Eur Spine J (2018) 27:2–12
https://doi.org/10.1007/s00586-017-5292-3

ORIGINAL ARTICLE

Structural vertebral endplate nomenclature and etiology: a study by the ISSLS Spinal Phenotype Focus Group

Uruj Zehra[1] · Cora Bow[1] · Jeffrey C. Lotz[2] · Frances M. K. Williams[3] · S. Rajasekaran[4] · Jaro Karppinen[5] · Keith D. K. Luk[1] · Michele C. Battiê[6] · Dino Samartzis[1]

Received: 10 April 2017 / Revised: 23 July 2017 / Accepted: 3 September 2017 / Published online: 12 September 2017

Abstract
Purpose Vertebral endplate abnormalities may be associated with disc degeneration and, perhaps, pain generation. However, consensus definitions for endplate findings on spine MRI do not exist, posing a challenge to compare findings between studies and ethnic groups. The following survey was created to characterize the variability among the global spine community regarding endplate structural findings with respect to nomenclature and etiology.
Methods A working group within the International Society for the Study of the Lumbar Spine (ISSLS) Spinal Phenotype Focus Group was established to assess the endplate phenotype. A survey which consisted of 13 T2-weighted sagittal MRIs of the human lumbar spine illustrating the superior and inferior endplates was constructed based on discussion and agreement by the working group. A list of nomenclature and etiological terms with historical precedence was generated. Participants were asked to describe the endplates of each image and select from 14 possible nomenclatures and 10 etiological terms along with the option of free text response. The survey was entered into RedCap and was circulated throughout the ISSLS membership for data capture. Participants' demographics were also noted.
Results The survey was completed by 55 participants (87% males; 85% above 45 years of age, 39 clinicians, and 16 researchers). Sixty-eight percent of researchers and seventy-four percent of clinicians reported more than 16 and 20 years of research and clinical experience. Considerable variation existed in selection of nomenclature, etiology, and degree of severity of the endplate structural findings (reliability coefficients for single measures in each case were 0.3, 0.08, and 0.2, respectively). Sixty-seven percent regarded Modic changes as being a structural endplate finding. Approximately 84 and 80% of clinicians and researchers, respectively, agreed that a standardized endplate nomenclature and understanding the etiology is clinically important and needed.
Conclusions This study found that variations exist with respect to endplate nomenclature and etiology between clinicians and basic scientists, and paves the way for a consensus process to formalize the definitions.

Keywords Endplate · Spine · Nomenclature · Classification · Etiology · Phenotype · Survey · ISSLS

✉ Dino Samartzis
dsamartzis@msn.com

[1] Department of Orthopedics and Traumatology, The University of Hong Kong, Professorial Block, 5th Floor, 102 Pokfulam Road, Pokfulam, Hong Kong, SAR, China

[2] Department of Orthopaedic Surgery, University of California at San Francisco, San Francisco, CA, USA

[3] Division of Genetics and Molecular Medicine, King's College London, London, UK

[4] Department of Orthopedics and Spine Surgery, Ganga Hospital, Coimbatore, India

[5] Medical Research Center Oulu, University of Oulu and Oulu University Hospital, Oulu, Finland

[6] Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, AB, Canada

Introduction

The vertebral endplates are located adjacent to the intervertebral discs throughout the spine and are important components of the spinal motion segment [1–4]. The endplates are the key regulators of nutritional support to the

disc, maintain the stress–strain relationship between the vertebral bodies and the disc material, prevent the loss of macromolecules, and support the positional integrity of the disc [1, 5–7]. Various alterations of the endplates have been identified and linked with disc degeneration changes on magnetic resonance imaging (MRI) and low back pain, stressing their clinical relevance [2, 3, 8–14].

Although computed tomography (CT) scans are ideal in defining the osseous architecture of the spine, such imaging is associated with increased and potentially harmful levels of ionizing radiation exposure to the individual. Although the radiation dose exposure by plain radiographs is less than CT, endplate architecture is often obscured by axially tilted vertebral body segments. As such, MRI (e.g., T2-weighted) has been commonly used to address structural endplate findings and is ideal to assess soft tissue changes of the disc. Based on this modality, numerous endplate classification schemes have been reported, emphasizing distinct variants that associate with more severe forms of disc degeneration [3, 8, 9]. Nonetheless, it is unclear whether these endplate changes are the cause or consequence of disc degeneration. For example, it is common that the conventional MRI sequences show some disc levels with endplate changes adjacent to a non-degenerated disc, yet, other levels may show disc degeneration without endplate changes [2, 3, 14].

In vivo diffusion studies on human volunteers suggest that endplate damage can play a crucial role in the initiation of disc degeneration [7, 15]. Various mechanical studies noted that even minor endplate damage may lead to "high stress gradients" within the disc that precipitate disc degeneration and failure [16–19]. Yet, controversy remains regarding links between endplate changes and spine degeneration [2, 3, 20–23] as well as pathogenesis, distribution throughout the spine, age effects, and ethnic propensities [21, 24–28].

The proposed causative factors of endplate changes are numerous, and there is variable understanding whether the etiology is congenital, developmental, or traumatic [21, 25, 29, 30]. Studies have noted that the prevalence of specific types of endplate change, although not entirely specific, may be heritable [14, 31, 32]. Few studies have yet reported genome-wide significant gene effects related to endplate change—not least because a standardized definition is not yet available for the phenotype, but despite attempts, this is also noted with disc degeneration on MRI [33, 34]. In addition, structural endplate findings (i.e., non-Modic changes) are not yet clearly related to low back pain and, in keeping with many MRI changes, may be evident in both symptomatic and asymptomatic people [35–38].

All these clinical and research ambiguities surrounding the endplate might be due to heterogeneity across studies in relation to phenotypic classification of endplate observations or findings [4, 38]. The most common structural alteration noted during radiological and qualitative visual observations of cadaveric endplates include fractures [4, 8, 39], erosions [4, 8, 40], micro-trauma [41], vertebral rim lesions [42], and calcifications [4, 8], while clinical MRI imaging interpretation mostly refer to these structural changes as "Schmorl's nodes". Schmorl's nodes were first described by Christian Georg Schmorl in 1927 based on plain radiography and dry specimen observations [43], but a contemporary interpretation of Schmorl's nodes is lacking [4, 3, 44]. The role of Schmorl's nodes in back pain also remains controversial, as there is great variability in the reported prevalence and association with disc degeneration and clinical findings [2, 14, 28, 36, 37, 45–47]. All these conflicting observations are highly suggestive that all endplate changes should not belong to a singular nomenclature type. The difference in the shape, size, and location of endplate structural architecture and findings likely influence the adjacent disc differently [3, 8, 40], which may affect the surrounding innervation and pain probability; however [10], whether every structural changes are highly innervated and linked with low back pain is questionable. Also important to note that most studies include both "endplate structural alterations" and "vertebral bone marrow lesions," (i.e. Modic changes), as "endplate changes". Modic changes are signal intensity changes on MRI in the subchondral bone marrow region, and are highly associated with disc degeneration and back pain [11, 48–52]. Modic changes appear as hypo- or hyper-intense signals over the area of the endplate, and believed to be associated with structural endplate breaks and changes; however, the exact pathogenesis of this phenomenon is not clearly understood [12, 53–58]. It is assumed that some of the endplate structural changes, such as micro-fractures and fissures, might be major cause of Modic changes [57, 59].

Currently, there is no consensus within the global spine community regarding phenotypic classification of "structural endplate" findings. In the absence of such an agreement, it remains challenging to determine the endplate's role in disc degeneration, as well as other spinal phenotypes, and pain generation through systematic aggregation of different studies and replication of findings, especially for various omics research platforms. As such, to advance the phenotypic classification and ultimately establish a standardized nomenclature scheme for structural endplate findings, it is important to start by summarizing the current perspective of the spine community. Therefore, our goal was to conduct a survey of a multidisciplinary group of spine experts to gauge the extent of variation in the interpretation of endplate structural findings as seen on MRI with respect to nomenclature and etiology.

Methods

The International Society for the Study of the Lumbar Spine (ISSLS: http://www.issls.org) was established in 1974 and is the oldest, multidisciplinary, and international society focusing on all aspects of the lumbar spine and low back pain. The society has a membership of approximately 250 members worldwide who are vetted and voted for inclusion based on their experience/contribution in spine research. In June of 2013, the International Spine and Pain Consortium (http://www.spine-consortium.org) was established based on a grant from ISSLS, whereby leading experts in the field of imaging, omics, and clinical profiling were brought together to address large-scale phenotyping and other risk factors related to spine changes and pain. An extension of that, in June of 2014, the ISSLS Spinal Phenotype Focus Group was established. Within that framework, a vertebral endplate working group was established to address the nomenclature, etiology, and other matters regarding the endplate. In October of 2016, a survey was initially drafted to address such objectives and was based on detailed discussion and agreement by the working group. The domains consisted on demographics of the participant, nomenclature, and etiological interpretation of structural endplate findings, and perception of endplate relevance. After subsequent refinements and consensus on question structure and material presented within the survey, it was uploaded upon a RedCap (Nashville, Tennessee, USA) online system for data capturing. The survey was circulated via email to the ISSLS membership in November of 2016 by the ISSLS Secretariat. Instructions were given to the participants to complete the survey within 2 weeks, with email reminders circulated at various time points to the membership to address the survey. Institutional Review Board approval and informed consent was obtained at the senior authors' institution to obtain images of subjects to assess their vertebral endplate integrity for research purposes. All images were anonymized. It was conveyed to all ISSLS participants in the invited emails that data gathered will be used for presentation and publication purposes.

The nomenclature and etiological domains consisted of 13 distinct T2-weighted sagittal 3T MRIs of lumbar spine motion segments, illustrating the superior and inferior endplates with the intervertebral disc fully visible. Images were chosen to represent common endplate findings by consensus. These 13 images showed endplates with several different forms and shapes of lesions along with some having no apparent finding. The working group developed a list of nomenclature and etiological terms with historical precedence based on the reported literature. Participants were asked to describe both endplates of each image and select one option from 14 possible nomenclatures and 10 etiological terms. The option of free text response was also included to invite qualitative comment to enhance interpretation. The list of nomenclature terms included Normal, Abnormal, Atypical, Changes, Defect, Erosion, Findings, Fracture, Irregular, Mixed lesion, Schmorl's node, Typical, Other, and Not sure/Don't know. The options for etiological terms given were Not applicable, Congenital, Degenerative, Developmental, Genetics, Infection, Metabolic, Traumatic, Other, and Not sure/Don't know.

The severity of each endplate finding was also rated from Not severe, Mild, Moderate, and Severe to Very severe. Participants' demographics including age, gender, country of residence, main specialty, educational background, and years in spine research or clinical practice were also asked. The questions regarding the clinical utility of having a standardized nomenclature and understanding the etiology of endplate findings were added at the conclusion of the survey

All data were captured and entered upon a spreadsheet. SPSS (Chicago, Illinois, USA) version 22 was utilized to perform the statistical analyses. Descriptive statistics involving frequency and percentage distributions were used to establish general trends of all domains. Intra-class correlation coefficient (ICC) was used to measure the reliability/agreement of responses and the following scales were considered to measure the strength of the coefficient: >0.90 = excellent, ≥ 0.80 = good, ≥ 0.70 = acceptable, and <0.69 = poor [60]. 95% confidence intervals (CI) were noted to assess the precision of the coefficient.

Results

Demographics

In total, 91 individuals logged in online to undertake the survey; however, 55 of these (87% male; 85% above 45 years of age) were able to complete the entire survey (Table 1). Among the respondents, 71% were clinicians, representing a variety of clinical backgrounds, whereas the rest were clinician-scientists or researchers (Table 1). Of all of the clinicians, 74% completed their final training since more than 20 years ago, while among researchers, 68% reported more than 16 years of research experience (Table 1). Almost 67% of the respondents reported experience of conducting research on the endplates and 47% of the participants were aware of an endplate classification scheme as reported in the literature.

Endplate nomenclature

Considerable variation existed in selection of name (i.e., nomenclature), etiology, and degree of severity of the

Table 1 Demographics and responses by ISSLS survey participants

Section (*n*)	Descriptor	Number of responses	Response rate (%)
Age (55)	25–34	4	7.3
	35–44	4	7.3
	45–54	14	25.4
	55–64	20	36.4
	65 or above	13	23.6
Gender (55)	Male	48	87.3
	Female	7	12.7
Country of residence (55)	Asia pacific	21	38.2
	Europe	18	32.7
	USA and Canada	16	29.1
Main specialty (55)	Basic Science/Clinical Researcher	16	29.1
	Clinician (surgical/non-surgical)	27	49.1
	Clinician and researcher	12	21.8
Education back ground-researchers (16)	Epidemiology + others	6	37.5
	Biomechanics +others	4	25
	Bioengineering + biomechanics + cell	3	18.7
	Biology	2	12.5
	Biochemistry + cell biology	1	6.2
	Neurophysiology		
Clinical specialty-clinicians (39)	Orthopedics	31	79.5
	Physical medicine and rehabilitation	2	5.2
	Physical- therapy	1	2.5
	Rheumatology	2	5.2
	Other	1	2.5
	Nuclear medicine	1	2.5
	Neuroradiology	1	2.5
Spine fellowship is completed (39)	Yes	28	71.8
	No	11	28.2
Type of spine fellowship (39)	Surgical	19	48.7
	Clinical	3	7.7
	Surgical/clinical	6	15.4
	NA	11	28.2
Years since clinical training completed (39)	1–5 years	3	7.7
	6–10 years	2	5.1
	11–15 years	2	5.1
	16–20 years	3	7.7
	21–25 years	7	18
	25–30 years	8	20.5
	30 years and above	14	35.9
Location of practice (39)	Urban	32	82
	Rural	5	12.8
	Urban/rural	2	5.2
Years in spine research (28)	1–5 years	3	10.7
	6–10 years	1	3.6
	11–15 years	5	17.8
	16–20 years	4	14.2
	21–25 years	1	3.6
	25–30 years	2	7.3
	30 years and above	12	42.8

Table 1 continued

Section (*n*)	Descriptor	Number of responses	Response rate (%)
Performed research into endplate (55)	Yes	37	67.2
	No	18	32.8
Aware of any endplate structural grading/classification scheme (55)	Yes	26	47.3
	No	29	52.7
Consider Modic changes as endplate findings (55)	Yes	37	67.3
	No	18	32.7
Involving both endplates is more significant (55)	Yes	38	69
	No	17	31
Endplate findings associated with- (option to select all that apply)	Disc bulge/protrusion	13	23.6
	Disc degeneration	45	81.8
	Disc herniation	21	38.1
	Facet joint alignment	4	7.3
	Facet joint degeneration	6	10.9
	High-intensity zones	6	10.9
	Modic changes	25	45.5
	Narrow disc height	23	41.8
	Narrow spinal canal	1	1.8
	Vertebral osteophytes	9	16.4
	None of the above	3	5.5
	Not sure/don't know	0	0
	Other	4	7.3
Clinical utility in understanding endplate findings (55)	Yes	44	80
	No	3	5.5
	Not sure/don't know	8	14.5
Clinical utility in having standardized nomenclature of endplate findings (55)	Yes	46	83.6
	No	1	1.8
	Not sure/don't know	8	14.5

ISSLS International Society for the Study of the Lumbar Spine

endplate structural findings among the respondents. The reliability coefficient in naming the structural finding was 0.3 (95% CI 0.20–0.45). The range of agreement on nomenclature items varied from endplate to endplate (2–83%). The naming of the structural findings for most of the endplates was very much variable among the respondents (Fig. 1). On almost 81% of the endplates ($n = 21$), not more than 50% of the respondents could agree on any one nomenclature item. The two most commonly selected nomenclature items were Schmorl's node and Normal. On few endplates ($n = 3$, 11.5%), more than half of the respondents agreed on the term Schmorl's node for the structural finding. The highest mutual agreement was 83% and entailed Schmorl's node whereby both of the endplates of one motion segment had distinct findings (Fig. 2). The second most commonly selected item was Normal. More than half of the respondents agreed on the item Normal on two endplates. Only one of the respondents suggested the nomenclature terms Adaptive and Vertebrae Height Increase in the open-ended option.

Endplate etiology

The reliability coefficient in the interpretation of endplate etiology was 0.08 (95% CI 0.04–0.15). The range of agreement for different etiological items varied between 2 and 78% (Fig. 3). On almost 62% of the endplates ($n = 16$), the maximum mutual agreement did not exceed more than 50% on any one of the etiology items. Maximum agreement of 78% was seen with the term Degenerative on one of the endplate examples (Fig. 3), whereas the second most commonly used term was Not applicable. The other terms suggested by few respondents were Adaptation/Remodeling, Inflammation, and Imaging Artefact.

The reliability coefficients to determine the severity of the motion segment were 0.2 (95% CI 0.1–0.6). The range of agreement was 2–53% (Fig. 4). Only on one of the motion segment examples, more than half of the respondents (53%) agreed on one item (i.e. moderate severity), whereas on the remaining motion segments ($n = 12$, 92%), the mutual agreement did not exceed more than 50% on any one of the items by the respondents.

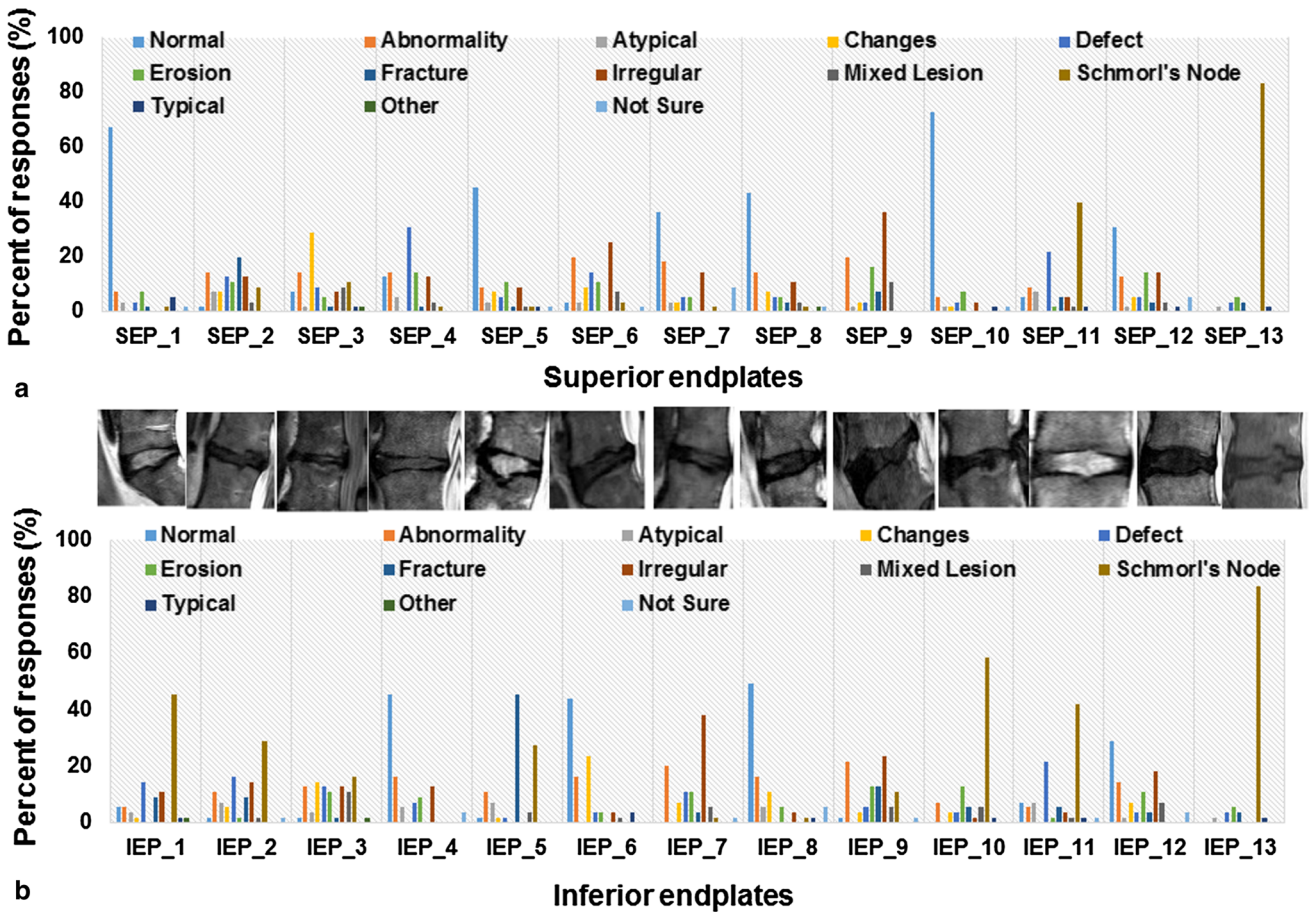

Fig. 1 Structural endplate nomenclature item responses for the **a** superior endplates (SEP) and the **b** inferior endplates (IEP) of each 13 motion segment sample on magnetic resonance imaging

General queries

Approximately 67% of the respondents noted Modic changes as endplate findings and 69% suggested that involvement of both (superior and inferior) endplates could be more significant as compared to one. Most commonly associated conditions with endplate findings were disc degeneration (82%), Modic changes (45%), and narrow disc height (42%). Approximately 84% of the respondents agreed that a standardized endplate nomenclature is needed and 80% agreed that understanding the etiology is clinically important. In terms of grading the importance to have a standardized endplate structural nomenclature scheme, the top three responses were as follows: pathogenesis of disease (33%), genetic research (31%), and identifying the pain source (29%). Due to the sample size of respondents, it was not practical to assess specific demographic factors in relation to the responses in the various domains.

Discussion

This study represents the first attempt to define the variability and/or agreement of the nomenclature and etiology of structural endplate findings among the global spine community of skilled and knowledgeable clinicians and scientists. Based on participation by members of the ISSLS, we noted that a significant variability exists as to how endplate findings on MRI are interpreted and perceived. Wide ranges of variability in the responses for endplate nomenclature, etiology, and rating of severity were seen on 13 different motion segments based on MRI. In the nomenclature section, only on 19% of the endplates, we noted that more than 50% of the respondents agreed on one item. Furthermore, regarding endplate etiology, only 38% of the endplates showed agreement of more than 50% of the respondents on any one item. In rating the severity of the motion segments, only one motion segment received agreement of more than half of the respondents.

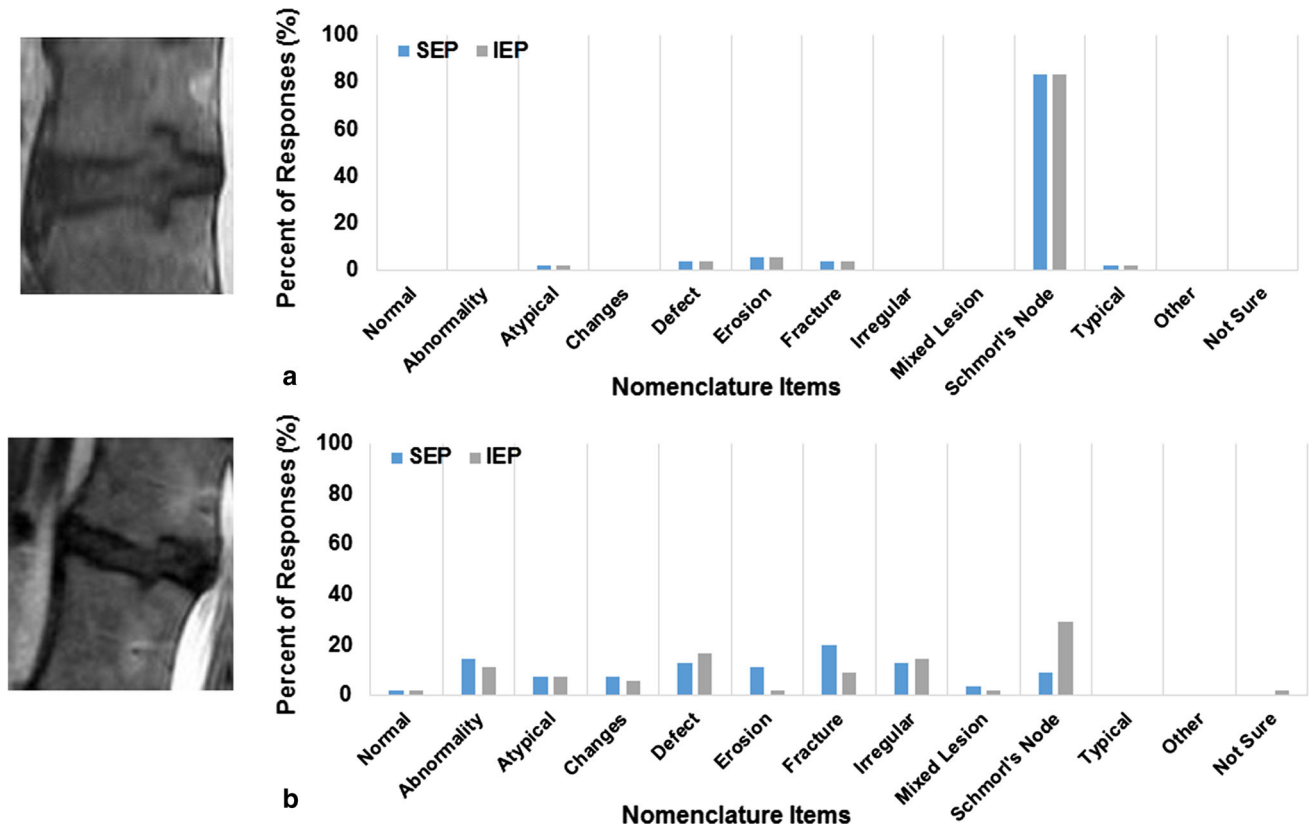

Fig. 2 Magnetic resonance images of two sample motion segments (left) and survey responses of their corresponding nomenclature. **a** Highest mutual agreement for Schmorl's node nomenclature selection was noted for this image for both endplates. **b** High variability in nomenclature selection is seen for this image for both endplates. *SEP* superior endplate, *IEP* inferior endplate

Approximately, 82% of the endplates did not receive mutual agreement on any one of the nomenclature items by more than 50% of the respondents. Normal and Schmorl's node were the only two nomenclature items on which more than half of the respondents agreed upon, while remaining items did not achieve mutual consensus on any one of the endplates. Those endplates with straight, concave, or mixed appearance were selected as Normal by most of the respondents and achieved more than 50% of the consensus. Although the morphometry and endplate shapes have been explored by many previous studies for various purposes [61–63], it is recognized and relatively accepted that endplate shape changes with degeneration [20, 63–65] and that flatter endplates are more associated with disc degeneration as compared to concave or other types; however, this concept can also be questionable [64–66]. The reported responses highlight the variability and difference of opinion based on this understanding. The rounded deep defects with smooth looking margins ($n = 3$ endplates) were the ones more likely regarded as Schmorl's nodes by more than half of the respondents. This trend illustrated that some unanimity existed on such typically rounded, slightly deep structural findings, even though there were still 20–60% of the respondents who selected other item options in these cases. However, the concept of what is a Schmorl's node is poorly defined [4], since it would appear in the literature that even this aforementioned definition and visual appearance seems to often be combined with other endplate findings and regarded as the same nomenclature [3, 44].

Regarding opinions addressing the etiology of endplate changes, considerable variation also existed between the participants, whereas Degenerative and Not applicable were the items of maximum consensus. Over the last 2 decades, studies addressing the most commonly occurring endplate finding, Schmorl's nodes, have suggested that they are highly heritable and also linked with a developmental origin [14, 21, 67, 68]. Interestingly, in the current study, the two endplates which were deemed as Schmorl's nodes by 83% of the respondents, the corresponding etiology showed variation whereby 42% of the respondents noted it to be Developmental, 17% as Degenerative, and 13% opted for Not Sure. This discrepancy of the etiology based on one of the more agreed upon nomenclature items further underscores the conflicting views of the spine community upon endplate findings.

Despite the fact that almost 70% of the respondents were clinicians, only one motion segment achieved more than

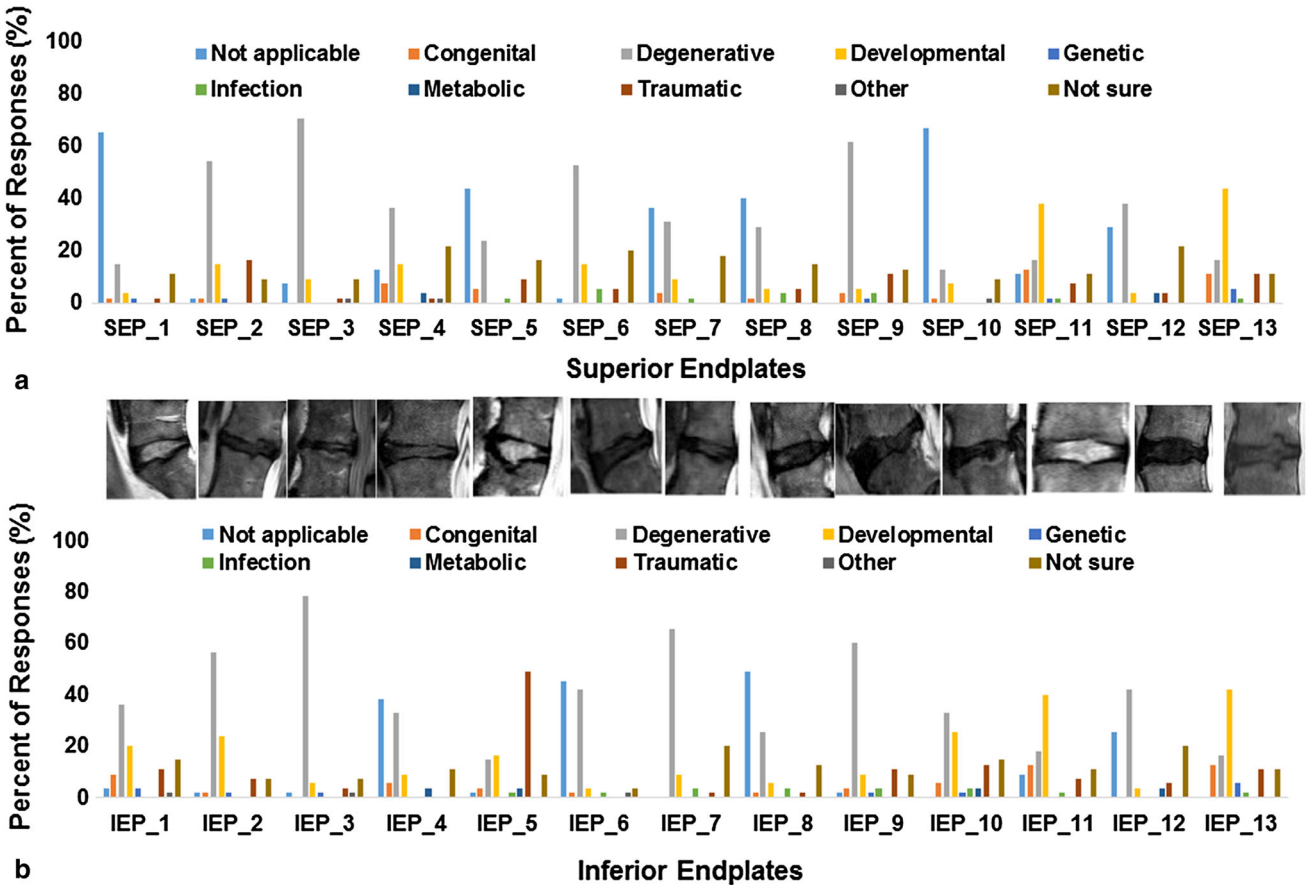

Fig. 3 Structural endplate etiology responses for the **a** superior endplates (SEP) and the **b** inferior endplates (IEP) of each 13 motion segment sample on magnetic resonance imaging

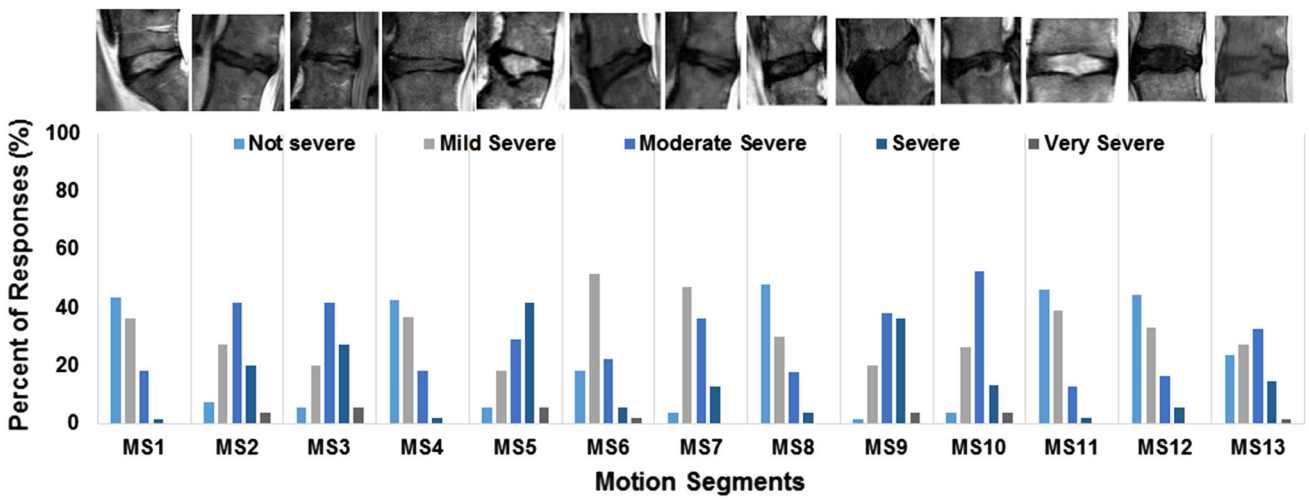

Fig. 4 Responses in rating the severity of each 13 motion segment (MS) samples on magnetic resonance imaging

50% of agreement with respect to rating its clinical severity. Defining and understanding the severity of certain structural endplate findings are important for treatment and future management of patients, while at the same time, its significance for research is also critical. In the current study, many of the respondents recognized Modic changes as an endplate structural finding and its corresponding grading scheme as the one most familiar [52].

Conceivably, lack of agreement on endplate structural findings and pathogenesis might be linked to significant

variability in the literature regarding the clinical relevance of the endplate findings on MRI. Over the last few years, vertebral endplate research has gathered tremendous momentum and its importance and association with disc degeneration and back pain has taken center stage [10, 18, 26, 69–71]. However, in determining the precise role of these morphological alterations in the disc degenerative process and pathogenesis of back pain, a deeper understanding and appreciation is required. Of particular interest, approximately 80% of the respondents felt that the clinical relevance and utility of an endplate nomenclature scheme is important and is greatly needed.

As with any clinical study and survey, limitations inherently exist. Although our study reflected the opinions of 55 individuals, equal amount of participation was seen from three major regions of the world (Asia Pacific, Europe, and North America). The MRIs selected for this survey were representative of some routinely observed findings whose selection for inclusion was brought upon by an expert working group of endplate researchers and clinicians. The majority of the researchers and clinicians who eventually participated in the online survey were adequately experienced and trained in their respective fields and had already some experience addressing the vertebral endplates. Along with the designated choices of items, open-ended options were also available and through this process additional terms/items were flagged for future consideration. Though 91 respondents attempted to complete the survey form, only 55 were able to complete and submit it. This 40% failure to complete the survey may have been a result to the amount of personal time that each participant had to address to complete the entire survey as it may have been deemed lengthy. As a result, it may be perceived that more dedicated and committed individuals with an interest in the endplate completed the survey; yet, if this assumption remains true, the variability and lack of agreement of endplate findings is rather substantial among the even more experienced demographic. Lack of participation of experienced radiologists might be another possible limitation of this study. Future work will aim to include experts from other relevant disciplines and to increase the sample size of participants to help determine the various factors that may contribute to individual and collective variation or lack of agreement with respect to endplate interpretation and its clinical relevance. Furthermore, survey consists of only T2-weighted sagittal MRIs and not T1-weighted. Although the aim of the current study was to assess variability based on the imaging that was provided, we hope that future studies can also include T1-weighted sequences in an attempt to further refine the interpretation of the structural endplate findings.

Conclusions

This is the first study to determine the variation/agreement of structural endplate findings on MRI with respect to their nomenclature and etiology among the global spine community. Our study found that substantial variation exists among clinicians and scientists with respect to this platform. Our study underscores the critical need for standardized nomenclature of endplate structural findings, and motivates future efforts to develop consensus between clinicians and researchers worldwide. In an age of big data studies consisting of genomics, metabolomics, proteomics, and other platforms, understanding the endplate phenotype is essential to identify cases of interest and to avoid false positive and questionable findings. With such knowledge, new and more precise molecular pathways of the condition could be identified and discovered, enhance biomechanical and animal model approaches, novel and targeted therapeutics can be developed, and a more personalized approach or patient profiling can be constructed to ultimately benefit the care and outcomes of patients. Furthermore, having a global consensus of endplate findings may facilitate a deeper understanding of the degenerative process of the disc as well as improve patient selection for biological therapies that aims to regenerate or halt the degeneration of the disc and subsequent discogenic pain. Along these same lines, having an understanding of the endplate may further broaden the field of vertebrogenic or endplatogenic origins of back pain with future development of endplate targeted therapies, and perhaps more advanced imaging to assess sub- or endplate phenotypes that are clinically relevant.

Compliance with ethical standards

Conflict of interest The authors have no financial or competing interests to disclose.

Funding This work was supported by grants from the Hong Kong Theme-Based Research Scheme (T12-708/12N), Hong Kong Research Grants Council (777111), and the International Society for the Study of the Lumbar Spine MacNab/LaRocca Award.

References

1. Moore RJ (2000) The vertebral end-plate: what do we know? Eur Spine J 9:92–96
2. Mok FP, Samartzis D, Karppinen J, Luk KD, Fong DY, Cheung KM (2010) ISSLS prize winner: prevalence, determinants, and association of Schmorl nodes of the lumbar spine with disc degeneration: a population-based study of 2449 individuals. Spine (Phila Pa 1976) 35:1944–1952
3. Samartzis D, Mok FP, Karppinen J, Fong DY, Luk KD, Cheung KM (2016) Classification of Schmorl's nodes of the lumbar spine and association with disc degeneration: a large-scale population-based MRI study. Osteoarthr Cartil 24:1753–1760

4. Wang Y, Videman T, Battie MC (2012) Lumbar vertebral endplate lesions: prevalence, classification, and association with age. Spine (Phila Pa 1976) 37:1432–1439
5. Grunhagen T, Shirazi-Adl A, Fairbank JC, Urban JP (2011) Intervertebral disk nutrition: a review of factors influencing concentrations of nutrients and metabolites. Orthop Clin North Am 42:465–477 **(vii)**
6. Urban JP, Smith S, Fairbank JC (2004) Nutrition of the intervertebral disc. Spine (Phila Pa 1976) 29:2700–2709
7. Rajasekaran S, Babu JN, Arun R, Armstrong BR, Shetty AP, Murugan S (2004) ISSLS prize winner: a study of diffusion in human lumbar discs: a serial magnetic resonance imaging study documenting the influence of the endplate on diffusion in normal and degenerate discs. Spine (Phila Pa 1976) 29:2654–2667
8. Wang Y, Videman T, Battie MC (2012) ISSLS prize winner: Lumbar vertebral endplate lesions: associations with disc degeneration and back pain history. Spine (Phila Pa 1976) 37:1490–1496
9. Maatta JH, Wadge S, MacGregor A, Karppinen J, Williams FM (2015) ISSLS prize winner: vertebral endplate (Modic) change is an independent risk factor for episodes of severe and disabling low back pain. Spine (Phila Pa 1976) 40:1187–1193
10. Fields AJ, Liebenberg EC, Lotz JC (2014) Innervation of pathologies in the lumbar vertebral endplate and intervertebral disc. Spine J 14:513–521
11. Mok FP, Samartzis D, Karppinen J, Fong DY, Luk KD, Cheung KM (2016) Modic changes of the lumbar spine: prevalence, risk factors, and association with disc degeneration and low back pain in a large-scale population-based cohort. Spine J 16:32–41
12. Määttä JH, Karppinen J, Paananen M et al (2016) Refined phenotyping of modic changes: imaging biomarkers of prolonged severe low back pain and disability. Medicine 95:e3495
13. Hsu KY, Zucherman JF, Derby R, White AH, Goldthwaite N, Wynne G (1988) Painful lumbar end-plate disruptions: a significant discographic finding. Spine (Phila Pa 1976) 13:76–78
14. Williams FM, Manek NJ, Sambrook PN, Spector TD, Macgregor AJ (2007) Schmorl's nodes: common, highly heritable, and related to lumbar disc disease. Arthritis Rheum 57:855–860
15. Rajasekaran S, Venkatadass K, Naresh Babu J, Ganesh K, Shetty AP (2008) Pharmacological enhancement of disc diffusion and differentiation of healthy, ageing and degenerated discs: results from in vivo serial post-contrast MRI studies in 365 human lumbar discs. Eur Spine J 17:626–643
16. Von Forell GA, Nelson TG, Samartzis D, Bowden AE (2014) Changes in vertebral strain energy correlate with increased presence of Schmorl's nodes in multi-level lumbar disk degeneration. J Biomech Eng 136:061002
17. Adams MA, McNally DS, Wagstaff J, Goodship AE (1993) Abnormal stress concentrations in lumbar intervertebral discs following damage to the vertebral bodies: a cause of disc failure? Eur Spine J 1:214–221
18. Adams MA, Freeman BJC, Morrison HP, Nelson IW, Dolan P (2000) Mechanical initiation of intervertebral disc degeneration. Spine 25:1625–1636
19. Dolan P, Luo J, Pollintine P, Landham PR, Stefanakis M, Adams MA (2013) Intervertebral disc decompression following endplate damage: implications for disc degeneration depend on spinal level and age. Spine 38:1473–1481
20. Wang Y, Videman T, Battie MC (2013) Morphometrics and lesions of vertebral end plates are associated with lumbar disc degeneration: evidence from cadaveric spines. J Bone Jt Surg Am 95:e26
21. Hilton RC, Ball J, Benn RT (1976) Vertebral end-plate lesions (Schmorl's nodes) in the dorsolumbar spine. Ann Rheum Dis 35:127–132
22. Pfirrmann CW, Resnick D (2001) Schmorl nodes of the thoracic and lumbar spine: radiographic-pathologic study of prevalence, characterization, and correlation with degenerative changes of 1,650 spinal levels in 100 cadavers. Radiology 219:368–374
23. González-Reimers E, Mas-Pascual M, Arnay-de-la-Rosa M, Velasco-Vázquez J, Santolaria-Fernández F (2002) Schmorl nodes: lack of relationship between degenerative changes and osteopenia. Radiology 222:293–294
24. Vernon-Roberts B, Pirie CJ (1977) Degenerative changes in the intervertebral discs of the lumbar spine and their sequelae. Rheumatol Rehabil 16:13–21
25. McCall IW, Park WM, O'Brien JP, Seal V (1985) Acute traumatic intraosseous disc herniation. Spine (Phila Pa 1976) 10:134–137
26. Wagner AL, Murtagh FR, Arrington JA, Stallworth D (2000) Relationship of Schmorl's nodes to vertebral body endplate fractures and acute endplate disk extrusions. AJNR Am J Neuroradiol 21:276–281
27. Kyere KA, Than KD, Wang AC et al (2012) Schmorl's nodes. Eur Spine J 21:2115–2121
28. Sward L, Hellstrom M, Jacobsson B, Peterson L (1990) Back pain and radiologic changes in the thoraco-lumbar spine of athletes. Spine (Phila Pa 1976) 15:124–129
29. Martel W, Seeger JF, Wicks JD, Washburn RL (1976) Traumatic lesions of the discovertebral junction in the lumbar spine. AJR Am J Roentgenol 127:457–464
30. Hauger O, Cotten A, Chateil JF, Borg O, Moinard M, Diard F (2001) Giant cystic Schmorl's nodes: imaging findings in six patients. AJR Am J Roentgenol 176:969–972
31. Sahlman J, Inkinen R, Hirvonen T et al (2001) Premature vertebral endplate ossification and mild disc degeneration in mice after inactivation of one allele belonging to the Col2a1 gene for Type II collagen. Spine (Phila Pa 1976) 26:2558–2565
32. Jim JJ, Noponen-Hietala N, Cheung KM et al (2005) The TRP2 allele of COL9A2 is an age-dependent risk factor for the development and severity of intervertebral disc degeneration. Spine (Phila Pa 1976) 30:2735–2742
33. Eskola PJ, Lemmela S, Kjaer P et al (2012) Genetic association studies in lumbar disc degeneration: a systematic review. PLoS ONE 7:e49995
34. Eskola PJ, Mannikko M, Samartzis D, Karppinen J (2014) Genome-wide association studies of lumbar disc degeneration–are we there yet? Spine J 14:479–482
35. Kokkonen SM, Kurunlahti M, Tervonen O, Ilkko E, Vanharanta H (2002) Endplate degeneration observed on magnetic resonance imaging of the lumbar spine: correlation with pain provocation and disc changes observed on computed tomography diskography. Spine (Phila Pa 1976) 27:2274–2278
36. Takahashi K, Miyazaki T, Ohnari H, Takino T, Tomita K (1995) Schmorl's nodes and low-back pain. Analysis of magnetic resonance imaging findings in symptomatic and asymptomatic individuals. Eur Spine J 4:56–59
37. Abu-Ghanem S, Ohana N, Abu-Ghanem Y, Kittani M, Shelef I (2013) Acute Schmorl node in dorsal spine: an unusual cause of a sudden onset of severe back pain in a young female. Asian Spine J 7:131–135
38. Chou D, Samartzis D, Bellabarba C et al (2011) Degenerative magnetic resonance imaging changes in patients with chronic low back pain: a systematic review. Spine (Phila Pa 1976) 36:S43–S53
39. Perey O (1957) Fracture of the vertebral end-plate in the lumbar spine; an experimental biochemical investigation. Acta Orthop Scand Suppl 25:1–101
40. Zehra U, Flower L, Robson-Brown K, Adams MA, Dolan P (2017) Defects of the vertebral endplate: implications for disc degeneration depend on size. Spine J 17:727–737
41. Yoganandan N, Maiman DJ, Pintar F et al (1988) Microtrauma in the lumbar spine: a cause of low back pain. Neurosurgery 23:162–168

42. Hilton RC, Ball J (1984) Vertebral rim lesions in the dorsolumbar spine. Ann Rheum Dis 43:302–307
43. Schmorl G (1927) Die pathologische Anatomie der Wirbelsaule. Verh Dtsch Path Ges 21:3–41
44. Hansson T, Roos B (1983) The amount of bone mineral and Schmorl's nodes in lumbar vertebrae. Spine (Phila Pa 1976) 8:266–271
45. Stabler A, Bellan M, Weiss M, Gartner C, Brossmann J, Reiser MF (1997) MR imaging of enhancing intraosseous disk herniation (Schmorl's nodes). AJR Am J Roentgenol 168:933–938
46. Smith DM (1976) Acute back pain associated with a calcified Schmorl's node: a case report. Clin Orthop Relat Res 117: 193–196
47. Lipson SJ, Fox DA, Sosman JL (1985) Symptomatic intravertebral disc herniation (Schmorl's node) in the cervical spine. Ann Rheum Dis 44:857–859
48. Albert HB, Kjaer P, Jensen TS, Sorensen JS, Bendix T, Manniche C (2008) Modic changes, possible causes and relation to low back pain. Med Hypotheses 70:361–368
49. Jensen TS, Bendix T, Sorensen JS, Manniche C, Korsholm L, Kjaer P (2009) Characteristics and natural course of vertebral endplate signal (Modic) changes in the Danish general population. BMC Musculoskelet Disord 10:81
50. Maatta JH, Karppinen J, Paananen M et al (2016) Refined phenotyping of Modic changes: imaging biomarkers of prolonged severe low back pain and disability. Med (Baltim) 95:e3495
51. Maatta JH, Karppinen JI, Luk KD, Cheung KM, Samartzis D (2015) Phenotype profiling of Modic changes of the lumbar spine and its association with other MRI phenotypes: a large-scale population-based study. Spine J 15:1933–1942
52. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR (1988) Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 166:193–199
53. Toyone T, Takahashi K, Kitahara H, Yamagata M, Murakami M, Moriya H (1994) Vertebral bone-marrow changes in degenerative lumbar disc disease. An MRI study of 74 patients with low back pain. J Bone Jt Surg Br 76:757–764
54. Kuisma M, Karppinen J, Niinimaki J et al (2007) Modic changes in endplates of lumbar vertebral bodies: prevalence and association with low back and sciatic pain among middle-aged male workers. Spine (Phila Pa 1976) 32:1116–1122
55. Kjaer P, Korsholm L, Bendix T, Sorensen JS, Leboeuf-Yde C (2006) Modic changes and their associations with clinical findings. Eur Spine J 15:1312–1319
56. Rahme R, Moussa R (2008) The modic vertebral endplate and marrow changes: pathologic significance and relation to low back pain and segmental instability of the lumbar spine. AJNR Am J Neuroradiol 29:838–842
57. Dudli S, Fields AJ, Samartzis D, Karppinen J, Lotz JC (2016) Pathobiology of Modic changes. Eur Spine J 25:3723–3734
58. Dudli S, Sing DC, Hu SS, et al. (2017) Intervertebral disc/bone marrow cross-talk with Modic changes. Eur Spine J 26:1362–4955
59. Zhang YH, Zhao CQ, Jiang LS, Chen XD, Dai LY (2008) Modic changes: a systematic review of the literature. Eur Spine J 17:1289–1299
60. Vavken P, Ganal-Antonio AKB, Shen FH, Chapman JR, Samartzis D (2015) Fundamentals of clinical outcomes assessment for spinal disorders: study designs, methodologies, and analyses. Global Spine J 5:156–164
61. Chen H, Jiang D, Ou Y, Zhong J, Lv F (2011) Geometry of thoracolumbar vertebral endplates of the human spine. Eur Spine J 20:1814–1820
62. Oetgen ME, Yue JJ, la Torre JJJ, Bertagnoli R (2008) Does vertebral endplate morphology influence outcomes in lumbar total disc arthroplasty? Part II: clinical and radiographic results as evaluated utilizing the Vertebral Endplate Yue-Bertagnoli (VEYBR) classification. Sas j 2:101–106
63. Lakshmanan P, Purushothaman B, Dvorak V, Schratt W, Thambiraj S, Boszczyk M (2012) Sagittal endplate morphology of the lower lumbar spine. Eur Spine J 21(Suppl 2):S160–S164
64. Yao-sheng L, Qi-xin C, Shu-bin L (2008) Endplate concavity variation of lumbar motion segments: a finite element analysis. J Clin Rehabil Tissue Eng Res 12:8765–8770
65. He X, Liang A, Gao W et al (2012) The relationship between concave angle of vertebral endplate and lumbar intervertebral disc degeneration. Spine (Phila Pa 1976) 37:E1068–E1073
66. Pappou IP, Cammisa FP Jr, Girardi FP (2007) Correlation of end plate shape on MRI and disc degeneration in surgically treated patients with degenerative disc disease and herniated nucleus pulposus. Spine J 7:32–38
67. Dar G, Peleg S, Masharawi Y, Steinberg N, May H, Hershkovitz I (2009) Demographical aspects of Schmorl nodes: a skeletal study. Spine (Phila Pa 1976) 34:E312–E315
68. Chandraraj S, Briggs CA, Opeskin K (1998) Disc herniations in the young and end-plate vascularity. Clin Anat 11:171–176
69. Dudli S, Haschtmann D, Ferguson SJ (2012) Fracture of the vertebral endplates, but not equienergetic impact load, promotes disc degeneration in vitro. J Orthop Res 30:809–816
70. Holm S, Holm AK, Ekstrom L, Karladani A, Hansson T (2004) Experimental disc degeneration due to endplate injury. J Spinal Disord Tech 17:64–71
71. Sahoo MM, Mahapatra SK, Kaur S, Sarangi J, Mohapatra M (2017) Significance of vertebral endplate failure in symptomatic lumbar disc herniation. Global Spine J 7:230–238