Chapter 5

Prognostic value of MRI in sciatica patients in relation to back pain

Abdelilah el Barzouhi MD, Carmen L.A.M. Vleggeert-Lankamp MD PhD, Geert J. Lycklama à Nijeholt MD PhD, Bas F. Van der Kallen MD, Wilbert B. van den Hout PhD, Bart W. Koes PhD, and Wilco C. Peul MD PhD for the Leiden–The Hague Spine Intervention Prognostic Study Group

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ABSTRACT

BACKGROUND

Patients with sciatica frequently do complain about associated back pain. It is not known whether there are prognostic relevant differences in Magnetic Resonance Imaging (MRI) characteristics between sciatica patients with and without disabling back pain.

METHODS

The study population contained patients with sciatica who underwent a baseline MRI to assess eligibility for a randomized trial designed to compare the efficacy of early surgery with prolonged conservative care for sciatica. Blinded evaluated MRI findings were compared between sciatica patients with and without disabling back pain. On the basis of significantly different MRI findings four subgroups were defined that were correlated with perceived recovery at one year: back pain with and without the MRI characteristic, and no back pain with and without the MRI characteristic.

RESULTS

Of 379 included sciatica patients, 158 (42%) had disabling back pain. Of the patients with both sciatica and disabling back pain 68% did reveal a herniated disc with nerve root compression on MRI, compared to 88% of patients with predominantly sciatica (P<0.001). The existence of low back pain in sciatica at baseline was negatively associated with perceived recovery at one year (Odds ratio [OR] 0.32, 95% CI 0.18-0.56, P<0.001). Sciatica patients with disabling back pain in absence of nerve root compression on MRI at baseline reported less perceived recovery at one year compared to those with predominantly sciatica and nerve root compression on MRI (50% vs 91%, P<0.001)

CONCLUSION

Sciatica patients with disabling low back pain reported an unfavorable prognosis at one-year follow-up compared to those with predominantly sciatica. If additionally a clear herniated disc with nerve root compression on MRI was absent, the results were even worse.

INTRODUCTION

Patients with sciatica frequently complain about associated back pain.[1] Sciatica is associated with significant short- and sometimes long-term morbidity. This affliction, certainly in the industrialized countries, ranks as one of the most costly and ubiquitous medical problems.[2] In classical literature sciatica has been of great interest to Greco-Roman and Eastern scientists and physicians.[3] For centuries an inflammation of the sciatic nerve was the origin of pain, described as sciatic neuritis,[4] until 1934 when Mixter and Barr revolutionized the understanding of sciatica into mechanical origin.[3,5] They asserted that sciatica was caused by a herniated disc pressing against a nerve root. Worldwide this mechanical compression theory has been accepted giving rise to a global implementation of disc surgery as the solution to remove the compression on the nerve root and with that resolve the disabling pain problem. However, does this theory still find ground or is it worthwhile to think about the renaissance of the old theory involving inflammation of the nerve root?

This scientific confusion has been caused by the introduction of modern imaging modalities such as Magnetic Resonance Imaging (MRI) which allowed many investigators to detect an enormous variety of previously unappreciated anatomical variations in patients undergoing diagnostic workups for sciatica.[6] For example, several studies show a high prevalence of disc herniations ranging from 20 to 76% in subjects without any symptoms.[7,8] Furthermore, it remains unclear to what extent morphological changes seen on MRI in sciatica patients are associated with back pain, rather than being a representation of irrelevant differences between individuals.[6,7,8] Back pain has been reported to be associated with worse prognosis in patients with sciatica,[9] but one could question whether it is the back pain itself that causes the worse prognosis or the possible MRI anatomical differences between sciatica patients with and without back pain.

The investigators previously reported the results of a randomized controlled trial comparing early surgery with prolonged conservative care for patients with sciatica.[10] The trial showed faster recovery after early surgery compared to a strategy of prolonged conservative care with surgery if needed, but without any differences in the clinical outcomes after one year. The randomized patients were part of a larger group of patients with sciatica who underwent MRI and were followed up for one year. In this large group of sciatica patients, we now report on the MRI differences between patients who suffered from sciatica with disabling back pain as compared to patients who suffered from sciatica only. Furthermore we report on the relevance of these MRI differences for prognosis.

MATERIALS AND METHODS

ETHICS STATEMENT

The medical ethics committees at the nine participating hospitals (Leiden University Medical Center, Medical Center Haaglanden, Diaconessen Hospital, Groene Hart Hospital, Reinier de Graaf Hospital, Spaarne Hospital, Bronovo Hospital, Rijnland Hospital and Lange Land Hospital) approved the protocol. Written informed consent was obtained from all patients.

STUDY POPULATION

Patients for this study were patients with intense lumbosacral nerve root pain who underwent a baseline MRI to assess the eligibility for the Sciatica Trial: a multicenter, randomized controlled trial designed to determine whether early surgery results in better outcome compared to a strategy of prolonged conservative treatment with surgery if needed among patients with 6-12 weeks sciatica.[10,11] Patients who had symptoms being so severe that they were eligible for surgery according to their family physicians were referred to the neurologist who subsequently evaluated whether these patients were eligible to participate in the trial. Patients were excluded if they were presenting with cauda equina syndrome, insufficient strength to move against gravity, identical complaints in the previous 12 months, previous spine surgery, pregnancy, and severe coexisting disease. Participants who were not meeting one or more of the aforementioned exclusion criteria and had a lumbosacral radicular syndrome lasting between 6-12 weeks underwent an MRI and qualified to be included in this present study (thus for the present study it was not necessary to have a herniated disc visible on MRI). All patients with sciatica who underwent MRI (regardless of participation in the randomized trial) were followed for one year. Details of the design and study protocol have been published previously.[11]

MRI PROTOCOL AND IMAGE EVALUATION

MRI scans were performed in all nine participating hospitals using standardized protocols tailored to a 1.5 Tesla scanner. Sagittal T1 and axial T1 spin echo images of the lumbar spine were acquired. In addition, T2 weighted sagittal and axial series, and contrast-enhanced (gadolinium-DTPA) T1 fat suppressed images were obtained.

Two experienced neuroradiologists (BK and GL) and one neurosurgeon (CV) independently evaluated all MR images. The readers were not provided any clinical information and had not been involved in the selection or care of the included patients.

Definitions of imaging characteristics were based on recommendations from the combined task forces of the North American Spine Society, the American Society of Spine Radiology, and the American Society of Neuroradiology for classification of lumbar disc pathology.[12] Vertebral Endplate Signal Changes were defined according to criteria of Modic.[13,14] Standardized case record forms with definitions were used to evaluate the images (Appendix Table S1).

First, the blinded readers had to decide which disc level showed the most severe nerve root compression. For both the presence of disc herniation and nerve root compression a four point scale was used: "definite about the presence", "probable about the presence", "possible about the presence" and "definite about the absence". The first two categories were combined and marked as having the abnormality present. The latter two categories were combined and marked as not having the abnormality present. Clinically relevant characteristics of the disc level and disc herniation were scored. Vertebral Endplate Signal Changes were evaluated from L2-L3 through L5-S1.

OUTCOMES

The patients were assessed by means of the Roland Disability Questionnaire for Sciatica (RDQ, scores range from 0 to 23, with higher scores indicating worse functional status)[15] the 100-mm visual-analogue scale (VAS) for leg and low back pain (with 0 representing no pain and 100 the worst pain ever experienced),[16] and a 7-point Likert self-rating scale of global perceived recovery with answers ranging from completely recovered to much worse. Perceived recovery was defined as "complete" or "nearly complete disappearance of symptoms" on the patient-reported 7-point Likert scale for global perceived recovery, while a score in the remaining five categories (varying from "minimally improved" to "very much worse") was marked as "no recovery".[10,11] Outcome measures were assessed at baseline, 2, 4, 8, 12, 26, 38 and 52 weeks.

STATISTICAL ANALYSIS

The majority opinion of the three readers regarding the MRI characteristics (answer independently given by minimum 2 out of 3 readers) was used in the statistical analysis. Interobserver agreement regarding the MRI findings was determined by use of absolute percentages of agreement and kappa values (weighted in case of ordered data).

Disabling back pain was defined in the SIPS research group consensus meeting as a VAS for back pain of at least 40, as this cutt-off value is regularly used when the VAS is categorized into favorable and unfavorable outcome.[17,18] Patients with missing VAS-back pain at baseline were excluded. Differences between patients with VAS-back pain of at least 40 and those with a VAS lower than 40 were assessed by using Student's t-test for continuous data and Chi-square tests for categorical data.

Logistic regression was used to determine the association between perceived recovery at one year and disabling back pain at baseline. On the basis of MRI characteristics that proved to be significantly different in proportions between patients with versus those without disabling back pain four subgroups were defined: back pain with and without the MRI characteristic, and no back pain with and without the MRI characteristic. Between group differences in continuous outcome measures (RDQ and VAS pain scores) during the first year were analyzed by repeated measurement analysis of variance.

We assumed clinical outcome data to be missing at random and used model-based multiple imputation to impute the outcome values, a method in which the distribution of the observed data is used to construct sets of plausible values for the missing observations (10 imputed datasets). Variables included in the imputation model were age, gender, body-mass index, duration of symptoms, smoking, treatment group, all used MRI variables (Table S1 Appendix), and baseline and other follow-up measurements of the outcomes being predicted. Complete case analysis (i.e. no imputation) was performed as a sensitivity analysis. Statistical significance was defined as P <0.05.

Table 1 Baseline characteristics stratified by presence of disabling back pain.

Variable	Sciatica with disabling back pain (n=158)	Sciatica with no disabling back pain (n=221)	P-value
Age at baseline MRI	42.8±10.9	43.4±9.6	0.56
Male-sex	92 (58)	147 (67)	0.09
Duration of sciatica (weeks)	9.0±2.4	9.5±3.8	0.11
BMI ‖	26.1±4.2	25.9±3.6	0.59
Treatment group			0.09
Non-randomized	48 (30)	50 (23)	
Randomized to early surgery	60 (38)	79 (36)	
Randomized to prolonged conservative care	50 (32)	92 (42)	
Smoking	67 (42)	80 (36)	0.24
Roland disability score for sciatica¶			
Baseline	17.4±3.3	15.0±4.5	<0.001
12 months	4.5±5.9	2.9±4.7	0.004
Visual-analogue scale of leg pain‡			
Baseline	66.6±20.3	60.7±22.7	0.009
12 months	13.7±22.4	8.7±16.5	0.014
Visual-analogue scale of back pain‡			
Baseline	63.3±16.2	12.1±11.6	<0.001
12 months	21.3±26.1	12.2±18.8	<0.001
Perceived recoveryò			
12 months	111 (70)	195 (88)	<0.001

Values are n (%) or means ± SD.

‖ Body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters

¶ The Roland disability questionnaire for sciatica is a disease-specific disability scale that measures functional status in patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.

‡ The intensity of pain was indicated on a horizontal 100 mm visual analogue scale, with 0 representing no pain and 100 the worst pain ever experienced.

ò Perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.

Table 2 Comparison of MRI characteristics between sciatica patients with and without disabling back pain at baseline.

	Sciatica with disabling back pain (n=158)	Sciatica with no disabling back pain (n=221)	P-value
MRI characteristic			
Presence of disc herniation	120 (76)	202 (91)	**<0.001**
Presence of nerve root compression	108 (68)	195 (88)	**<0.001**
Presence of Vertebral Endplate Signal Changes at one or more lumbar level ¶	63 (41)	94 (43)	0.91
Type 1	3 (5)	6 (6)	
Type 2	58 (92)	84 (89)	
Type 3	0 (0)	1 (1)	
Mixed Type 1 and 2	2 (3)	3 (3)	
Presence of Schmorl's nodules (herniation of the disc into the vertebral-body endplate) at one or more levels	18 (12)	25 (11)	0.94

Values are n (%)

¶ Vertebral Endplate Signal Changes were defined according to criteria of Modic and their presence was assessed from vertebral endplates L2-L3 through L5-S1. Type 1 lesions: hypointense in T1-weighted sequences and hyperintense in T2-weighted sequences. Type 2 lesions: increased signal on T1 weighted sequences and isointense or slightly hyperintense signal on T2 weighted sequences. Type 3 lesions: hypointense both in T1- and T2-weighted sequences.

RESULTS

Of the 599 patients screened for the study, 395 patients underwent MRI of whom 283 patients were randomized.[10,19] In total, 283 baseline MRI's of the 283 randomized patients and 106 MRI's of 112 non-randomized patients could be retrieved, bringing the total to 389 MRI's. Of the randomized patients 91% depicted a disc herniation with nerve root compression on MRI compared to 49% of the non-randomized patients. Baseline VAS of back pain was not available for 10 (2.6%) patients. Of the 379 eligible patients, 158 (42%) had a VAS of at least 40 with a mean of 63.3 (95% Confidence Interval [CI] 61-66) and 221 (58%) patients had a VAS of back pain of less than 40 with a mean VAS of 12.1 (95% CI 11-14). At baseline, sciatica patients with and without disabling back pain had a statistically significant but clinically small difference in RDQ and VAS-leg pain (17.4 vs. 15.0 and 66.6 vs. 60.7 respectively) (Table 1). Clinical outcome at 52 weeks was missing in 12-13% of patients (Appendix Table S2). Baseline RDQ and VAS for leg and back pain were comparable among patients for whom clinical outcome at 52 weeks was available and those for whom not (P-value range 0.21-0.42).

Substantial agreement was found for the MRI assessed presence of disc herniation (kappa range 0.67-0.75) and nerve root compression (kappa range 0.60-0.80) (Appendix Table S3).

Moderate agreement was found for the size of the disc herniation (kappa range 0.35-0.55) and presence of vertebral endplate signal changes (kappa range 0.49-0.67).

MRI DIFFERENCES WITH AND WITHOUT DISABLING BACK PAIN

Of patients with both sciatica and disabling back pain 76% had a disc herniation on MRI compared to 91% of patients without disabling back pain (P<0.001) (Table 2). Nerve root compression on MRI was observed less frequently in patients with both disabling sciatica and back pain compared to patients with predominantly sciatica (68% vs. 88%, P<0.001). No significant differences existed in prevalence of Vertebral Endplate Signal Changes between sciatica patients with and without disabling back pain (41% vs. 43%, P=0.70).

A comparison of the characteristics of the herniated disc itself between sciatica patients with and without disabling back pain is shown in Table 3**.** Large disc herniations (size >50% of spinal canal) were observed in an equal percentage (18%) between patients with and without disabling back pain. Also, no significant difference existed in extrusions between patients with and without disabling back pain (64% vs. 67%, P=0.66).

CLINICAL OUTCOME IN RELATION TO DISABLING BACK PAIN AND MRI DIFFERENCES

The existence of disabling back pain in sciatica at baseline was negatively associated with perceived recovery at one year (Odds ratio [OR] 0.32, 95% CI 0.18-0.56, P<0.001). This result was consistent with the continuous outcomes RDQ and VAS pain scores (Appendix Figure S1). By contrast, presence of disc herniation on MRI at baseline was positively associated with perceived recovery at one year (OR 3.18, 95% CI 1.6-6.4, P=0.001). Same holds for nerve root compression (OR 4.99, 95% CI 2.7-9.2, P<0.001).

The reported prevalence of perceived recovery at one year was 81% for sciatica patients who had at baseline disabling back pain and nerve root compression, 50% for patients who had at baseline back pain but no nerve root compression, 91% for patients who had at baseline no back pain but depicted nerve root compression on MRI, and 73% for patients who had at baseline no back pain and no nerve root compression (P<0.001) (Table 4). In the stratified analysis according to treatment group the overall trends were comparable with the non-stratified analysis (Appendix Table S4).

In patients with disabling back pain, those who also had nerve root compression on MRI significantly reported more favorable recovery from their back pain at one year compared to those who had not depicted nerve root compression at baseline (Figure 1).

The sensitivity analyses yielded comparable results (with complete case analysis instead of multiple imputation of missing data) (Appendix Table S5).

Table 3 Comparison of the characteristics of the herniated disc on MRI between sciatica patients with and without disabling back pain at baseline. Values are n (%). N=330

	Sciatica with disabling back pain (n=125)	Sciatica with no disabling back pain (n=205)	P-value
Size of disc herniation			
Size > 50% in relation to spinal canal	23 (18)	37 (18)	0.95
Size < 50% in relation to spinal canal	102 (82)	167 (81)	
Not classifiable	0 (0)	1 (1)	
Location of disc herniation			
Central and/or subarticular	111 (89)	183 (89)	0.70
Foraminal and/or extraforaminal	14 (11)	20 (10)	
Not classifiable	0 (0)	2 (1)	
Morphology of disc herniation			
Extrusion	80 (64)	138 (67)	0.66
Protrusion	42 (34)	65 (32)	
Not classifiable	3 (2)	2 (1)	
Loss of disc height at the disc level of the disc herniation			
Yes	112 (90)	186 (91)	0.96
No	10 (8)	17 (8)	
Not classifiable	3 (2)	2 (1)	
Signal intensity of nucleus pulposus on T2 images at the disc level of the disc herniation			
Hypointensity	110 (88)	185 (90)	0.72
Normal	10 (8)	15 (7)	
Hyperintensity	(0)	1 (1)	
Not classifiable	5 (4)	4 (2)	
Presence of Vertebral Endplate Signal Changes at the disc level of the disc herniation ¶			
Type 1	2 (4)	6 (7)	0.70
Type 2	51 (93)	76 (91)	
Type 3	0 (0)	0 (0)	
Mixed Type 1 and 2	2 (4)	2 (2)	

Values are n (%)

¶ Vertebral Endplate Signal Changes were defined according to criteria of Modic. Type 1 lesions: hypointense in T1-weighted sequences and hyperintense in T2-weighted sequences. Type 2 lesions: increased signal on T1 weighted sequences and isointense or slightly hyperintense signal on T2 weighted sequences. Type 3 lesions: hypointense both in T1- and T2-weighted sequences.

Table 4 Clinical outcome measures at one year according to subgroups at baseline. Subgroups defined by the presence of disabling back pain and the presence of a disc herniation or nerve root compression on MRI at baseline. Values are n (%) or means ± SD. N=379

	Clinical outcome at one year			
	Perceived recoveryò	Roland Disability‡	VAS-Leg pain¶	VAS-back pain¶
Subgroups according to back pain and presence of nerve root compression on MRI at baseline				
Back pain and nerve root compression (n=108)	87 (81)	3.6±5.8	11.8±21.7	17.4±23.9
Back pain and no nerve root compression (n=50)	25 (50)	6.4±5.8	17.8±23.5	29.6±28.8
No back pain and nerve root compression (n=195)	177 (91)	2.7±4.4	7.6±14.1	11.4±17.2
No back pain and no nerve root compression (n=26)	19 (73)	4.5±6.6	16.7±27.9	18.7±27.4
Subgroups according to back pain and presence of disc herniation on MRI at baseline				
Back pain and disc herniation (n=120)	90 (75)	4.2±6.2	14.4±23.9	20.0±26.2
Back pain and no disc herniation (n=38)	22 (58)	5.4±5.1	11.6±16.8	25.2±25.8
No back pain and disc herniation (n=202)	181 (90)	2.8±4.5	7.7±14.1	11.6±17.3
No back pain and no disc herniation (n=19)	14 (74)	4.1±6.5	18.8±31.7	18.3±29.9

ò Perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.
‡ The Roland Disability Questionnaire for Sciatica is a disease-specific disability scale that measures the functional status of patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.
¶ The intensity of pain is indicated on a horizontal 100 mm visual analogue scale (VAS) with 0 representing no pain and 100 the worst pain ever experienced.

DISCUSSION

In this study of patients with sciatica who were followed for one year, those with disabling back pain at baseline reported an unfavorable prognosis at one-year follow-up compared to those with predominantly sciatica. If additionally a herniated disc with nerve root compression on MRI was absent, the results were even worse. Herniated discs and nerve root compression on MRI were more prevalent among patients with predominantly sciatica compared to those who suffered from additional disabling back pain. However, vertebral endplate signal changes were equally distributed between those with and without disabling back pain. Remarkably large disc herniations and extruded disc herniations were also equally distributed between the two groups.

Over the past two decades there has been an ongoing scientific debate about the clinical relevance of MRI morphological variations.[7,8] To uncover the relevance of imaging findings, knowledge regarding their prevalence and relation with symptoms in different (sub)groups is needed. However, in most clinical studies, patients with herniated discs have been reported as a single pathological group.[20] Comparable to this study, some researchers have attempted to

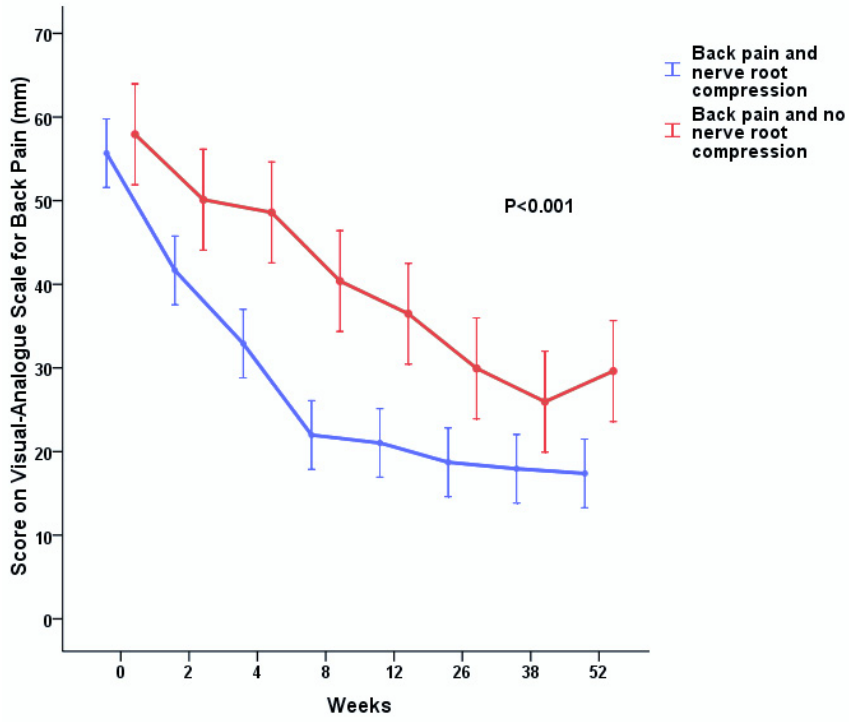


Figure 1 Repeated measurement analysis curve of Mean Scores for back pain on the Visual-Analogue Scale. Sciatica patients with both disabling back pain and nerve root compression on MRI were compared with patients with disabling back pain but who did not depict nerve root compression on MRI at baseline. The vertical bars represent 95% confidence intervals.

identify MRI differences between (sub)groups. MRI differences have been reported between patients with both sciatica and low back pain compared to asymptomatic control subjects,[7] and between sciatica patients compared to low back pain patients.[21] The finding that vertebral endplate signal changes was equally distributed between those with and without disabling back pain was surprising as they are hypothesized to be a causative factor in low back pain.[22,23] The finding that extruded disc herniations and large disc herniations were also equally distributed between the two groups was also surprising as both findings have been reported to correlate with the severity of symptoms in sciatica.[6,7] However, these studies did not compare these findings between sciatica patients with and without back pain. Comparable to this study, Vroomen described a more favourable prognosis for patients with compared to those without nerve root compression on MRI.[24]

The preoccupation with the herniated disc as a source of disabling low back and leg pain has led disc surgery to become one of the most commonly performed operative procedures. However, disc herniations are often seen on imaging studies in patients without symptoms.[7,8] Contrary, in this study, a substantial number of patients without disc herniation or nerve

compression suffered from sciatica. The worldwide accepted mechanical compression theory therefore seems not to offer a sufficient explanation for the cause of the disabling back and leg symptoms in sciatica. Some researchers suggested that inflammation of the nerve root may also be a major factor in sciatica.[25,26] Back in time, Cotugnio, an 18th Century Italian physician, explained the sciatic complaints as a consequence of neuritis or edema of the sciatic nerve.[3,4] If this hypothesis is correct, the finding that sciatica patients with back pain less often had a herniated disc compared to patients with predominantly sciatica may be explained by a higher inflammatory component in sciatica patients with back pain. This may also explain why sciatica patients with back pain fared worse compared to patients with predominantly sciatica as the extent of inflammation may be a causative factor in the cases with persistent pain and functional disability.

The results after lumbar disc surgery do not seem to have improved during recent decades. Depending upon the used outcome measure, both classical studies and recent randomized controlled trials show that during longer follow-up treatment results for sciatica are satisfactory in 60 to 85% of the patients.[10,19,27,28,29] The number of proposed interventions, developed by numerous disciplines, is overwhelming. The results of this study indicate that in sciatica subgroups with different prognostic profiles can be identified. A shift from a "one-size fits all" approach, where heterogeneous groups of patients receive broadly similar treatments, towards targeted treatments according to prognostic profiles or specific characteristics, may help to improve the treatment results.[30]

A strength of this study was the blinded MRI assessment and follow-up of all patients with 6-12 weeks sciatica who underwent MRI, regardless of participation in the randomized trial. A limitation of the present study is that the study population consisted of sciatica patients who had severe symptoms and were referred to the neurologists. These patients were willing to undergo surgery, so patients with a clear preference for conservative treatment are underrepresented. Some might view the agreement among MRI readers as suboptimal. However, the kappa values are comparable with those found in previous studies [8,31,32] and therefore one might consider them to reflect existing agreement among expert readers in clinical practice.

CONCLUSIONS

Sciatica patients with disabling low back pain reported an unfavorable prognosis at one-year follow-up compared to those with predominantly sciatica. If additionally a clear herniated disc with nerve root compression on MRI was absent, the results were even worse. Further research is needed to identify the reasons behind the different prognostic profiles in sciatica and how to apply new or existing therapeutic strategies accordingly.

REFERENCES

1. Koes BW, van Tulder MW, Peul WC (2007) Diagnosis and treatment of sciatica. BMJ 334: 1313-1317.
2. Dagenais S, Caro J, Haldeman S (2008) A systematic review of low back pain cost of illness studies in the United States and internationally. Spine J 8: 8-20.
3. Robinson JS (1983) Sciatica and the lumbar disk syndrome: a historic perspective. South Med J 76: 232-238.
4. Cotugnio D (1764.) De ischiade nervosa commentarius. Neapoli apud frat Simonios 12 ed. Viennæ:.
5. Mixter WJ, Barr JS (1934) Rupture of Intervertebral Disc with Involvement of Spinal Canal. N Engl J Med 211: 210-215.
6. Beattie PF, Meyers SP, Stratford P, Millard RW, Hollenberg GM (2000) Associations between patient report of symptoms and anatomic impairment visible on lumbar magnetic resonance imaging. Spine (Phila Pa 1976) 25: 819-828.
7. Boos N, Rieder R, Schade V, Spratt KF, Semmer N, et al. (1995) 1995 Volvo Award in clinical sciences. The diagnostic accuracy of magnetic resonance imaging, work perception, and psychosocial factors in identifying symptomatic disc herniations. Spine (Phila Pa 1976) 20: 2613-2625.
8. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, et al. (1994) Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 331: 69-73.
9. Haugen AJ, Brox JI, Grovle L, Keller A, Natvig B, et al. Prognostic factors for non-success in patients with sciatica and disc herniation. BMC Musculoskelet Disord 13: 183.
10. Peul WC, van Houwelingen HC, van den Hout WB, Brand R, Eekhof JA, et al. (2007) Surgery versus prolonged conservative treatment for sciatica. N Engl J Med 356: 2245-2256.
11. Peul WC, van Houwelingen HC, van der Hout WB, Brand R, Eekhof JA, et al. (2005) Prolonged conservative treatment or 'early' surgery in sciatica caused by a lumbar disc herniation: rationale and design of a randomized trial [ISRCT 26872154]. BMC Musculoskelet Disord 6: 8.
12. Fardon DF, Milette PC (2001) Nomenclature and classification of lumbar disc pathology. Recommendations of the Combined task Forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology. Spine (Phila Pa 1976) 26: E93-E113.
13. Modic MT, Masaryk TJ, Ross JS, Carter JR (1988) Imaging of degenerative disk disease. Radiology 168: 177-186.
14. Modic MT, Steinberg PM, Ross JS, Masaryk TJ, Carter JR (1988) Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 166: 193-199.
15. Patrick DL, Deyo RA, Atlas SJ, Singer DE, Chapin A, et al. (1995) Assessing health-related quality of life in patients with sciatica. Spine (Phila Pa 1976) 20: 1899-1908; discussion 1909.
16. Collins SL, Moore RA, McQuay HJ (1997) The visual analogue pain intensity scale: what is moderate pain in millimetres? Pain 72: 95-97.
17. Peters ML, Sommer M, de Rijke JM, Kessels F, Heineman E, et al. (2007) Somatic and psychologic predictors of long-term unfavorable outcome after surgical intervention. Ann Surg 245: 487-494.
18. Yamashita K, Ohzono K, Hiroshima K (2006) Patient satisfaction as an outcome measure after surgical treatment for lumbar spinal stenosis: testing the validity and discriminative ability in terms of symptoms and functional status. Spine (Phila Pa 1976) 31: 2602-2608.
19. Peul WC, van den Hout WB, Brand R, Thomeer RT, Koes BW (2008) Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial. BMJ 336: 1355-1358.
20. Carragee EJ, Han MY, Suen PW, Kim D (2003) Clinical outcomes after lumbar discectomy for sciatica: the effects of fragment type and anular competence. J Bone Joint Surg Am 85-A: 102-108.

21. Modic MT, Obuchowski NA, Ross JS, Brant-Zawadzki MN, Grooff PN, et al. (2005) Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. Radiology 237: 597-604.
22. Albert HB, Kjaer P, Jensen TS, Sorensen JS, Bendix T, et al. (2008) Modic changes, possible causes and relation to low back pain. Med Hypotheses 70: 361-368.
23. Jensen TS, Karppinen J, Sorensen JS, Niinimaki J, Leboeuf-Yde C (2008) Vertebral endplate signal changes (Modic change): a systematic literature review of prevalence and association with non-specific low back pain. Eur Spine J 17: 1407-1422.
24. Vroomen PC, Wilmink JT, de KM (2002) Prognostic value of MRI findings in sciatica. Neuroradiology 44: 59-63.
25. Chen C, Cavanaugh JM, Ozaktay AC, Kallakuri S, King AI (1997) Effects of phospholipase A2 on lumbar nerve root structure and function. Spine (Phila Pa 1976) 22: 1057-1064.
26. Saal JS, Franson RC, Dobrow R, Saal JA, White AH, et al. (1990) High levels of inflammatory phospholipase A2 activity in lumbar disc herniations. Spine (Phila Pa 1976) 15: 674-678.
27. Jacobs WC, van Tulder M, Arts M, Rubinstein SM, van Middelkoop M, et al. (2011) Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review. Eur Spine J 20: 513-522.
28. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE (2005) Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. Spine (Phila Pa 1976) 30: 927-935.
29. Weber H (1983) Lumbar disc herniation. A controlled, prospective study with ten years of observation. Spine (Phila Pa 1976) 8: 131-140.
30. Konstantinou K, Beardmore R, Dunn KM, Lewis M, Hider SL, et al. (2012) Clinical course, characteristics and prognostic indicators in patients presenting with back and leg pain in primary care. The ATLAS study protocol. BMC Musculoskelet Disord 13: 4.
31. Brant-Zawadzki MN, Jensen MC, Obuchowski N, Ross JS, Modic MT (1995) Interobserver and intraobserver variability in interpretation of lumbar disc abnormalities. A comparison of two nomenclatures. Spine (Phila Pa 1976) 20: 1257-1263; discussion 1264.
32. Jarvik JG, Haynor DR, Koepsell TD, Bronstein A, Ashley D, et al. (1996) Interreader reliability for a new classification of lumbar disk disease. Acad Radiol 3: 537-544.

Table S1 MRI study variables. The three readers (2 neuroradiologists and one neurosurgeon) independently used the same case record form.

MRI variable	Type	Categories
Disc level with the most severe nerve root compression	Disc level	1. L2L3 2. L3L4 3. L4L5 4. L5S1 5. Not applicable, all disc levels have a normal disc contour: no disc extension beyond the normal margins of the intervertebral disc space at any disc level
	Disc contour at this disc level	1. Bulging: presence of disc tissue circumferentially (50-100%) beyond the edges of the ring apophyses 2. Herniation: localized displacement of disc material beyond the normal margins of the intervertebral disc space 3. Not applicable, all disc levels have a normal disc contour: no disc extension beyond the normal margins of the intervertebral disc space at any disc level
	Certainty about the presence of this disc herniation	1. Definite about the presence: no doubt about the presence 2. Probable about the presence: some doubt but probability > 50% 3. Possible about the presence: reason to consider but probability < 50% 4. Definite about the absence: no doubt about the absence
	Loss of disc height (distance between the planes of the end-plates of the vertebrae craniad and caudad to the disc) at this disc level	1. Yes 2. No
	Signal intensity of nucleus pulposus on T2 images at this level	1. Hypointensity 2. Normal 3. Hyperintensity
If a herniation at the disc level is considered	Side of this disc herniation	1. Right 2. Left 3. Right and left
	Location on axial view of this disc herniation	1. Central zone: zone within the vertebral canal between sagittal planes through the medial edges of each facet 2. Sub-articular zone: zone, within the vertebral canal, sagittally between the plane of the medial edges of the pedicles and the plane of the medial edges of the facets, and coronally between the planes of the posterior surfaces of the vertebral bodies and the under anterior surfaces of the superior facets. 3. Foraminal zone: zone between planes passing through the medial and lateral edges of the pedicles 4. Extra-foraminal zone: the zone beyond the sagittal plane of the lateral edges of the pedicles, having no well-defined lateral border.

	Size of this disc herniation in relation to spinal canal	1. Large stenosing: size >75% of the spinal canal 2. Large: size 75-50% of the spinal canal 3. Average: size 25-50% of the spinal canal 4. Small: size <25% of the spinal canal
	Morphology	1. Protrusion: localized displacement of disc material beyond the intervertebral disc space, with the base against the disc of origin broader than any other dimension of the protrusion. 2. Extrusion: localized displacement of disc material beyond the intervertebral disc space, with the base agains the disc of origin narrower than any one distance between the edges of the disc material beyond the disc space measured in the same plane, or when no continuity exists between the disc material beyond the disc space and that within the disc space.
Nerve root compression	Certainty about the presence of nerve root compression	1. Definite about the presence: no doubt about the presence 2. Probable about the presence: some doubt but probability > 50% 3. Possible about the presence: reason to consider but probability < 50% 4. Definite about the absence: no doubt about the absence
Separate for every end plate from level L2-L3 through L5-S1	Presence of vertebral endplate signal changes (VESC)	1. No VESC 2. VESC type 1: hypointense in T1-weighted sequences and hyperintense on T2-weighted sequences 3. VESC type 2: increased signal on T1 weighted sequences and isointense or slightly hyperintense signal on T2 weighted sequences 4. VESC type 3: hypointense both on T1- and T2-weighted sequences 5. VESC type 1 and 2
	Presence of Schmorl's nodes (herniation of the disc into the vertebral-body end plate)	1. Yes 2. No

Table S2 Outcome measurements available at 52 weeks after baseline MRI. The mentioned outcome measures were assessed at baseline, 2, 4, 8, 12, 26, 38, and 52 weeks. Values are n (%). Total n=379

	Number of patients (%)
Visual Analogue scale for back pain at 52 weeks¶	
Outcome available at 52 weeks	332 (88)
At least one follow-up examination	37 (10)
Lost to follow-up after baseline examination	10 (3)
Global perceived recovery on a 7-point Likert scale at 52 weeksò	
Outcome available at 52 weeks	330 (87)
At least one follow-up examination	39 (10)
Lost to follow-up after baseline examination	10 (3)
Roland disability questionnaire at 52 weeks‡	
Outcome available at 52 weeks	333 (88)
At least one follow-up examination	36 (9)
Lost to follow-up after baseline examination	10 (3)
Visual Analogue scale for leg pain at 52 weeks¶	
Outcome available at 52 weeks	334 (88)
At least one follow-up examination	35 (9)
Lost to follow-up after baseline examination	10 (3)

¶ The intensity of pain is indicated on a horizontal 100 mm visual analogue scale (VAS) with 0 representing no pain and 100 the worst pain ever experienced.
ò Global perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.
‡ The Roland Disability Questionnaire for Sciatica is a disease-specific disability scale that measures the functional status of patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.

Table S3 Interobserver agreement regarding the MRI characteristics. Reader A en B represent the two neuroradiologists, while reader C represents the neurosurgeon. Kappa values and percentages of agreement for the characteristics of disc herniation were only calculated if the observers agreed about their presence (e.g. when a reading pair showed disagreement about the presence of disc herniation, this patient did not contribute to the interagreement analysis regarding the characteristics of the herniated disc).

	A vs B		A vs C		B vs C		All observers	
	% agree-ment	kappa	% agree-ment	kappa	% agree-ment	kappa	% agree-ment	multi-rater kappa
Disc level with the most severe nerve root compression ¶	92.0	0.86	88.4	0.81	90.5	0.84	86.4	0.84
Probability of disc herniation (2 categories) ‡	93.6	0.75	91.8	0.71	90.0	0.67	87.7	0.71
Probability of nerve root compression (2 categories) ‡	94.1	0.80	85.4	0.62	84.6	0.60	82.0	0.66
Presence of vertebral end plate changes ò	73.8	0.49	83.4	0.67	81.0	0.60	69.1	0.58
Presence of Schmorl's nodes ò	80.3	0.25	81.6	0.47	82.6	0.26	72.2	0.33
Characteristics disc herniation								
Location axial view ╞	94.2	0.88	95.5	0.90	96.7	0.93	95.6	0.92
Size disc herniation in relation to spinal canal (2 categories) ‖	82.1	0.55	76.3	0.35	86.3	0.47	71.5	0.44
Protrusion versus extrusion	77.4	0.48	75.0	0.50	73.7	0.44	63.2	0.46
Loss of disc height of the disc level ò	97.9	0.86	72.2	0.26	72.4	0.26	71.5	0.31
Signal intensity of nucleus pulposus on T2 images §	95.3	0.75	90.4	0.64	90.7	0.57	88.6	0.61

¶ The 5 categories were: 1) L2L3 2) L3L4 3) L4L5 4) L5S1 5) Not applicable, all disc levels have a normal disc contour: no disc extension beyond the normal margins of the intervertebral disc space at any disc level.

‡ The categories "Definite and probable about the presence" were combined to one category and the categories "possible about the presence" and "definite about the absence" were also combined to one category.

ò Categories were: yes versus no.

╞ Categories were: 1) Central zone 2) Sub-articular zone 3) Foraminal zone 4) Extra-foraminal zone.

‖ The categories "large stenosing" and "large" were combined to one category and the categories "average" and "small" were also combined to one category.

§ Categories were: 1) Hypointensity 2) Normal 3) Hyperintensity.

Table S4 Clinical outcome measures at one year stratified according to subgroups at baseline and treatment group. Values are n (%) or means ± SD.

	Clinical outcome at one year			
	Perceived recoveryò	Roland Disability‡	VAS-Leg pain¶	VAS-back pain¶
Patient not randomized				
Back pain and nerve root compression (n=14)	11 (79)	3.4±4.2	5.9±8.5	18.5±21.3
Back pain and no nerve root compression (n=34)	16 (47)	6.3±5.2	14.8±17.3	29.2±2.6
No back pain and nerve root compression (n=33)	31 (94)	2.7±3.9	7.3±13.6	7.5±13.0
No back pain and no nerve root compression (n=17)	11 (65)	5.7±7.1	20.6±32.3	22.8±31.2
Patients assigned to surgery				
Back pain and nerve root compression (n=52)	42 (81)	3.4±6.2	12.9±22.2	15.6±22.2
Back pain and no nerve root compression (n=8)	4 (50)	8.7±7.4	34.7±33.6	36.6±34.4
No back pain and nerve root compression (n=73)	69 (95)	2.4±4.4	6.7±14.5	10.9±18.6
No back pain and no nerve root compression (n=6)	4 (67)	4.3±7.0	11.7±18.0	15.3±20.7
Patients assigned to conservative care				
Back pain and nerve root compression (n=42)	34 (81)	4.1±5.9	13.0±23.7	19.5±26.9
Back pain and no nerve root compression (n=8)	2 (25)	9.8±5.0	31.8±25.4	39.2±32.0
No back pain and nerve root compression (n=89)	77 (87)	3.1±4.5	9.1±14.0	13.1±17.2
No back pain and no nerve root compression (n=3)	3 (100)	1.0±1.7	2.3±2.3	3.7±4.0

ò Perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.

‡ The Roland Disability Questionnaire for Sciatica is a disease-specific disability scale that measures the functional status of patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.

¶ The intensity of pain is indicated on a horizontal 100 mm visual analogue scale (VAS) with 0 representing no pain and 100 the worst pain ever experienced.

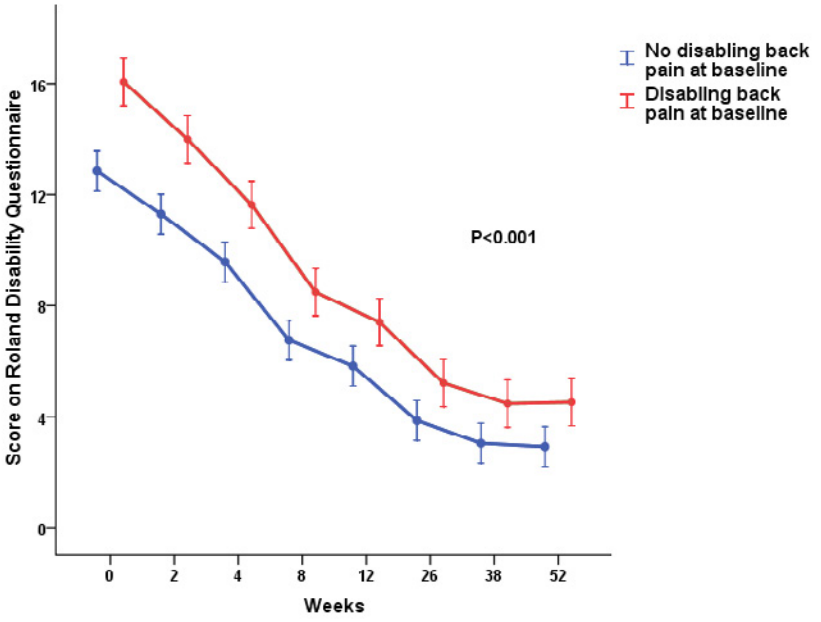
Table S5 Clinical outcome measures at one year according to subgroups at baseline. Subgroups defined by the presence of back pain and disc herniation or nerve root compression on MRI at baseline. *This analysis only included patients with available clinical outcome at one year.* Values are n (%) or means ± SD. N=330

	Clinical outcome at one year			
	Perceived recoveryò	Roland Disability‡	VAS-Leg pain¶	VAS-back pain¶
Subgroups according to back pain and presence of nerve root compression on MRI at baseline				
Back pain and nerve root compression (n=101)	80 (79)	3.8±5.9	12.1±22.0	17.9±24.4
Back pain and no nerve root compression (n=30)	10 (33)	8.3±5.8	22.8±25.6	35.9±30.5
No back pain and nerve root compression (n=176)	161 (91)	2.6±4.4	7.1±13.1	10.9±16.5
No back pain and no nerve root compression (n=23)	16 (70)	4.7±6.9	17.9±28.8	19.7±28.3
Subgroups according to back pain and presence of disc herniation on MRI at baseline				
Back pain and disc herniation (n=111)	82 (74)	4.4±6.3	14.9±24.4	20.8±26.8
Back pain and no disc herniation (n=20)	8 (40)	6.9±5.2	12.9±15.6	28.3±27.1
No back pain and disc herniation (n=185)	167 (90)	2.8±4.5	7.3±13.2	11.3±16.7
No back pain and no disc herniation (n=14)	10 (71)	4.1±7.0	22.3±34.8	21.1±33.2

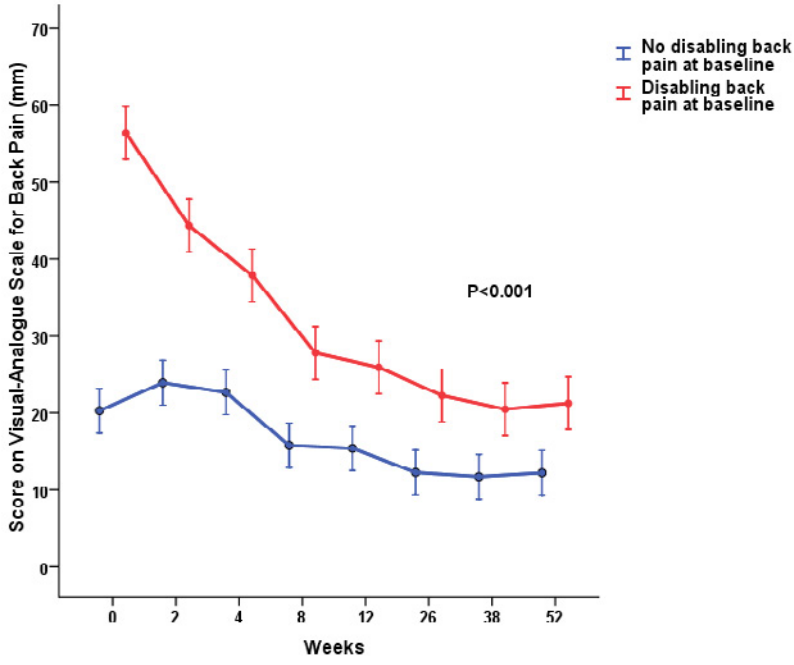
ò Perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.

‡ The Roland Disability Questionnaire for Sciatica is a disease-specific disability scale that measures the functional status of patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.

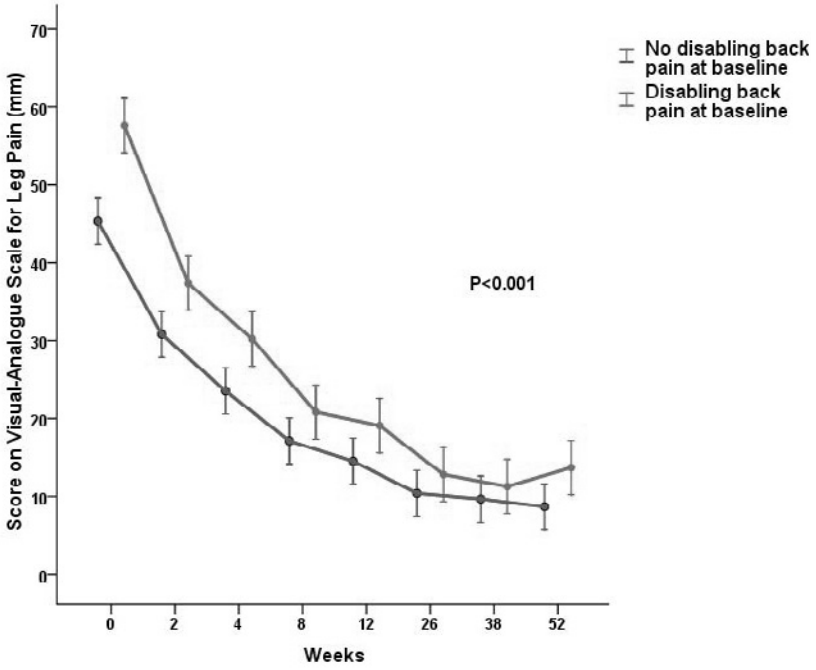
¶ The intensity of pain is indicated on a horizontal 100 mm visual analogue scale (VAS) with 0 representing no pain and 100 the worst pain ever experienced.



S1A Curve for the mean Roland Disability Questionnaire (scores range from 0 to 23, with higher scores indicating worse functional status) in relation to disabling back pain at baseline.



S1B Curve for the mean scores on the visual-analogue scale for intensity of back pain (scale ranges from 0 to 100 mm, with higher scores indicating more intense pain) in relation to disabling back pain at baseline.



S1C Curve for the mean scores on the visual-analogue scale for intensity of leg pain (scale ranges from 0 to 100 mm, with higher scores indicating more intense pain) in relation to disabling back pain at baseline.
Figure S1 Repeated measurement analysis curves of Mean Scores on the Roland Disability Questionnaire (1A), the Visual-Analogue Scale for back pain (1B), and the Visual-Analogue Scale for leg pain (1C) in relation to disabling back pain at baseline. The vertical bars represent 95% confidence intervals.