Quantitative MRI analysis of the surface area, signal intensity and MRI index of the central bright area for the evaluation of early adjacent disc degeneration after lumbar fusion

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Abstract

Purpose The aim of this study was to evaluate early ASD at short-term follow-up in fused and unoperated patients with degenerative disc disease, using quantitative magnetic resonance imaging (MRI) analysis of the area, signal intensity and their product, i.e., MRI index of the central bright area of the disc as well as measures of intervertebral disc height and Pfirrmann grading scale. The further purpose was to determine whether fusion accelerates ASD compared with non-surgical treatment in short-term follow-up.

Methods One hundred and eight chronic low back patients diagnosed as L4/L5 degeneration undertook either one-level instrumented posterior lumbar interbody fusion or conservative treatment. They were followed up for about 1 year. Finally 46 fused and 45 conservatively treated patients with MRI follow-up were included. Pre- and post-treatment MRIs were compared to determine the progression of disc degeneration at the two cranial adjacent segments.

Results The area, signal intensity and MRI index of the central bright area of the adjacent discs decreased in the operated and unoperated groups from pre-treatment to follow-up, except for an insignificant decrease of signal intensity at the second adjacent segment in the unoperated

group. The changes in these parameters were statistically greater at the first than the second adjacent segment in the fused group, but not in the unoperated group. And the changes in the fused group were more pronounced than those at both neighbouring levels in the unoperated group. However, the Pfirrmann grading scale and intervertebral disc height did not detect any changes at adjacent discs in either group.

Conclusions Decrease in the parameters of quantitative MRI analysis indicated early degeneration at discs adjacent to lumbar spinal fusion. Fusion had an independent effect on the natural history of ASD during short-term follow-up. Continued longitudinal follow-up is required to determine whether these MRI changes lead to pathologic changes.

Keywords Adjacent segment degeneration · Lumbar fusion · Quantitative MRI analysis · Signal intensity

Introduction

Despite numerous publications on the subject [1–10], few studies have investigated adjacent segment degeneration (ASD) at an early postoperative stage. Most report the occurrence of ASD at follow-up of >3 years [1–8], with varying manifestations such as disc space narrowing, listhesis, or stenosis. Unfortunately, when these pathologic conditions arise, they are difficult to reverse. Some reports describe certain cases of early ASD during long-term follow-up [9–12], the earliest occurring 1 year postoperatively, but the general degenerative status of adjacent segments at the early stage in their fused patients was not reported. Furthermore, in these investigations ASD was not identified until pronounced pathologic changes appeared, probably because of the insensitive measures they applied,

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such as reduction of disc height and aggravation of grade of disc degeneration. Since underlying degenerative changes can occur before pathologic conditions emerge, monitoring ASD at short-term follow-up is important. Early detection can alert the surgeons and patients to the possible progression of adjacent degenerative conditions and enable measures to retard or prevent the development of ASD at the initial stage.

Measurement sensitive to the early degenerative changes is therefore needed. With the well-established correlations between the signal intensity on magnetic resonance imaging (MRI) and disc composition and condition [13–16], quantitative analysis of MRI has been developed to capture the early disc degeneration [16–18]. The method introduced by Sobajima et al. [18] measures the surface area and signal intensity of the nucleus pulposus, and their product provides an MRI index from T2-weighted images. This effectively identifies degenerative changes in rabbit lumbar discs beginning at 3 weeks after a stab injury, along with histologic analysis. It shows advantages in identifying early disc degeneration by capturing the initial biochemical changes within the disc and it is sensitive, reliable and accurate [18]. This method has not yet been used to evaluate ASD in humans.

The aim of this study was to evaluate early ASD at short-term follow-up in fused and unoperated patients with degenerative disc disease, using quantitative MRI analysis as well as the frequently used measures of intervertebral disc height (DH) and Pfirrmann grading scale. The further purpose was to determine whether fusion accelerates ASD compared with non-surgical treatment in short-term follow-up.

Materials and methods

Population and follow-up

From April 2007 to December 2009, 108 eligible patients were prospectively included in this study. There were 65 males and 43 females aged from 25 to 65 years (mean 47.2 ± 6.9). The average age for males was 46.6 ± 8.1 (range 25–64) and for females 48.1 ± 6.3 (range 31–65). They complained of low back pain with or without radicular pain for at least 1 year, and each was examined by plain radiography, computed tomography (CT) and MRI. The pain was interpreted as emanating from L4/L5 according to the patients' history, physical examination and radiographic signs including loss of signal on T2-weighted MRIs, disc space narrowing, endplate sclerosis, vacuum phenomenon, and Modic changes. Patients with previous spine surgery (18 cases), spondylolisthesis (48), spinal stenosis with reduced walking distance and neurologic

signs (37), degenerative scoliosis (19), acute spinal fracture (31), infection (8), osteoporosis (23), tumour (17), or ongoing psychiatric illness (9) were precluded. Further, patients with one or more of the following pre-existing changes at the adjacent segments were also precluded (65 cases): disc degeneration of Pfirrmann grade $\geq$ III; spondylolisthesis >3 mm; angular motion $>10^\circ$ between the adjacent vertebral endplates on flexion–extension radiographs; symptomatic disc herniation or spinal stenosis; hypertrophy of facet; osteophyte >3 mm; scoliosis; and compression fracture [7, 19, 20]. The included participants were divided into two groups according to treatment: one-level instrumented posterior lumbar interbody fusion (fusion group, $n = 55$) and non-surgical treatment (control group, $n = 53$). They all gave informed consent prior to participation.

All fusion procedures were performed with a uniform technique by one team of surgeons in our institution. Flexion–extension radiographs and/or CTs were obtained at 6 months to determine the fusion status. Patients in the control group followed a program that was constructed on a consensus basis. It consisted of physiotherapy with other supplementary forms of treatments including information and education, cognitive intervention and exercise. MRIs were performed in both groups at the last follow-up. Finally, 91 patients were available: 5 with fusion and 5 with non-surgical treatment were lost to follow-up; in the fused group, 2 refused to take the final MRI examination and 2 were considered as non-fusion; and in the unoperated group, three patients were operated in other hospitals for worsening or continuation of severe symptoms. Thus, 46 were left in the operated group and 45 in the unoperated group.

To focus on the effects of lumbar fusion, and to reduce the effects of natural degeneration and other potential confounding factors, pre-treatment intergroup variables were determined to be comparable (Table 1).

MRI measurements

The lumbar spine was imaged using a 1.5-T System (Siemens, Germany) with a surface coil. All patients were placed supine and the center of the localizing laser was set at 3 cm proximal to the umbilicus (corresponding to the center of L3 vertebral column approximately) to keep a uniform scanning positioning for each patient. Midsagittal T2-weighted MRIs were selected for evaluation of the degenerative changes in adjacent discs. Sagittal scans used a T2-weighted fast spin echo sequence, with TR/TE times of 3,000/100 ms, slice thickness and interslice gap of 4 and 1 mm, matrix size 255×512 , field of view 260×260 mm, bandwidth 120 Hz/Px, and echo factor 15. Magnet shimming was not used for any of the scanings.

Table 1 Baseline characteristics of patients who underwent fusion (Group I) and non-surgical treatment (Group II) (mean $\pm$ SD)

	Group I (<i>n</i> = 46)	Group II (<i>n</i> = 45)	<i>P</i> value
Sex (M/F)	30/16	24/21	0.290
Age (years)	48.4 $\pm$ 8.0	46.2 $\pm$ 6.0	0.129
Weight (kg)	66.7 $\pm$ 7.9	65.9 $\pm$ 7.5	0.614
Height (cm)	166.0 $\pm$ 8.1	166.9 $\pm$ 6.4	0.571
BMI (kg/m ²)	24.2 $\pm$ 2.6	23.6 $\pm$ 1.9	0.201
Duration of FU (months)	11.7 $\pm$ 0.7 (9–12)	11.8 $\pm$ 0.5 (10–12)	0.424
Disc degeneration at first adjacent segment (I/II)	6/40	3/42	0.485
Disc degeneration at the second adjacent segment (I/II)	9/37	7/38	0.784
Spinal canal diameter (mm)	12.8 $\pm$ 2.8	13.2 $\pm$ 1.9	0.489
Lumbar lordosis (degrees)	43.8 $\pm$ 8.9 ^a	41.5 $\pm$ 9.2	0.226
Segmental lordosis (degrees)	10.4 $\pm$ 2.7 ^a	10.6 $\pm$ 2.8	0.786
Sacral inclination (degrees)	49.3 $\pm$ 7.4 ^a	50.7 $\pm$ 6.5	0.331

The grade of disc degeneration at adjacent segments was evaluated by the Pfirrmann grading system; the spinal canal diameter at the affected level was measured as the minimum sagittal diameter at the level of the disc space on T2-weighted MRIs

FU follow-up, BMI body mass index

^a The segmental and lumbar lordosis and sacral inclination in the operated group were collected from the immediate postoperative radiographs to achieve better comparability between the two groups

All MRIs were obtained at about 3:00 pm, to minimize the effect of water influx within the discs due to overnight bed rest, which can increase the T2-weighted disc signal up to 25 % [21]. And the patient weight at the first and last MRIs was not significantly different (data not shown), thus eliminating its potential effect on the disc signal [22].

MRIs were analyzed on a picture archiving and communication system workstation (Jin YeXiang, Beijing, China) with embedded region of interest (ROI) and gray-scale histogram software. A uniform window width of 1,800 and window level of 700 was set for all analyses. As the region of “nucleus pulposus”, or more appropriate the central bright area (CBA) of the disc illustrated by Sobajima et al. [18], is suggested to correspond to the inner annulus fibrosus and nucleus pulposus by comparative histologic and radiologic studies [23, 24], we considered it better to call our analysis as quantitative analysis of the area, signal intensity and their product, i.e., MRI index of the CBA of the disc. Briefly, the CBA of each disc was outlined on a screen using the computer mouse to define the ROI (Fig. 1). The area and mean signal intensity of the ROI were then computed, and their product calculated. The MRI index is considered a comprehensive measure of degenerative changes since a degenerating disc can exhibit changes in area, signal intensity, or both on MRIs [18]. For each disc, the signal intensity of the CBA was normalized to the signal of the adjacent cerebrospinal fluid to compensate for the inhomogeneity of the magnetic fields between subjects and discs [13, 25]. As only patients with preoperative adjacent discs of Pfirrmann grade I or II were included (clear distinction of nucleus and annulus [26], and

in this study, to say “clear distinction of the central bright portion and peripheral dark portion” is more appropriate), the measurement error of ROI outlining was minimal. As ASD is more common at the cranial than the caudal segments in floating fusion [27, 28], only the cranial unfused levels were investigated.

The Pfirrmann score [26] and intervertebral DH of adjacent discs were also measured on the same midsagittal T2-weighted images, to compare the sensitivity of different measures in detecting early ASD. The measurement of DH is described elsewhere [29], and the mean of the anterior and posterior heights was used.

Fig. 1 Measurement of the surface area, signal intensity and MRI index of the CBA of an adjacent disc. The contour of the CBA was outlined in gray as ROI. The ROI was automatically computed for surface area and average signal intensity. MRI index was calculated as the product of surface area and average signal intensity

Two independent, attending radiologists experienced in reading musculoskeletal images and blinded to the study design analyzed all selected images, and then the differences between pre-treatment and follow-up MRIs were calculated to determine the progression of ASD. Inter-observer repeatability was calculated using the intra-class correlation coefficient (ICC), and the means of the readings were used. The inter-observer ICCs were 0.79 for Pfirrmann score and 0.85 for DH. ICCs for the area, signal intensity and MRI index of the CBA ranged from 0.88 to 0.93.

IRB consideration

The Ethics Committee of our institution approved this study.

Statistical analysis

Student's *t* test was used to evaluate intersegment and intergroup differences for continuous variables. The χ^2 test or Fisher's exact test was used to compare the distributions of categorical variables. $P < 0.05$ indicated statistical significance. Data analyses were performed with SPSS 16.0 software.

Results

Changes of Pfirrmann score and intervertebral DH from pre-treatment to follow-up

None of the discs at the two cranial adjacent levels showed progression of Pfirrmann score in either group at 1 year follow-up. The intervertebral DH showed a slight but insignificant decrease at the two neighbouring segments in the fused group (first segment: pre-treatment 10.48 ± 0.77 mm, follow-up 10.38 ± 1.03 mm, $P = 0.096$; second segment: pre-treatment 9.66 ± 0.92 mm, follow-up 9.59 ± 1.05 mm, $P = 0.107$). The trends were similar in the control group (first segment: pre-treatment 10.55 ± 1.14 mm, follow-up 10.50 ± 1.20 mm, $P = 0.465$; second segment: pre-treatment 9.47 ± 1.10 mm, follow-up 9.43 ± 1.04 mm, $P = 0.400$).

Changes in the area, signal intensity and MRI index of the CBA from pre-treatment to follow-up

Both groups showed decreases in the area, signal intensity and MRI index of the CBA at the adjacent levels ($P < 0.05$), except that the signal intensity decreases at the second segment was insignificant in the non-surgical group ($P = 0.057$) (Table 2).

The MRI index in the fused group decreased 23.6 and 15.3 % in the first and second adjacent segment discs, compared with 5.5 and 4.3 %, respectively, in the non-surgical group. In total, 58.7 % (27/46) of fused patients had an MRI index decrease >20 % at the first adjacent segment, and 23.9 % (11/46) at the second adjacent level. The corresponding proportions were 4.4 % (2/45) and 0 % in the unoperated group.

Intersegment and intergroup comparisons of changes in the area, signal intensity and MRI index of the CBA from pre-treatment to follow-up

The percentage changes in the area, signal intensity and MRI index of the CBA were greater at the first than the second segment in the operated group ($P < 0.05$). However, no intersegment differences were found in the unoperated group ($P > 0.05$) (Fig. 2).

Intergroup comparison showed that the percentage changes of MRI index and area were greater in the fused than the conservatively treated group for both adjacent segments ($P < 0.001$), as was the rate of change of signal intensity ($P < 0.05$) (Table 3).

Comparison of baseline characteristics in fused patients with different MRI index changes from pre-treatment to follow-up

Patients in the fused group were divided into two subgroups according to their percentage change of MRI index at the first adjacent segment: those with a decrease >20 % of the pre-treatment value and those with <20 %. A smaller sacral inclination angle was found in patients in the former subgroup, while no significant differences were identified in gender, age, body mass index, duration of follow-up, spinal canal diameter, grade of disc degeneration, lumbar lordosis or segmental lordosis between the subgroups (Table 4).

Discussion

Our main finding was that the area, signal intensity and MRI index of the CBA decreased in the operated and unoperated groups from pre-treatment to follow-up, except for an insignificant decrease of signal intensity at the second adjacent segment in the unoperated group. The changes in these parameters were statistically greater at the first than the second adjacent segment in the fused group, but not in the unoperated group. And the changes in the fused group were more pronounced than those at both neighbouring levels in the unoperated group. However, the Pfirrmann score and DH did not detect any changes at adjacent discs in either group.

Table 2 The area, signal intensity and MRI index of the CBA in surgical and non-surgical groups pre-treatment and at follow-up (mean $\pm$ SD)

	Surgical group (<i>n</i> = 46)			Non-surgical group (<i>n</i> = 45)		
	Pre-tre	Follow-up	<i>P</i> value	Pre-tre	Follow-up	<i>P</i> value
First adjacent discs						
Area (mm ²)	217.9 $\pm$ 42.9	190.7 $\pm$ 43.2	<0.001	201.1 $\pm$ 43.7	197.4 $\pm$ 42.9	<0.001
Signal intensity (%)	42.4 $\pm$ 14.5	36.6 $\pm$ 12.7	<0.001	46.6 $\pm$ 12.7	44.2 $\pm$ 10.5	0.001
MRI index (mm ²)	93.4 $\pm$ 40.3	70.3 $\pm$ 31.3	<0.001	94.5 $\pm$ 33.8	87.8 $\pm$ 28.9	<0.001
Second adjacent discs						
Area (mm ²)	203.3 $\pm$ 43.8	183.5 $\pm$ 41.9	<0.001	191.7 $\pm$ 43.3	186.8 $\pm$ 43.0	<0.001
Signal intensity (%)	43.2 $\pm$ 12.6	40.8 $\pm$ 13.2	<0.001	49.2 $\pm$ 7.6	47.9 $\pm$ 6.2	0.057
MRI index (mm ²)	90.7 $\pm$ 41.4	77.9 $\pm$ 38.7	<0.001	94.0 $\pm$ 24.8	89.6 $\pm$ 24.2	0.002

CBA central bright area, *Pre-tre* pre-treatment **Fig. 2** Percentage changes of the area, signal intensity, MRI index at the two cranial adjacent segment discs in surgical (a) and non-surgical groups (b) (*1st*, the first adjacent segment; *2nd*, the second adjacent segment)

Disc degeneration at the initial stage, characterized by proteoglycan degradation and a subsequently reduced capacity of the nucleus pulposus to bind water, can be

revealed by loss of disc signal on T2-weighted MRIs [14]. So, we interpret the changes in MRI parameters as indicating the presence of early ASD. The high ICCs for the three parameters (between 0.89 and 0.92) indicate good to excellent repeatability [30].

The insensitivity of the Pfirrmann grading system was possibly due to the loss of information when the digital data provided by MRIs were reduced to a 5-level categorical assessment [31]. The failure of DH to detect early ASD was not surprising, because DH reduction usually occurs in later stages following the biochemical changes and thus seen in discs with advanced degeneration [27, 29].

The major strength of this study was that we prospectively selected a valid control group and attempted to eliminate potential confounding factors, identifying fusion as the major factor to explain the differing severity of ASD in the two groups. Although previous studies sporadically reported cases of early ASD, the retrospective design and the fact that heterogeneous patients were enrolled without a valid control group made it difficult to distinguish the effects of fusion from those of natural degeneration or genetic predisposition [9–11, 20].

We interpreted the changes in the non-surgical group as the results of natural degeneration and genetic predisposition, while the greater changes of the three parameters in the surgical group at both adjacent segments were accelerated by fusion (Table 3). Further, the differences between the first and second adjacent segments in the surgical group, but not in the non-surgical group, also supported this hypothesis (Fig. 2), as ASD is more prone to affect the segment immediately neighbouring the fusion than more distant segments [7, 27].

Risk factor analysis showed that patients with a greater decrease in MRI index had a smaller sacral inclination ($P = 0.009$). This is similar to the finding by Disch et al. [32], who found a reduced sacral inclination in patients suffering from ASD compared with non-ASD patients. A rigid lumbar arthrodesis combined with a more vertical

Table 3 Intergroup differences in percentage change of the area, signal intensity and MRI index of the CBA at the two upper adjacent discs (mean $\pm$ SD)

	Surgical group (<i>n</i> = 46)	Non-surgical group (<i>n</i> = 45)	<i>P</i> value
First adjacent segment			
Area (%)	12.7 $\pm$ 7.7	1.8 $\pm$ 2.6	<0.001
Signal intensity (%)	12.2 $\pm$ 13.7	3.7 $\pm$ 9.3	0.001
MRI index (%)	23.6 $\pm$ 12.7	5.5 $\pm$ 9.4	<0.001
Second adjacent segment			
Area (%)	9.9 $\pm$ 5.3	2.6 $\pm$ 2.0	<0.001
Signal intensity (%)	6.1 $\pm$ 9.2	1.8 $\pm$ 8.9	0.028
MRI index (%)	15.3 $\pm$ 10.1	4.3 $\pm$ 9.0	<0.001

CBA central bright area

Table 4 Baseline characteristics of fused patients with different percentage changes of MRI index (mean $\pm$ SD)

	MRI index decrease ≥ 20 % (27/46)	MRI index decrease < 20 % (19/46)	<i>P</i> value
Sex (M/F)	17/10	13/6	0.762
Age (years)	47.4 $\pm$ 8.5	49.9 $\pm$ 7.3	0.307
BMI (kg/m ²)	24.7 $\pm$ 1.8	23.5 $\pm$ 3.3	0.125
Duration of FU (months)	11.8 $\pm$ 0.6	11.6 $\pm$ 0.9	0.417
Pre-treatment Pfirrmann score (I/II)	3/24	2/17	1.000
Spinal canal diameter (mm)	13.2 $\pm$ 3.1	12.3 $\pm$ 2.4	0.316
LL (degrees)	43.3 $\pm$ 8.0	44.6 $\pm$ 10.3	0.636
SL (degrees)	10.2 $\pm$ 2.3	10.8 $\pm$ 3.1	0.415
SI (degrees)	46.9 $\pm$ 7.2	52.6 $\pm$ 6.9	0.009

FU follow-up, BMI body mass index, LL lumbar lordosis, SL segmental lordosis, SI sacral inclination

sacral inclination may enhance the load shift towards the cranial segments, and thus may cause anticipatory degenerative changes [5, 32]. However, the sacral inclination of those with greater changes in MRI index did not reach the criteria for a “vertical sacrum” [5] in this study. A possible explanation is that the follow-up time was not long enough, leading to a statistically but not clinically significant difference between patients with different degrees of ASD.

ASD is detectable as early as 6 months postoperatively in patients treated with the Dynesys stabilization system [31]. Moreover, animal model experiments have identified the early development of ASD radiologically and

histologically, sometimes as early as at 3 months after fusion, although the authors point out that ASD is likely to progress more rapidly in animal models than in humans [33–35]. The progression of post-fusion ASD we identified was based on the initial biochemical changes, and highlights the utility of quantitative MRI analysis to reveal changes during early follow-up. In that case, prompt preventive measures can be taken before pathologic changes arise, and the development of ASD may be effectively delayed or halted.

The main weaknesses of this study was the limited number of patients enrolled and the lack of continued longitudinal follow-up.

Conclusion

Decrease in the parameters of quantitative MRI analysis indicated early degeneration at discs adjacent to lumbar spinal fusion. Fusion had an independent effect on the natural history of ASD during short-term follow-up. Continued longitudinal follow-up is required to determine whether these MRI changes lead to pathologic changes.

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Ethical considerations The clinical study has been approved by Medical Ethic Committee of Sir Run Run Shaw hospital. The doctors of this clinical study have obeyed the ethic principles, and respected the patients’ right. The study has been performed with the patients’ permissions.

Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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