

Do lumbar magnetic resonance imaging changes predict neuropathic pain in patients with chronic non-specific low back pain?

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Abstract

The aim of this observational, cross-sectional study was to analyse lumbar magnetic resonance imaging (MRI) findings in patients with non-specific chronic low back pain (CLBP), and to evaluate any correlation with pain intensity and their capacity to predict neuropathic pain (NP) in these patients.

Fifty-two patients with non-specific CLBP, between 21 and 62 years of age, 50% men, were investigated. Lumbar MRI was employed to assess disc degeneration, endplate changes, Modic changes, disc displacement, facet degeneration, foraminal stenosis and central lumbar spinal stenosis. The characteristics of pain were evaluated and patients were divided into 2 subgroups: with NP (24 patients) and without NP (28 patients), based on the results of a DN4-interview. Correlations between particular MRI changes and their relations to the intensity of pain were evaluated. Logistic regression was used to disclose predictors of NP.

Lumbar spine degenerative features were frequent in patients with non-specific CLBP, with L4/5 the most affected level. A significant correlation emerged between the severity of degenerative changes in particular lumbar spine structures (correlation coefficient ranging between 0.325 and 0.573), while no correlation was found between severity of degenerative changes and pain. Multivariate logistic regression revealed only 2 independent predictors of NP – female sex (odds ratio [OR]= 11.9) and a mean pain intensity of ≥ 4.5 in the previous 4 weeks (OR= 13.1).

Degenerative changes in the lumbar spine are frequent MRI findings, but do not correlate with the intensity of pain and do not predict NP. However, female sex and pain intensity do predict NP.

Abbreviations: BMI = body mass index, CLBP = chronic low back pain, CT = computed tomography, DD score = disc degeneration score, DD sum score = disc degeneration summary score, DN4 = Douleur Neuropathique en 4 Questions, EP score = endplate score, EP sum score = endplate summary score, FD score = facet degeneration score, FD sum score = facet degeneration summary score, FS score = foraminal stenosis score, FS sum score = foraminal stenosis summary score, LBP = low back pain, MC = Modic changes, MRI = magnetic resonance imaging, NCS/EMG = nerve conduction studies/needle electromyography, NP = neuropathic pain, NPSI_{CZ} = Neuropathic Pain Symptom Inventory–Czech version, NPT = neuropathic pain treatment, NRS = numerical rating scale, NSAIDs = non-steroidal anti-inflammatory drugs, OR = odds ratio, SD = standard deviation, TEP score = total endplate score, TFD score = total facet degeneration score, TFS score = total foraminal stenosis score.

Keywords: DN4, low back pain, magnetic resonance imaging, neuropathic pain

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1. Introduction

Non-specific low back pain (LBP) is defined as a pain not attributable to a recognisable, known specific pathology (e.g., tumour, osteoporosis, infection, fracture, structural deformity, radicular syndrome, or cauda equina syndrome).^[1] LBP is considered chronic when it persists for ≥ 12 weeks. The prevalence of chronic LBP (CLBP) is about 23%, functional disability due to chronic LBP has increased in recent decades.^[1] It appears that LBP may come to rank among the greatest concerns for public health systems.^[1,2] The pain may originate from a range of structures in the spine. Available systematic reviews and studies have demonstrated that a number of lesions identified by MRI, such as disc protrusion, nerve root displacement/compression, disc degeneration, disc high-intensity zone, Modic changes (MC, particularly type I), facet joint osteoarthritis, and spinal stenosis are all associated with LBP.^[3–9] Nonetheless, a systematic review with meta-analysis concluded that, at individual level, none of these lesions provides a strong indication that LBP is attributable to underlying pathology since such MRI abnormalities are also very common when symptoms are absent.^[3] Clear understanding of any associations between degenerative changes in particular lumbar spine structures is still lacking. Recent studies have shown that degenerative processes in

the disc, the adjacent endplate and the bone marrow are inter-correlated^[9–12] and it has been established that MCs and disc degeneration are significant parameters that affect lumbar facet osteoarthritis.^[13]

CLBP is considered a mixed pain syndrome, consisting of both nociceptive and neuropathic components.^[14] Neuropathic back pain is a term describing pain arising from injury or disease directly affecting the nerve roots that innervate the spine and lower limbs, and from pathological invasive innervation of the damaged lumbar discs.^[15] Neuropathic pain (NP) is not restricted to typical radiculopathy. Attal et al have further identified NP in patients with CLBP restricted to the lumbar area.^[16] NP must be correctly diagnosed for optimal treatment.^[17] Although a recent study has revealed an association between disc space narrowing and NP in LBP^[18], the risk factors for NP in these patients have yet to be made clear.

The aim of this study was to analyse MRI findings from the lumbar spine in patients with non-specific CLBP, to assess any inter-correlation between severity of morphological changes in particular lumbar spine structures (disc, facet joint, intervertebral foramen) and their relation to pain intensity, and to evaluate risk factors for the neuropathic component of the pain.

2. Materials and methods

2.1. Study design

The study was cross-sectional and observational; no existing pain management was delayed or altered by participation in it. It was reviewed and approved by the local medical research Ethics Committee of the University Hospital Brno and all participants gave written informed consent. Most of the patients were referred by collaborating out-patient neurologists over a period of 2 years. Patients were eligible for inclusion if they presented with non-specific CLBP (pain restricted to the lumbar area or pain radiating above the knee lasting for at least 12 weeks). Exclusion criteria were: age < 18 years, presence of lumbosacral radicular pain or neurogenic claudication in the medical history, clinical neurological examination and/or NCS/EMG (nerve conduction studies/needle electromyography) showing signs of lumbosacral radiculopathy or polyneuropathy, previous surgery of the lumbar spine, vertebral fracture, developmental deformities of the spine, spine infection or tumour, mental disorders or impairment of cognitive function, presence of risk factors in the medical history and/or laboratory abnormalities indicating a disease, condition or treatment that might be a potential cause of polyneuropathy, severe comorbid conditions (e.g., malignancy), diffuse widespread pain (e.g., fibromyalgia), and other chronic pain.

2.2. Pain assessment

Baseline demographic characteristics were recorded and body mass index was calculated. All patients underwent a comprehensive clinical neurological examination, including extensive evaluation of the lower limbs to exclude radiculopathy or polyneuropathy.

Assessment of pain included its descriptors, distribution, duration, intensity, time-course, pain-relieving position, and current intake of analgesics or any other drugs known to moderate pain. The intensity of pain was quantified by means of an 11-step numerical rating scale (NRS: 0–10). Current pain intensity at rest and in movement, together with mean and maximum pain intensity in the previous 4 weeks, were noted. The

presence of NP was assessed by means of the DN4-interview (Douleur Neuropathique en 4 Questions), which has been suggested as a suitable questionnaire for screening for NP in mixed pain conditions, including LBP patients.^[19–22] The score of DN4-interview ≥ 3 means that neuropathic pain is likely (the maximum score is 7).^[19] For a detailed description of the intensity of particular NP symptoms, a validated Czech version of the Neuropathic Pain Symptom Inventory (NPSIcz) was employed.^[23,24] Nerve conduction studies/needle electromyography of the lower limbs was performed to exclude incidental polyneuropathy or radiculopathy. Basic blood tests were screened to exclude potential causes of polyneuropathy (vitamin B12 and folate levels, thyroid hormones, serum protein electrophoresis, blood count, serum creatinine, bilirubin and transaminases, blood glucose and glycated haemoglobin (HbA1C), and serum lipid spectrum).

2.3. MRI of the lumbar spine

All MRI scans were obtained on a 1.5T scanner (Philips Achieva, Netherlands, or Siemens Magnetom Essenza, Munich, Germany) at a slice thickness 3 mm for all imaging sequences in both scanners. Grading was performed on sagittal T1-weighted, sagittal T2-weighted turbo spin echo (TSE) sequences and axial T2-weighted TSE sequences. Each participant was supine during the examination for approximately 30 minutes. All MRI images were assessed by a trained radiologist blinded to the patients' clinical data.

A range of grading systems was used to assess degenerative features of the lumbar spine and evaluate degeneration of intervertebral discs, adjacent endplates, vertebral bodies, facet joints and foramina. Five lumbar spinal levels (from L1/2 to L5/S1) were investigated in all patients.

Lumbar disc degeneration (DD) was classified on T2-weighted MRI according to the 5-grade Pfirrmann classification, in which grade 1 corresponds to no disc degeneration and 5 represents the most severe disc degeneration.^[25] Disc degeneration summary score L1-S1 (DD sum score) was calculated by summation of individual Pfirrmann scores at each lumbar level.

Vertebral endplate (EP) changes were evaluated on T1-weighted images and classified (as EP score) into 6 types in terms of the severity of the damage, with type 1 corresponding to a normal EP and type 6 representing extensive EP damage, taking into consideration EP breaks, defects or sclerosis, alteration in shape, presence of Schmorl nodes and associated MCs.^[11] A total endplate score (TEP score) was derived for each disc by adding up the EP scores of rostral and caudal endplates. Endplate summary score L1-S1 (EP sum score) was calculated by summation of individual TEP scores at each level.

Disc displacement was coded at each lumbar disc level as absent, bulging, protrusion or extrusion/sequestration, following widely-accepted lumbar disc nomenclature recommendations.^[26]

MCs were evaluated as previously defined in the literature.^[27] In this study, MCs were coded as absent or present at each lumbar disc level.

Facet degeneration score (FD score) was graded for both sides from L1/2 to L5/S1 spinal levels after the classification by Weishaupt et al.^[28] This grading system classifies facet degeneration progressively from 0 to 3 according to the degree of facet joint space narrowing and the presence of hypertrophy of the articular process, osteophytes, subarticular bone erosions and/or subchondral cysts. Total facet degeneration score (TFD score) was

calculated by summing the FD scores of both left and right sides at each lumbar spinal level. Facet degeneration summary score L1-S1 (FD sum score) was calculated by summation of individual TFD scores at each lumbar level (L1/2-L5/S1).

Foraminal stenosis was rated separately on each side (left, right), following Lurie et al.^[29] This classification is based on compromise of the foraminal zone (0 – no stenosis, 1 – mild stenosis, that is, compromise of <1/3 of its normal size, 2 – moderate stenosis, that is, compromise of 1/3–2/3 of its normal size, 3 – severe stenosis, that is, compromise of >2/3 of its normal size). A total foraminal stenosis score (TFS score) at each level was established by summing up right and left foraminal stenosis scores (FS score). Foraminal stenosis summary score L1-S1 (FS sum score) was calculated by summation of TFS scores at each lumbar level (L1/2-L5/S1).

Degenerative summary score was calculated for all patients by addition of DD sum score, FD sum score and FS sum score; it thus characterises disc degeneration, facet degeneration and foraminal stenosis for the whole lumbar spine.

The presence and severity of central lumbar spinal stenosis was assessed by Schizas qualitative morphological classification.^[30] This scale evaluates the morphology of the dural sac on MRI and the grading is based on the cerebrospinal fluid/rootlet ratio as seen on axial T2-weighted images at the level of the intervertebral disc. Grade A refers to absence of, or mild, stenosis, grade B moderate stenosis, grade C severe stenosis, and grade D extreme stenosis. For the purposes of this study, LSS was graded as absent (grade A) or present (B, C or D).

To assess intra-observer reliability, a random subsample of 5 MRIs was selected and re-read by the same radiologist at least 2 weeks after the initial reading. Later, the same sample of 5 selected

MRI scans was independently assessed by another experienced, data-blinded radiologist for inter-observer reliability.

2.4. Statistical analyses

Standard descriptive statistics were applied in the analysis. Continuous variables were described by mean and standard deviation (SD), categorical variables were characterised by absolute and relative frequencies. The statistical significance of the score differences among lumbar levels was analysed by means of the Friedman test, with post-hoc analysis of it by Wilcoxon signed-rank test. Correlations among scores and between particular scores and pain intensities were computed by Spearman correlation coefficient. The statistical significance of differences between the groups of patients with neuropathic and non-neuropathic pain was established by the Mann-Whitney test for continuous variables and Fisher exact test for categorical variables. To determine the statistical significance of predictors for NP with their odds ratios, univariate and multivariate logistic regression were computed. Intra-observer and inter-observer reliabilities were evaluated using mean and SD, Wilcoxon signed-rank test, Spearman correlation coefficient and Bland-Altman plots. The analysis was processed by an SPSS 25.0 (IBM Corporation, 2017).

3. Results

3.1. Patient characteristics

Fifty-two patients with non-specific CLBP were included in the study. Figure 1 summarises subject recruitment. The basic characteristics of these patients are presented in Table 1: mean

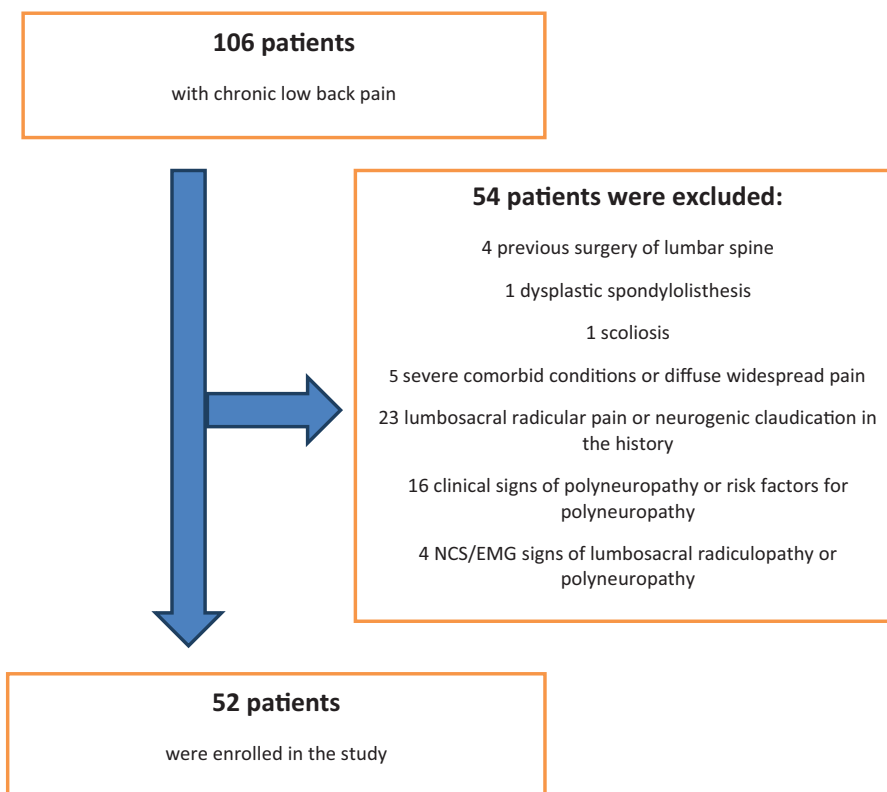


Figure 1. Study flowchart, including subject recruitment.

Table 1
Characteristics of patients with chronic non-specific low back pain.

Parameter	Patients (N=52)
Demographic	
Sex	
Male	26 (50.0%)
Female	26 (50.0%)
Age	40.8 (± 9.9)
BMI	26.1 (± 3.3)
Pain	
Pain duration (months)	66.1 (± 80.2)
Current pain at rest (0–10 scale)	2.4 (± 1.8)
Current pain at movement (0–10 scale)	5.4 (± 2.6)
Maximum pain in the previous 4 weeks (0–10 scale)	7.2 (± 2.1)
Mean pain in the previous 4 weeks (0–10 scale)	4.6 (± 1.8)
DN4-interview (0–7)	2.7 (± 1.5)
NPSI _{CZ} score (0–100)	19.5 (± 13.8)
Analgesic medication	
Yes	17 (32.7%)
Analgesic medication (if yes)	
Monotherapy	17 (100.0%)
Polytherapy	0 (0.0%)
Type of medication (multiple choice)	
NSAIDs	14 (82.4%)
Paracetamol	2 (11.8%)
Opioids	1 (5.9%)
NPT	0 (0.0%)

Data are presented as absolute and relative frequencies or mean (± SD).

BMI=body mass index, DN4=Douleur Neuropathique en 4 Questions, NPSI_{CZ}=Neuropathic Pain Symptom Inventory–Czech version, NPT=neuropathic pain treatment, NSAIDs=non-steroidal anti-inflammatory drugs.

age was 40.8 (SD 9.9) years and the proportions of male and female were the same (50.0%).

3.2. Pain characteristics

The mean duration of chronic pain was 66.1 (range 3–360) months and the mean pain intensity in the previous 4 weeks was 4.6 (SD 1.8) (NRS: 0–10) (Table 1). Only 32.7% of patients were taking analgesic medication. The most frequent type of pain treatment consisted of monotherapy with non-steroidal anti-inflammatory drugs (NSAIDs), used by 82.4% of patients with analgesic medication. None of the patients was using specific neuropathic pain treatment. The mean score at the DN4-interview was 2.7 (SD 1.5).

3.3. MRI characteristics

The MRI findings appear in Tables 2 and 3 and Figure 2. MCs were found in 17 patients (32.7%), predominantly at levels L4/5 and L5/S1. Findings of disc displacement were made most frequently at L4/5 level and L5/S1 levels, less frequently at L3/4 level and rarely at L1/2 or L2/3 levels. There were statistically significant differences in values of DD score, TFD and TFS score at particular levels of the lumbar spine (Tables 2 and 3). The L1/2 and L2/3 levels were least affected by degenerative changes and did not differ significantly in scores. In general, the most pronounced degenerative changes were at L4/5 and L5/S1 (slightly more at L4/5 for foraminal stenosis). The values of TEP score increased from proximal to more distal lumbar segments but the differences between particular levels did not reach statistical significance. The most pronounced changes of

Table 2
MRI characteristics of patients.

MRI parameter	Patients* (N=52)	P value (Friedman Test)
DD score		
L1/2	2.3 (± 0.6)	<.001
L2/3	2.4 (± 0.7)	
L3/4	2.6 (± 0.8)	
L4/5	3.3 (± 1.0)	
L5/S1	3.0 (± 1.0)	
DD sum score L1-S1	13.6 (± 2.9)	–
TEP score		
L1/2	2.9 (± 1.9)	.504
L2/3	3.1 (± 1.9)	
L3/4	2.9 (± 1.6)	
L4/5	3.9 (± 3.3)	
L5/S1	4.3 (± 3.6)	
EP sum score L1-S1	17.1 (± 8.0)	–
Modic changes		
No	35 (67.3%)	–
Yes	17 (32.7%)	–
Disc displacement		
No	7 (13.5%)	–
Yes	45 (86.5%)	–
Bulging	32 (61.5%)	–
Protrusion	21 (40.4%)	–
Extrusion/sequestration	8 (15.4%)	–
TFD score		
L1/2	1.6 (± 1.3)	<.001
L2/3	1.9 (± 1.3)	
L3/4	3.4 (± 1.5)	
L4/5	4.5 (± 1.4)	
L5/S1	4.2 (± 1.4)	
FD sum score L1-S1	15.5 (± 5.9)	–
TFS score		
L1/2	0 (± 0)	<.001
L2/3	0.1 (± 0.4)	
L3/4	0.7 (± 1.2)	
L4/5	2.2 (± 1.9)	
L5/S1	1.1 (± 1.7)	
FS sum score L1-S1	4.1 (± 4.0)	–
Degenerative summary score L1-S1	33.2 (± 10.5)	–
Central lumbar spinal stenosis (at least moderate)		
No	46 (88.5%)	–
Yes	6 (11.5%)	–

DD score=disc degeneration score, DD sum score=disc degeneration summary score, EP sum score=endplate summary score, FD sum score=facet degeneration summary score, FS sum score=foraminal stenosis summary score, TEP score=total endplate score, TFD score=total facet degeneration score, TFS score=total foraminal stenosis score.

* N (%) or mean (±SD).

the endplates (EP score 6) were disclosed at L4/5 and L5/S1 only (Fig. 2).

A significant positive correlation (low to moderate) emerged between some scores characterizing the severity of degenerative changes in lumbar spinal structures (correlation coefficient ranging between 0.33 and 0.57). The highest correlations occurred between the severity of disc degeneration and facet degeneration ($P < .001$) and between the severity of facet degeneration and foraminal stenosis ($P < .001$) (Table 4).

The results for intra-observer and inter-observer reliabilities (DD score, EP score, FD score and FS score) appear in Supplemental Digital Contents 1–10, <http://links.lww.com/MD/C939> (Supplemental Tables 1, 2 and Supplemental Figures 1–8, <http://links.lww.com/MD/C939>). In summary, the

Table 3
Post hoc tests of Friedman test from Table 2.

	DD score*	TFD score*	TFS score*
L1/2 vs L2/3	1.000	0.097	0.633
L1/2 vs L3/4	0.180	<0.001	0.008
L1/2 vs L4/5	<0.001	<0.001	<0.001
L1/2 vs L5/S1	0.001	<0.001	<0.001
L2/3 vs L3/4	0.550	<0.001	0.015
L2/3 vs L4/5	<0.001	<0.001	<0.001
L2/3 vs L5/S1	0.005	<0.001	0.002
L3/4 vs L4/5	<0.001	<0.001	<0.001
L3/4 vs L5/S1	0.183	0.006	0.718
L4/5 vs L5/S1	1.000	0.362	0.006

DD score=disc degeneration score, TFD score=total facet degeneration score, TFS score=total foraminal stenosis score.
 * Wilcoxon signed-rank test.

intra-individual and inter-individual agreement in particular scores was high (correlation coefficients for intra-observer reliability ranged between 0.79 and 0.96, for inter-observer reliability between 0.67 and 0.77, and the differences between the 2 checking measurements were low and clinically insignificant).

3.4. Correlation between severity of degenerative changes and pain

No correlation between the pain intensity (mean pain in the previous 4 weeks) and severity of degenerative changes (Table 5) was found.

3.5. Predictors of neuropathic pain

The patients were divided into 2 subgroups based on the results of the DN4-interview (the score of DN4-interview ≥3 means

Table 4
Correlation between particular MRI scores in all lumbar spine levels.

	Correlation coefficient*	P value
DD score and TEP score	0.325	.019
DD score and TFD score	0.573	<.001
DD score and TFS score	0.459	.001
TFD score and TFS score	0.474	<.001

DD score=disc degeneration score, TEP score=total end plate score, TFD score=total facet degeneration score, TFS score=total foraminal stenosis score.
 * Spearman coefficient.

neuropathic pain). The subgroup with NP included 24 patients (46.2%) and the subgroup with non-NP 28 patients (53.8%). Differences between demographics, pain and radiological (MRI) parameters were evaluated (Table 6). No statistically significant difference in any of the potential MRI predictors emerged. Not surprisingly, the 2 subgroups of patients differed in statistically significant fashion in their results for DN4-interview and NPSI_{cz}, the questionnaires that evaluate NP. Patients with NP showed significantly higher intensity of mean pain in the previous 4 weeks on NRS (5.7 vs 3.6, $P < .001$) and a higher proportion of females (79.2% vs 25.0%, $P < .001$). The odds ratios (OR) for these potential predictors of NP were also calculated (Table 7). Univariate analysis led to statistically significant OR for female sex (OR=11.4) and intensity of mean pain the previous 4 weeks (OR=2.3). ROC (receiver operating characteristic) analysis of intensity of mean pain in the previous 4 weeks disclosed this parameter as an effective discriminating factor between the 2 subgroups of patients, at a sensitivity of 87.5% and specificity 64.3%, using an optimal cut-off point of 4.5 (Fig. 3). Multivariate logistic regression confirmed female sex (OR=11.9) and

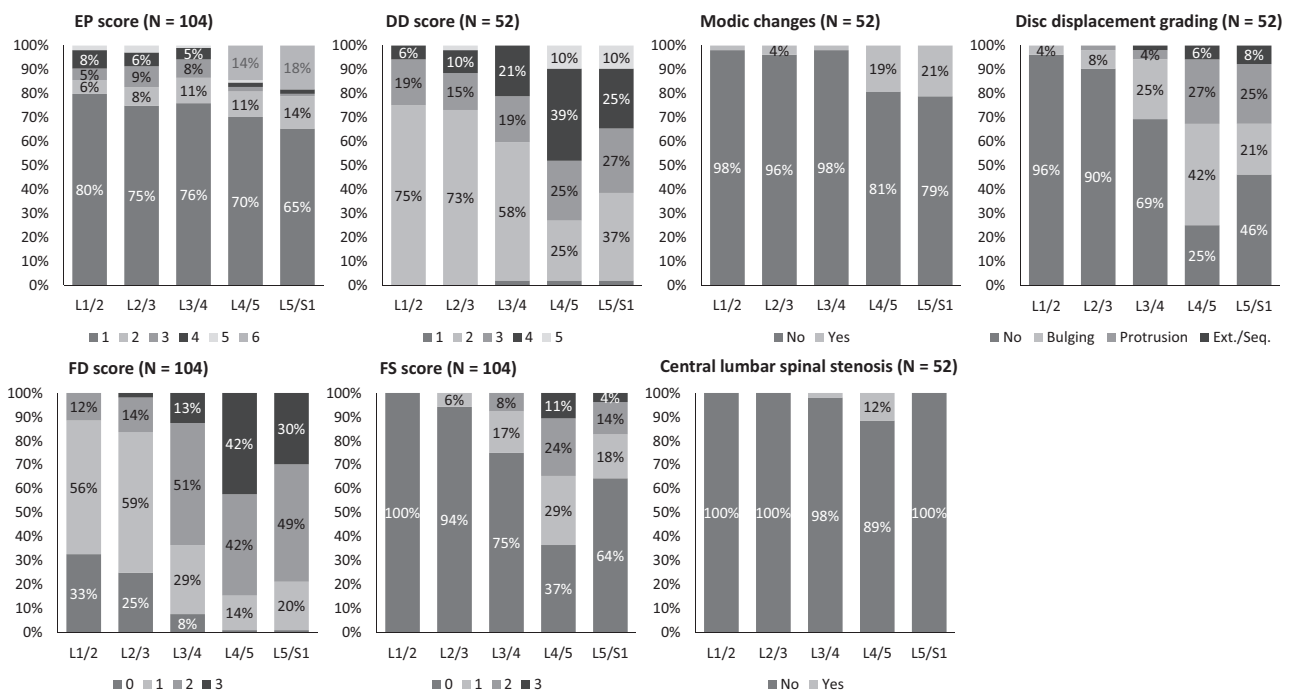


Figure 2. Occurrence and severity of degenerative changes at each level. DD score=disc degeneration score, EP score=endplate score, Ext./seq.=extrusion/sequestration, FD score=facet degeneration score, FS score=foraminal stenosis score.

Table 5
Correlation between pain intensity and severity of degenerative changes.

	Correlation coefficient*	P value
DD sum score L1-S1	0.057	.689
FD sum score L1-S1	0.009	.952
FS sum score L1-S1	0.061	.669
Degenerative summary score L1-S1	0.077	.589

DD sum score=disc degeneration summary score, FD sum score=facet degeneration summary score, FS sum score=foraminal stenosis summary score.

* Spearman coefficient.

intensity of mean pain in the previous 4 weeks 4.5 (NRS, 0–10) or more (OR=13.1) as independent predictors of NP in patients with non-specific LBP.

4. Discussion

This study focused on the analysis of the MRI findings in patients with non-specific CLBP and assessment of their relations to pain intensity and the presence of a neuropathic component of pain. The findings suggest that degenerative changes in the lumbar spine are frequent and that the L4/5 segment is the most affected level. The severity of degenerative changes in particular structures of the vertebral segments inter-correlates and thus seems to constitute a complex degenerative impairment of vertebral

Table 6
Comparison of patient characteristics in the 2 subgroups (with neuropathic pain and non-neuropathic pain).

	Non-neuropathic pain (N=28)*	Neuropathic pain (N=24)*	P value†
Sex			
Female	7 (25.0%)	19 (79.2%)	<.001
Male	21 (75.0%)	5 (20.8%)	
Age	38.5 (± 7.6)	43.6 (± 11.4)	.065
BMI	25.5 (± 2.6)	26.8 (± 3.8)	.160
Duration of pain (months)	64.1 (± 77.5)	68.5 (± 83.2)	.686
Mean pain in the previous 4 weeks	3.6 (± 1.6)	5.7 (± 1.4)	<.001
DN4-interview	1.5 (± 0.6)	4.1 (± 1.0)	<.001
NPSI _{CZ}	9.9 (± 4.5)	30.8 (± 12.3)	<.001
DD sum score L1-S1	13.1 (± 2.8)	14.3 (± 2.9)	.131
EP sum score L1-S1	17.2 (± 7.6)	16.9 (± 8.5)	.778
FD sum score L1-S1	14.5 (± 4.8)	16.6 (± 6.8)	.185
FS sum score L1-S1	3.4 (± 3.5)	4.9 (± 4.3)	.260
Degenerative summary score L1-S1	31.0 (± 8.7)	35.8 (± 11.8)	.095
Modic changes			
Yes	8 (28.6%)	9 (37.5%)	.562
No	20 (71.4%)	15 (62.5%)	
Disc displacement			
Yes	23 (82.1%)	22 (91.7%)	.430
No	5 (17.9%)	2 (8.3%)	
Central lumbar spinal stenosis			
Yes	2 (7.1%)	4 (16.7%)	.397
No	26 (92.9%)	20 (83.3%)	

BMI=body mass index, DD sum score=disc degeneration summary score, DN4=Douleur Neuropathique en 4 Questions, EP sum score=endplate summary score, FD sum score=facet degeneration summary score, FS sum score=foraminal stenosis summary score, NPSI_{CZ}=Neuropathic Pain Symptom Inventory–Czech version.

* Data are presented as absolute and relative frequencies or mean (± SD).

† Mann-Whitney test for continuous variables; Fisher exact test for categorical variables.

segments rather than degeneration confined to particular structures. The extent of degenerative changes is not directly related to the intensity of pain in general and is not a predictor of its neuropathic component. The only independent predictors of NP in patients with non-specific CLBP are female sex and pain intensity.

The study indicated a general trend to more frequent and more pronounced degenerative changes in the lower lumbar spinal segments (especially at L4/L5 and L5/S1 levels) with a slight predominance of degeneration at the L4/5 level compared with L5/S1. This is in agreement with other studies, in which the most commonly affected levels have been determined at the L4/5 and L5/S1 segments.^[6,11] Comparison of MRI abnormality prevalence between studies is difficult, since the results are affected by particular definitions of changes and the age structures of study groups (the severity of degenerative changes increases with advancing age). In the present study, the prevalence of MC was 32.7%, largely located at the 2 lowest lumbar levels. The prevalence of MC varies widely between reported studies. Jensen et al established a median prevalence of Modic changes of 43% in patients with non-specific LBP and/or sciatica, based on a systematic review^[31], which is relatively close to the findings herein. Disc protrusion and/or extrusion/sequestration were found in 46.2% of patients in this study, while the prevalence of these findings reported elsewhere ranged from 15% to 96% of patients with LBP.^[3] In the present study, at least moderate central lumbar spinal stenosis did not frequently (11.5%), while the prevalence of central lumbar spinal stenosis in patients with LBP was 29.7% for relative stenosis and 18.9% for absolute stenosis in the Kalichman et al study, but their criteria for spinal stenosis (anteroposterior diameter of the canal using CT scans) were different from those reported here, and the age structure of the study group was different too (older comparing to the sample herein).^[4]

The present study has demonstrated positive inter-correlation between the severity of degenerative changes of particular lumbar spinal structures, and thus supports the idea that the progress of degenerative changes in vertebral segments is a complex and interlinked process. Previous studies have disclosed a positive correlation between lumbar disc degeneration and vertebral endplate changes,^[11,12] which is in agreement with this study. Similarly, the data presented herein support a relationship between facet joint osteoarthritis and disc degeneration that has also been described in a previous study.^[13]

Any association between radiological findings and severity of symptoms (e.g., pain) remains unclear and is a matter for debate. This work found no correlation between pain intensity and severity of degenerative changes. According to these results, it is not possible to estimate intensity of pain in patients with non-specific CLBP on the basis of MRI findings. Berg et al also demonstrated that MRI findings are not related to the intensity of LBP in patients with chronic non-radicular LBP.^[32] Similarly, in a previous study performed by the current authors, pain intensity displayed no correlation with MRI parameters in patients with clinically symptomatic lumbar spinal stenosis.^[33] Relationships between degree of degenerative changes disclosed by MRI and symptoms will probably be more complex.

Baron et al draw special attention to the fact that CLBP often has an under-recognized neuropathic component, which may be challenging to manage and requires better diagnosis and treatment.^[15] A knowledge of predictors can increase capture of NP. In this study, the presence of NP was assessed using the

Table 7
Potential predictors of neuropathic pain (endpoint) in logistic regression.

	N	Endpoint*	OR†	P value
Univariate logistic regression				
Sex				
Male	26	5 (19.2%)	–	–
Female	26	19 (73.1%)	11.400 (3.092–42.026)	<.001
Age	52	–	1.056 (0.995–1.121)	.072
BMI	52	–	1.135 (0.954–1.350)	.152
Duration of pain (months)	52	–	1.001 (0.994–1.007)	.844
Mean pain in the previous 4 weeks	52	–	2.301 (1.429–3.707)	.001
DD sum score L1-S1	52	–	1.148 (0.945–1.395)	.166
EP sum score L1-S1	52	–	0.996 (0.931–1.066)	.907
FD sum score L1-S1	52	–	1.065 (0.967–1.173)	.202
FS sum score L1-S1	52	–	1.100 (0.000–0.000)	.187
Degenerative summary score L1-S1	52	–	1.046 (0.990–1.104)	.110
Modic changes				
No	35	15 (42.9%)	–	–
Yes	17	9 (52.9%)	2.600 (0.432– 15.646)	.297
Disc displacement				
No	7	2 (28.6%)	–	–
Yes	45	22 (48.9%)	1.500 (0.468– 4.805)	.495
Central lumbar spinal stenosis				
No	46	20 (43.5%)	–	–
Yes	6	4 (66.7%)	2.391 (0.419– 13.636)	.326
Multivariate logistic regression				
Sex				
Males	26	5 (19.2%)	–	–
Females	26	19 (73.1%)	11.870 (2.540– 55.464)	.002
Mean pain in the previous 4 weeks				
less than 4.5	21	3 (14.2%)	–	–
4.5 and more	31	21 (67.7%)	13.143 (2.468–69.994)	.003

BMI=body mass index, DD sum score=disc degeneration summary score, EP sum score=endplate summary score, FD sum score=facet degeneration summary score, FS sum score=foraminal stenosis summary score.

*Data are presented as absolute and relative frequencies.

†Odds ratio with 95% confidence interval (in parentheses).

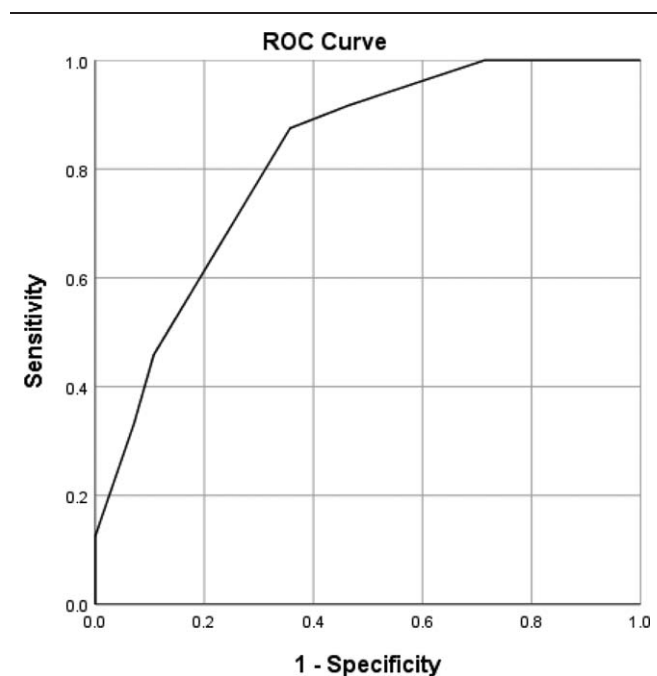


Figure 3. Mean pain intensity in the previous 4 weeks as a predictor of neuropathic pain—ROC (receiver operating characteristic) curve. AUC=area under the ROC curve with corresponding 95% confidence interval.

DN4-interview, as has previously been done in other studies.^[18,21] NP was recognized in 46.2% of non-specific CLBP patients in this study. Attal et al reported NP in 8% of patients with pain restricted to the lumbar area and in 29% of patients with CLBP radiating proximally.^[16] In an unselected cohort of CLBP patients, 37% were found to have predominantly NP.^[34] The probable reason for a higher proportion of patients with NP in this study is that it is not population-based and patients not responding to standard treatment were referred by collaborating out-patient neurologists. In such a cohort, a higher prevalence of NP is thus not unexpected. The statistically significant difference in the results for NPSI between the 2 subgroups of patients supports a correct classification of the NP-related subgroups. A literature search found only one study that has explored the association between radiographic findings (radiographic features of lumbar disc degeneration) and NP.^[18] This study found no association between osteophytes and NP but disc space narrowing was significantly associated with the presence of NP; however OR was relatively low (OR = 1.7).^[18] It was pointed out that further research is required to confirm this association. Our study demonstrated no radiological predictors of NP; however, female sex and the mean pain intensity in the previous 4 weeks with a cut-off of 4.5 appeared as significant independent predictors of NP. The van der Berg study and the present work, however, differ in many ways, mainly in the imaging methods employed (radiography vs MRI of the lumbar spine, patients with coexisting pain of the hip and/or knee vs patients without other

pain). In agreement with our study, other workers have also noted that NP is more prevalent in women than in men and the intensity of chronic pain with neuropathic characteristics is higher in comparison with chronic pain without neuropathic characteristics.^[21,35] Duration of pain has been shown to be longer in patients with chronic NP than in patients without NP and prevalence increases with age^[21,35]. In our study, however, duration of pain and age did not significantly differ between subgroups (with NP and with non-NP).

The present study has some limitations. The number of patients recruited is relatively low, which could impact especially on the determination of predictors and OR values. However, the results of our study do not contradict the results of larger studies evaluating neuropathic pain predictors.^[21,35] Strict inclusion and exclusion criteria were essential to eliminate factors that might influence the intensity and characteristics of pain. Patients with incidental polyneuropathy or radiculopathy and with severe comorbid conditions were excluded. These strict criteria led to a low age range (21–62 years). A further limitation is the use of analgesic medication by a number of patients, which could have influenced pain intensity. On the other hand, analgesic medication was used by only a third of the patients and NP was not probably affected by medication, since only one patient was taking a weak opioid and none of the patients was using specific neuropathic pain treatments. The advantage of this study is that it reports a comprehensive clinical examination and detailed MRI examination of the lumbar spine.

5. Conclusions

A general trend towards more frequent and more severe MRI degenerative features in lower, rather than upper, lumbar spinal segments was demonstrated in CLBP patients. A correlation between the severity of degenerative changes of particular structures in vertebral segments was established, suggesting that degenerative changes affect vertebral segment as a complex interaction, rather than being confined to only selected structures. MRI degenerative changes in the lumbar spine did not correlate with the intensity of pain and did not predict NP. The only independent predictors of NP in patients with non-specific CLBP were female sex (OR 11.9) and mean pain intensity in the previous 4 weeks ≥ 4.5 (OR 13.1). A multicentre study with a higher number of patients is needed to validate these results in a similar population.

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References

- Airaksinen O, Brox JI, Cedraschi C, et al. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J* 2006;15(Suppl 2):S192–300.
- Deyo RA, Dworkin SF, Amtmann D, et al. Report of the NIH Task Force on research standards for chronic low back pain. *J Pain* 2014;15:569–85.
- Endean A, Palmer KT, Coggon D. Potential of magnetic resonance imaging findings to refine case definition for mechanical low back pain in epidemiological studies: a systematic review. *Spine* 2011;36:160–9.
- Kalichman L, Cole R, Kim DH, et al. Spinal stenosis prevalence and association with symptoms: the Framingham Study. *Spine J* 2009;9:545–50.
- Kalichman L, Kim DH, Li L, et al. Computed tomography-evaluated features of spinal degeneration: prevalence, intercorrelation, and association with self-reported low back pain. *Spine J* 2010;10:200–8.
- Cheung KM, Karppinen J, Chan D, et al. Prevalence and pattern of lumbar magnetic resonance imaging changes in a population study of one thousand forty-three individuals. *Spine* 2009;34:934–40.
- Suri P, Hunter DJ, Rainville J, et al. Presence and extent of severe facet joint osteoarthritis are associated with back pain in older adults. *Osteoarthritis Cartilage* 2013;21:1199–206.
- Määttä JH, Wadge S, MacGregor A, et al. ISSLS Prize Winner: vertebral endplate (modic) change is an independent risk factor for episodes of severe and disabling low back pain. *Spine* 2015;40:1187–93.
- Mok FP, Samartzis D, Karppinen J, et al. Modic changes of the lumbar spine: prevalence, risk factors, and association with disc degeneration and low back pain in a large-scale population-based cohort. *Spine J* 2016;16:32–41.
- Farshad-Amacker NA, Hughes A, Herzog RJ, et al. The intervertebral disc, the endplates and the vertebral bone marrow as a unit in the process of degeneration. *Eur Radiol* 2017;27:2507–20.
- Rajasekaran S, Venkatadass K, Naresh Babu J, et al. Pharmacological enhancement of disc diffusion and differentiation of healthy, ageing and degenerated discs: Results from in-vivo serial post-contrast MRI studies in 365 human lumbar discs. *Eur Spine J* 2008;17:626–43.
- Rade M, Määttä JH, Freidin MB, et al. Vertebral endplate defect as initiating factor in intervertebral disc degeneration: strong association between endplate defect and disc degeneration in the general population. *Spine* 2018;43:412–9.
- Paholpak P, Dedeogullari E, Lee C, et al. Do modic changes, disc degeneration, translation and angular motion affect facet osteoarthritis of the lumbar spine. *Eur J Radiol* 2018;98:193–9.
- Freyenhagen R, Baron R. The evaluation of neuropathic components in low back pain. *Curr Pain Headache Rep* 2009;13:185–90.
- Baron R, Binder A, Attal N, et al. Neuropathic low back pain in clinical practice. *Eur J Pain* 2016;20:861–73.
- Attal N, Perrot S, Fermanian J, et al. The neuropathic components of chronic low back pain: a prospective multicenter study using the DN4 Questionnaire. *J Pain* 2011;12:1080–7.
- Sommer C, Richter H, Rogausch JP, et al. A modified score to identify and discriminate neuropathic pain: a study on the German version of the Neuropathic Pain Symptom Inventory (NPSI). *BMC Neurol* 2011;11:104.
- van den Berg R, Jongbloed LM, Kuchuk NO, et al. The association between self-reported low back pain and radiographic lumbar disc degeneration of the cohort hip and cohort knee (CHECK) study. *Spine* 2017;42:1464–71.

- [19] Attal N, Bouhassira D, Baron R. Diagnosis and assessment of neuropathic pain through questionnaires. *Lancet Neurol* 2018;17:456–66.
- [20] Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005;114:29–36.
- [21] Bouhassira D, Lantéri-Minet M, Attal N, et al. Prevalence of chronic pain with neuropathic characteristics in the general population. *Pain* 2008;136:380–7.
- [22] Bursova S, Vlckova E, Hnojckikova M, et al. Validity and predictive value of screening tests in prediabetic and early diabetic polyneuropathy. *Cesk Slov Neurol N* 2012;75/108:562–72.
- [23] Bouhassira D, Attal N, Fermanian J, et al. Development and validation of the neuropathic pain symptom inventory. *Pain* 2004;108:248–57.
- [24] Srotova I, Vlckova E, Strakova J, et al. Validation of the Czech Version of the Neuropathic Pain Symptom Inventory (NPSIcz). *Cesk Slov Neurol N* 2015;78/111:45–56. (Czech).
- [25] Pfirrmann CW, Metzendorf A, Zanetti M, et al. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine* 2001;26:1873–8.
- [26] Fardon DF, Williams AL, Dohring EJ, et al. Lumbar disc nomenclature: version 2.0: Recommendations of the combined task forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. *Spine J* 2014;14:2525–45.
- [27] Modic MT, Steinberg PM, Ross JS, et al. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. *Radiology* 1988;166(1 Pt 1):193–9.
- [28] Weishaupt D, Zanetti M, Boos N, et al. MR imaging and CT in osteoarthritis of the lumbar facet joints. *Skeletal Radiol* 1999;28:215–9.
- [29] Lurie JD, Tosteson AN, Tosteson TD, et al. Reliability of readings of magnetic resonance imaging features of lumbar spinal stenosis. *Spine* 2008;33:1605–10.
- [30] Schizas C, Theumann N, Burn A, et al. Qualitative grading of severity of lumbar spinal stenosis based on the morphology of the Dural sac on magnetic resonance images. *Spine* 2010;35:1919–24.
- [31] Jensen TS, Karppinen J, Sorensen JS, et al. Vertebral endplate signal changes (Modic change): a systematic literature review of prevalence and association with non-specific low back pain. *Eur Spine J* 2008;17:1407–22.
- [32] Berg L, Hellum C, Gjertsen Ø, et al. Do more MRI findings imply worse disability or more intense low back pain? A cross-sectional study of candidates for lumbar disc prosthesis. *Skeletal Radiol* 2013;42:1593–602.
- [33] Andrasinova T, Adamova B, Buskova J, et al. Is there a correlation between degree of radiological lumbar spinal stenosis and its clinical manifestation? *Clin Spine Surg* 2018;31:E403–8.
- [34] Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22:1911–20.
- [35] Harifi G, Amine M, Ait Ouazar M, et al. Prevalence of chronic pain with neuropathic characteristics in the Moroccan general population: a national survey. *Pain Med* 2013;14:287–92.