ORIGINAL RESEARCH

Correlation of Modic Changes with Sagittal Lumbopelvic Parameters

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Purpose: The main aim of this retrospective study was to analyze lumbopelvic sagittal parameters among the three different types of Modic changes (MCs). Furthermore, correlations between the sizes of MCs and the number of involved lumbar levels with lumbopelvic parameters are investigated.

Methods: A total of 263 adult subjects with MCs at a single institution from September 2015 to October 2020 who underwent lumbar x-ray examinations and magnetic resonance imaging were included in this retrospective study. Types of MCs, sizes of MCs, lumbar levels involved by MCs as well as lumbopelvic sagittal parameters from each subject were evaluated by two authors.

Results: Lumbar lordosis (LL), sacral slope (SS), and pelvic incidence (PI) in subjects with MC grade 1 were significantly smaller than in those with MC grade 2 and grade 3 ($p < 0.05$). Lumbopelvic sagittal parameters decreased significantly as the sizes aggravated ($p < 0.01$). Triple lumbar levels with MCs showed a significant increase in PI-LL ($p < 0.05$) and decrease in LL ($p < 0.01$), SS ($p < 0.01$), and PI ($p < 0.01$) when compared to MCs at single and double lumbar levels.

Conclusion: MC grade 1, severe MCs, and lumbar multi-segmental MCs were significantly linked to lumbar sagittal imbalance.

Keywords: Modic changes, sagittal balance, lumbopelvic parameter, pelvic incidence, lumbar lordosis, sacral slope

Introduction

Chronic low back pain (CLBP) is the most common symptom of patients with degenerative disc disease who are seeking professional treatment.[1] Considering its essential impact on the individual, communities, and health care systems,[1] much more attention should be paid to it. As a potential source for CLBP,[2–5] abnormal signal changes in the subchondral bone marrow adjacent to the endplates, also known as Modic changes (MCs), were first discussed by Modic et al[6,7] in 1988.

In the decades since the preliminary elaboration of MCs by Modic et al, there has been an ongoing dispute about their pathogenesis. Biomechanical injury, inflammatory, and low-grade bacterial infection are generally considered to be the main causes of the development of MCs.[3,8,9] These 3 models may not be independent of each other but are closely interrelated, each of them potentially triggering a cascade of events leading to the development of MCs.[8] However, biomechanical injury of the endplates can provide good anatomical conditions for the "cross-talk" of pro-inflammatory mediators between the disc and subchondral bone marrow as well the colonization and spread of bacteria, which may be one of the important

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prerequisites for the development of MCs.[10] The increased shear force acting on the degenerative disc would cause the micro-fracture of the vertebral endplates,[11,12] showing bone marrow edema related to MC1.

The sagittal spinopelvic contour plays an important role in the normal function of the spine and in various diseased states.[13] Knowledge of its normal composed elements would be crucial for understanding its significance in body balance and alignment.[14] Once abnormal, the body needs to expend more energy to compensate for the abnormal sagittal alignment for balance.[15] Recently, several studies[10,13,16] have investigated sagittal parameters among patients with and without MCs. The strong relationships between MCs and spinal sagittal imbalance might potentially provide new insight into the mechanism of MCs leading to CLBP.

However, previous studies did not investigate the potential effects of the sizes of MCs and the number of lumbar levels affected by MCs on lumbar sagittal parameters. Therefore, the purpose of this study was to analyze lumbopelvic sagittal parameters in correlation to MC grades, sizes, and number of involved lumbar levels.

Materials and Methods

This study is a part of the research program"the imaging study of the intervertebral disc and endplate degeneration for patients with cervical/lumbar degenerative diseases"approved by our Institutional Ethical Committee in 2016. We conceived and implemented this study in April 2021.

Study Population

According to the aims of this study, the inclusion and exclusion criteria were formulated for this study before selecting the appropriate subjects. The subjects who met the following criteria were included in this study: (1) Age over 18 years on admission; (2) Subjects underwent lumbar X-ray examination in the standing position and lumbar magnetic resonance imaging (MRI) scanning in the supine position from September 2015 to October 2020; (3) There was evidence of the imaging appearance of one of three types of MCs occurring at any lumbar level on MRI; (4) Radiological examinations complied with the standard operating procedures and the images were of high quality. The subjects were excluded if they had a prior history of lumbar surgery, significant spinal deformities (spinal scoliosis ≥15°), spinal tumor, spinal trauma, spinal infections

or inflammations, or abnormal postures caused by lower extremity diseases.

Finally, 263 adult subjects who met the above-mentioned criteria were included in this retrospective study. All images included in this study were coded and covered subjects' personal information. The study protocol was approved by the ethics committee of The People's Hospital of Guangxi Zhuang Autonomous Region (No. 2016-12) and we implemented this study in strict accordance with the principles of the Declaration of Helsinki. Patients who participated in this study signed an informed consent form with knowledge of the study's purposes and relevant details.

Imaging Evaluation and Measurement

All subjects were examined by lumbar MRI (supine position) and X-ray (standing position). The scanning area was included at least L1 to the femoral heads. Subjects' images were recorded in the electronic medical system of our hospital.

MRI Protocol

All included patients were examined with 3.0 T magnetic resonance units (Siemens, Germany) with the following parameters: (1) the sagittal T1-weighted images (T1WI): time to echo (TE): 8 ms, time of repetition (TR): 400 ms, slice thickness (ST): 4 mm, and field of view (FOV): 512*512 pixel; (2) the sagittal T2-weighted images (T2WI): TE: 100 ms, TR: 3000 ms, ST: 4 mm, FOV: 512*512 pixel.

Assessment of Three Types of MCs

Two spinal surgeons (X.P.M and C.Q.Y) with more than 3-year experience were allocated to independently evaluate all MR images for identifying the type of MCs. Three types of MCs (Figure 1) proposed by Modic et al[6,7] were defined by their appearances on both TIWI and T2WI. Modic type 1 change (MC1) indicates a hypointense signal on T1WI and a hyperintense signal on T2WI. Modic type 2 change (MC2) reflects the hyperintense signals both on T1- and T2WIs. Whereas, Modic type 3 change (MC3) is characterized by the hypointense signals both on T1- and T2WIs.

Parameters Measurement

The above-mentioned 2 reviewers independently measured all radiological parameters on X-ray images from 15 randomly selected subjects and calculated the inter-observer reliability thereafter. In addition, the measurement of these
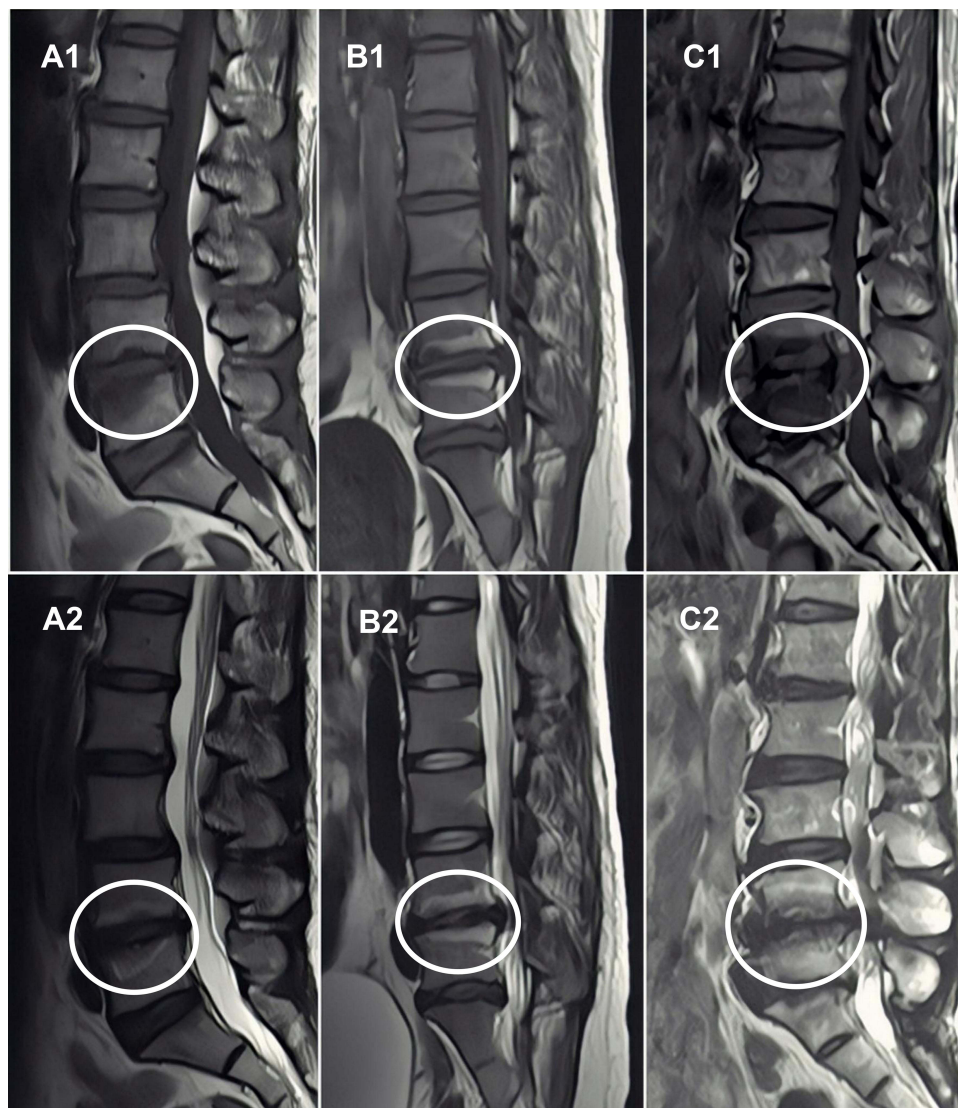
Figure 1 The imaging presentations of the three types of Modic changes (MCs) on magnetic resonance imaging. Modic type 1 change: decreased signal intensity on T1-weighted images (T1WIs, (**A1**)) and increased signal intensity on T2-weighted images (T2WIs, (**A2**)); MC2: increased signal intensity both on T1WIs (**B1**) and T2WIs (**B2**); MC3: decreased signal intensity both on T1WIs (**C1**) and T2WIs (**C2**).

parameters were repeated 10 days after the first measurement and the intra-observer reliability was calculated.

Surgimap® 2.3.2.1 software (Nemaris Inc., New York, USA) was used to measure the parameters on X-ray images. The sagittal parameters were measured in the neutral position on X-ray images (Figure 2). Lumbar lordosis (LL) was the angle between by two lines which were parallel to the superior endplate of L1 and the inferior endplate of L5. The conformation of sacral slope (SS) was similar to LL, but it consisted of one line parallel to the superior endplate of S1 and the horizontal line. Pelvic tilt (PT) was an angle formed by a line through the midpoint of the S1 superior endplate and the center of the

femoral head and a vertical line through the center of the femoral head. Pelvic incidence (PI), which is an angle that based on a line perpendicular to the sacral endplate and a line through the midpoint of the S1 superior endplate and the center of the femoral head, is a fixed value determined by the sum of the SS and PT.

Size of MCs

We adopted a classification proposed by Hanımoğlu et al[2] to categorize the distribution of three types of MCs at the endplate and vertebral bodies. This classification method allowed us to divide the vertebrae into 4 equal parts including 16 small units across the horizontal and vertical
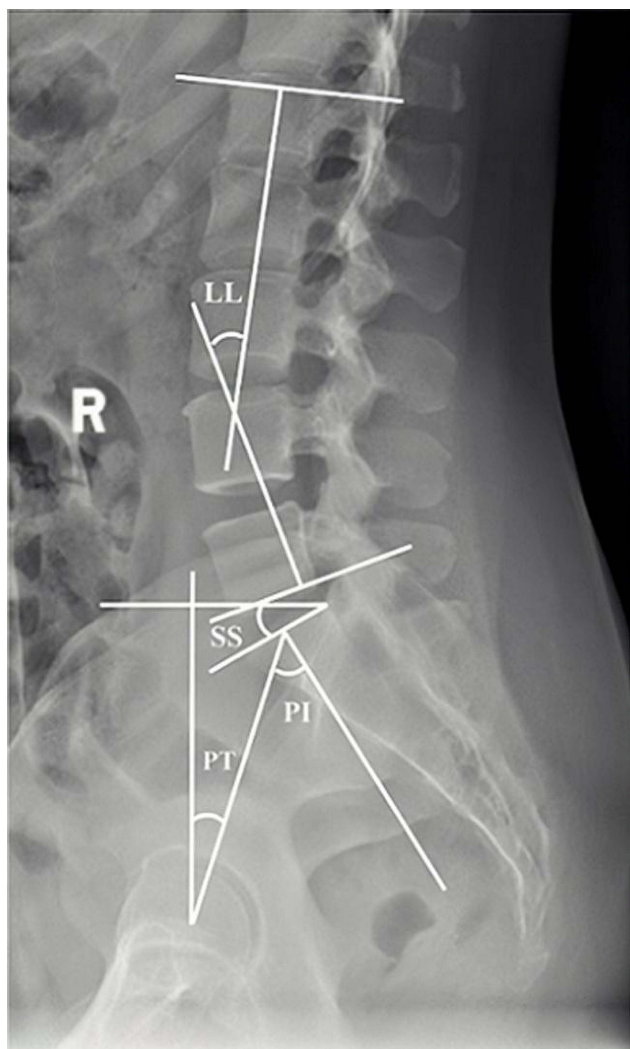
Figure 2 Measurement of sagittal spinopelvic parameters in the lumbar spine.
Abbreviations: LL, lumbar lordosis; SS, sacral slope; PI, pelvic incidence; PT, pelvic tilt.

Figure 3 Evaluation the sizes of Modic changes in the horizontal and vertical planes.

variables complied with the normal distribution. Otherwise, the Mann-Whitney *U*-test or Kruskal-Wallis test was used. Categorical variables were expressed as percentages (%) and numbers. A *p*-value with two-tail less than or equal to 0.05 was considered as a significant difference. We used the intra-class correlation coefficient (ICC) to evaluate the inter-and intra-observer reliability.[17] The ICC value of inter-and intra-observer reliability for types of MCs and radiological parameters were all more than 0.8 and were graded as good to excellent.

Results
Baseline Characteristics
A total of 263 subjects were included in this retrospective study, with a mean age of 57 (SD: 9.9) years and a mean body mass index (BMI) of 22.7 kg/m^2 (SD: 3.0). There were 150 females (57%) and 113 males (43%). The incidence of MC1, MC2, and MC3 among the included population was 30% (79/263), 46% (121/263), and 24% (63/263), respectively. According to the sizes of MCs, 113 subjects were defined as slight, 82 subjects as moderate, and the remaining 68 subjects as severe. In the present work, we did not identify any MCs occurring at the segment of L1/2 or L2/3. Over 70% of MCs (189/263) were observed at a single lumbar level, of which 27 MCs (14.3%) occurred at L3/4, 64 (33.9%) at L4/5, and 98 (51.8%) at L5/S1. The incidence of MCs at double and

planes (Figure 3). The total sizes of MCs were calculated by summing each small unit of MCs involvement. Therefore, we could determine the involvement area of MCs as from 0 to IV4 (Table 1). The involvement area of MCs with less than 1/4 of the vertebral body horizontally or vertically was defined as slight, larger than 1/4 but smaller than 3/4 of the vertebral body as moderate, and more than 3/4 of the vertebral body as severe.

Statistical Analysis
IBM SPSS 22.0 (SPSS Inc., Armonk, New York) was employed to perform statistical analysis. We used mean ± standard deviation (SD) to describe continuous variables. Two independent samples *t*-test or one-way variance analysis was applied to analyze them if these continuous
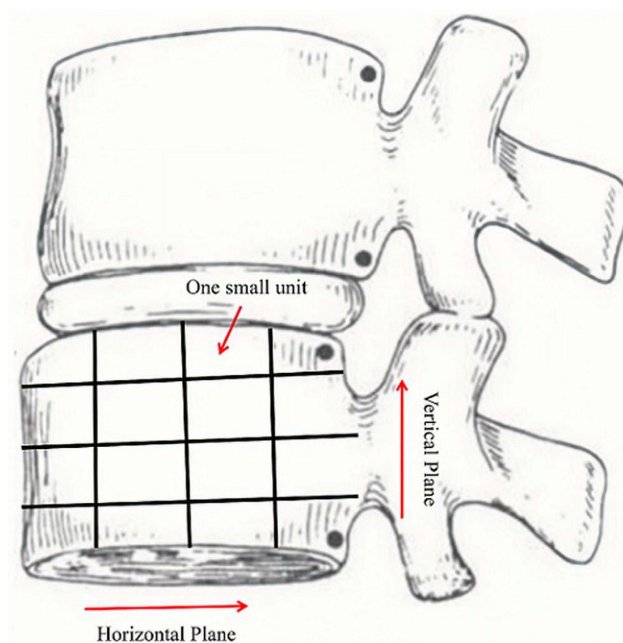
Table 1 The Grading System Regarding the Involvement Area of Modic Changes (MCs)

Groups		Involvement Area of MCs at the Horizontal Plane			
		1 Small unit	2 Small units	3 Small units	4 Small units
Involvement Area of MCs at the Vertical Plane	1 Small unit	I1	I2	I3	I4
	2 Small units	II1	II2	II3	II4
	3 Small units	III1	III2	III3	III4
	4 Small units	IV1	IV2	IV3	IV4

Note: Red: slight; blue: moderate; brown: severe.

Table 2 Baseline Characteristics of the Included Subjects

Number of Patients	n= 263
Gender	male: 113 female: 150
Age (years)*	57.0±9.9
Body mass index (kg/m^2)*	22.7±3.0
Types of Modic changes (MCs)	Modic type 1 change: 79 (30.0%) Modic type 2 change: 121 (46.0%) Modic type 3 change: 63 (24.0%)
Extents of MCs	Slight: 113 (43.0%) Moderate: 82 (31.2%) Severe: 68 (25.8%)
Lumbar levels with MCs	Single level: 189 (71.9%) 27 (14.3%, L3/4) 64 (33.9%, L4/5) 98 (51.8%, L5/S1) Double levels: 46 (17.5%) 18 (39.1%, L3-5) 28 (60.9%, L4-S1) Triple levels: 28 (10.6%, L3-S1)

Note: *Mean±SD.

triple lumbar levels was 17.5% (46/263; L3-5: 18; L4-S1: 28) and 10.7% (28/263, L3-S1). Baseline characteristics of the included subjects are shown in Table 2.

Lumbar Sagittal Parameters

The results of lumbar sagittal parameters among the three types of MCs are shown in Table 3. The statistical analysis revealed that several lumbar sagittal parameters in subjects with MC1 (LL: −25.0±9.6; SS: 22.3±7.7; and PI: 39.8 ±7.4) were significantly smaller than the groups of MC2 (LL: −29.0±10.5; SS: 26.4±8.5; and PI: 43.9±7.6) and MC3 (LL: −29.1±9.8; SS: 26.7±7.8; and PI: 43.5±6.5) (p<0.05), However, we did not detect any statistical differences in PT and PI-LL between MC1 (PT:17.4±4.0; PI-LL :14.8±6.9), MC2 (PT:17.4±4.0; PI-LL:14.9±7.6), and MC3 (PT:16.8±3.8; PI-LL:14.3±6.5) (p>0.05).

263 subjects were allocated to three groups (slight, moderate, and severe) based on the sizes of MCs (Table 4). The subjects with severe MCs (LL: −21.5±7.9; SS: 19.9±7.0; and PI: 37.0±6.2) were significant smaller LL, SS, and PI values than those of slight (LL: −32.6 ±10.4; SS: 29.9±7.7; and PI: 46.7±6.6) or moderate MCs (LL: −26.4±8.3; SS: 23.3±6.5; and PI: 41.4±6.1), with statistical differences among the three groups (p<0.01). However, no significant differences in PT and PI-LL were detected between the 3 groups (p>0.05).

Considering that the potential influence of lumbar levels involved by MCs on lumbar sagittal parameters,

Table 3 Lumbar Sagittal Parameters Among Three Types of Modic Changes (MCs)

Types Characteristics		MC1 (n= 79)	MC2 (n= 121)	MC3 (n= 63)	p
Sagittal parameters	Lumbar lordosis (LL, degrees)	−25.0±9.6*	−29.0±10.5	−29.1±9.8	<0.05
	Sacral slope (degrees)	22.3±7.7*	26.4±8.5	26.7±7.8	<0.01
	Pelvic tilt (degrees)	17.4±4.0	17.4±4.0	16.8±3.8	n.s.
	Pelvic incidence (PI, degrees)	39.8±7.4*	43.9±7.6	43.5±6.5	<0.01
	PI-LL (degrees)	14.8±6.9	14.9±7.6	14.3±6.5	n.s.

Notes: mean±SD; *Compared with MC2 and MC3, P<0.05.
Abbreviation: n.s., no significance.

Table 4 Lumbar Sagittal Parameters in Subjects with Different Involvement Extents of Modic Changes

Extents Characteristics		Slight (n= 113)	Moderate (n= 82)	Severe (n= 68)	p
Sagittal parameters	Lumbar lordosis (LL, degrees)	−32.6±10.4*	−26.4±8.3*	−21.5±7.9	<0.01
	Sacral slope (degrees)	29.9±7.7*	23.3±6.5*	19.9±7.0	<0.01
	Pelvic tilt (degrees)	16.8±3.8	18.1±3.8	17.1±4.1	n.s
	Pelvic incidence (PI, degrees)	46.7±6.6*	41.4±6.1*	37.0±6.2	<0.01
	PI-LL (degrees)	14.1±7.7	15.0±6.7	15.4±6.7	n.s.

Notes: mean±SD; *Compared with group of severe, P<0.05.
Abbreviation: n.s., no significance.

Table 5 Lumbar Sagittal Parameters in Subjects with Different Lumbar Levels Involved by Modic Changes

Lumbar Segments Characteristic		Single Level (n= 189)	Double Levels (n= 50)	Triple Levels (n= 24)	p
Spinopelvic parameters	Lumbar lordosis (LL, degrees)	−28.9±10.5	−28.3±8.3	−18.5±6.3*	<0.01
	Sacral slope (degrees)	26.0±3.9	25.5±7.6	18.6±5.3*	<0.01
	Pelvic tilt (degrees)	17.3±3.9	16.5±3.7	18.3±4.1	n.s
	Pelvic incidence (PI, degrees)	43.4±7.6	42.0±6.6	36.9±5.6*	<0.01
	PI-LL (degrees)	14.5±7.3	13.7±6.1	18.5±6.5#	<0.05

Notes: mean±SD; *Compared with the groups of single and double levels, P<0.01. #Compared with the group of double levels, P<0.05.
Abbreviation: n.s., no significance.

the included 263 subjects were divided into 3 groups: single lumbar level with MCs, double lumbar levels with MCs, and triple lumbar levels with MCs (Table 5). The analysis showed that triple lumbar levels with MCs had a significant decrease in LL (−18.5±6.3), SS (18.6±5.3), and PI (36.9±5.6) (p<0.01) and a significant increase in PI-LL (18.5±6.5, p<0.05) when compared to those MCs at single (LL: −28.9±10.5; SS: 26.0±3.9; PI: 43.4±7.6; and PI-LL: 14.5±7.3) and double lumbar levels (LL: −28.3 ±8.3; SS: 25.5±7.6; PI: 42.0±6.6; and PI-LL: 13.7±6.1).

Discussion

Previous studies[13,16] have reported that lumbar sagittal parameters are generally related to the development of MCs, whereas the correlation of the MC type, the size, and the levels involved with lumbopelvic parameters is not well understood. The results of this study showed that LL, SS, and PI are closely linked to MC1 and negatively correlated to the size of MCs. Despite MCs mainly involving one lumbar level, triple lumbar levels with MCs tend to influence sagittal balance to a major extent.

Radiographic parameters including LL, SS, PT, PI, and PI-LL are the most commonly used to evaluate the sagittal spinopelvic alignment in clinical practice and studies. LL and SS reflect the overall balance of the lumbar spine.

A loss of LL or SS may be strongly associated with the development of CLBP by disrupting the local balance of the lumbar spine.[18,19] However, in response to the changes of LL and SS, subjects could change their PT via the movement of a hip joint to maintain normal sagittal balance.[20] Therefore, PT can be thought of as a compensatory mechanism for sagittal imbalance and spinal deformity.[21] PI, a well-known pelvic morphological parameter, always maintains a constant value at the end of growth and is significantly associated with other radiographic parameters such as LL, SS, and PT.[22,23] However, since PI is constant, a mismatch between PI and LL may be caused by a loss of LL, thus affecting the global sagittal balance. A PI-LL of 10 degrees or less is usually considered the ideal sagittal matching between the lumbar spine and the pelvis.[24]

The relationship between MCs and the sagittal parameters is currently controversial and is considered to be interactive. The damage to the endplate generally precedes the intervertebral disc: the calcification and lesion of the endplate would decrease its permeability, and therefore, impede the nutritional supply of the disc to a certain extent, which accelerates degenerative changes of the intervertebral disc.[25,26] Additionally, the degeneration of the vertebral endplates causes the tilts of the upper and

lower edges, the superior and inferior edge of the vertebral body, and the inconsistency of the anterior and posterior intervertebral space,[27] resulting in the instability of the adjacent vertebral body and the changing of the sagittal balance.

Due to the unique anatomy of the lumbar spine, it is subjected to relatively high mechanical stress.[28] In the process of degeneration including the endplate calcification, a slight change in the sagittal parameters can be anticipated and compensated by the local postural adjustment. However, the localized postural adjustment may cause mechanical compensatory changes in the whole spine. Therefore, LL, SS, and PI have to be changed to accommodate this mechanical compensatory mechanism over time.[29]

Previous studies[13,16,30–32] have shown strong relationships between MCs and sagittal spinopelvic parameters. The lower LL and SS are more often seen in subjects with lumbar degenerative disease. Recent studies[13,16] have demonstrated that LL and SS were significantly decreased in subjects with MCs compared to those without MCs. However, the relationship between MCs and PI is not well-understood, as the results of existing studies on this topic vary greatly.[13,22]

In the present work, we performed a detailed stratification analysis based on the type of MCs, the sizes, and lumbar segments involved by MCs. The results indicated that subjects with MC1, severe MCs, and triple lumbar levels with MCs had significantly smaller LL as well as SS. As mentioned before, biomechanical injury to the vertebral endplates plays an important role in the development of MCs. We speculate that the lower values of the LL and SS not only reduce the resistant capacity of the intervertebral disc for the axial loading but also increase the axial forces on the vertebral endplates, leading to the endplates microfractures, which may be able to respond to why the lower LL and SS cause MCs. However, their processes might not be disparate but are interactive. Rapid progression of degenerative changes in the disc with MCs and the loss of disc height[33] may both contribute to the lower LL.[21] A loss of LL has the potential to lead to the anterior translation of the gravitational axis. The value of SS is passively decreased to maintain the normal gravitational axis in the compensation process.[22]

A lower PI significantly alters the transmission of mechanical load in the spine and imposes excessive axial compressive stresses on the discs and their adjacent vertebral endplates.[34] Once mechanical loading exceeds the bearing capacity of the vertebral endplates, microfractures may occur, further inducing the occurrence of MCs. Moreover, the alteration of mechanical loading caused by a lower PI could substantially increase the level of collagen type X, a protein that accelerates the process of cartilage calcification,[35] thus aggravating the degenerative extents by affecting the nutritional pathways of the intervertebral disc.[36] The degenerated vertebral endplates are vulnerable to damage under lesser mechanical loads and then lose their barrier function between the intervertebral disc and subchondral bone marrow, triggering "cross-talk"[37] and the initial stage of MC1. In the present work, PI-LL is high in all groups but pronounced in the triple-level group, probably because of a more pronounced loss of lordosis.

This study also suffers from some deficiencies. First, the present work may have inherent limitations of the retrospective study and selection bias compared to the prospective and randomized studies. Second, the small sample size, especially a relatively small number of MCs at double and triple lumbar levels, could reduce the statistical power and affect the reliability of the study findings. Additionally, we were restricted by the nature of the retrospective study from obtaining complete clinical information.

Conclusions

The present work supports the previously found connection between MCs and lumbar sagittal parameters. Further, our study identifies the MC-related characteristics, such as their types, sizes, as well as the number of involved lumbar levels by MCs, that are significantly linked to lumbar sagittal imbalance. Overall, MC1, severe MCs, and lumbar multi-segmental MCs might contribute to lumbopelvic sagittal imbalance.

Compliance with Ethics Guidelines

Our institutional ethical committee reviewed and approved the study protocol (No. 2016-12). The present work was implemented under the guide of the principles of the Declaration of Helsinki.

Acknowledgments

Author Contributions

Xiaoping Mu and Jianxun Wei conceived the research topic. Jianxun wei supervised the implement of this study.

Disclosure

The authors report no conflicts of interest in this work.

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