

Prevalence of Degenerative Imaging Findings in Lumbar Magnetic Resonance Imaging Among Young Adults

Jani Takatalo, MSc,* Jaro Karppinen, MD, PhD,*† Jaakko Niinimäki, MD,‡
Simo Taimela, MD, PhD,§ Simo Näyhä, MD, PhD,†¶ Marjo-Riitta Järvelin, MD, PhD,¶
Eero Kyllönen, MD, PhD,* and Osmo Tervonen, MD, PhD‡

Study Design. A cross-sectional imaging study of young adults.

Objective. To investigate the prevalence of disc degeneration (DD) and displacement, anular tears, and Modic changes in lumbar magnetic resonance imaging (MRI) among young adults.

Summary of Background Data. Although low back pain in young adulthood is common, the prevalence of spinal MRI findings at this age remains virtually unknown.

Methods. The study population was a subcohort of the Northern Finland Birth Cohort 1986. Subjects living within 100 km of Oulu (n = 874) were invited to participate in lumbar MRI at 20 to 22 years of age (mean: 21.2 years). Degree of DD, type of Modic changes, and presence of disc bulges, herniations, high intensity zone (HIZ) lesions, and radial tears at all lumbar levels were assessed.

Results. Three hundred twenty-five women and 233 men (n = 558) attended the MR imaging. DD was significantly more frequent in men (54% vs. 42%, $P = 0.005$), as was multiple DD (21% vs. 14%, $P = 0.036$). The prevalences of disc bulges and radial tears were 25% and 9.1%, respectively, without gender differences. HIZ lesions were more common among women than men (8.6% vs. 4.3%, $P = 0.046$), whereas herniations were significantly more common among men (5.6% vs. 2.5%, $P = 0.047$). Only 2 disc extrusions were observed, one in each gender. All degenerative disc findings were more common at the L5–S1 level except HIZ lesions, which were most likely at L4–L5. The prevalence of the Modic changes was 1.4%, without gender difference, type I being more common than type II. Typically, Modic changes were located adjacent to a DD Grade 4 disc and at the 2 lowest levels.

Conclusion. Almost half of young Finnish adult aged 21 years had at least one degenerated disc, and a quarter had a bulging disc. Modic changes and disc herniations were, however, relatively rare.

Key words: magnetic resonance imaging, lumbar spine, prevalence, intervertebral disc degeneration, Modic changes, anular tears, herniations, young adults. **Spine 2009; 34:1716–1721**

Low back pain (LBP) is common already among children and the prevalence increases with age,^{1–4} lifetime prevalence being up to 50% of 20-year-old men.² The etiology of LBP in adolescence remains largely unknown. Some authors claim that adolescent LBP is primarily related to psychosocial factors,^{5,6} but a discogenic origin has also been suggested since intervertebral disc degeneration (DD) at 15 years of age was strongly associated with recurrent or continuous LBP at 18 and 23 years.⁷ Furthermore, the likelihood of LBP increases with higher grade of DD in adults.⁸ Studies of the prevalence of magnetic resonance imaging (MRI) findings and their relationships with LBP have mainly been conducted in adult populations. Although LBP is quite common among young adults, the prevalence of MRI findings at this age is virtually unknown.

DD is known to be common among asymptomatic.^{9,10} In addition to DD, other lumbar degenerative changes on MRI have been reported to occur in adult populations without LBP. The prevalence of DD (56%–72%), disc bulging (20%–81%), protrusions (27%–33%), extrusions (0%–18%), high intensity zone (HIZ) lesions (6%–33%), and anular tears (56%) ranges widely in asymptomatic subjects.^{10–12} Moreover, the prevalence of endplate and bone marrow changes (Modic changes) varies from 2% to 7% among asymptomatic.¹² We investigated the prevalence of DD, anular tears, degree of disc displacement, and Modic changes in lumbar MRI in a population-based cohort of young adults.

Materials and Methods

Study Population

The study population consisted of a subcohort of the Northern Finland Birth Cohort 1986 (NFBC 1986), which originally included data on 9479 children born in Northern Finland between July 1, 1985 and June 30, 1986. In 2003 to 2004, a postal questionnaire about symptoms and personal characteristics was sent to 2969 cohort members living within 100 km of the city of Oulu. The respondents were included in the Oulu Back Study (OBS). The response rate was 67% (1987 responses). All respondents to the postal questionnaire were invited to participate in a clinical and laboratory examination (isometric strength measurements, body sway, blood samples, weight, height, and questionnaire about symptom and personal

From the *Department of Physical and Rehabilitation Medicine, Institute of Clinical Sciences, University of Oulu, Oulu, Finland; †Finnish Institute of Occupational Health, Oulu, Finland; ‡Institute of Diagnostics, University of Oulu, Oulu, Finland; §Department of Public Health, University of Helsinki, Helsinki, Finland; and ¶Institute of Health Sciences, University of Oulu, Finland.

Acknowledgment date: September 30, 2008. Acceptance date: January 19, 2009.

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

Supported by the Academy of Finland grant (200868) (to J.K.).

Address correspondence and reprint requests to Jaro Karppinen, MD, PhD, Department of Physical and Rehabilitation Medicine, Institute of Clinical Sciences, University of Oulu, PL 5000, 90014 Oulu, Finland; E-mail: jaro.karppinen@ttl.fi

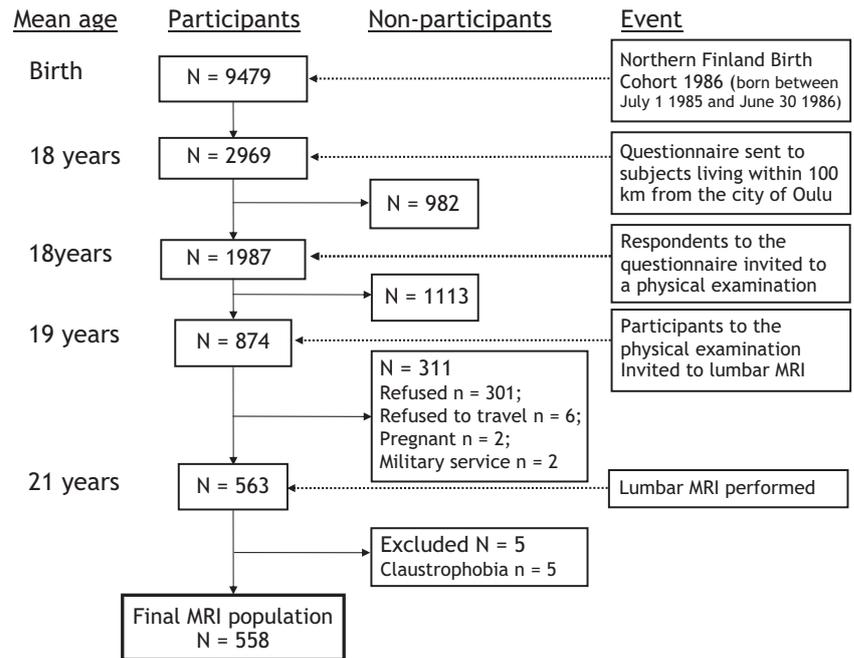


Figure 1. Flow-chart of the study population.

characteristics), performed in 2005 to 2006. All 874 who were examined at the age of 19 were further invited to lumbar spine MRI about 2 years later (Figure 1). The present study was conducted in accordance with The Declaration of Helsinki. The ethical committee of Oulu University Hospital approved the study protocol before its initiation.

Magnetic Resonance Imaging

MRI scans were obtained with a 1.5-T unit (Sigma, General Electric, Milwaukee, WI) using the imaging protocol for sagittal T1-weighted (440/14 [repetition time msec/echo time msec]) spin echo and T2-weighted (3960/116) fast spin echo of the entire lumbar spine. The number of excitations for T1-weighted images was 1 and for T2-weighted images 4. Echo train length for T2-weighted images was 29. Image matrix was 256×224 for T1-weighted images and 448×224 for T2-weighted images. Field of view was 28×28 cm and slice thickness 4 mm with 1-mm interslice gap.

Disc Degeneration

The degree of DD was graded on T2-weighted images with a modified Pfirrmann¹³ scale as grade 1 (normal shape, no horizontal bands, distinction of nucleus, and anulus is clear), grade 2 (nonhomogeneous shape with horizontal bands, some blurring between nucleus and anulus), grade 3 (nonhomogeneous shape with blurring between nucleus and anulus, anulus shape still recognizable), grade 4 (nonhomogeneous shape with hypointensity, anulus shape not intact and distinction between nucleus and anulus impossible, disc height usually decreased), and grade 5 (same as grade 4 but collapsed disc space). The modification of Pfirrmann scale was that the hyperintensity and isointensity of intervertebral disc to cerebrospinal fluid were not used as criteria for grades 1 through 3, because the cerebrospinal fluid was always hyperintense to the discs with the used MR sequences. Grades 1 to 2 were classified as normal discs, while grades 3, 4, and 5 were defined as degenerated (Figure 2).

Modic Changes

The vertebral endplate and bone marrow changes were graded as absent, type I (hypointense in T1-weighted sequences and

hyperintense in T2-weighted sequences), type II (hyperintense in both sequences) (Figure 3), and type III (hypointense in T1-weighted sequences and hypointense in T2-weighted sequences), as presented by Modic *et al.*¹⁴

Anular Tears

A radial tear of the intervertebral disc is characterized as an abnormal finding on MRI where nucleus pulposus protrudes into the horizontally separated anulus fibrosus. It is defined as a hyperintense linear area from the nucleus pulposus towards the outer anulus fibrosus as observed on T2-weighted image (Figure 3).¹⁵⁻¹⁷ HIZ lesions are defined as a high intensity signal located in the substance of the posterior anulus fibrosus, being brighter than nucleus pulposus (Figure 2).¹⁸

Degree of Disc Displacement

The herniated disc was subdivided into bulging, (subligamentous) herniation, and extrusion. Bulging was defined as displacement of the disc material greater than 50% of the disc circumference. When disc displacement was less than 50% of the disc circumference, the herniation was evaluated as either protrusion (subligamentous herniation), or extrusion. The disc was defined as protrusion if the greatest distance between the edges of the disc material beyond the disc place was less than the distance between the edges of the base in any of the same planes. The extrusion was characterized as a greater diameter of the extruded fragment than of its base in any one plane. This classification of disc displacement is published by Fardon *et al.*¹⁷ The total number of herniations (subligamentous herniations and extrusions combined) and number of extrusions were recorded as 2 variables.

Data Analysis

The MRI images were read by 3 observers. One (J.T.) evaluated the Modic changes and DD, while 2 more experienced observers (J.K., J.N.) evaluated in addition to these, anular tears (HIZ lesions and radial tears separately) and degree of disc displacement. The inter-rater agreement in DD and Modic changes evaluation was performed with kappa statistics with each level (or end plate in case of Modic changes) evaluated as indepen-



Figure 2. HIZ lesions (arrows) at L3–L4 and L4–L5 levels of an individual (female) with the 3 lowest lumbar discs showing degenerative signal loss without marked height reduction in T2-weighted image.

dent finding. Inter-rater agreement was found to be very good ($\kappa = 0.841$) in DD and moderate ($\kappa = 0.513$) in Modic changes. To evaluate selection bias the MRI participants were compared with the rest of the OBS survey respondents ($n = 1424$) and the rest of the invited subjects ($n = 311$). The 95% confidence intervals for the prevalence of symptoms were based

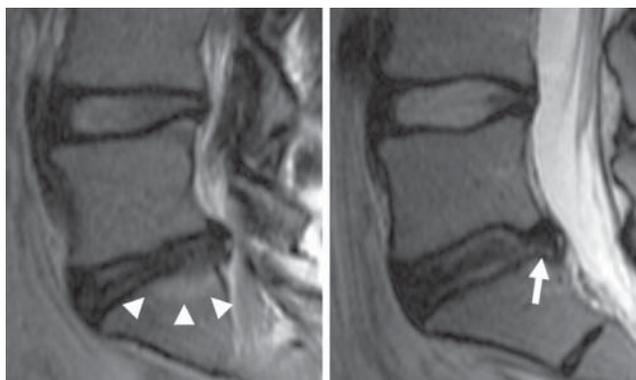


Figure 3. Modic type 2 change (arrowheads) and radial tear (arrow) at L5–S1 level in the same individual in T1- (left) and T2-weighted images.

Table 1. Comparison of the MRI Study Population ($n = 563$) and the Rest of OBS Survey Respondents ($n = 1424$) Characteristics at the Age of 18

	MRI Study Participants			Rest of the OBS Survey Respondents		
	Female	Male	All	Female	Male	All
Gender	58%	42%	100%	53%	47%	100%
Weight (mean; kg)	57	72	63	59	71	65
Height (mean; cm)	165	179	170	165	177	171
BMI (mean; kg/m ²)	21	22	22	22	23	22
Smoking						
Non-smoker	60%	67%	63%	51%	52%	52%
Current smoker*	19%	17%	18%	28%	31%	30%
Sitting† (mean; h)	7.6	8.1	7.2	8.5	9.5	9.0
Physically active‡	13%	23%	17%	7%	15%	11%
Reporting LBP§	58%	45%	52%	56%	41%	49%
Consultation for LBP§	6%	8%	7%	6%	5%	5%

*Smoking on 5 to 7 days per week.
 †Total mean self-reported sitting hours (leisure time and motor vehicle) per day.
 ‡Exercising at least 3 hours a week on leisure time.
 §“Reporting LBP” (LBP = low back pain) includes individuals who had not consulted a physician, physiotherapist, nurse, or a health professional because of LBP during the past 6 months, whereas “Consultation for LBP” includes those individuals who had consulted a physician, physiotherapist, nurse, chiropractic, or any health care professional because of LBP.

on binomial distribution. The χ^2 test and Fisher exact test were used in the statistical analyses stratified by gender. Data analyses were performed using SPSS software for Windows (version 15.0, SPSS Inc., Chicago, IL) and The NAG Fortran Mark 21 software library (The Numerical Algorithms Group Ltd., Oxford, UK).

Results

Subjects were scanned with MR imaging at Oulu University Hospital between November 2005 and February 2008 while they were 20 to 22 years old (mean: 21.2 years). Scans were obtained from 558 (325 women, 233 men) subjects (64% of the invited). The male participants in the MRI study were more likely to report LBP (45% vs. 41%) and have consulted a physician, physiotherapist, nurse, or a health professional during the past 6 months (8% vs. 5%) compared with the rest of the OBS survey male respondents ($n = 1424$) at the age of 18 years (Table 1). In women, no significant difference in LBP was observed. The participants were more likely to sit less (7.2 vs. 9.0 hours a day), be nonsmokers (63% vs. 52%), women (58% vs. 53%), and physically active (17% vs. 11%; Table 1). There were no significant differences in parents’ socioeconomic status at the age of 16 years (data not shown). When participants were compared with those who were invited to the scans, but did not participate ($n = 316$), the participants were slimmer (BMI: 21.6 vs. 22.4) but no other significant differences were observed.

Disc Degeneration

The number of evaluated intervertebral discs was 2789, of which 373 (13.4%) were degenerated. One disc was not evaluated due to a previous operation. At least one degenerated disc occurred in 47.2% of all subjects. Men had a significantly higher prevalence of lumbar DD (at

Table 2. Percentages (Numbers) of Degenerative Imaging Findings in Males and Females and the Gender Difference in Percentage Together With Its 95% Confidence Interval (CI)

	Male (n = 233)	Female (n = 325)	Difference % (CI)
DD	55% (127)	43% (138)	12 (3.7–20) %
Bulge	26% (61)	24% (78)	2 (0–10) %
Herniation	5.6% (13)	2.5% (8)	3.1 (0–6.5) %
Radial tear	10.7% (25)	8.0% (26)	2.7 (0–7.7) %
HIZ	4.3% (10)	8.6% (28)	4.3 (0.3–8.3)%
Modics	1.7% (4)	1.2% (4)	0.5 (0–1.5) %

least one level degenerated) compared with women (54.5% vs. 42.5%, $P = 0.006$) (Table 2). Degenerated discs occurred typically at the 2 lowest lumbar levels (L4–L5 and L5–S1), representing 85% of all degenerated discs, and men had a significantly higher prevalence at both levels ($P = 0.048$ and $P = 0.009$, respectively) (Figure 4). In addition, the prevalence of DD per disc was significantly higher in men than women (15.5% vs. 11.9%, $P = 0.02$). Almost half (47%) of the degenerated discs at L4–L5 and L5–S1 were grade 4, in contrast to 29% at the higher levels. Grade 5 degeneration was not detected at all. Overall, grade 4 degenerated discs were more commonly observed in women than men (49% vs. 39%, $P = 0.027$).

Of all subjects scanned, 95 (17%) had multiple level DD, *i.e.*, 2 or more degenerated discs. The prevalence of multiple level degeneration was significantly higher in men than women (21% vs. 14%, $P = 0.036$); the most

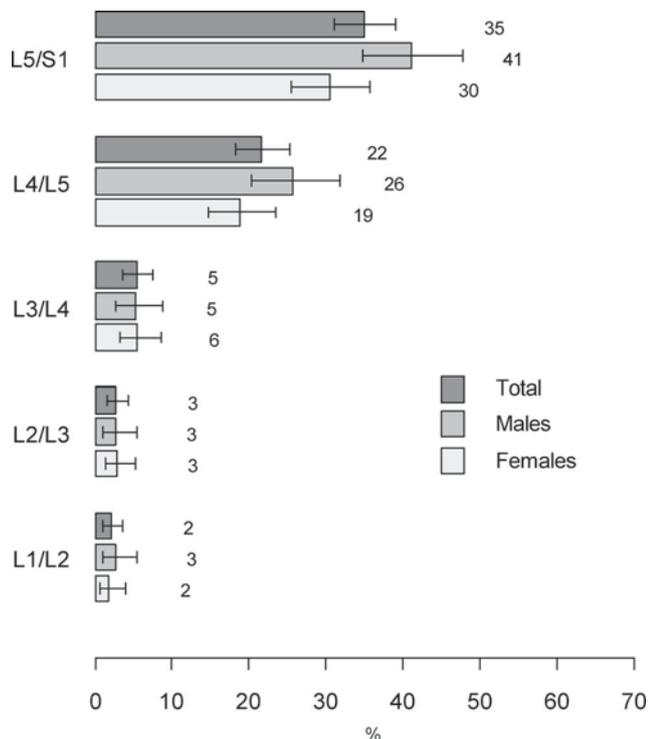


Figure 4. Percentages of degenerated discs according to lumbar level and gender. Numbers are prevalences and horizontal bars indicate their 95% confidence intervals.

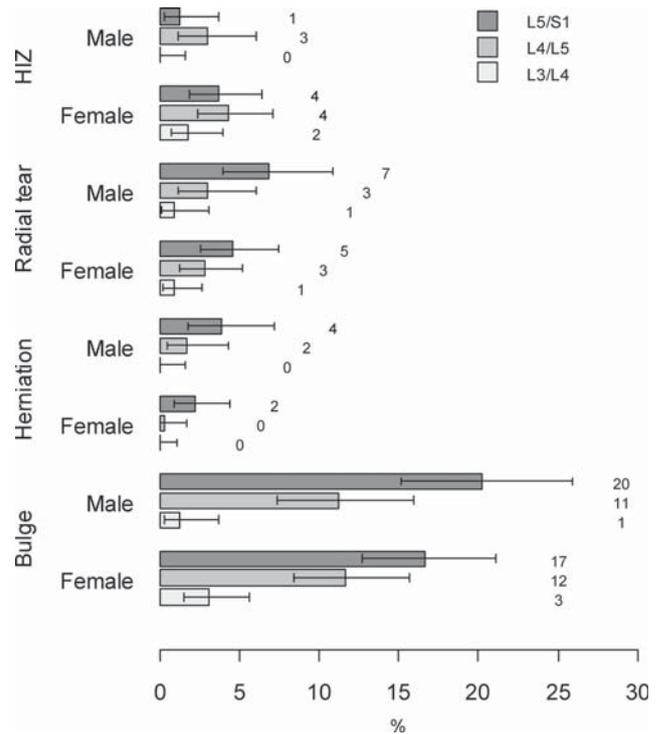


Figure 5. Percentages of HIZ lesions, radial tears, intervertebral disc herniations, and bulges according to lumbar level and gender. Numbers are prevalences and horizontal bars indicate their 95% confidence intervals.

common pattern was a combination of DD at L4–L5 and L5–S1 (65% of all cases with multiple level DD).

Degree of Disc Displacement

A quarter of subjects had at least one bulging disc. The prevalence of bulging discs did not differ between genders (Table 2). Disc bulges were typically observed at the 3 lowest intervertebral discs being highest at L5–S1 level in both genders (Figure 5). The prevalence of disc bulging was 6% from all discs analyzed, and highest at L5–S1 (18.1%). Of all subjects with bulging discs, 6% of men and 7% of women had multiple disc bulges.

Herniations (subligamentous herniations and extrusions combined) were rare among the scanned subjects, at 3.8% (Table 1). Herniations occurred either at L4–L5 or L5–S1 (24% vs. 76%, respectively; Figure 5). Only 1 female and 1 male subject had an extrusion, both located at L5–S1. Herniations were slightly more prevalent in men than women. (5.6% vs. 2.5%, $P = 0.047$). No multiple herniations were found.

Anular Tears

Of all subjects, 9.1% had at least 1 radial tear with no significant differences between genders (Table 2). Only 1 female subject had multiple radial tears at L4–L5 and L5–S1. Typically radial tears were located at the 2 lowest intervertebral discs (Figure 5).

The prevalence of HIZ lesions was slightly lower than radial tears, being 1.5% of all evaluated discs. Of the subjects, 6.8% had at least one HIZ lesion. The prevalence of HIZ lesions was significantly higher in women

than men (8.6% vs. 4.3%, $P = 0.046$) (Table 2). Four women had multiple lesions. HIZ lesions were typically observed at L4–L5 or L5–S1 (Figure 5).

Modic Changes

The prevalence of Modic changes (at least 1) was 1.4%, with no significant difference between genders. Of all Modic changes, 7 (64%) were of type I while 4 type II changes were observed. Ten of 11 findings were adjacent to a grade 4 degenerated disc. One Modic change (type I) was observed adjacent to a grade 3 disc at the lower L3 end plate. Moreover, in 6 of 9 subjects Modic changes occurred only at one side of the degenerated disc. Multiple findings were observed in 3 subjects. All Modic changes adjacent to a grade 4 disc were at the 2 lowest levels.

Discussion

The results of this study indicate that DD and bulging are common MRI findings in the lumbar spine among young adults aged 20 to 22 years. Radial tears and HIZ lesions were frequent as well, while protrusions and Modic changes were relatively rare. The prevalence of extrusions was very low at this age. Women had significantly higher prevalence of HIZ lesions whereas men had significantly higher prevalence of DD and herniations.

A straightforward comparison with earlier research is not possible due to lack of studies in the same age group. Salminen *et al*⁷ studied the prevalence of DD in adolescence and reported 31% and 42% of subjects to have at least 1 level DD at the age of 15 and 18, respectively. In a Danish study, 21% of 13-year-old school children were reported to have at least one disc with decreased disc signal intensity in the lumbar spine.¹⁹ Thus, our finding (47% prevalence of DD) is in accordance with the earlier results if we assume that the prevalence of degenerative findings increases with age. Our 13% prevalence of DD per analyzed disc is lower than the prevalence of 20% in an adult population reported by Weishaupt *et al*,¹² and is most likely due to the young age of the scanned subjects in our study. Higher prevalence of DD per all discs in men has not been reported earlier. In addition, multiple DD was more frequent in men. Interestingly, women had a higher prevalence of grade 4 DD.

The prevalence of DD found here was highest at the 2 lowest lumbar levels, in accordance with observations by others.^{12,19,20} Our results show that collapsed discs (grade 5 degeneration) are rare among young adults. Eighteen percent of subjects in this study had multiple DD. The most typical pattern of multiple level DD was a combination at the 2 lowest levels, which is not surprising as DD most typically occurs at these levels.

The prevalence of bulging discs was 25% in the present study. In a cohort study of 13-year-old school children bulging discs occurred in 14% of subjects,¹⁹ whereas among 40-year-old Danes the prevalence was 28%.²¹ Thus, our findings are in accordance with the results from these Danish population-based cohorts. Bulging discs were mainly localized at L4–L5 and L5–S1

in the present study, as also observed elsewhere.^{10–12,19} In our study, the occurrence of bulging was over 1.6 times higher at L5–S1 than at L4–L5, whereas studies on asymptomatic older subjects reported bulging to occur slightly more often at L4–L5 than L5–S1.^{10,12} This disparity might be age-related.

The prevalence of protrusions in this study was 3.4%. Only 2 disc extrusions and no multiple herniations were found. Kjaer *et al*²¹ published similar results among 13-year-old children. They found the prevalence of protrusions to be 3% and found neither multiple herniations nor extrusions. In previous studies, protrusions have been observed at the 2 lowest lumbar levels, in accordance with our results.^{9,10,12,19} In the 40-year-old Danish cohort,²¹ men had higher prevalence of protrusions although the gender difference was less in the present study. On the other hand, in a 13-year-old population no difference between genders was found.¹⁹

Previous studies have concluded that radial tears are more likely to occur at the lowest 2 levels, as in our study.^{11,15,19,20} However, our finding of a preponderance of radial tears at L5–S1 level and a higher prevalence in men is supported by the Danish study on 13-year-old children.¹⁹ On the other hand, among 40-year-old Danes the prevalence of radial tears was higher in women.²¹

We found the prevalence of HIZ lesions to be highest at the 2 lowest levels, as in earlier studies of older subjects.^{12,20} Among Danish children, HIZ lesions were most likely at L5–S1 and in boys,¹⁹ whereas no significant difference between the 2 lowest levels or genders was observed in the 40-year-old Danish population.²¹ Our results showed that HIZ lesions occurred significantly more often in women. The prevalence of HIZ lesion per disc was lower here than in earlier studies among older subjects.^{12,22} We found a few multiple HIZ lesions, as also reported earlier.¹⁸ Furthermore, in some individuals HIZ lesions co-occurred with radial tears, as observed earlier.¹⁸

Previous studies have reported prevalences of Modic changes ranging from 12% to 58%, depending on whether subjects were symptomatic or not.²³ Comparison of these studies to the present one is difficult because our subjects were so young. In the 13-year-old Danish population only 2 Modic changes were observed, 1 at L1 and 1 at S1.¹⁹ The prevalence of Modic changes was reported at 0.5%, whereas in the present study it was 1.4%. We found mostly type I Modic changes. The L4–L5 and L5–S1 levels are reportedly those typically affected,^{20,24} in accordance with our results. However, we found no gender association with Modic changes as earlier reported.²⁴

The strength of the present study is the large general population-based cohort of young adults. Despite their healthier lifestyle habits the MRI study male participants had a higher prevalence of LBP compared with the rest of OBS survey male respondents. This may have some impact on the generalizability of our results in the general population, the extent of which can be determined only af-

ter studying the association between LBP and sciatica symptoms and MRI findings. The invitations to the MR imaging were sent only to those who participated in a clinical examination in 2005 to 2006. No marked selection bias was found between the scanned and the invited nonparticipants. In the present study, the kappa statistics showed the inter-rater agreement to be very good in DD but only moderate in case of Modic changes. Thus, DD can be graded quite reliably with only little experience in evaluating MRI images, while evaluation of Modic changes requires more experience. In practice, the most misclassified Modic changes were Schmorl's nodes with a halo of bone marrow signal change around them.

Gene therapy has been suggested as a potential treatment method for DD in the near future.²⁵⁻²⁷ However, as our results have shown, the prevalence of DD is high already among young adults. Although DD at young ages has been recognized as a risk factor for LBP in early adulthood,⁷ not all subjects with DD at young age will suffer chronic or recurrent LBP. As knowledge about the pathophysiology of DD increases, we hope it will become possible to recognize vulnerable individuals who are likely to develop chronic disabling LBP. As almost a half of the population of young adults have DD on MRI, this is not yet possible. Future studies are needed to assess the associations between these abnormalities in MRI and LBP and sciatica symptoms and limitations in activities of daily living.

In summary, lumbar DD and bulges are already very common at the age of 20. Modic changes and disc herniations are, however, relatively rare at this age. DD and herniations are more common in men than women, whereas HIZ lesions are found more frequently in women.

■ Key Points

- This large (n = 558) population-based cross-sectional MRI study investigated the prevalence of degenerative findings of the lumbar spine among young adult members of a birth cohort.
- DD and bulging were common whereas Modic changes and herniations were relatively rare (1.4% and 3.8% of subjects, respectively) at 21 years of age. Almost half of these young Finnish adults had at least one degenerated disc, and a quarter had a bulging disc.
- DD at single or multiple levels and herniation were more frequent in men (55% vs. 43%, 21% vs. 14%, and 5.6% vs. 2.5%, respectively), whereas HIZ lesions were more prevalent in women (8.6% vs. 4.3%).
- The prevalence of the Modic changes was 1.4%, without gender difference, type I being more common than type II.

References

1. Taimela S, Kujala UM, Salminen JJ, et al. The prevalence of low back pain among children and adolescents. A nationwide, cohort-based questionnaire survey in Finland. *Spine* 1997;22:1132-6.
2. Leboeuf-Yde C, Kyvik KO. At what age does low back pain become a common problem? A study of 29,424 individuals aged 12-41 years. *Spine* 1998;23:228-34.
3. Wedderkopp N, Leboeuf-Yde C, Andersen LB, et al. Back pain reporting pattern in a Danish population-based sample of children and adolescents. *Spine* 2001;26:1879-83.
4. Jones A, Clarke A, Freeman BJ, et al. The Modic classification: inter- and intraobserver error in clinical practice. *Spine* 2005;30:1867-9.
5. Balague F, Skovron ML, Nordin M, et al. Low back pain in schoolchildren: a study of familial and psychological factors. *Spine* 1995;20:1265-70.
6. Watson KD, Papageorgiou AC, Jones GT, et al. Low back pain in schoolchildren: the role of mechanical and psychosocial factors. *Arch Dis Child* 2003;88:12-7.
7. Salminen JJ, Erkintalo MO, Pentti J, et al. Recurrent low back pain and early disc degeneration in the young. *Spine* 1999;24:1316-21.
8. Buirski G, Silberstein M. The symptomatic lumbar disc in patients with low-back pain. Magnetic resonance imaging appearances in both a symptomatic and control population. *Spine* 1993;18:1808-11.
9. Boden SD, Davis DO, Dina TS, et al. Abnormal magnetic-resonance scans of the lumbar spine in asymptomatic subjects: a prospective investigation. *J Bone Joint Surg Am* 1990;72:403-8.
10. Jensen MC, Brant-Zawadzki MN, Obuchowski N, et al. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med* 1994;331:69-73.
11. Stadnik TW, Lee RR, Coen HL, et al. Annular tears and disc herniation: prevalence and contrast enhancement on MR images in the absence of low back pain or sciatica. *Radiology* 1998;206:49-55.
12. Weishaupt D, Zanetti M, Hodler J, et al. MR imaging of the lumbar spine: prevalence of intervertebral disc extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. *Radiology* 1998;209:661-6.
13. Pfirrmann CW, Metzford A, Zanetti M, et al. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine* 2001;26:1873-8.
14. Modic M, Steinberg P, Ross J, et al. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology* 1988;166:193-9.
15. Yu SW, Sether LA, Ho PS, et al. Tears of the annulus fibrosus: correlation between MR and pathologic findings in cadavers. *AJNR Am J Neuroradiol* 1988;9:367-70.
16. Yu S, Haughton VM, Sether LA, et al. Criteria for classifying normal and degenerated lumbar intervertebral disks. *Radiology* 1989;170:523-6.
17. Fardon DF, Milette PC, the Combined task forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology. Nomenclature and classification of lumbar disc pathology. *Spine* 2001;26:E93-113.
18. Aprill C, Bogduk N. High-intensity zone: a diagnostic sign of painful lumbar disc on magnetic resonance imaging. *Br J Radiol* 1992;65:361-9.
19. Kjaer P, Leboeuf-Yde C, Sorensen JS, et al. An epidemiologic study of MRI and low back pain in 13-year-old children. *Spine* 2005;30:798-806.
20. Braithwaite I, White J, Saifuddin A, et al. Vertebral end-plate (Modic) changes on lumbar spine MRI: correlation with pain reproduction at lumbar discography. *Eur Spine J* 1998;7:363-8.
21. Kjaer P, Leboeuf-Yde C, Korsholm L, et al. Magnetic resonance imaging and low back pain in adults: a diagnostic imaging study of 40-year-old men and women. *Spine* 2005;30:1173-80.
22. Rankine JJ, Gill KP, Hutchinson CE, et al. The clinical significance of the high-intensity zone on lumbar spine magnetic resonance imaging. *Spine* 1999;24:1913-9.
23. Jensen TS, Karppinen J, Sorensen JS, et al. Vertebral endplate signal (Modic) changes: a systematic literature review of prevalence and association with non-specific low back pain. *Eur Spine J* 2008;17:1407-22.
24. Karchevsky M, Schweitzer ME, Carrino JA, et al. Reactive endplate marrow changes: a systematic morphologic and epidemiologic evaluation. *Skeletal Radiol* 2005;34:125-9.
25. Chen Y. Orthopedic applications of gene therapy. *J Orthop Sci* 2001;6:199-207.
26. Chadderdon RC, Shimer AL, Gilbertson LG, et al. Advances in gene therapy for intervertebral disc degeneration. *Spine J* 2004;4:S341-7.
27. Levicoff EA, Gilbertson LG, Kang JD. Gene therapy for disc repair. *Spine J* 2005;5:S287-96.