Disc degeneration of young low back pain patients: A prospective 30-year follow-up MRI study

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30-YEAR FOLLOW-UP ON DISC DEGENERATION

ABSTRACT

Study Design: A prospective follow-up study.

Objective: To investigate if early lumbar disc degeneration (DD) in young low back pain (LBP) patients predicts progression of degenerative changes, pain, or disability in a 30-year follow-up.

Summary of Background Data: MRI is an accurate method for studying degenerative changes in intervertebral discs. Decreased signal intensity (SI) can be used as indication of decreased water content. Long-term prognosis of early DD remains unclear.

Methods: In an earlier study, 75 conscripts aged 20 years with LBP, had their lumbar spine examined by MRI. At a follow-up of 30 years, the subjects were contacted; 35/69 filled a pain and disability questionnaire, and 26/35 were also re-examined clinically and by MRI. The images were evaluated for decreased SI and other degenerative changes. Association between decreased SI of a disc at baseline and the presence of more severe degenerative changes in the same disc space at follow-up was analyzed using Fisher's exact test. Association between decreased baseline SI and pain/disability scores from the questionnaire was analyzed with Kruskal-Wallis H test.

Results: The total number of lumbar discs with decreased SI increased from 23/130 (18%) to 92/130 (71%) -from 0.9 to 3.5 per subject during the follow-up. Distribution of DD changed from being mostly in L4 – L5 and L5 – S1 discs to being almost even between the four lowermost discs. Discs that had even slightly decreased SI at baseline were more likely to have severely decreased SI at follow-up, compared to healthy discs (57% vs 11%, p<0.001).

Other degenerative changes were also more common in these discs. Severity of DD at baseline did not have a significant association with current pain or disability.

Conclusions: In young LBP patients, early degeneration in lumbar discs predicts progressive degenerative changes in the respective discs, but not pain, disability, or clinical symptoms. *Key Words:* Disc degeneration; Low back pain; Lumbar spine; Magnetic resonance imaging; Signal intensity; Disc protrusion; Modic changes; Endplate lesions; Oswestry disability index *Level of Evidence:* 4

KEY POINTS

- Lumbar discs with decreased signal intensity in MRI at baseline were more likely to show severe degenerative changes after the follow-up.
- The mean number of lumbar discs with decreased signal intensity increased from 0.9 to 3.5 per subject.
- Early disc degeneration did not predict future pain or disability.

1 INTRODUCTION

Low back pain (LBP) is a persistent and growing issue in healthcare. An estimated 70-80% of the population in industrialized countries suffer from LBP at some point in their life.^{1,2} One of the important background factors is intervertebral disc degeneration (DD), which begins early during youth.³ Magnetic resonance imaging (MRI) gives information about morphological and biochemical changes in the intervertebral disc without risk of harmful effects. Therefore, MRI is widely used for assessing the early phases of DD. Decreased signal intensity (SI) of the nucleus pulposus of the intervertebral disc correlates with its water content and grade of DD.^{4,5} Degenerative disc changes have an association with clinical LBP symptoms.^{6,7} On the other hand, 80% of asymptomatic adults have disc abnormalities on lumbar MRI.^{8,9} Long-term effects and prognosis of early DD remain unclear.

12 In a prospective MRI study of 20-year-old men, one or more lumbar discs were 13 demonstrated to be degenerated in 57% of those with chronic LBP compared with 35% of 14 the asymptomatic controls.¹⁰ The aim of the present study was to investigate the value of 15 DD detected in early adulthood as a predictor of progression of degenerative changes and 16 changes in LBP symptoms and disability in middle age.

MATERIALS AND METHODS

18 Subjects

In 1987, 75 young Caucasian male conscripts in Finland (mean age 20 years, SD 1.0) suffering
from LBP, severe enough to hinder their participation in military service, were recruited into
an MRI study in a military hospital. 34 age-matched asymptomatic controls were also
recruited, consisting of conscripts and medical students volunteering for the study. The
prevalence of lumbar discs with decreased SI was significantly higher among the study
subjects (57%) than among the controls (35%).¹⁰

In 2017, the original study subjects were invited by mail (submitted twice) to participate in a follow-up study consisting of a questionnaire, clinical examination and MRI. Six of them were not reached (four dead, two did not have a permanent address). Of the contacted 69 subjects, 35 replied to the questionnaire and 26 additionally attended the clinical examination and MRI (Fig.1). The mean age was 51 (SD 1.4) for all the 35 subjects who replied, and 51 (SD 0.7) years for the 26 subjects in the re-examined subgroup.

32 MRI of the lumbar spine and assessment of degenerative changes

A 0.02 T low-field MRI scanner (Acutscan, Instrumentarium Corp.)¹⁰ was used in 1987, and a
 1.5 T scanner (Avanto^{fit}, Siemens Healthineers, Erlangen, Germany) in 2017. Routine T2 weighted and T1-weighted sagittal and T2-weighted axial spin-echo sequences and
 additional T1-weighted coronal and T2 TIRM-weighted sagittal images were obtained in
 2017.

SI of the intervertebral discs was determined in 2017 with the same method as in 1987 as previously reported.¹⁰ A region of interest (ROI) was determined in the nucleus pulposus of each disc at levels Th12/L1 – L5/S1 in sagittal T2-weighted images and the SI of that region measured. The disc with the highest SI value was regarded as the healthiest in each subject and it was used as a reference for his other discs. SI value (ROI measurement) of each lumbar disc was compared with that of the reference disc. A relative SI-value was calculated for each lumbar disc as a percentage of the reference disc's SI-value. The degree of SI decrease was presented using a three-grade scale: normal (0 – 20% decreased SI), moderately decreased (21 – 60% decreased SI), and severely decreased (>60% decreased SI). To assess the intraobserver repeatability of the SI measurements, the SI in six discs of five subjects (n=30 discs) was measured twice and the intraclass correlation coefficient was calculated. It was 0.98.

Additional degenerative changes in discs and adjacent subchondral bone were visually evaluated in 2017, by two radiologists separately who were blinded to the 1987 MRI findings. Height of each disc (DH) was graded by comparing it with that of the normal one above. It was graded on a four-grade scale as normal, decreased by 1 - 33%, decreased by 34 - 66% or decreased by 67 - 100%. Disc protrusion or bulging were graded as present or absent. Sign of an annular fissure was graded as absent, high intensity zone (small HIZ) or a large annular fissure present. Modic changes (subchondral SI changes in bone marrow) were divided into three grades according to the presence of different combinations of Modic types representing subchondral bone marrow changes (M1=edema, M2=fat and M3=sclerosis)¹¹ adjacent to each disc. Grade 0 included disc spaces with no Modic changes.

Grade 1 included any disc spaces with M1 type changes (with or without M2 or M3 types). Grade 2 included those with M2 and/or M3 type changes (without M1). Lesions in adjacent bony endplates (EPL) were graded as no lesions, a minor lesion, a Schmorl node type defect, an uneven or irregular border between disc and vertebra, and a combination of a Schmorl node and an irregular border. Furthermore, the grades with Schmorl nodes and/or an irregular border were regarded as severe EPLs. Interobserver agreement for visual analyses ranged from 0.45 to 0.66 (Cohen's kappa). Analysis of these additional degenerative findings was not available for the 1987 MRI images. Questionnaire and clinical examination in 2017

The questionnaire included questions about health and lifestyle, employment status, history of spinal surgery, a visual analogue pain scale (VAS; scale 0 - 10), and the Oswestry disability index (ODI; Table 1). VAS was interpreted as mild (0 - 3.4), moderate (3.5 - 6.4), or severe pain (6.5 - 10). The clinical examination included sensory, motor and jerk reflex tests, the straight leg raise test and Schober's test. These test results were reported as positive or negative.

77 Statistical analysis

To examine the progress of degeneration in individual discs and find out if early decrease of SI in a disc predicted more severe degenerative changes in the same disc or disc space, we used the dichotomized SI decrease (SI decreased >20% vs. 0 – 20%) of the individual disc in 1987 as predictor and the SI decrease (SI decreased 0 – 20%, 21 – 60% or >60%) and the

visually evaluated degenerative changes in the same disc in 2017 as outcomes (n=130 discs; 26 subjects with 5 lumbar discs each). Cross tabulation was used to show whether a disc with decreased SI (SI decrease of >20%) at baseline (1987) was more likely to have a higher grade of SI decrease (>60%) or other types of degenerative changes in that disc or adjacent subchondral bone at follow-up (2017) than a disc with no SI decrease (SI decreased 0 – 20%) in 1987. The statistical significance of the associations was analyzed using Fisher's exact test. Presence of decreased SI (dichotomized) at baseline was used as a predictor and VAS and ODI scores from the 2017 questionnaire were used as outcomes. Subjects were divided into two groups according to the presence or absence of decreased SI at any disc level in 1987. The means of VAS and ODI were determined for both groups. The statistical significance of the difference between the means was determined with the Kruskal-Wallis H test. The calculations were done for all subjects who replied to the questionnaire (n=35) in 2017 and separately for the smaller subgroup of subjects who additionally had MRI (n=26). The association of the subject's employment status with his VAS/ODI score was analyzed with the same method.

To find out if moderately or severely decreased SI at any disc level in 1987 predicted findings in clinical tests in 2017, association of the graded baseline SI decrease (SI decreased 0 - 20%, 21 - 60% or >60%) with the dichotomized clinical findings in 2017 was analyzed with cross-tabulation and Fisher's exact test. The "maximal decreased SI grade" in each subject, meaning the highest grade of SI decrease in any lumbar disc of that subject in 1987, was the predictor. The presence of clinical findings (positive or negative) were outcomes.

B RESULTS

In the 2017 MR images, 25 of the 26 subjects had more degenerated lumbar discs (with SI
decreased >20%) than in 1987. Every subject had at least one disc with decreased SI in 2017,
while only 15/26 did in 1987. Of all lumbar discs, 92/130 (71%) were degenerated in 2017
while 23/130 (18%) in 1987. Furthermore, 73/107 (67%) of the normal discs in 1987
degenerated during the 30-year follow-up. The mean number of degenerated discs per
person increased from 0.9 (SD 0.9) in 1987 to 3.5 (SD 1.0) in 2017 (p<0.001, Kruskal-Wallis).
While most degenerated discs were at disc levels L4/L5 or L5/S1 in 1987, the distribution
was more even in 2017 with nearly the same number of discs with decreased SI at each of
the four lowest disc levels (Figure 2).

113 A significant association was found between decreased SI of individual discs (n=130) 114 at baseline and any type of degenerative change in the same discs or disc levels at follow-115 up. In a disc with even a slight SI decrease (>20%) in 1987, the presence of severely 116 decreased SI (>60% decrease), decreased disc height (DH), disc protrusion, high intensity 117 zone (HIZ), Modic changes, or severe endplate lesions was more common in 2017 than in a 118 disc without decreased SI (0 – 20%) in 1987 (Table 2). Figure 3 shows grade of SI decrease 119 and disc protrusions in 2017 in relation to grade of SI decrease in 1987. The associations 120 were statistically significant (p<0.01).

Of the 35 subjects who replied to the questionnaire in 2017, 28 (80%) reported
 currently suffering from LBP. The mean VAS in 2017 was 3.3 (SD 3.4) in subjects with no
 discs with decreased SI in 1987 (SI decreased >20%) and 2.7 (SD 2.8) in those with one or
 more degenerated discs (p=0.68). Using 3.5 as the cut-off point, 23/35 (66%) had only mild

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125	or no pain at all. Five (14%) had severe pain with VAS 6.5 or more. Mean ODI in 2017 was
126	20.1 (SD 21.9) and 15.1 (SD 13.4) respectively (p=0.71) (Table 3). One subject was on
127	extended sick leave for back pain, six were retired due to disability (not necessarily back-
128	pain related), and four were currently unemployed. Occupational status was not
129	significantly associated with VAS (p=0.22), ODI (p=0.13), or SI in 1987 (p=0.71).
130	In comparison, 23/26 (89%) subjects participating in both the clinical and MRI
131	examination reported having LBP. The mean VAS in 2017 was 3.4 (SD 3.2) in subjects with
132	no discs with decreased SI in 1987 and 3.1 (SD 2.7) in those with one or more degenerated
133	discs (p=0.90). Mean ODI was 20.2 (SD 19.7) and 17.3 (SD 13.9) respectively (p=0.66). One
134	subject was on extended sick leave, four were retired, and two unemployed. During the 30-
135	year follow-up, four of the 26 subjects had undergone spinal surgery – two of them had
136	discs with decreased SI in 1987.
137	In the clinical examination, five of the subjects had weakened lower leg motor

function, eight had abnormal lower limb skin sensations (such as numbness, hypo- or hyperesthesia), five had weakened patellar reflexes, one had a positive straight leg raise test, and 21 had under 5 cm increase in Schober's test. Results of the 2017 clinical tests did not have an association with the subjects' maximal grade of SI decrease in 1987 (p=0.54 –

⁸ 142 1.00)

DISCUSSION

This study is a prospective long-term follow-up of the progression of intervertebral DD in young LBP patients. We found that decreased SI of the disc at the age of 20 was associated with further decrease of SI and other advanced degenerative changes in the same disc and disc space after follow-up, including disc protrusions and adjacent bony endplate lesions. Our MRI study suggests that decreased SI of a disc may have a predictive value for multiple other types of degenerative changes, in addition to further decreasing SI in that specific disc. One explanation could be that early lumbar DD predisposes to an accelerated degenerative process in that specific disc space, as suggested in an earlier study.¹¹ Recent research has identified important genetic factors behind disc degeneration.¹² It's possible that heritability could partly explain both the early DD and the changes during follow-up in our study.

The progression of degeneration (as measured by SI) in general during follow-up was evident. This was anticipated and in line with current understanding of the degenerative process.¹³⁻¹⁷ DD is known to progress with increasing age. In a previous study on the same group of 75 original subjects the results were similar.¹⁸ The mean number of degenerated discs per subject was 3.0 in 2003 and 3.5 in 2017.

However, the severity of DD at baseline or at follow-up did not have a significant
 correlation with current LBP (VAS) and disability (ODI). Research results on the relation
 between MRI findings and pain symptoms are conflicting.^{9,19,20} Some studies have shown an
 increased prevalence of degenerated discs in subjects with LBP.⁸ On the other hand,
 degenerative changes have also been detected in the lumbar spine among symptomless
 individuals.⁶

We did not have the MR images from the original study available – only the recorded relative numerical SI values from 1987 for comparison. Assessment of morphological changes in 1987 was not possible, neither was their long-term follow-up. Therefore, we chose to use the relative numerical value of the measured SI for grading of DD also in 2017. The relative SI of the disc in 1987 was the predictor for DD and LBP in 2017. The repeatability of the measurements both in 2017 and in 1987 with the low-field scanner was excellent. The same SI measurement method was used at baseline and follow-up although the rater was not the same.

The SI measurement method has limitations. Since SI is determined by relaxation times T2 and T1, and T1 is significantly dependent on the field strength, a significant difference can be seen in SI measurement values and even a visually detectable SI decrease observed between images of low-field and high-field MRI devices.²¹ Since SI in each disc was ³⁵ 177 measured with the same method at baseline and follow-up, the same measurement error and DD-grading error is expected in each disc of the subject. Thus, that error has a similar effect for the comparison of SI and DD in both 1987 and 2017. Since we compared the relative SI values of 1987 and 2017, and not the absolute measurements, the comparison should be fairly reliable. However, since the disc with the highest SI is used as a reference ⁴⁸ 182 for the other discs of the subject, those discs may be graded as normal if the "healthiest" disc has a low SI. In such an extreme case the grade and number of discs with decreased SI may be underestimated rather than exaggerated. This grading error is more likely in follow-up images where more discs – also the healthiest – may have age dependent SI decrease.

In addition to SI, several other MRI measures including disc height have been used for grading DD in spine studies.²² Visual morphological assessment for grading DD is becoming more reliable with the increasing resolution of modern MRI.²¹

Lack of clinical data at baseline prevented us from accurately analyzing the development of LBP symptoms during the follow-up. The lack of contact information of the original control group made the comparison of the DD progression of our LBP patients to asymptomatic controls impossible. The small sample size in our study may have reduced the power of the statistical tests regarding e.g. pain symptoms. We don't know how well the MRI subgroup of subjects in 2017 represents all the baseline study subjects but in 2017 the MRI subgroup reported slightly more LBP than those only participating in the questionnaire. We know that every subject in 1987 had LBP severe enough to hinder them from military duty. Yet, after 30 years most of them had only mild pain or no pain at all. According to our results, LBP experienced in early adulthood does not necessarily become chronic and SI of the disc on MRI cannot be used as an accurate prognostic finding for these patients. The timeframe of the present MRI study is exceptionally long. Even with the limitations of sample size and loss to follow-up, this study shows that decreased SI of the disc in early adulthood seems to predict further decrease and other degenerative changes

and clinical information will be needed to clarify the relationship between DD and LBP.

but not current pain or disability. Future studies with larger cohorts including genetic data

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0% to 20%: minimal	The patient can cope with most living activities. Usually no	
disability	treatment is indicated apart from advice on lifting, sitting and	
	exercise.	
21%-40%: moderate	The patient experiences more pain and difficulty with sitting,	
disability	lifting and standing. Travel and social life are more difficult and	
	they may be disabled from work. Personal care, sexual activity	
	and sleeping are not grossly affected and the patient can	
	usually be managed by conservative means.	
41%-60%: severe	Pain remains the main problem in this group but activities of	
disability	daily living are affected. These patients require a detailed	
	investigation.	
61%-80%: crippled	Back pain impinges on all aspects of the patient's life. Positive	
	intervention is required.	
81%-100%:	These patients are either bed-bound or exaggerating their	
	symptoms.	

Table 1. Interpretation of the Oswestry Disability Index (ODI)

	SI of the disc i		
Degenerative change in 2017	SI decrease >20% (n=23)	SI normal (n=107)	p-value
SI decrease >60%	13 (57%)	12 (11%)	<0.001
Any Modic change	18 (78%)	41 (38%)	0.001
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Disc protrusion or bulge Severe bony endplate lesion	21 (91%) 18 (78%)	57 (53%) 39 (36%)	0.001 <0.001
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Disc height decrease >33%	14 (61%)	31 (29%)	0.007
Annular fissure or HIZ	10 (44%)	15 (14%)	0.003

Table 2. Advanced degenerative changes (dichotomized variables) in a lumbar disc in 2017 in relation to its level of SI decrease in 1987.

Table 3. Severity of pain and disability in 2017 as the mean and 95% confidence interval of VAS and ODI, according to presence (none / at least one) of discs with decreased (>20%) SI in 1987.

No discs with decreased SI in	ODI	20.1 (7.95 – 32.3)
1987 (n=15)	Pain VAS	3.3 (1.4 – 5.2)
At least one disc with SI	ODI	15.1 (8.82 – 21.4)
decrease >20% in 1987 (n=20)	Pain VAS	2.7 (1.4 – 4.0)

Mean value (95% confidence interval)

30-YEAR FOLLOW-UP ON DISC DEGENERATION

FIGURE LEGENDS

Figure 1. Subject recruitment process

Figure 2. Anatomical distribution of degenerated discs in 26 subjects as the number of discs with >20% SI decrease at baseline 1987 and follow-up 2017.

Figure 3. The grade of SI decrease of a disc in 1987 in relation to a) grade of SI decrease and b) protrusion of the same disc in 2017 (n=130). The percentages in the columns are in relation to the number of discs with the respective grade in 1987.







