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Original Article

Magnetic resonance imaging findings of the lumbar spine, back symptoms and physical function among male adult patients with Scheuermann's disease

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ARTICLE INFO	A B S T R A C T		
<i>Ceywords:</i> Scheuermann's disease	<i>Background:</i> There are only a few studies on untreated Scheuermann's disease and magnetic resonance imaging (MRI) findings in the lumbar spine. The primary aim of this study was to clarify lumbar MRI findings in patients		
umbar MRI	with Scheuermann's disease and to compare with subjects without diagnosed spine disease.		
ow back pain	Methods: Twenty-two male adult Scheuermann's patients (mean age 64.7 years (Standard Deviation [SD] 6.4)		
	and 26 males (mean age 59.7 years [SD 7.4]) from a national health survey were included in this study. From MR images, the dimensions of the vertebral bodies, intervertebral discs and the dural sac were measured.		
	Spondylolisthesis, Modic changes (MC), high intensity zone values (HIZ), and Schmorl's nodes were registered		
	from both groups as well as self-reported data concerning general health, quality of life, and back pain symp-		
	toms.		
	Results: Significantly more patients with Scheuermann's disease had at least one MC compared to the controls at		
	the level L1/L2 (Odds Ratio [OR] 21.11, 95% Confidence Interval [95% CI] 2.31–192.96), at the level L3/L4 (OR		
	13.62, 95% CI 1.41-131.26), and at the level L5/S1 (OR 6.11, 95% CI 1.50-24.83). Patients had significantly		
	more Schmorl's nodes compared to the controls (64% vs. 8%, $p < 0.001$). The area of the dura sac (L3/L4) was		
	larger (mean 201 mm ² vs. 152 mm ² , $p = 0.017$) in the patients compared to controls. At level L1/L2 patients		
	had higher disc than controls (mean 7.9 mm vs. 6.8 mm, $p = 0.038$). After adjusting for age patients had more		
	commonly constant back pain (OR 9.4, 95% CI 1.56–56.97), and difficulties in walking up one floor without		
	resting (OR 9.8, 95% CI 1.01–95.34) than controls.		
	Conclusions: Schmorl's nodes and Modic changes on lumbar MRI, back pain and physical function restrictions		

Conclusions: Schmorl's nodes and Modic changes on lumbar MRI, back pain and physical function restrictions seem to be more prevalent among patients with Scheuermann's disease than in the general population.

1. Introduction

I

Scheuermann's disease was originally defined as a growth disturbance of the thoracic spine, characterized by a rigid hyperkyphosis due to wedge-shaped vertebral bodies.¹ At least three consecutive vertebral bodies with a minimum of 5° of wedging have to be present to justify the diagnosis,² sometimes only one or two vertebrae may be affected.³ Besides vertebral wedging, typical radiographic findings are: irregularities of the vertebral endplates, disc material herniation through the endplates (Schmorl's nodes), narrowing of the disc spaces, and lengthening of the vertebral bodies.^{3,4}

Few long follow-up studies have been shown that patients with Scheuermann's disease had more pain than those of a control group.^{5–7} The pain symptoms, however, did not interfere with activities of daily living or employment.⁵ Ristolainen et al.^{6,7} reported in their long-term follow-up studies that the degree of kyphosis was not associated with the self-reported quality of life, general health or any back pain issue. However, they concluded that patients with Scheuermann's disease had more common back pain than a control group without Scheuermann's disease. Secondary lumbar hyperlordosis due to thoracic hyperkyphosis

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is thought to be the reason for the occurrence of low back pain. There is no clear data proving this assumption. However, Paajanen and coworkers⁸ studied 21 young patients on average 20 years old, and they found that over 55% of the thoracolumbar discs were abnormal and degenerated among patients with Scheuermann's disease in Magnetic Resonance (MR) images compared to 10% in asymptomatic controls.

Studies about radiological findings are usually made in young patients with Scheuermann's disease,^{8,9} and MR images are taken from the thoracic or thoracolumbar spine.^{8,10} In a hospital staff MR study, the authors concluded lumbar Scheuermann changes were associated with the severity and progressive nature of low back pain.¹¹

The primary aim of this study was to clarify differences in lumbar MR images between patients with Scheuermann's disease and controls. Secondly, we wanted to compare back symptoms and physical function between the patients and controls. We were also interested associations between MR findings and back symptoms and physical function.

2. Patients and methods

2.1. Patients with Scheuermann's disease

Sixty-four patients (46 males, 18 females) with Scheuermann's disease attended the outpatient clinics of our institution on average 46 years ago (35–59 years). They were invited for a follow-up examination in 2013. Thirty patients accepted the invitation to come to the hospital. Eight patients were excluded: three had lumbar Scheuermann's changes, four were female and one refused MRI. Thus, the study group (called "patients" in the following) consisted of 22 male patients. Their mean age was 64.7 years (Standard Deviation [SD] 6.4). MR images were taken using Siemens Symphony 1.5T in T2 sag and T2 tra. MR images were taken in TSE-sequence (Turbo Spin Echo) with section thickness 4 mm.

2.2. Control group

A male control subjects (called "controls" in the following) of 26 individuals was served as controls in a previous spine study.¹² Controls with physician diagnosed severe spine diseases were excluded from that study but subjects with possible non-specific spine symptoms were included. Their mean age was 59.7 (SD 7.4) years. From them, MR images had been taken utilizing a 1.5 T scanner.

2.3. Questionnaire and physical function measurements

From both groups, we obtained also self-reported data concerning general health (Visual analogue scale [VAS]), quality of life (VAS), where 0 means the worst general health or quality of life, 10 means the best general health or quality of life. Pain symptoms were measured by asking for back pain, constant back pain, and disability because of back pain during last 5 years, back pain, neck pain and shoulder pain during last 30 days, sciatica and constant sciatica. The questions were obtained Health 2000 study.¹³ Beside this, physical function was measured by five-repetition sit-to-stand test,¹⁴ and by walking speed in 6.1 m test.

2.4. Measurements of the MR images

An orthopaedic surgeon measured the posterior height of the lumbar vertebral bodies (mm) and the anterior and posterior height of the lumbar discs (mm). The sum of the anterior plus posterior disc height was divided by two to get the mean disc height for each level. Also spondylolisthesis (mm) and spondylolysis (0 = no, 1 = unilateral, 2 = bilateral) were checked. Modic changes (MC) (11) were not subdivided in the different types but only registered as present or not. High Intensity Zone (HIZ) is defined as a high-intensity signal on T2-weighted magnetic resonance (MR) images, located in the posterior annulus fibrosus, clearly separated from the nucleus pulposus.^{15,16} HIZ was registered if present. Periradicular fat tissue, sagittal diameter of the dura sac and area of the dura sac were also measured from both groups. The location and the number of Schmorl's nodes were registered in both groups.

Another orthopaedic surgeon classified lumbar disc degeneration according to Pfirrmann. In Pfirrmann Grade I the disc is homogenous, bright white, Grade II is inhomogenous with or without horizontal bands, Grade III is inhomogenous and grey, Grade IV is inhomogenous, grey to black and Grade V is inhomogenous and black.¹⁷ Pfirrmann classification was checked in the patient group, this data were not available for the controls from the Health 2000 national health survey.

2.5. Statistics

IBM SPSS Statistics (version 25.0) was used to carry out all analyses. T-tests and analysis of variance (ANOVA, ANCOVA) were applied to calculate statistical differences in distributions among patients and correlation back pain symptoms and disability. While the patients were on average five years older than the controls, the results were adjusted for age. Logistic regression was used to study the associations between patients and controls in MR images variables. Odds Ratios [OR] and their 95% Confidence Intervals [95% CIs] were calculated for the occurrence of back symptoms and activities of daily living in patients compared to controls. The statistically significant threshold was accepted at $p \leq 0.05$ (two-tailed).

2.6. Ethical aspects

Ethical permissions for the study was obtained from the authorities (HUS 163/13/February 03, 2012).

3. Results

The basic characteristics of the patients and the controls are seen in Table 1. In the study group patients were on average five years older compared to the control group (p = 0.015).

3.1. MRI findings

The number of patients with MC was higher compared to the controls at the levels L1/L2, L3/L4, and L5/S1. After adjusting for age the differences still remain at the level L1/L2 (OR 21.11, 95% CI 2.31–192.96), at the level L3/L4 (OR 13.62, 95% CI 1.41–131.26), and at the level L5/S1 (OR 6.11, 95% CI 1.50–24.83). Fifteen patients (68%) among the study group and five (19%) of the controls had MC in more than one segment. Only two patients did not have MC at all, while in the controls, 12 (46%) did not have any MC in the lumbar spine. No differences in HIZ was found between patients and the controls. The location of HIZ was similar, at L4/L5 and L5/S1 levels in 79% of patients and 76% of controls.

Fourteen patients (64%) had at least one Schmorl's node between T11 and L5 levels, all together 35 Schmorl's nodes. Forty percent of the patients had nodes in more than one vertebra. Usually the location of the nodes was at the levels L1 to L3 (30/35, 86%). Patients had significantly more Schmorl's nodes compared to the controls (64% vs. 8%, p < 0.001).

The mean sagittal diameter of the dura sac at the L4/L5 level was smaller among patients compared to the controls (10.9 mm, SD 3.1 vs. 12.6 mm, SD 2.9, p = 0.049), but after adjusting for age the difference disappeared (age-adjusted mean difference -0.78, 95% CI -2.60 - 1.04, p = 0.394). The area of the dura sac at the L3/L4 level was larger in patients than in the controls (201 mm², SD 73.8 vs. 152 mm², SD 63.4, p = 0.017). This difference remained after adjusting for age (age-adjusted mean difference 52.73, 95% CI 9.42–96.03, p = 0.018). Five patients and ten controls had relative spinal stenosis; the area of the dura sac being less than 100 mm². Two of ten controls had stenosis at

Table 1

The characteristics of the patients with Scheuermann's disease and Health 2000 control group.

	Patients with Scheuermann's disease	Health 2000 controls	p-value ^a
	n = 22	n = 26	
Age at MRI ^b , mean (SD)	64.7 (6.4)	59.7 (7.4)	0.015
Height, mean (SD)	177.2 (7.1)	176.8 (6.1)	0.838
Weight, mean (SD)	83.3 (12.0)	83.0 (13.3)	0.932
BMI ^c , mean (SD)	27.1 (3.9)	26.8 (4.0)	0.752
Basic education			0.630
Less than elementary	13 (61.9)	13 (50.0)	
Elementary school or part of the highschool	4 (19.0)	5 (19.2)	
Secondary school	4 (19.0)	8 (30.8)	
Working status, n (%)			0.152
Full-time or part time job	5 (22.7)	9 (34.6)	
Student	0 (0.0)	1 (3.8)	
Retirement	17 (77.3)	12 (46.2)	
Unemployed	0 (0.0)	3 (11.5)	
Other	0 (0.0)	1 (3.8)	
Retirement years, mean	10.9 (8.6)	7.9 (6.0)	0.024
Betirement n (%)			0.676
Disability pension	6 (35 3)	4 (33 3)	0.070
Betired because of age	10 (58.8)	+ (33.3) 8 (66 7)	
Other	1 (5.9)	0 (0.0)	

^a p-values are distributed between patients with Scheuermann's disease and Health 2000 controls.

^b MRI = Magnetic Resonance Imaging.

^c BMI = Body Mass Index, kg/m².

all measured levels. Five patients (19%) had lumbar disc herniation; one of the patients had two herniations (at L1/L2 and L2/L3 levels). In the controls, only one control subject had lumbar disc herniation at the level L4/L5.

No differences were found concerning the height of the vertebral bodies, and periradicular fat tissue between groups. Periradicular fat tissue was mainly seen at L5/S1 levels in both groups. There was a tendency that the mean disc heights in all disc levels of the lumbar spine were on average higher among patients compared to controls, but at level L1/L2 the difference was significant (7.9 mm vs. 6.8 mm, p = 0.038), also after adjusting for age (age-adjusted mean difference 1.10, 95% CI 0.02–2.17, p = 0.046).

Four persons had spondylolysis, one patient and one control had unilateral spondylolysis. Two persons in the controls had bilateral spondylolysis. Six patients had spondylolisthesis, one at L3, two at L4, and three at level L5. Four of them were degenerative. In the controls, seven persons had spondylolisthesis, three at level L2, two at level L3 and two at level L5.

Among the patients, 46% had disc changes Pfirrmann Grade IV or V in the L1/2 disc, the percentage increasing linearly downwards being 77% at L5/S1.

3.2. Back symptoms and physical function

On the VAS, patients' general health was on average worse compared to the controls (mean 6.6, SD 2.4 vs. 8.0, SD 1.7, p = 0.024). However, after adjusting it for age, the difference disappeared (ageadjusted mean difference -1.02, 95% CI -2.50 - 0.96, p = 0.069) (Table 2). Adjusted for age, patients had more constant back symptoms (OR 9.4, 95% CI 1.56–56.97) compared to the controls (Table 2). Patients had also more back pain (OR 45.0, 95% CI 4.92–411.32, p = 0.001), neck pain (OR 27.3, 95% CI 3.95–188.05, p = 0.001) and shoulder pain (OR 14.1, 95% CI 2.48–80.55,p = 0.003) during the last 30 days compared to the controls (Table 2). Adjusted for age, patients had more difficulties in walking up one floor without resting (OR 9.8, 95 CI 1.01–95.34, p = 0.049). Patients also needed slightly more time for the five-repetitions sit-to-stand test compared to the controls (mean 15.1 s, SD 6.6 vs. 11.7 s, SD 2.8, (p = 0.047) compared to the controls. But after adjusting for age, the significance disappeared (age-adjusted mean difference 3.37, 95% CI -0.11 - 6.85, p = 0.057). There were no further differences between groups in other functional tests (Table 2).

4. Discussion

Our aim was to clarify lumbar MRI findings among adult patients with Scheuermann's disease and to look for possible differences between patients and controls without known spinal pathology. In addition, associations between back symptoms and physical function and MRI findings were studied.

Modic changes (MC) were seen in the lumbar spine more often among patients than in the controls. In an earlier population-based study in 831 twin volunteers, discs and endplates were studied in lumbar MR Images. Volunteers were mainly women (96%) and on average 54 years old.¹⁸ One third of the subjects had MC and the highest prevalence was at the levels L4/L5 and L5/S1.^{18,19} In our study, 91% of patients and half of controls had at least one MC in the lumbar spine, also mainly at levels L4/L5 and L5/S1. However, our patients had MC at all levels, only two patients did not have changes at all. In an adolescent idiopathic scoliosis (AIS) study, middle age patients without surgery were compared to healthy individuals to find out if spinal deformities have an effect on lumbar spine degeneration.²⁰ AIS patients had more lumbar MC than controls, no difference in disc degeneration was found.²⁰ It may be possible that thoracic spinal deformities such as Scheuermann's disease and AIS are associated with MC changes in lumbar spine. But there is a difference in alignment: Scheuermann's patients have a secondary lumbar hyperlordosis in opposite to AIS patients who do have a flat back i.e. a decreased lumbar lordosis. The risk to develop MC likely depends on the inflammatory potential of the disc and the capacity of the bone marrow to respond to it.²¹ Määttä et al.¹⁸ also concluded that the endplate defect is strongly associated with MC at every lumbar level. In a recent study, the most common endplate lesions in the lumbar spine were "notched" and "Schmorl's nodes".²² Irregularities of the vertebral endplates and Schmorl's nodes are typical findings in Scheuermann's disease.^{4,5,8}

In the large population study the association between disc degeneration, end plate signal changes, Schmorl's nodes and low back pain was examine.²³ The prevalence of the Schmorl's nodes in the lumbar spine in abovementioned study was 1.5%. They found that these lumbar MRI findings were significantly associated with low back pain. Paajanen et al.⁸ found that Schmorl's nodes were related to the enhanced rate of disc degeneration. However, in their study Schmorl's nodes were seen at the levels T10/T11 to L2/L3, mainly between T11/T12-L1/L2 levels and in our study 86% of nodes were seen at levels L1/L2- L3/L4.

The finding that a large amount of lumbar Schmorl's nodes were found in the majority of patients with classic (thoracic) Scheuermann's but almost not at all in the controls seems to indicate that endplate weakness in Scheuermann's affects the whole spine. But for biomechanical reasons, it becomes obvious during growth in the kyphotic thoracic spine and rarely in the lordotic lumbar area. Disc degeneration and loss of lumbar lordosis during ageing may be the reasons for the appearance of Schmorl's nodes in the lumbar area in adult Scheuermann's patients. It would be interesting to see how the cervical spine of adult Scheuermann's patients looks in comparison to normal controls.

In the study of Jensen et al.,²⁴ low back pain patients were included who were partly or fully sick-listed from work for 4–12 weeks due to low back pain with and without radiculopathy. Low back pain was associated with type 1 MC, whereas leg pain was associated with HIZ, disc herniation and all sorts of MR images nerve root compromise. However, in our study

Table 2

Back pain and physical function between male patients with Scheuermann's disease and control group Health 2000.

	Patients with Scheuermann's disease	Health 2000 controls	Patients with Scheuermann's disease	p-values ^b
	n = 22	n = 26		
	mean (SD)	mean (SD)	mean difference (95 %CI)a	
General health ^c	6.6 (2.4)	8.0 (1.7)	-1.02 (-2.50-0.96)	0.069
The quality of life ^c	6.9 (2.5)	7.9 (1.7)	-0.92 (-2.22-0.39)	0.163
Five-repetition sit-to-stand test (seconds)	15.1 (6.6)	11.7 (2.8)	3.37 (-0.11-6.85)	0.057
Walking time in 6.1 m (seconds)	4.0 (1.8)	3.6 (1.0)	0.53 (-0.43-1.50)	0.269
Number of steps during 6.1 m	8.4 (2.3)	7.4 (1.1)	1.05 (-0.12-2.22)	0.076
Walking speed (m/s)	1.7 (0.5)	1.8 (0.4)	-0.10 (-0.40-0.10)	0.485
	%	%	OR (95% CI) ^d	
Constant back pain, (%)	41	8	9.41 (1.56–56.97)	0.015
Disability because of back pain during last 5 years, (%)	50	12	5.48 (1.19-25.23)	0.029
Back pain during last 30 days, (%)	68	4	45.00 (4.92-411.32)	0.001
Sciatica, (%)	50	46	1.21 (0.36-4.09)	0.755
Constant sciatica, (%)	14	4	4.76 (0.40-56.89)	0.217
Neck pain during last 30 days, (%)	59	8	27.26 (3.95-188.05)	0.001
Shoulder pain during last 30 days, (%)	55	8	14.13 (2.48-80.55)	0.003
Difficulties carrying 5-kg load at least 100 m, (%)	36	0		
Difficulties in walking up one floor without resting, (%)	27	4	9.82 (1.01-95.34)	0.049
Other chronic diseases, (%)	77	46	3.36 (0.89–12.63)	0.073

^a ANCOVA, age-adjusted mean difference and its 95% CI confidence intervals [95% CI] for general health, quality of life and physical function in male patients with Scheuermann's disease (n = 22) compared to male controls (n = 26), adjusted for age.

^b p-values are distributed between patients and controls.

^c Self-reported outcomes measured by visual analogue scale (VAS), 0 to 10, where 0 is the worst and 10 is the best possible.

^d Odds Ratios [OR] and their 95% confidence intervals [95% CI] for back symptoms and activities of daily living in male patients with Scheuermann's disease (n = 22) compared to male controls (n = 26), adjusted for age.

we found no association between MC and constant back pain. Aprill & Bogduk¹⁶ in 1992 found a diagnostic sign of painful lumbar disc. HIZ. They considered HIZ as a disrupted annulus and symptomatic intervertebral disc. In a recent study, Wang & Hu25 studied 637 patients (3185 lumbar discs) from lumbar MR images. All patients were included except if the records were incomplete, the MR image quality was poor, the structure of spine was disordered, or other painful diseases, such as infection and tumor, were present. The mean age of the subjects were 49 years, range 16-86 years, and 54% of subjects were male. They concluded that HIZ is associated with aging, high body weight, and low back pain symptoms. They found a significant difference in HIZ prevalence between symptomatic and asymptomatic patients. However, they indicated HIZ is a part of the natural history of disc degeneration, not actual cause of low back pain. In our study, no differences were found between patients and control group in HIZ prevalence. This may be due to normal aging and its influence to the disc degeneration process. In this study, every second had HIZ and nearly 80% of findings were seen at L4/L5 and L5/S1 levels. Also earlier studies found HIZ location being mostly at L4/L5 and L5/S1 levels.²⁶ No associations between constant back pain and HIZ were found in either group.

We looked at lumbar disc degeneration in the patient group using Pfirrmann's grading system for Scheuermann's patients. Nearly 80% of the discs were grade IV or grade V. In the firefighters' lumbar intervertebral disc degeneration study,²⁷ Pfirrmann grade were increased with lumbar intervertebral disc level, and age was significantly associated with lumbar intervertebral disc degeneration. We also found among the patients that a higher Pfirrmann grade was the most common at L5/S1 level.

In the study of Paajanen et al.,⁸ MR images were assessed of the thoracolumbar spine (T10 to S1). They reported that 55% of all thoracolumbar discs were degenerated in the 20-years-old patients with Scheuermann's disease. It was more commonly seen among patients with Scheuermann's disease compared to asymptomatic control subjects of the

same age.²⁸ The degree of disc degeneration was calculated as a percentage decrease of signal intensity relative to the value of healthy disc. The disc degeneration was found in the most of cases at the levels L4/L5 and L5/S1.

The cross-sectional area of dura sac is a sensitive measure and it is significantly associated with lumbar central canal spinal stenosis.²⁹ Among our patients, the mean sagittal diameter of the dura sac at L4/L5 level was smaller compared to the controls. But at the L3 level, the area of the dura sac was on average larger among the patients compared to the controls. Spinal stenosis is found to be common in radiologic evaluations at level L4/L5.³⁰ Also our patients had spinal stenosis more common at level L4/L5, controls had spinal stenosis more often at level L3/L4. But the number of cases is very small and no conclusions can be drawn concerning this point.

There were no differences between patients and controls in the posterior height of the lumbar vertebral bodies. Anterior vertebral body height was not measured in the patients because this data was not available from the controls.

Patients were older on average than the controls. This was taken into account and statistical analyzes were adjusted for age. Patients had worse general health compared to the controls, but this difference disappeared when it was adjusted for age. However, a trend for worse general health remained also after adjustment. Similar results have also been found earlier.⁶

Likewise as in earlier studies,^{5,6} our patients had more commonly constant back pain than controls. Besides, the patients had back, neck and shoulder pain during the last 30 days more commonly than the controls. The patients had also more radiologic findings compared to the controls, which may partly explain the differences between the groups in back pain. However, single MR findings are not always correlated with back pain.^{31,32}

Patients had more functional disabilities compared to the controls and more often back symptoms restricting function significantly. This was seen especially in five-repetition sit-to-stand test and walking up one floor without resting. There was a trend for worse sit-to-stand test among Scheuermann's patients compared to the controls.

Faingold et al.³³ found in their systematic review that thoracic MR images play an important diagnostic role, particularly with severe and painful kyphosis in children and adolescents. Liu et al.¹¹ found in their retrospective cohort study including nearly 200 staff members from one hospital that lumbar MR images meet the diagnostic criteria of the atypical Scheuermann's disease in 18% of subjects in the general population. In our study, there were only few differences in MR images between our groups, such as Modic changes, Schmorl's nodes, the mean sagittal diameter of the dura sac, the area of the dura sac, so healthy individuals may also have similar lumbar radiological changes than patients with Scheuermann's disease.

The differences between the groups and back pain maybe biomechanical due to the increased thoracic kyphosis and secondary lumbar hyperlordosis causing increased stress on the lumbar intervertebral joins or due to the growth disturbance and disc degeneration and dysfunction.

Scheuermann's disease is more commonly seen among males.^{34,35} Therefore the small number of females in our original patient study group was excluded. In Europe twenty-seven centers participated in a population-based study where prevalence and geographic variation in vertebral Scheuermann's disease were studied.³⁶ They reported an overall prevalence of Scheuermann's disease of 8% with no significant difference between the sexes.

Limitation of our study is the small number of cases, a typical problem for long-term follow-up studies. However, we used a control group from a representative national health survey. All patients were from a single institution. At the time when the patients were seen for the first time, on average 46 years ago, nearly all Scheuermann's patients of the country were treated at this hospital. The same self-reported questionnaires were applied in both groups.

5. Conclusions

Schmorl's nodes and Modic changes on lumbar MRI, back pain and physical function restrictions seem to be more prevalent among Scheuermann's patients than in the general population. The high frequency of lumbar Schmorl's nodes in comparison to normal controls suggests that endplate weakness affects the whole spine and not only the thoracic area. Although patients with Scheuermann's disease had more symptoms compared to the controls, there was no statistically significant difference in general health and quality of life between groups.

Author contribution

Leena Ristolainen: Conceptualization, Methodology, Investigation, Software, Writing- Original draft preparation.

Jyrki A. Kettunen: Conceptualization, Methodology, Writing-Reviewing and Editing.

Heidi Danielson: Conceptualization, Investigation, Writing- Reviewing and Editing.

Markku Heliövaara: Conceptualization, Methodology, Writing-Reviewing and Editing.

Dietrich Schlenzka: Conceptualization, Methodology, Investigation, Writing- Reviewing and Editing.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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