis values were evident: at L1 between groups 1 and 3 and groups 2 and 3, and ; at L3 between groups 1 and 2 and groups 1 and 3.

In the distal spine (L4-L5), significant differences in the vertebral segmental lordosis values were evident: at L4 between groups 1 and 2 and age groups 1 and 3, and; at L5 between groups 1 and 2.

Considering combined vertebral body lordosis in each region, there was no significant difference between age groups in the proximal lumbar vertebral body lordosis while in the distal lumbar spine there were significant differences between groups 1 and 2 and groups 1 and 3. Globally, vertebral body lordosis was significantly different only between groups 1 and 2.

Correlation analysis of the entire cohort did not show meaningful relationships between PI and age ($r=0.07$). In general, stronger associations were seen between PI and measured parameters with increasing age.

DISCUSSION

As children age, segmental contributions by the vertebral bodies to global lordosis evolve and in adolescence appear to approach those seen in the adult population. The relationship between PI and segmental and regional lordosis also undergoes maturation. Further research should define the point of adoption of the adult PI-LL relationship.

Impact of diffuse idiopathic skeletal hyperostosis on sagittal spinal alignment in the general elderly population: A Japanese cohort survey randomly sampled from a basic resident registry

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Introduction: Interest is mounting on diffuse idiopathic skeletal hyperostosis (DISH) as the elderly rate increases. Although some studies have demonstrated an effect of DISH on sagittal spinal alignment, the pathogenetic mechanism remains unknown. We recently conducted an epidemiological musculoskeletal examination in the community-dwelling elderly. Random sampling from the basic resident registry of a rural Japanese town was adopted to minimize selection bias and obtain a cohort representative of the general population [Spine J (in press)]. This study aimed to investigate the impact of DISH on sagittal spinal alignment in this cohort.

Methods: Registered citizens of 50 to 89 years old were targeted for this survey. We established 8 groups based on age (50's, 60's, 70's, and 80's) and gender (male and female) after random sampling from the resident registry of Obuse town in 2014. A total of 411 participants (202 male and 209 female) were enrolled and underwent a single whole-spine lateral radiographic examination. We investigated the spinal level of DISH occurrence, measured sagittal spinal alignment parameters, and analyzed the effects of clinical factors on DISH using multivariate analysis.

Results: A total of 72 (17.5%) participants were identified as having DISH in our population cohort. Regarding DISH involving the thoracic spine, sagittal vertical axis (SVA), cervical SVA, T1 slope, thoracic kyphosis, aging, and male had significant influences on DISH in univariate analysis. Aging and male were also independent factors according to multivariate analysis, with odds ratios (ORs) of 1.70 and 3.75, respectively. SVA, lumbar lordosis (LL), sacral slope, pelvic tilt, aging, and male had significant influences on DISH involving the lumbar spine in univariate analysis, with LL, aging, and male as independent factors in multivariate analysis (OR: 1.82, 4.35, and 10.7, respectively).

Conclusions: In this study examining the impact of DISH on sagittal spinal alignment in a general population, LL was significantly associated with DISH involving the lumbar spine in the healthy community-dwelling elderly, while no sagittal spine parameters were significantly related to DISH affecting the thoracic spine.

EOS Analysis of Sagittal Alignment of Spine and Pelvis in Korean Adult Population

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Introduction: To investigate the spinal and sagittal values of Korean adults using EOS. In Korea, there is no study to know the value of the spinal and pelvic sagittal alignment.

Materials and Methods: From February, 2017 to April, 2019, 426 patients who have no symptoms of spine or pelvis were underwent EOS evaluation. The patients were divided into 5 groups according to their age. The groups were 20s, 30s, 40s, 50s, 60s and above. All patients who don't have any operation record were healthy and asymptomatic. Measured parameters were pelvic incidence (PI), sacral slope (SS) and Sagittal pelvic tilt (SPT). Sagittal balance was measured by sagittal vertical axis (SVA). Thoracic kyphosis, Lumbar lordosis were measured in kyphosis and lordosis

Results: The PI of 20s was an average of $44.96 \pm 2.71^\circ$, the SS was an average of $34.41 \pm 2.04^\circ$, and the SPT was an average of $10.54 \pm 2.01^\circ$. SVA averaged $-10.69 \pm 6.30\text{mm}$, Thoracic kyphosis averaged $35.94 \pm 2.45^\circ$, and Lumbar lordosis averaged $49.22 \pm 2.89^\circ$. The PI of 30s averaged $47.23 \pm 1.50^\circ$, the SS averaged $36.58 \pm 1.03^\circ$, and the SPT averaged $10.63 \pm 1.14^\circ$. SVA averaged $-8.91 \pm 3.80\text{mm}$, Thoracic kyphosis averaged $37.40 \pm 1.53^\circ$, and Lumbar lordosis averaged $51.01 \pm 1.59^\circ$. The PI of 40s averaged $46.71 \pm 1.50^\circ$, the SS averaged $35.46 \pm 1.33^\circ$, and the SPT averaged $11.27 \pm 1.13^\circ$. SVA averaged $-10.86 \pm 3.77\text{mm}$, Thoracic kyphosis averaged $40.49 \pm 1.55^\circ$, and Lumbar lordosis averaged $51.03 \pm 1.84^\circ$. The PI of 50s averaged $49.81 \pm 1.98^\circ$, the SS averaged $35.65 \pm 1.67^\circ$, and the SPT averaged $14.24 \pm 1.75^\circ$. SVA averaged $-4.95 \pm 4.54\text{mm}$, Thoracic kyphosis averaged $41.01 \pm 2.29^\circ$, and Lumbar lordosis averaged $51.31 \pm 2.46^\circ$. The PI of 60s and above group averaged $46.53 \pm 3.22^\circ$, the SS averaged $34.29 \pm 3.42^\circ$, and the SPT averaged $12.47 \pm 2.29^\circ$. SVA averaged $1.59 \pm 12.69\text{mm}$, Thoracic kyphosis averaged $43.06 \pm 4.80^\circ$, and Lumbar lordosis averaged $49.24 \pm 6.58^\circ$. The PI, SS, and SPT of each group were not statistically significant. There was no statistically significant difference in SVA and lumbar lordosis of each group. The thoracic kyphosis of each group was the smallest in the 20s group, and the 30s, 40s, and 50s groups were not different from each other, and the 60s and above groups were statistically significant.

Conclusions: It is important to measure and accurately analyze the spine and pelvic sagittal values of healthy adults. The normoactive values according to the patient's age can help to estimate pre-operative lumbar lordosis restoration and can also be used as a guideline for spinopelvic sagittal balance.

Minimally invasive versus conventional open approach for correction and posterior spinal fusion in patients with adolescent idiopathic scoliosis

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INTRODUCTION: The most popular surgical treatment method for adolescent idiopathic scoliosis (AIS) is posterior spinal fusion. Recent advances in implant designs allow for minimally invasive (MISS) or less invasive (LISS) approaches in spinal surgery. However, for various reasons, these have not yet made a breakthrough in the treatment of spinal deformity. Tissue damage is less when using MISS/LISS techniques, but intraoperative orientation is more challenging because of the decreased overview. Few previous studies have analysed surgical/patient outcomes in patients with AIS undergoing MISS/LISS; even fewer have compared MISS/LISS with the open approach. We compared the results of AIS patients treated using MISS/LISS with those of a historical cohort treated using traditional open methods.

METHODS: This was a single-center retrospective analysis of data collected prospectively within the EUROSPINE Spine Tango Registry framework. Inclusion criteria were: idiopathic scoliosis; posterior spinal fusion as surgical treatment; major coronal Cobb <80°; aged ≤30 years. We identified 66 patients operated using conventional methods (OPEN) between 2005 and 2015, and 26 patients operated using a minimally invasive posterior transmuscular approach (MINI-OPEN) between 2016 and Feb 2020. Complications, blood loss, operation time, and length of stay were documented on Tango surgery forms. Pre and postop whole spine standing X-rays were analysed. Patients completed the Core Outcome Measures Index (COMI) preoperatively and at 3 and 12mo postoperatively.

RESULTS: Baseline characteristics (age, gender) were similar in both groups, as was the preop main curve (57.5±9.1° in the MINI-OPEN and 59.4±9.7° in the OPEN group; p=0.39). Blood loss was significantly less in the MINI-OPEN than the OPEN group (472±273 mL vs 1218±731 mL, respectively; p<0.0001). Operating time was significantly longer in the MINI-OPEN than the OPEN group (473±92 min vs 320±104 min, respectively; p<0.0001). Length of stay (surgery to discharge) was almost half as long in the MINI-OPEN as the OPEN group (5.4±1.4 days vs 9.19±2.7 days, respectively; p<0.0001). The % coronal correction of the main curve was not significantly different between the groups (76.5±9.6% for MINI-OPEN vs 71.9±11.7% for OPEN; p=0.08). The pattern of reduction in COMI from preop to 3mo FU and from preop to 12mo FU (in those who had reached 12 mo FU) was significantly different (p<0.05) between the groups, with MINI-OPEN showing slightly better results.

DISCUSSION: Compared with the conventional open approach, the minimally invasive approach using a free-hand pedicle screw insertion technique was associated with a significantly lower blood loss and shorter hospital stay and slightly better short-term (3-12 months postop) patient rated outcomes. Refining the surgical technique and decreasing the surgical invasiveness reduces the suffering of the patients immediately after surgery, and is associated with slightly better patient outcomes at 3 and 12 months.

Risk Factors for Worsening of Sagittal Imbalance after Revision Posterior Fusion Surgery in Patients with Adjacent Segment Disease

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Introduction

Recent studies have emphasized restoring sagittal balance during lumbar spinal fusion. Considering sagittal balance is particularly important in adjacent segment disease (ASD) patients because they frequently show hypolordotic prior fusion. Worsening of sagittal imbalance after additional posterior lumbar fusion is also frequently encountered. This study aimed to identify the risk factors of sagittal imbalance after posterior lumbar fusion in ASD patients.

Methods

Fifty-nine patients who underwent revision surgery via a posterior approach for ASD between 2014 and 2018 and were followed up for >2 years were included. Radiographic parameters were measured in whole-spine lateral view of plain radiographs. Clinical results were analyzed using the visual analog scale, Oswestry Disability Index, and EuroQol 5-domain. Patients were divided into two groups according to the postoperative sagittal balance status, determined as the pelvic incidence minus lumbar lordosis (PI-LL) value, based on the age-adjusted Schwab classification (group A: ideal correction, N=20; group B: undercorrection, N=39). Preoperative and operation-related factors were compared between the groups by univariate and multivariate analyses.

Results

The PI-LL improved postoperatively from 19.4° to 12.5° in group A ($p=0.019$) and unchanged (from 38.6° to 38.6°, $p=1.000$) in group B. Although the clinical outcomes improved postoperatively in both groups, they did not any inter-group differences pre- and postoperatively. In multivariate analysis, better preoperative PI-LL ($p=0.001$), slippage of the vertebral body at the ASD level ($p=0.022$), higher disc height ($p=0.048$), and absence of L4-5-S1 fusion ($p=0.041$) in the index surgery were significantly correlated with better postoperative sagittal balance.

Discussion

Better preoperative PI-LL value, slippage of the vertebral body at the ASD level, higher disc height, and absence of L4-5-S1 fusion in the index surgery were significantly correlated with better postoperative sagittal balance following ASD surgery. Thus, surgeons should pay attention for obtaining sagittal balance after surgery in patients with preoperative sagittal imbalance, a rigid segment, or an already fused L4-S1 segment.

The impact of lower lumbar lordosis on surgical results after long spinal fusion

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Introduction: Lower lumbar lordosis has been reported to account for two-thirds of all cases of lumbar lordosis (LL) in the standing alignment of physiologically healthy persons. However, in long spinal fusion, which is a non-physiological state, reconstruction of the standing alignment is not always appropriate for healthy persons.

Aim: To investigate the effect of lower LL on the postoperative results of long spinal fusion.

Materials and Methods: 39 patients (4 men and 35 women; mean age, 72.2 years) who underwent spinal fusion from the lower thoracic vertebra to the pelvis for an adult spinal deformity were evaluated retrospectively. The ratio of L4–S lordosis to LL was defined as %L4–S. 24 cases with %L4–S between 55% and 75% immediately postoperatively were assigned to the H group (mean %L4–S, 64.2%) and 15 cases with %L4–S less than 55%, in the L group (46.1%). We compared postoperative sagittal alignment, instrument-related adverse events, and clinical outcome (Oswestry disability index [ODI], Scoliosis Research Society 22 [SRS22] and Visual analogue scale [VAS] for satisfaction with surgery) between the two groups.

Results: The mean values of the parameters measured immediately postoperatively were as follows (group H/group L): pelvic incidence (PI; 49.0°/44.1°), PI-LL (4.1°/6.9°), sacral slope (SS; 29.3°/26.4°), T1 pelvic angle (TPA; 16.7°/15.1°), and sagittal vertical axis (SVA; 25.5 mm/33.9 mm). No significant differences were found between the groups. Two years postoperatively, PI-LL (12.2°/5.9°), SS (25.0°/23.7°), TPA (25.2°/21.9°), and SVA (56.3 mm/46.7 mm) were not significantly different. The instrument-related adverse events were proximal junctional kyphosis (46.7%/37.5%), proximal junctional failure (0%/0%), adjacent vertebral fractures (12.5%/20.0%), screw loosening (4.2%/13.3%), and rod fracture (16.7%/0%), with no significant differences between the groups. Moreover, no significant differences in ODI (26.2%/20.7%), SRS22 total score (2.5/2.4) and VAS for satisfaction with surgery (8.4/8.8) were found 2 years postoperatively.

Conclusion: In long spinal fusion, LL formation mainly in the lower lumbar vertebrae may not affect the spinal alignment and clinical outcome in the postoperative mid-term.

The comparison of the spinopelvic parameters between the decompression and the fusion for degenerative lumbar disease at L5-S1

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Introduction: The spinopelvic parameters are divided into fixed parameter (pelvic incidence, PI) and non-fixed parameters (pelvic tilt, PT; sacral slope, SS). Recently, several literatures demonstrated PI increase with sagittal imbalance or aging due to degenerative change in sacroiliac joint by shear force. PT represents pelvic compensations, which is combined motion of lower lumbar spine and hip joint. Spinal fusion at L5-S1 may influence spinopelvic parameters. However, there was no previous study. The aim of this study is to reveal the change in spinopelvic parameters after spinal fusion at L5-S1 comparing to decompression surgery at L5-S1.

Methods: We retrospectively reviewed 61 consecutive patients who were surgically treated for single-level lumbar degenerative disease at L5-S1 (31 patients in fusion group and 30 patients in decompression group). We measured spinopelvic parameters including PI, PT, and SS, lumbar lordosis (LL), and L4-S1 lower lumbar lordosis (LLL) on standing radiograph at the initial visit and postoperative 1 year. We analyzed changes in parameters of overall subjects and subgroups subjects between baseline and follow-up using paired t-test. We also compared parameters between fusion and decompression groups using student t-test.

Results: Overall, PI changed significantly ($47.1 \pm 8.1^\circ$ to $46.0 \pm 7.9^\circ$, $P=0.022$). However, the magnitude of change was small. LL increased ($40.6 \pm 14.6^\circ$ to $43.4 \pm 13.1^\circ$, $P=0.36$) and PI-LL decreased ($6.5 \pm 13.1^\circ$ to $2.6 \pm 11.3^\circ$, $P=0.006$) significantly after both surgeries. There were no differences in baseline parameters between fusion group and decompression group (All $P < 0.05$). Mean value of PT increased after fusion and decreased after decompression. However, those changes did not reach statistical significance.

Discussion: At postoperative 1 year follow-up, spinopelvic parameters did not change significantly after both L5-S1 fusion and decompression. Spinal fusion at L5-S1 may not make significant change in spinopelvic parameter in comparison with decompression surgery at postoperative 1 year follow-up.

Predicting spondylolisthesis correction with prone traction radiographs

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Introduction: Degenerative spondylolisthesis with radiological instability is commonly defined using dynamic flexion-extension radiographs. Radiological instability accounts for three radiological changes including slip distance, slip angle and disc height changes. Traction radiographs can assess disc height and segmental translation better in the presence of vertical instability. However, the significance of degree of vertical instability in relationship to postoperative outcomes and the need for interbody fusion is unknown. The aim of study is to determine preoperative radiological predictors for postoperative spondylolisthesis correction.

Methods: 112 consecutive patients with degenerative spondylolisthesis with preoperative prone traction radiographs obtained since 2010 were studied. Only patients who subsequently had one- or two-level lumbar fusions were included. Patients without fusion surgery or long-segment deformity corrections were excluded. Measurements of slip distance, slip angle, disc height, segmental lordosis and global lordosis (L1-S1) were performed on preoperative lateral standing radiographs, flexion-extension lateral radiographs, prone traction lateral radiograph and postoperative lateral standing radiographs. Patients were divided into two groups: posterolateral fusion or posterolateral fusion with interbody fusion. Spearman's correlation was performed between preoperative and postoperative parameters. Predictors were studied with non-linear regression and receiver operating characteristic was used to determine the cut-off value of disc height changes for interbody fusion.

Results: A total of 63 patients were included with mean age of 60.9±10.9 years. Two levels were fused in 10 patients giving rise to 73 lumbar levels for analysis. L4-5 was the most common level (72.6%), followed by L3-4 (16.4%) and L5-S1 (11.0%). The average change in segmental lordosis and global lordosis was 7.1±6.7° and 2.9±9.9° respectively for the interbody fusion group, and 0.8±5.1° and -0.4±10.1° respectively for the posterolateral fusion only group. Strong correlations were observed for all preoperative dynamic parameters with the postoperative images. Segmental lordosis ($\rho=0.794$, $p<0.001$) corrected with interbody fusion was best correlated with prone traction radiographs. Global lumbar lordosis ($\rho=0.788$, $p<0.001$) was best correlated with the interbody fusion group and preoperative lateral standing radiographs. The least difference in slip distance (-0.3±1.7mm, $p<0.001$), slip angle (0.9±5.2°, $p<0.001$) and disc height (0.02±2.4mm, $p<0.001$) was observed between prone traction and postoperative radiographs. Regression analyses suggest that prone traction parameters best predict slip distance correction ($R^2=0.631$) and disc height correction ($R^2=0.338$), while slip angle correction ($R^2=0.511$) is best predicted by extension radiographs. ROC cut-off showed that a prone traction disc height of 8.4mm warranted an interbody fusion with 69.6% sensitivity and 69.2% specificity.

Conclusion: Prone traction radiographs provide the best prediction of slip distance and disc height corrections that are achieved with interbody fusion for lumbar degenerative spondylolisthesis. To achieve this maximum correction, interbody fusion should be performed if a disc height of 8.4mm is achieved on preoperative prone traction radiographs.

Functional Ability Classification based on Moderate and Severe Kinesophobia and Demoralization Scores in Degenerative Spine Patients

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Introduction: Fear avoidance and demoralization are crucial components of mental health that impact the outcomes in spine surgery. However, interpreting their effect on patient function remains challenging. Further establishing this correlation and identifying a threshold of severity can aid in identifying patients in whom a portion of their altered gait and balance may amplified by underlying psychologic distress. Therefore, the purpose of this study was to assess the relationship of fear avoidance and demoralization on gait and balance and determine a threshold score for the Tampa Scale for Kinesophobia (TSK) and the Demoralization Scale (DS) that identifies spine patients with gait and balance dysfunction amplified by underlying psychological factors.

Methods: 405 symptomatic spine patients were given the TSK and DS questionnaires. Symptomatic adult patients were drawn from one of five cohorts of degenerative spinal conditions: adult degenerative scoliosis (ADS), cervical spondylotic myelopathy (CSM), degenerative lumbar spondylolisthesis (DLS), single-level lumbar degeneration (LD), sacroiliac joint dysfunction (SIJD). Patient's gait and balance were tested with a human motion capture system. A TSK score of 41 and DS score of 30 were chosen as thresholds to classify moderate vs severe dysfunction based on literature and statistical analysis.

Results: In this study, a combination of statistical analysis and literature data was used to analyze gait and balance differences at the proposed thresholds of 41 for TSK and 30 for DS. After allocating patients to moderate and severe groups for fear avoidance, we found significant differences across walking speed, stride time, step length/width, and head sway across planes. Patients with TSK > 41, on average, had 0.08 (m/s) slower walking speed and 0.08 (s) longer stride time. Higher TSK and DS scores were correlated with worse walking speed (p<0.001), longer stride time (p=0.001), decreased stride length (p<0.048) and wider step width (<0.001) during gait as well as increased sway across planes (p=0.001) during standing balance. When classified by TSK scores > 41, patients with more severe fear avoidance had slower walking speed (p<0.001), longer stride time (p=0.001), shorter stride length (p=0.004), increased step width (p<0.001) and increased sway (p=0.001) compared to their lower scoring counterparts. Similarly, patients with DS > 30, had slower walking speed (p=0.012), longer stride time (p=0.022), and increased sway (p=0.003) compared to their lower scoring counterparts.

Conclusions: This study demonstrates that fear avoidance and demoralization directly correlate with worsening gait and balance. Furthermore, patients with TSK >41 and DS >30 have more underlying psychological factors that contribute to significantly worse function compared to lower scoring peers. Understanding this relationship and using these guidelines can help identify and treat patients whose gait dysfunction may be amplified by psychologic distress.

Table 1. One way ANOVA comparison of Functional Parameters between Moderate to Severe Scores

Score	Walking Speed	Stride Time	Stride Length	Step Width	Head Coronal Sway	Head Sagittal Sway	Head Total Sway	
TSK with a Median of 41								
Low	35.49	0.89	1.24	1.08	0.16	3.21	6.43	65.52
SD	4.88	0.18	0.20	0.14	0.05	3.09	2.91	36.09
N	217	217	217	217	217	217	217	217
High	47.56	0.81	1.32	1.04	0.18	3.90	7.40	80.62
SD	5.01	0.19	0.25	0.15	0.05	3.31	3.53	50.56
N	188	188	188	188	188	188	188	188
41	0.000	0.000	0.001	0.004	0.000	0.032	0.003	0.001
DS with a Median of 30								
Low	13.07	0.87	1.27	1.06	0.17	3.34	6.72	69.36
SD	7.71	0.18	0.22	0.14	0.05	2.93	3.17	38.74
N	325	325	325	325	325	325	325	325
High	44.76	0.81	1.33	1.04	0.17	4.30	7.55	85.42
SD	10.41	0.20	0.24	0.16	0.05	4.10	3.48	59.48
N	80	80	80	80	80	80	80	80
30	0.000	0.012	0.022	0.227	0.365	0.017	0.039	0.003

ETIOLOGY AND CLINICAL MANIFESTATIONS OF DOUBLE-LEVEL VERSUS SINGLE-LEVEL LUMBAR DEGENERATIVE SPONDYLOLISTHESIS

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Background: The differences in etiology, clinical manifestation, and whole body standing alignment between single-level LDS (sLDS) and double-level LDS (dLDS) have not been sufficiently clarified. We hypothesized that the etiology and manifestations of dLDS differ from those of sLDS. This study aimed to test this hypothesis.

Methods: A total of 112 cases with sLDS, 25 cases with dLDS, and 50 healthy volunteers as a normal control were enrolled in the study. Following the data collection on demographic and Health-related quality of life (HRQOL) by ODI and SRS-22, radiologic measurement by EOS system and MRI examination including lumbar spinal stenosis (LSS) were performed. All the parameters were compared among the groups. Correlations among radiologic parameters and HRQOL were analyzed. Risk factors for sLDS and dLDS were investigated respectively using multivariate logistic analysis.

Results: The alignment summary of the three groups are shown in Table 1. Age (cutoff >62y) is the most important etiologic factor of sLDS; whereas high PI (>57deg), age (>79y), and sagittally oriented facet joints (>22.8deg) are the important factors for dLDS. HRQOL significantly correlates with sagittal alignment. HRQOL does not, however, significantly differ between patients with sLDS and dLDS. Although the mean value of %slip was higher in the dLDS group than in the sLDS group, the difference was not statistically significant. %slip positively correlated with the PI. The number of spinal stenoses (LSS) per patient is significantly higher in patients with dLDS than in patients with sLDS. The HRQOL does not, however, correlate with the number of LSS.

Conclusions: Age is the most important etiologic factor of sLDS; whereas high PI, age, and sagittally oriented facet joints are the important factors for dLDS.

Table 1. Radiographic parameters

Parameters	Normal (50)		sLDS (112)		dLDS (25)	ANOVA p-value
	mean±SD (95% CI)	p-value	mean±SD (95% CI)	p-value	mean±SD (95% CI)	
		v.s. sLDS		v.s. dLDS		
SVA (cm)	1.2±2.7 (0.4/1.9)	0.0005 < 0.0001	3.7±4.3 (2.9/4.5)	0.0135	8.5±7.9 (5.2/11.7)	< 0.0001
TPA (°)	10.2±7.6 (8.0/12.4)	< 0.0001 < 0.0001	17.7±9.1 (16.0/19.4)	< 0.0001	32.7±15.2 (26.4/38.9)	< 0.0001
C2-7 lordosis (°)	2.2±9.9 (-0.6/5.0)	N.S. N.S.	5.8±12.4 (3.4/8.1)	N.S.	7.0±13.8 (1.1/12.8)	N.S.
TK (°)	44.3±9.9 (41.4/47.1)	N.S. N.S.	40.4±12.2 (38.1/42.7)	N.S.	35.4±18.3 (27.8/42.9)	0.0160
LL (°)	52.9±11.6 (49.6/56.2)	< 0.0001 0.0033	43.7±13.6 (41.1/46.2)	N.S.	37.2±20.9 (28.5/45.8)	< 0.0001
%slip	/	/	20.8±7.7 (19.4/22.3)	< 0.0001 (v.s. dLDS)	24.0±8.2 (20.7/27.4)	/
Pth (cm)	10.8±0.7 (10.6/11.0)	0.0003 N.S.	10.3±0.7 (10.2/10.4)	N.S.	10.4±1.0 (10.0/10.8)	0.0007
PI (°)	53.4±12.1 (50.0/56.8)	N.S. < 0.0001	54.9±8.2 (53.3/56.4)	< 0.0001	65.8±8.3 (62.4/69.3)	< 0.0001
PI-LL (°)	0.5±9.6 (-2.3/3.2)	< 0.0001 < 0.0001	11.2±13.3 (8.7/13.7)	0.0001	28.7±22.0 (19.6/37.8)	< 0.0001
SS (°)	39.8±8.8 (37.3/42.3)	0.0001 N.S.	35.0±7.4 (33.7/36.4)	N.S.	35.2±9.0 (31.5/38.9)	0.0020
PT (°)	13.6±7.7 (11.4/15.8)	< 0.0001 < 0.0001	19.8±7.7 (18.4/21.3)	< 0.0001	30.5±9.6 (26.5/34.5)	< 0.0001
Knee flexion (°)	0.4±4.1 (-0.8/1.6)	< 0.0001 0.0002	5.4±5.9 (4.3/6.5)	N.S.	7.9±7.2 (4.9/11.0)	< 0.0001

Normal: healthy volunteer group, sLDS: single-level spondylolisthesis group, dLDS: double-level spondylolisthesis group
Post-hoc test using Steel-Dwass analysis following ANOVA analysis was performed for all the parameters.

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The Effect of Scoliosis Support Orthosis Bracing on Adult Spinal Deformity Patients: Evaluation of Gait and Dynamic Balance

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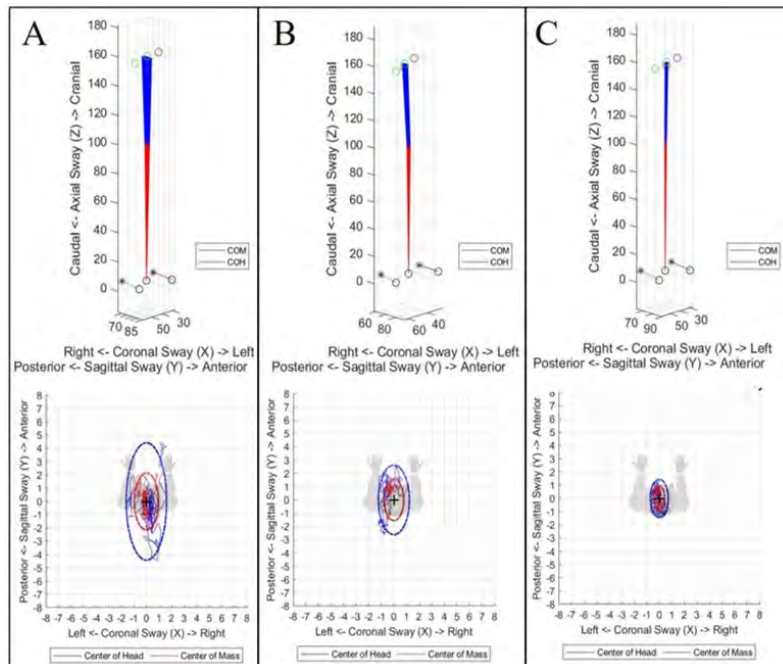
INTRODUCTION: Non-operative treatment is regarded as the first-line therapy for patients with adult spinal deformity (ASD) without neurologic deficits or significant impairment. While there is high-level evidence supporting the use of rigid bracing in adolescent idiopathic scoliosis, there is a paucity of literature pertaining to the use of scoliosis support orthosis (SSO) in ASD patients. Therefore, the purpose of this study was to investigate the impact of an SSO on pain, gait parameters, and functional balance measures in symptomatic ASD patients.

METHODS: This study was a non-randomized, prospective study. Thirty ASD patients (26 Females, Age: 72.7, Cobb Angle: 47.1°) were evaluated on 3 different occasions: first day of bracing: baseline (Pre), and 45-min post fitting (Post45m), and after 8-weeks of bracing for 4 hours a day (Post8w). Each patient performed a 6-minute walk (over-ground gait), a dynamic balance test, and completed VAS, ODI, and SRS22r.

RESULTS: A total of 30 patients were included in our analysis (26 Females, Age: 72.7±4.5 years, Height: 1.58±0.1 m, Weight: 67.7±16.1 kg, BMI: 26.9±5.2, Cobb Angle: 47.1±21.2°). Significant short- and long-term improvements using SSO were found in the 6-minute walk (Pre: 278.6; Post45m: 322.2; Post8w: 338.8 m, p<0.001), walking speed (Pre: 0.88; Post45m: 0.97; Post8w: 0.97 m/s, p<0.001), head total sway distance during the balance test (Pre: 81.33; Post45m: 68.63; Post8w: 60.72 cm, p=0.048), low-back pain (VAS: Pre: 5.5; Post45m: 3.5; Post8w: 3.3, p<0.001), and for the ODI (Pre: 41.9; Post45m: 32.9; Post8w: 30.1, p=0.005).

DISCUSSION: This study demonstrated clinically significant improvements in PROMs, spatiotemporal gait parameters and functional balance measures with the use of a SSO for patients with ASD. Some improvements were established immediately following brace fitting and many improvements were observed after wearing SSO for 8 weeks. In addition, this is the first SSO study for ASD to examine gait parameters and functional balance measures in order to understand the benefits of non-operative treatment from a functional and activity of daily living perspective. Based on the results of this study, it is reasonable to consider custom-fitted SSO as a treatment option to provide a measurable degree of pain relief and improvement of function for patients with ASD, if the goals of treatment match the measured benefits demonstrated in our paper. Future studies are warranted to investigate if the observed benefits can be maintained over longer periods, possibly with reduced wear times for patients with ASD.

Figure 1. Cone of Economy Measurements of Baseline (A), Post 45-Minutes (B), and Post 8-Weeks (C) Fitting of Scoliosis Support Orthosis Bracing



Hip extensor strength affects dynamic postural change on walking in the patients with adult spinal deformity; A three-dimensional motion analysis

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Introduction: In adult spinal deformity (ASD) patients, it has been reported that trunk and pelvic anteversion increases on walking. However, the precise dynamic mechanism remains to be clarified. The purpose of this study is to investigate what muscle strength can affect the dynamic postural change in walking in ASD patients.

Subjects and Methods: A total of thirty female subjects with ASD (Mean age, body height, weight, respectively; 72.8±8.2 years, 147.9±5.9 cm, 50.8±8.1 kg) were evaluated. Based on the SRS-Schwab classification, the ASD was defined as the following; 1) sagittal vertical axis (SVA) was 40 mm or more, 2) pelvic tilt (PT) was 20 degrees or more, 3) pelvic incidence minus lumbar lordosis (PI-LL) was more than 10 degrees. All the subjects complained of low back pain on walking. The subjects with a history of previous spinal surgery, neurological symptoms, and inability to walk independently were excluded. Trunk and hip extensor muscle strength were measured with a hand-held dynamometer. The spinal alignment was measured when standing and walking by using a 3D-motion analysis system (VICON with 8-cameras and 2-force plates). The sampling rate was 100 Hz. The sagittal alignment was represented as a sagittal trunk shift (STS), which was calculated as the difference of measured value between standing and walking. The STS is the distance between the C7-S1 markers in the sagittal plane, in millimeters. Univariable analysis was performed to examine the relationship between the x-p parameters (SVA, PT, PI-LL) and trunk/ hip extensor strength for Δ STS. Next, a multivariable analysis was conducted to examine the effects on Δ STS, using only items that showed a significant correlation. Significant correlations were defined as the items that met the requirement of a P-value of less than 0.05. The multivariable analysis was adjusted for confounding factors (age and BMI). P values less than 0.05 were considered statistically significant.

Results: Univariable analysis demonstrated that hip extensor strength was significantly correlated with Δ STS ($r_s = -0.40$). Multivariable analysis showed that reduced hip extensor strength was a factor that increased Δ STS ($\beta = -0.41$).

Conclusion: The current study demonstrated that hip extensor strength influenced dynamic postural change in patients with ASD. This implies that the hip joint can play an important role to control appropriate walking posture in patients with ASD. Although the trunk function should be the main target of rehabilitation programs in ASD, exercise for hip extensors may be a key to prevent abnormal walking posture with pelvic anteversion in patients with ASD.

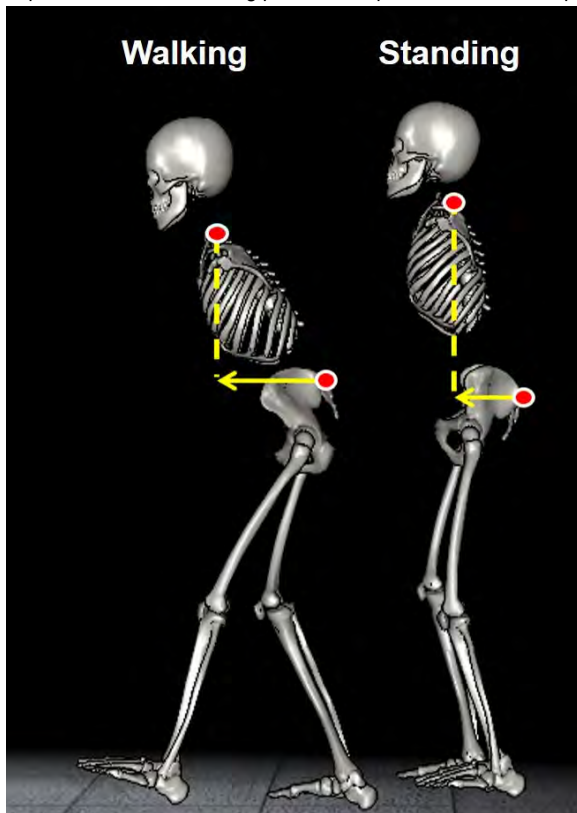


Figure 1: Sagittal trunk shift (STS) measurement

Radiographic and Clinical results using dual rod for adult spinal deformity surgery

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Introduction: Rod fractures are a major problem in adult spinal deformity (ASD) surgery. In our facility, rod fractures were observed in 14 of 28 cases (50%) who performed from the thoracic spine to sacral pelvic fixation between 2011 and 2015. Therefore, since 2015, spinal fusion using dual rod has been carried out.

Aim: The purpose of this study is to verify whether fusion using a dual rod is useful.

Materials and Methods: Forty-one patients with ASD were underwent spinal fusion from the thoracic vertebra to sacral pelvic between March 2011 and July 2018. There were 24 cases fixed with Simple rod (S group). There were 17 patients fixed with dual rod (DR group). Radiographic evaluation (Cobb angle, SVA, TK, TL, LL, PT, SS, PI) and clinical results (JOABPEQ, SRS22r) were measured before surgery, immediately after surgery, and 1 year after surgery in both group. Rod fracture rate was examined at postoperative one year.

Results: There was no significant difference of radiographic evaluation and clinical results between before and immediately after surgery. At postoperative 1 year, Significant differences were found in the Radiographic evaluation : TK (S / DR group = 30.3 / 38.5, p = 0.03), SS (S / DR group = 29.6 / 20.4, p = 0.00), PI (S / DR group = 52.6 / 43.8, p = 0.00). Significant differences were observed in SRS22r : pain (S / DR group = 3.2 / 4.1, p = 0.01), mental health (S / DR group = 3.0 / 3.8, p = 0.02), subtotal (S / DR group = 3.1 / 3.7, p = 0.02), total (S / DR group = 3.1 / 3.7, p = 0.02). Significant differences in JOABPEQ were pain relation (S / DR group = 53.8 / 84.6, p = 0.01), lumbar function (S / DR group = 31.9 / 54.0, p = 0.01), gait function (S / DR group = 34.7 / 54.7, p = 0.04), psychology (S / DR group = 43.6 / 58.1, p = 0.02), leg pain VAS (S / DR group = 43/16, p = 0.01) Numbness VAS (S / DR group = 34/9, p = 0.00). The rod breakage rate at 1 year after surgery was S group / DR group = 23.3 / 3.8%.

Conclusion: The rod breakage was reduced by using dual rod at postoperative one year. In the DR group, PI and SS in the DR group decreased .And further, lower back pain and numbness were alleviated, and pain-related and gait functions as well as psychological disorders were positively affected.

Correlation between Morphological Parameters of Vertebral Foramen and Aging

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INTRODUCTION: Trans foraminal approach for spinal surgery is getting popular in recent years. We sometimes resected superior articular process when diameter of endoscopic catheter was larger than vertebral foramen. In accordance with the spread of this approach, some surgeon fear of lumbar facet joint instability and morphological investigation about vertebral foramen was needed.

AIM: This study was conducted to present morphological features of the vertebral foramen and lumbar facet joint and indicate the safety and stability of facet joint after SAP (Superior Articular Process) resection. Furthermore, we researched morphological tendency of vertebral foramen when patients were getting older.

MATERIALS AND METHODS: From January 2016 to December 2018, eight hundred patients who were hospitalized in Anan Medical Center, Tokushima Municipal Hospital and Tokushima University Hospital (400 female and 400 male, average age was 58 yrs.) were included in this study. We measured several parameters from L1 to S1 on the reconstruction CT sagittal scans. Parameters that we evaluated were disc height, SAP facet contact (ratio of the contact distance between SAP and the total facet contact distance), SAP position (distance from the SAP's top to the underline of the upper vertebral body), foraminal distance (distance from the posterior border to the SAP's base), and foraminal area. In addition, we calculated the correlation between parameters and aging. SPSS soft-ware (version 22.0; IBM) was used for statistical analyses.

RESULTS: Disc height were tallest at L3/4 and L4/5. SAP facet contact was smallest at L4/5. SAP position was getting smaller from L1/2 to L3/4 and getting larger from L3/4 to L5/S. Foraminal distance had been decreasing trend and especially smallest at L4/5.

Foraminal area and SAP facet contact was smallest at L4/5. There was positive correlation between SAP position and aging. It meant that according to aging, SAP's top displaced to cranial side and it caused to foraminal stenosis. There was negative correlation between foraminal area and ageing, it suggested that aging was tend to come up foraminal stenosis. There was slightly negative correlation between SAP facet contact and aging. Comparing with younger patients, there was less risk that lumbar facet joint became instable by resecting SAP in elderly patients. On the other hand, aging was not high correlation between disc height and foraminal distance. Although we expected that as we aged intervertebral disc became degenerated and disc height was getting smaller, disc height didn't collapse by aging as we expected.

CONCLUSIONS: In this study, we found that SAP's top displaced to cranial side and foraminal area was getting smaller as patients were aging. These phenomena caused foraminal stenosis. SAP facet contact became smaller by aging and it meant that if SAP was resected in trans-foraminal surgery, stability of lumbar facet joint could be maintained in elderly patients.

Validity of the Global Alignment Proportion (GAP) Score in Predicting Mechanical Complications and Proximal Junctional Failure after Adult Spinal Deformity Surgery in Elderly Patients

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Introduction

Surgical correction, including multilevel fusion, is generally believed to be the only reasonable treatment option for patients with adult spinal deformity (ASD) who do not satisfactorily respond to conservative treatments and/or have a severe progressive deformity. Although the Scoliosis Research Society (SRS)-Schwab sagittal modifiers have been used as a guideline for ASD surgery, the cutoff value is set based on health-related quality of life (HR-QOL) measures, which was unclearly associated with mechanical failure. Global alignment and proportion (GAP) score is a concept that has recently been introduced and attracts much attention and predicts mechanical complications in patients undergoing surgery for ASD.

This study aimed to validate the usefulness of the global alignment proportion (GAP) score to predict postoperative mechanical failure in the elderly (mean age, 70.5 years) individuals with severe sagittal imbalance.

Methods

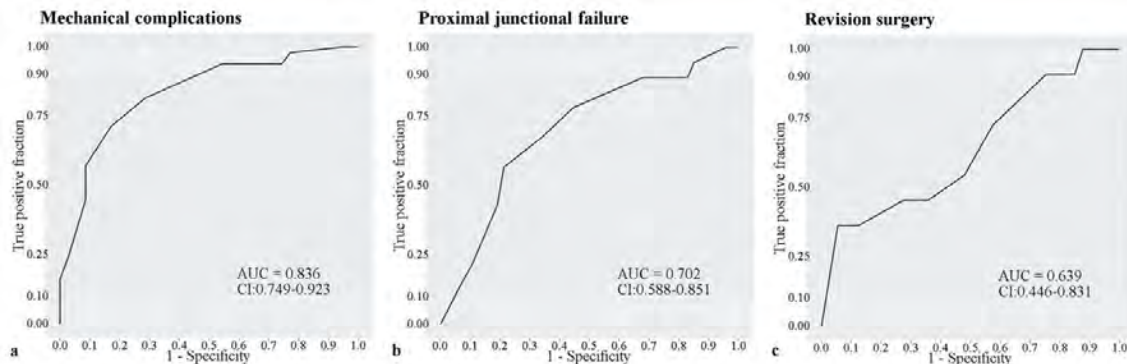
A total of 84 patients were enrolled and assigned to mechanical complications (n=49), proximal junctional failure (PJF; n=37), and revision surgery (n=11) groups. The GAP score was calculated using the X-ray obtained in the early postoperative period. The validity of the GAP score's predictive ability was evaluated by calculating the area under the curve (AUC) of the receiver operating characteristics (ROC) curve. Univariate logistic regression analysis and Cochran–Armitage test of trend were performed to determine the association between mechanical failure and GAP score.

Results

The discriminatory power of GAP score to predict mechanical complications and PJF were “moderately accurate,” with an AUC of 0.836 (confidence interval [CI]: 0.749–0.923, $p < 0.001$) and 0.702 (CI: 0.588–0.851, $p < 0.001$), respectively, in the ROC curve (Figure). The discriminatory power to predict revision surgery was “less accurate” with an AUC of 0.639 (CI: 0.446–0.831, $p < 0.001$). The GAP score showed a statistically significant association with mechanical complications and PJF in univariate logistic regression analysis and Cochran–Armitage test for trend. However, it was not significantly associated with revision surgery.

Discussion

The present study showed the favorable validity of the GAP score's prediction power for mechanical complications and even the PJF in the elderly population. Therefore, the GAP score could be used to determine the patient's specific correction goal preoperatively to prevent mechanical failure based on an individual patient's characteristics such as pelvic incidence.



The comparison of clinical and radiological parameters between degenerative scoliosis patients between with and without vertebral rotatory subluxation

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Introduction: Vertebral rotatory subluxation (VRS) frequently found in degenerative lumbar scoliosis patients. However, there have been a paucity literatures regarding VRS in degenerative lumbar scoliosis patients. We evaluated the relationship between the presence of VRS and the clinical and radiological parameters in degenerative lumbar scoliosis patients.

Methods: We prospectively recruited 45 consecutive patients who had *de novo* degenerative lumbar scoliosis ($>10^\circ$). Patients were divided into VRS group (n=26) and non-VRS group (n=19) depending on the presence of VRS ($>5\text{mm}$ lateral listhesis with rotation on computed tomography). Radiological parameters include coronal measurements (coronal C7 plumb line, Cobb angle of lumbar curve, pelvic obliquity, and length of subluxation), sagittal measurements (sagittal C7 plumb line, SVA; thoracic kyphosis, TK; lumbar lordosis, LL; sacral slope, SS; pelvic incidence, PI; pelvic tilt, PT), rotational measurements (apical axial vertebral rotation, AVR; axial intervertebral rotation, AIR; torsion index, TI), and facet-joint-related-measurements (count of facet joints with osteoarthritis $>$ grade 2, FOA). Clinical parameters include back and leg visual analogue scale (VAS), short-form 36 physical and mental component summary (SF36; PCS and MCS), and Oswestry disability index (ODI). Two groups were compared.

Results: Mean length of lateral listhesis in VRS group was $7.6\pm 1.8\text{mm}$ (Range: 5.1 - 11.4mm). Between VRS group and non VRS group, there was no difference of gender (male gender, 30.8% vs. 10.5%), age (69.1 ± 9.6 years vs. 70.1 ± 9.6 years), and count of involved vertebrae in scoliosis curve (5.7 ± 1.4 vs. 6.0 ± 1.3). VRS group had larger Cobb angle ($22.4\pm 10.2^\circ$ vs. $15.1\pm 15.4^\circ$). There was no significant differences in sagittal measurements between groups. Apex AVR ($9.4\pm 4.9^\circ$ vs. $4.4\pm 2.7^\circ$), AIR ($5.1\pm 2.5^\circ$ vs. $2.6\pm 2.0^\circ$), maximal AIR ($7.7\pm 3.0^\circ$ vs. $4.7\pm 1.6^\circ$), upper ($7.3\pm 4.3^\circ$ vs. $2.9\pm 2.1^\circ$) and lower AIR ($8.1\pm 4.7^\circ$ vs. $4.4\pm 2.8^\circ$), and TI ($15.3\pm 8.1^\circ$ vs. $7.3\pm 3.7^\circ$) were significantly different between groups (All $P<0.05$). FOA were greater in VRS group (4.6 ± 2.7 vs. 3.4 ± 2.8). However, it was not significant ($P=0.16$). There was no difference in clinical parameters between groups.

Discussion: Patient with VRS had the larger coronal curve and rotational deformity. However, there was no significant difference in sagittal parameters and clinical parameters between VRS and non-VRS groups. VRS may be compensatory mechanism in large degenerative lumbar scoliosis, rather than spinal pathology needing treatment.

Junctional Kyphosis/Failure after Long Instrumentation for Posttraumatic Thoracolumbar Kyphosis: Characteristics and Risk Factors

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Introduction: Junctional kyphosis/failure have become an important concern after long spinal fusion surgery for adult deformities, while there is a paucity of data on such an issue after long segmental correction for posttraumatic thoracolumbar kyphosis. So the purpose of this study was to investigate the characteristics and risk factors for junctional kyphosis and/or failure after long segment correction for posttraumatic thoracolumbar kyphosis.

Methods: This study recruited a total of 58 patients with posttraumatic thoracolumbar kyphosis who had undergone posterior long segmental correction and had been followed up for at least 1 year. Based on the follow-up results, these patients were divided into those with junctional kyphosis and/or failure (Group J) and those without junctional kyphosis and/or failure (Group NJ). Patients in group J were then subdivided into junctional kyphosis subgroup (Group JK) and junctional failure subgroup (Group JF). Occurrence timing, symptoms of junctional disorders and treatment were recorded. Radiological assessments included pelvic parameters, sagittal balance, bone quality on CT axial scans, and measurements of the cross-sectional area (CSA) and the fat saturation fraction (FSF) of the paraspinal muscles (multifidus and erector spinalis). The CSA of paraspinal muscles and the FSF of paraspinal muscles were measured on axial T2-weighted MR images. Comparison analyses were performed to test differences between groups and regression was carried out to identify risk factors of junctional kyphosis/failure.

Results: After a mean follow-up of 14.6 months, junctional kyphosis or failure were detected in 16 cases (Group J; incidence, 23.9%), including proximal junctional kyphosis in 11, proximal junctional failure in 2, and distal junctional failure in 3 cases. Eleven of them (68.8%) occurred within 6 months after the primary surgery. Only 5 patients in Group J showed clinical symptoms associated with junctional problems and one of them underwent revision surgery because of distal failure and cauda equine syndrome. Compared with the Group NJ, patients in Group J had older age (64.0 vs. 53.0, $p=0.001$), lower bone quality on CT (HU: 102.4 vs. 159.0, $p<0.001$), larger TK before surgery (46.8° vs. 27.8° , $p<0.001$) and larger TK correction (22.4° vs. 6.7° , $p<0.001$), larger CSA (188.3 vs. 208.8, $p<0.001$) and higher FSF (51.5 vs. 40.1, $p=0.003$) of paraspinal muscles. Patients in group JF has significantly lower bone quality than patients in group JK (CT values: 89.3 ± 4.5 vs 102.8 ± 5.3 , $P<0.05$). Logistic regression analysis revealed that the preoperative TK $>39.7^\circ$ ($p=0.001$, odds ratio 1.113) and the FSF of paraspinal muscles >47.3 ($p=0.018$, odds ratio 1.182) were independent risk factors of junctional kyphosis/failure.

Conclusion: Larger preoperative TK and higher fatty infiltration of paraspinal muscles might be involved in the occurrence of junctional disorders after long segmental instrumented correction for posttraumatic thoracolumbar kyphosis. Patients with lower bone quality were more likely to develop into junctional failure.

Surgical management of sagittal imbalance in adult degenerative thoracolumbar kyphoscoliosis: preoperative planning using computed tomography in the supine position

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INTRODUCTION: Sagittal imbalance in severe adult degenerative lumbar kyphoscoliosis (DLKS) requires surgical correction to relieve pain and improve mobility and quality of life. Surgical correction of severe and rigid sagittal imbalance in DLKS requires surgical techniques such as pedicle subtraction osteotomy (PSO) and posterior vertebral column resection (VCR). However, if the preoperative diagnosis is flexible-type DLKS, PSO, and VCR are not required. In this study, we assessed the utility of preoperative computed tomography (CT) in the supine position for surgical planning.

METHODS: Surgery was performed in 10 patients with painful compensated DLKS (mean sagittal vertical axis [SVA] 120 mm, mean pelvic incidence – lumbar lordosis [PI-LL] 46°). Mean age at surgery was 77.5 (range 73–82) years and mean follow-up duration was 12.9 (6–25) months. All patients were female. PI, LL, and SVA were measured on standing lateral radiographs and LL on CT (CTLL) was measured in the supine position. Surgical outcomes were evaluated using Japanese Orthopedic Association (JOA) and visual analog scale (VAS) scores. If we expected that DLKS may be compensated on preoperative CT in the supine position, we performed grade 2 posterior osteotomy and posterior lumbar interbody fusion at L4/5, L5/S1, and T10–S2 with posterior fixation (as in adolescent idiopathic scoliosis) for patients with kyphosis (K group). We performed 2-stage surgery, comprising 3-level oblique lumbar interbody fusion and posterior fixation 1 week later for patients with scoliosis (S group).

RESULTS: Mean operating time was 452.8 (range 334–610) min and mean intraoperative blood loss was 590.0 (230–1120) mL. Mean SVA, PI-LL, LL, and CTLL values changed from 125.6 mm, 43.9°, 5.7°, and 25.4°, respectively, before surgery to 38.1 mm, 15.8°, 34.1°, and 37.3° postoperatively. Only operating time was significantly different between the K and S groups. Mean JOA and VAS scores improved from 19.5 (18–22) and 3.0 (1–4), respectively, before surgery to 7.8 (range 4–8) and 7.6 (range 5–9) at final follow-up.

DISCUSSION: Flexible DLKS could be identified using preoperative CT in the supine position. Multiple grade 2 posterior osteotomy and posterior lumbar interbody fusion at L4/5 and L5/S1 can improve sagittal plane correction with a target PI-LL of 10°–20°. Preoperative CT in the supine position was useful for evaluation and calculation of optimal LL.

1. Surgical Outcomes of Multilevel Posterior Lumbar Interbody Fusion versus Lateral Lumbar Interbody Fusion for the Correction of Adult Spinal Deformity: A Comparative Clinical Study Masayoshi Iwamae,1 Akira Matsumura,1 Takashi Namikawa,1 Minoru Kato,1 Yusuke Hori,2 Akito Yabu,2 Yuta Sawada,3 Noriaki Hidaka,1 and Hiroaki Nakamura2 Asian Spine J. 2020 Aug; 14(4): 421–429.

Different disc characteristics between young elite skiers with diverse training histories revealed with a novel quantitative magnetic resonance imaging method

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INTRODUCTION

Skiing is a high-risk sport¹. Not only spinal traumas but also the repetitive loading might damage the spinal tissues². The incidence of spinal abnormalities has been reported to be significant already at a young age^{3,4}. This might be an effect of the increased level of competition and higher doses of training without long rest in-between. Also, the specialization in one singular sport with concomitant limitation in training-variability may increase the risk of overuse injuries.

Back pain is a common complaint in athletes^{5,6}, especially after training progression⁶. However, an association between pain and radiological findings has not been fully established in all sports. This may be due to the fact that most studies are based on plain radiographs or on conventional MRI. Such methods lack objective markers that can detect changes in detail on a continuous scale.

New methods, which rely on MRI and on advanced image analysis, have recently been proposed for quantitative assessment of disc characteristics^{7,8}. The methods have been shown to detect not only global but also detailed characteristics associated to annular fissuring and remodeling of the nucleus pulposus in chronic low back pain patients. The methods may also have the feasibility to detect subtle disc changes in athletes related to training histories.

The aim was to evaluate if there are differences in thoraco-lumbar disc characteristics between elite skiers and non-athletic controls as well as between different types of elite skiers, with diverse training histories, using a novel quantitative MRI method.

METHODS

The thoraco-lumbar spine of 58 elite skiers (age=18.2±1.1years, 30males) and 26 non-athletic controls (age=16.4±0.6years, 9males) was examined using T2-weighted MRI. Disc characteristics were compared quantitatively between groups using histogram and regional image analyses to determine delta peak and T2-values in five subregions.

RESULTS

A statistical difference in the delta peak value was found between skiers and controls (p<0.001, Figure), reflecting higher degree of disc degeneration. The histogram analysis also revealed that the type of training determines where and to what extent the changes occur. Alpine skiers displayed lumbar changes, while mogul skiers displayed changes also in the thoracic spine. Alpine skiers with diverse training dose differed in delta peak value (p=0.005), where skiers with highest training dose displayed less changes. Regional T2-value differences were found in skiers with divergent training histories (p<0.05, Figure), reflecting differences in disc degeneration patterns, foremost within the dorsal annulus.

DISCUSSION

Differences in quantitative disc characteristics were found not only between elite skiers and non-athletic controls but also between subgroups of elite skiers with diverse training histories. The differences in the disc markers, reflecting tissue degeneration, are likely related to type and intensity of the physical training. Future studies are encouraged to explore the relation between disc functionality, training history and pain to establish adequate prevention and rehabilitation programs for prevention of future spinal injuries.

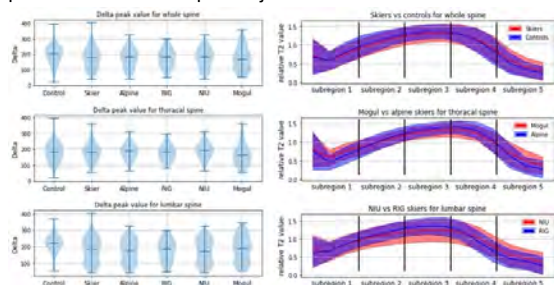


Figure. Delta peak values displayed as a violin plots for different skier groups (left). Regional distribution of T2-values for subregion 1 (anterior) to 5 (posterior), represented as overlapping patches with height representing mean T2-value±1SD.

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Deep learning based fully automated pathology classification of lumbar spine

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Introduction:

The analysis of lumbar MRI lacks a fast and consistent method. Manual analyses conducted by the surgeon based on their judgment and experience are subjective. Thus, we aim to develop a deep learning based method for the automated systematic analysis of lumbar MRI.

Methods:

The dataset based on the southern Chinese population contained MRI series from 2473 subjects (mean age 45.2; 39.5% male), with multiple lumbar degenerative features labelled by a spine specialist including Schmorl's nodes, high intensity zones (HIZs), Spondylolisthesis, and Marrow changes. Our deep learning model adopted the basic architecture of GoogLeNet, a state of art network for the classification of natural images, and several modifications were introduced to better process MRIs. A 5-fold cross-validation was conducted to assess the performance of the method. The model was trained to simultaneously produce the auto-analysis of these radiological features. The prediction difference analysis method was applied for the interpretation of the deep learning model, which could visualize the significant features and regions for the auto-assessment of each specific pathology.

Results:

Preliminary results showed that the model achieved satisfactory performances on the detections of: Schmorl's nodes (Accuracy: 87.4% \pm 2.9%), HIZ (Accuracy: 85.3% \pm 1.7%), Spondylolisthesis (Accuracy: 86.8% \pm 1.3%), and Marrow change (Accuracy: 88.9% \pm 2.0%).

Discussion:

A deep learning network for fully automated pathology assessment of LDD is implemented and tested. The visualization of the features can assist clinicians in interpreting the auto-diagnosis process. The preliminary results show that our model can achieve good performance on the assessment of multiple pathologies without relying on any human intervention. A prospective clinical study needs to be performed to further validate our model.

Effect of Pelvic Retroversion on Lumbopelvic Geometry and Muscle Morphometry from Upright MRI

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INTRODUCTION: In adult spinal deformity patients with positive sagittal imbalance, pelvic retroversion is typically an initial compensatory step. Consequently, there is interest to better understand the underlying mechanisms in such compensatory changes. First however, groundwork in studying both the lumbopelvic musculature and geometry synchronously in upright and retroverted postures in asymptomatic individuals would help confirm repeatability of image segmentation and feasibility before moving to patients. Therefore, the aim of this study was to assess the effect of pelvic retroversion on lumbopelvic musculature and geometry in asymptomatic adults using upright magnetic resonance imaging (MRI).

METHODS: Six healthy volunteers were imaged in a 0.5T upright MRI (MROpen, Paramed) using T1-weighted Spin Echo sequences (TR/TE=323/10//586/12ms, FOV 24/40cm, scan matrix 224*160, slice thickness 10/7mm, gap 1/7mm, NEX=1, time 139/114s). Each volunteer was scanned in 4 postures: standing, standing pelvic retroversion, standing 30° flexion, and supine. A sagittal stack including the sacral endplate and femoral head enabled geometric measurements (pelvic tilt (PT), pelvic incidence (PI), sacral slope (SS), L3-S1 lumbar lordosis (LL)). An oblique stack aligned to the sacral endplate, L5/S1-S4/S5, enabled musculature measurements (muscle cross-sectional area (CSA), circularity, radius, angle) for the gluteus (maximus, medius, minimus combined) and iliopsoas (iliacus, psoas major at L5/S1). The effect of posture and level on muscle morphometry and geometry was evaluated by ANOVA ($p < 0.05$) and correlations between muscle and geometric parameters were analyzed using Pearson's correlation coefficient ($p < 0.05$). Four volunteers repeated select postures, and repeatability was assessed with three raters using intraclass correlation coefficient (ICC(3,1)).

RESULTS: Posture and level had a significant effect and interaction on the gluteus (CSA, circularity, radius, angle). For example, generally CSA/circularity decreased from supine to standing and CSA/circularity increased from standing/standing flexion to retroversion (up to 22%)(Fig.1). Posture and level also significantly affected the iliopsoas (angle), with some significant interactions (circularity, radius). For example, at S1/S2, angle/radius increased from supine to standing and from standing/standing flexion to retroversion (up to 16%). Posture also affected PT, SS, and LL, but not PI. For example, average PT increased 6° from supine to standing and 7° from standing to retroversion. Muscle CSA/circularity also had significant correlation with PT, SS and LL at specific levels. For muscle CSA, posture repeatability in 3 rescanned volunteers was 0.86-0.97, intra-rater repeatability was 0.76-0.98, and inter-rater repeatability was 0.54-0.96. For pelvic geometry, posture repeatability was 0.94-0.99, intra-rater repeatability was 0.95-0.99, and inter-rater repeatability was 0.79-0.94. Across postures, PI repeatability was 0.85-0.92.

DISCUSSION: The effects, interactions, and correlations of posture and level with lumbopelvic muscles and geometry notably between standing to retroversion, with increases in CSA and circularity, confirms some expected trends such as muscle narrowing with elongation. This may be reflecting both passive and active muscle changes to achieve this retrovert posture as previous studies have shown gluteus maximus activation with pelvic tilt through electromyographic measures. Furthermore, the promising repeatability supports feasibility of imaging both musculature and geometry in upright postures in tandem and is critical groundwork for future adult spinal deformity patients imaging.

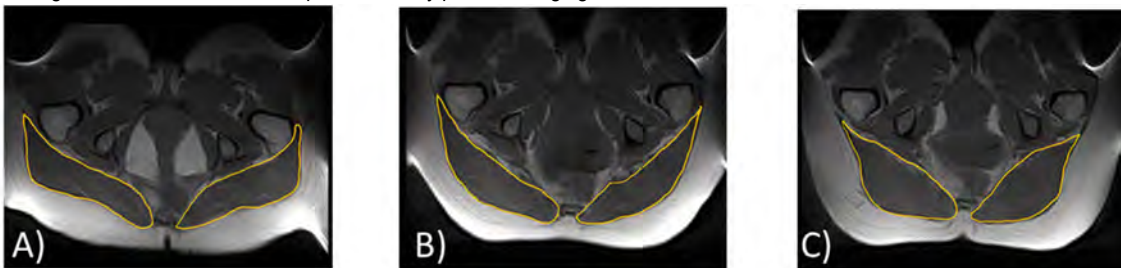


Fig.1: Gluteus A)supine, B)standing, C)retroversion

Investigation of Thoracic Muscle Morphology with Open Upright MRI

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Introduction: MRI-derived spinal-muscle morphology measurements have potential diagnostic, prognostic, and therapeutic applications in spinal health. While the focus to date has been on cervical and lumbar regions, recent findings have associated kyphosis severity with smaller paraspinal musculature in the thoracic spine [1]. Moreover, most imaging studies are carried out in supine; a posture that does not replicate subjects' clinical symptoms. Hence, there is a need to investigate thoracic musculature in upright weight-bearing postures as they likely relate to paraspinal muscle health in other regions.

Objectives: (i) To quantify muscle geometric parameters—cross-sectional area (CSA) and position (radius and angle with respect to the vertebral body center) in supine and upright postures. (ii) To study the effect of spinal level and posture on these parameters.

Materials and Methods: Six healthy participants (age 26±6 years) were imaged (0.5T vertical MROpen, Paramed Italy) at two thoracic regions (T4-T5 and T8-T9) in four postures (supine, standing, 30° forward flexion, sitting). Three muscle—erector spinae (ES), transversospinalis (TS), and trapezius (TZ) were manually segmented on axial MR images. Intra- and inter-rater segmentation repeatability was found to be good/excellent. Muscle geometric parameters, CSA, radius, and angle were computed for each muscle (averaged for right and left side). The effects of spinal level and posture on these muscle parameters were evaluated using 2-way repeated measures ANOVA ($p < 0.05$) for the two thoracic regions separately.

Results: Spinal level and posture showed significant effects on muscle morphology and position. Trapezius CSA decreased (40%, $p = 0.0027$) from level T8 to T9. The erector spinae CSA increased from T4 to T5 (12%, $p = 0.0048$) and from T8 to T9 (10%, $p = 0.0018$). Transversospinalis CSA showed opposite trends at the two spinal regions with a decrease (16%, $p = 0.0047$) from T4 to T5 and an increase (11%, $p = 0.0009$) from T8 to T9. At T4-T5, the trapezius CSA increased (up to 23%), and the erector spinae and transversospinalis CSA decreased (up to 10%) in upright postures compared to supine (Fig 1).

Conclusion: The magnitude of muscle data were in good consensus with supine-imaging literature. The spinal-level specific trends align with anatomical descriptions. The increase in trapezius CSA in upright postures could result from greater activation of the muscle. The decrease in CSA of all muscles from neutral to flexed posture represents passive stretching of the muscle. Our data have implications for making clinical comparisons and in the development and validation of spine biomechanical models.

Acknowledgments: We thank NSERC, CIHR, and Medtronic Canada for funding.

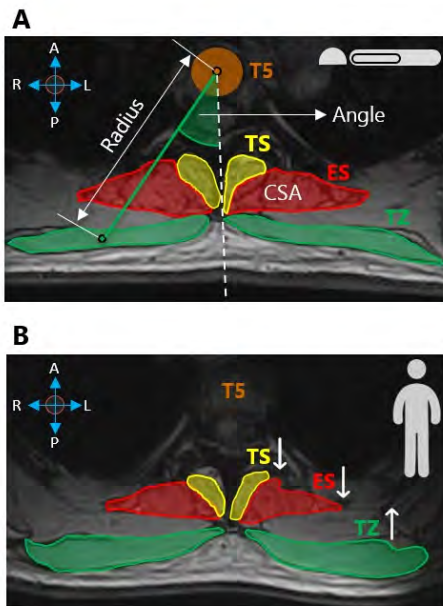


Fig 1. Illustration showing change in muscle CSA and position at T5 in A) supine. B) Upright standing.

[1] A. L. Lorbergs et al., "A Longitudinal Study of Trunk Muscle Properties and Severity of Thoracic Kyphosis in Women and Men: The Framingham Study," *Journals Gerontol. Ser. A*, vol. 74, no. 3, pp. 420–428, 2018.

Morphological Analysis of Paraspinal Muscles Using Magnetic Resonance Imaging and a novel software to Diagnose Sarcopenia

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Introduction: Sarcopenia is defined as age associated loss of skeletal muscle mass and function. There is a scarcity of literature in assessing the Sarcopenia of lumbar paraspinal muscle and its association with age in Indian population. Our aim was to determine the age and sex dependent lumbar paraspinal muscle morphology in Indian population.

Materials And Methods: The objectives of this study were To calculate the mean of morphological variables such as Total Cross Sectional Area (TCSA), Relative Cross Sectional Area (RCSA), Functional Cross Sectional Area (FCSA), Percentage of Fat Infiltration(FI%) and their asymmetry between right and left side in multifidus , erector spinae and psoas major muscle in different sex and age group of Indian population using MRI. To identify the normal trend of lumbar paraspinal muscle degeneration due to ageing. To find the association between BMI and FI% of paraspinal muscles. Study population was divided into six groups based on age.

Results:

Total number of samples included in the study was 210, (98 females and 112 males), with a mean age of 38.8±15.04 years. The mean height was 162±8.14 cm and mean weight of 65.85±11.17kgs with a mean BMI of 25±3.82. Statistically significant asymmetry was found between Left and Right side of TCSA of psoas muscle (P=0.022), FCSA of psoas muscle (p=0.001), TCSA of erector spinae (p=0.014), FCSA of Multifidus (p=0.001). However FCSA of erector spinae and TCSA of Multifidus did not show significant asymmetry between the Left and Right side (p=0.072 and p=0.983 respectively). On considering the Fat Infiltration Percentage Psoas and Multifidus muscle showed statistically significant asymmetry(p=0.006 and p=0.001 respectively) unlike Erector spinae (p=0.341). Psoas muscle Total Cross Sectional Area, Functional Cross Sectional Area, and Fat Infiltration Percentage showed statistically significant correlation (p=0.020,p=0.008, and p=0.016 respectively) with BMI. Erector spinae had the larger TCSA followed by Psoas and the Multifidus had the least TCSA in all age group. TCSA of Erector spinae had increasing trend in early decades and had decreasing trend in the late decades of life. However TCSA of Psoas and Multifidus did not showed significant trend. The Multifidus muscle degenerated significantly at higher rate, than the erector spinae muscle. Psoas degenerated at lower rate on comparing to other paraspinal muscles.

Conclusion: Digital analysis of MRI images with ImageJ software serves as an ideal tool to investigate morphological feature of paraspinal muscle. Normative value of paraspinal muscle morphology will be useful to investigate other spinal pathologies. Paraspinal muscle degenerates more qualitatively rather than quantitatively. Females had higher degeneration rate than males. Although there was an asymmetry between paraspinal muscle morphology, the difference is less. Thus we have to be cautious while considering asymmetry in spinal musculature as a cause of spinal pathology. Like osteoporosis, sarcopenia of paraspinal muscle will determine the late life disability. MRI could be used as a reliable stand alone investigation tool to assess Sarcopenia and related disorders.

GP153

Trunk muscle analysis using dual-energy X-ray absorptiometry and magnetic resonance imaging

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Introduction

Limb muscle mass measured by dual-energy X-ray absorptiometry (DXA) is widely used for sarcopenia screening. On the contrary, trunk lean mass measured by DXA cannot accurately separate the actual amount of trunk muscle mass from the internal organs. Therefore it remains unclear as to whether trunk lean mass measured by DXA reflects actual trunk muscle mass. In general, trunk muscle mass is estimated from its cross-sectional area (CSA) in magnetic resonance imaging (MRI) or computed tomography (CT), and its efficacy has been shown in previous studies. The aim of this study is to investigate the correlation between DXA measurement of trunk muscle mass and the CSA of trunk muscles measured by MRI in healthy volunteers.

Methods

Forty healthy volunteers participated in our study after providing informed consent. They were 20 male and 20 female with a mean age of 48.1 ± 11.5 years. The correlation between DXA measurement and the CSA of psoas muscle and back muscles (erector spinae and multifidus) at the L3 axial level, gluteus maximus at the center of femoral head axial level and trunk muscles were calculated by gender. The sum of the CSA of back muscles, psoas muscle and gluteus maximus was calculated and defined as the CSA of trunk muscles. Pearson correlation coefficient was used for statistical analysis with $P < 0.05$ considered to indicate statistical significance.

Results

Trunk lean mass (g) measured with DXA was 23475 ± 2841 for men and 17551 ± 2202 for women. CSA (mm^2) of psoas muscle, back muscles, gluteus maximus and trunk muscles were 2213 ± 412 , 5072 ± 687 , 9922 ± 1229 and 17208 ± 1897 for men, and 1114 ± 264 , 3595 ± 568 , 7740 ± 1356 and 12450 ± 1985 for women. The correlation coefficient between DXA trunk muscle mass measurement and CSA of each musculature (psoas muscle, back muscles, gluteus maximus and trunk muscles) were 0.13 ($P=0.2939$), 0.66 ($P < 0.05$), 0.86 ($P < 0.05$) and 0.83 ($P < 0.05$) for men and 0.81 ($P < 0.05$), 0.63 ($P < 0.05$), 0.82 ($P < 0.05$) and 0.88 ($P < 0.05$) for women, respectively. DXA measurement and the CSA of back muscles, gluteus maximus and trunk muscles were significantly correlated in both men and women.

Discussion

Regardless of gender, trunk lean mass measured by DXA was significantly correlated with the CSA of back muscles, gluteus maximus and trunk muscles in MRI. These data suggested that trunk lean mass measured by DXA was potentially effective for measuring trunk muscle mass. DXA is relatively low cost compared with MRI or CT, and with minimal radiation exposure ($< 1 \mu\text{Sv}$ for whole-body scans) as well. It may become the reference standard for measuring trunk muscle mass as well as limb muscle mass.

MRI-SegFlow V2.0: a novel unsupervised deep learning pipeline enabling accurate semantic segmentation of lumbar MR images with preliminary validation

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Introduction:

Segmentation is an essential part of many lumbar MRI automated analysis tasks, such as pathology detection and spinal 3D reconstruction for further mechanical simulations or 3D printing. Most deep learning based MRI segmentation methods require manual labelling tasks, which are normally laborious and time consuming. Besides, when transferring a well-trained deep learning model to the MRI with different image features and quality, new labels are still required for finetuning the model, which makes conventional deep learning based methods very expensive. In our previous work, we have developed an unsupervised deep learning based pipeline, called MRI-SegFlow, for the segmentation of the vertebral body in the sagittal lumbar MRI. We aim to improve our existing work and propose MRI-SegFlow V2.0 for the segmentation of multiple spinal tissues. The quantitative validation is also conducted to evaluate the performance of our method.

Methods:

The dataset used for the evaluation of our method contained 50 sagittal lumbar MRI series, each of them had 17 slices (totally 850 images), with masks of multiple spinal tissues labeled by 4 spine specialists as the ground truth (GT). The spinal tissues included the vertebrae, intervertebral discs, and neural tissue. The rule-based method of the original MRI-SegFlow was improved to generate suboptimal region of interests (ROIs) for multiple spinal tissues simultaneously, and then the ROIs were integrated through a voting mechanism to provide supervision in the training process of a deep learning model, which would generate the final optimal segmentation results. The Dice Coefficient and Intersection-over-Union (IoU) were used for the evaluation of the segmentation performance against the GT, which indicated the similarity (position similarity and shape similarity) between model segmentation results and manually masked ground truth.

Results:

We achieved high segmentation accuracy on the vertebral body (Dice Coefficient: 0.904 ± 0.009 , IoU: 0.834 ± 0.029), intervertebral disc (Dice Coefficient: 0.939 ± 0.035 , IoU: 0.899 ± 0.022), and neural tissue (Dice Coefficient: 0.903 ± 0.069 , IoU: 0.814 ± 0.079).

Discussion:

We advanced our unsupervised deep learning pipeline, which can produce accurate segmentation results for multiple spinal tissues in sagittal MRIs of the lumbar spine without relying on any manual labelling process.

Fusion pattern analysis of posterior lumbar interbody fusion using CT scan multi-planer reconstruction images: difference between L5/S1 level and the other levels

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Introduction

Previous studies have revealed some important CT scan findings such as endplate cyst formation, cage subsidence, trabeculated bone formation in anterior, posterior and lateral zones of cage after posterior lumbar interbody fusion (PLIF). It is well known that L5/S1 level has unique and different anatomical characteristics in comparison with other lumbar levels. However, fusion pattern difference between L5/S1 and the other levels have not been reported previously. In this study, we evaluated postoperative CT multi-planer images to reveal the fusion progression pattern of L5/S1 and the other lumbar levels in patients who underwent PLIF.

Methods

A total 61 consecutive patients with 77 treated levels underwent PLIF in a single institution (30 men, 31 women, age 31-83 years old, average 64 years old). Levels above L4/5 (L group: 47 levels) and L5/S1 (5S group: 30 levels) were assessed and compared by CT scans taken at 3 months, 6 months, 12 months and 24 months postoperatively. Reconstructed sagittal two slices which include left and right cages, and a coronal slice were assessed. Bone formation inside cages, anterior/posterior/lateral zones of intervertebral disc space, anterior/posterior/lateral disc marginal zones were evaluated and bone continuity observed more than two parts was considered fusion. Endplate cysts, cage subsidence, screw loosening were also evaluated. Chi-square test was used for statistical analysis, and $p < 0.05$ was considered statistically significant.

Results

Fusion rate was 84% overall, and 83.0% in L group, 87% in 5S group ($p=0.xx$). Fused after 12 months in 35% of L group and 27% of 5S group. Bridging bone formation in disc marginal zones were observed in 43% of L group and 61% of 5S group. Endplate cysts, cage subsidence and screw loosening were observed 26%, 60%, 23% in L group and 27%, 73%, 17% of 5S group, respectively. Fusion despite screw loosening or endplate cysts were observed in 13%, 18% of L group and 7%, 10% of 5S group. There were not any statistical significance in any evaluated items between two groups. There were three reoperation cases, and non-union was the reason for re-op in only one case.

Discussion

There was not any difference of fusion progression pattern between L5/S1 and the other lumbar levels in patients who underwent PLIF. The lower fusion rate compared to the previous study might be due to severer criteria for fusion. Fusion despite endplate cyst formation, cage subsidence or screw loosening were not uncommon, so long-term follow up with CT scans until fusion is encouraged.

A Comprehensive MRI Analysis of Paraspinal and Psoas Muscle Size, Lean Muscle, and Fatty Infiltration in Patients undergoing Lumbar Spinal Fusion

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Introduction: The paraspinal muscles have an important stabilizing function. Atrophy and fatty infiltration of these muscles have been associated with increased age and various spinal pathologies. Comprehensive data of lumbar paraspinal muscle size/fatty infiltration in patients undergoing spine surgery is limited. The objective of this study was to 1) assess the reliability of a manual segmentation protocol to measure paraspinal muscle size/fatty infiltration, 2) determine possible variation in muscle measurements throughout the lumbar spine 3) assess the correlation between percentage of fat-free muscle of the levels L1-S1.

Methods: Patients undergoing posterior fusion with available preoperative lumbar MRI were included. Muscle measurements were performed at the inferior L1 endplate, superior/inferior L2-5 and the superior S1 endplate (Figure1). Using a free software program, we manually defined the following 4 regions of interest per slice on T2-weighted axial images: left/right psoas, and left/right posterior muscles (combined erector spinae/multifidus) (Figure2). Muscle measurements included the total cross-sectional area (CSA), percentage of fat-free muscle and the functional cross-sectional area (FCSA) (area of muscle isolated from fat). The FCSA was calculated with a custom written Matlab™ program, which identified pixels as either muscle or fat by selecting an automatic threshold signal following intensity bias correction by quadratic fitting (Figure3). Pixel values below the threshold were classified as muscle and pixels above as fat. To assess inter-observer reliability of the manual segmentation, a validation study was performed. Pairwise comparison of CSA/percentage of fat-free muscle was conducted and correlations between each level/location were evaluated.

Results: The study population consisted of 21 men and 29 women (86% Caucasian). The mean age was 62 years and the mean BMI was 30.2 kg/m². The inter-rater reliability for the measurement of the CSA and the FCSA was excellent (ICC of 0.975 and 0.961, respectively). Overall, the percentage of fat-free muscle was significantly higher in the psoas compared to the posterior muscles (92.0% vs 57.7%, p<0.001). Men demonstrated higher posterior muscle CSA and percentage of fat-free muscle compared to women (60.4% vs 55.6%, p<0.001). While men also had higher CSA of the psoas, there was no difference in percentage of fat-free muscle between men and women (91.9% vs 92.1%, p=0.727). Overall the CSA of the psoas was highest at the inferior endplate of L4 and decreased in cranial and caudal directions. The percentage of fat-free muscle was over 90% for the psoas at all levels. In contrast, the posterior muscles FCSA was highest at L1 and decreased in the caudal direction, with almost 50% fatty infiltration at L5/S1. Despite level-dependent differences in percentage of lean muscle, significant correlations among all measured levels were observed within the same muscle group (Pearson's correlation coefficient 0.43-0.97). Multivariate analysis revealed that age, female sex, BMI and lower lumbar levels were associated with decreased lean muscle and increased fatty infiltration of the paraspinal/psoas muscles.

Discussion: This study provides comprehensive level-specific muscle data in a large cohort of patients undergoing spine surgery. There is significant variation in muscle size/fatty infiltration depending on muscle group, anatomical level and demographic factors.



Figure 1: Location of the 10 axial cuts

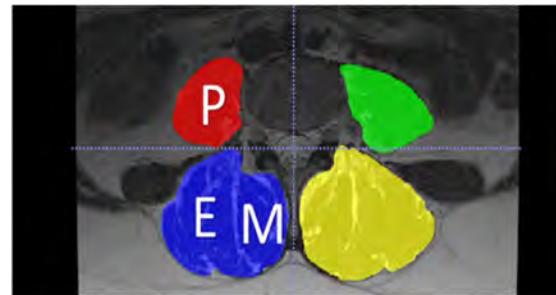


Figure 2: Example of segmentation for psoas (P) and combined erector spinae (E) and multifidus (M) muscle measurements

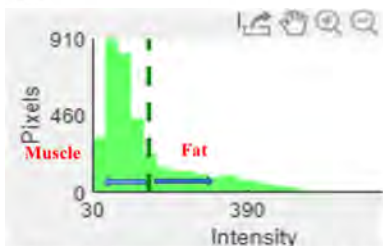


Figure 3: Representative histogram of pixel intensities across a spectrum of fat and muscle

Toxic annular tear and high signal intensity zone of patients with discogenic low back pain

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Introduction: Toxic annular tear (TAT) which Yeung et al. reported in 2017 is the condition of a patient discogenic low back pain, and the patients who had TAT were good candidates for transforaminal full-endoscopic lumbar discectomy and thermal annuloplasty (TELD and TA). High signal intensity zone (HIZ) of the posterior part of the intervertebral disc on lumbar MRI and posterior leakage of contrast media to the annulus fibrosus in CT discogram (CTD) are important radiological findings. In this study, we retrospectively evaluated the preoperative radiological findings who were diagnosed as having discogenic low back pain and TELD and TA under local anesthesia.

Materials and methods: Twenty-three patients who were diagnosed as having discogenic low back pain at our hospital from February 2014 to May 2020 and underwent TELD and TA were included in this study. Among 23 patients (man 17, woman 6), 38 intervertebral discs were treated. We retrospectively assessed the intervertebral disc level, the disc degeneration in Pfirrmann classification, the presence and location of HIZ on preoperative magnetic resonance T2-weighted image (T2-MRI), the morphometric evaluation of the contrast media leakage in CTD (presence of posterior annular tear: positive TAT, absence of posterior annular tear: negative TAT), and the relationship between the location of HIZ and the direction of TAT.

Results: Average age of the patients included in this study was 35.1 years old. Among 38 intervertebral discs, 21 were L4-L5 disc level, 15 were L5-S1 disc level, 1 was L2-L3 and L3-L4 respectively. The twenty-eight intervertebral disc had grade 3 disc degeneration on T2-MRI. Twenty-nine intervertebral discs had HIZ on T2-MRI and they had positive TAT in 26 intervertebral discs (90%). In all positive TAT, the direction of TAT went forward to the location of HIZ. However, 9 intervertebral discs without HIZ had only one positive TAT (11.1%).

Discussion: TELD-TA is one of the surgical procedures for patients with discogenic low back pain. Accurate diagnosis of discogenic low back pain is the most important point to treat this disease. From the result of the present study about preoperative radiological features, we treated the lower moderate degenerated intervertebral disc levels. We think that noninvasive T2-MRI is the first step as screening check-up of the discogenic low back pain and CTD is the second step which can detect positive TAT.

Importance of the Epiphyseal Ring in OLIF Stand-alone Surgery: A Biomechanical Study on Cadaveric Spines

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Introduction: 'OLIF stand-alone' refers to decompression of the intervertebral disc and insertion of a fusion cage through an oblique approach, without posterior pedicle instrumentation. Strength of the endplate seems crucial for a successful outcome because endplate damage can cause endplate collapse and cage subsidence. The epiphyseal ring is a relatively strong structure around the periphery of the endplate and the present cadaveric study aimed to investigate its role in preventing endplate damage and cage subsidence following OLIF stand-alone surgery.

Materials and Methods: 24 cadaveric lumbar functional spinal units were randomly assigned to two groups. The first was instrumented with long fusion cages which engaged with both the inner and outer regions of the epiphyseal ring (Complete Span Epiphyseal ring group, or CSER). Specimens in the second group received shorter cages which engaged with only the inner half of the epiphyseal ring (Half Span Epiphyseal Ring group, or HSER). Each group was divided into two subgroups: (higher cage height (HH) group, and normal cage height (NH) group. According to standard OLIF procedure, the appropriate size of the fusion cage was inserted into the intervertebral space. Each specimen was compressed at approximately 2.5 mm/s, until a minor injury was indicated by the first sign of structural failure (a slight reduction in the gradient of the real-time displacement-force graph). Preoperative cage location and post-operative structural failure were confirmed by X-ray and CT imaging. Trabecular structural damage was analyzed by Micro-CT.

Results: Endplate collapse was mainly evident in the inner region of the epiphyseal ring, where trabecular injury of sub-endplate bone was most concentrated. The incidence of endplate collapse, and of cage subsidence, was significantly higher in the HSER than CSER specimens. A structural failure occurred at a lower force in the HSER group (1.41 ± 0.34 kN) compared to the CSER group (2.44 ± 0.59 kN). Results for the two subgroups (HH and NH) were similar. The HH subgroups failed at a lower average force than the NH subgroups, but this was significant only for the HSER specimens. Micro-CT results showed a more extensive trabecular fracture in the HSER specimens compared to the CSER specimens, especially in the HH subgroup.

Conclusion: Endplate collapse is more likely to occur with short half-span cages because they are not supported at both ends by the epiphyseal ring structure. Collapse is also more likely to occur if the cage height exceeds disc space height. During OLIF surgery, we should choose cages to match intervertebral disc space height, and place the cages over the whole epiphyseal ring in order to improve support strength.