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Chapter 5

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

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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.\textsuperscript{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.\textsuperscript{2} In classical literature sciatica has been of great interest to Greco-Roman and Eastern scientists and physicians.\textsuperscript{3} For centuries an inflammation of the sciatic nerve was the origin of pain, described as sciatic neuritis,\textsuperscript{4} until 1934 when Mixter and Barr revolutionized the understanding of sciatica into mechanical origin.\textsuperscript{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.\textsuperscript{6} For example, several studies show a high prevalence of disc herniations ranging from 20 to 76\% in subjects without any symptoms.\textsuperscript{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.\textsuperscript{6,7,8} Back pain has been reported to be associated with worse prognosis in patients with sciatica,\textsuperscript{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.\textsuperscript{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)\(^\text{15}\) 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),\(^\text{16}\) and a 7-point 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”.\(^\text{10,11}\)

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 cut-off value is regularly used when the VAS is categorized into favorable and unfavorable outcome.\(^\text{17,18}\) 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.

| MRI characteristic                                      | Sciatica with disabling back pain (n=158) | Sciatica with no disabling back pain (n=221) | P-value |
|--------------------------------------------------------|------------------------------------------|---------------------------------------------|---------|
| 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. 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 (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.
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.\textsuperscript{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.\textsuperscript{20} Comparable to this study, some researchers have attempted to

\begin{table}
\centering
\caption{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}
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Subgroups according to back pain and presence of nerve root compression on MRI at baseline} & Perceived recovery\textsuperscript{0} & Roland Disability\textsuperscript{‡} & VAS-Leg pain\textsuperscript{¶} & VAS-back pain\textsuperscript{¶} \\
\hline
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 \\
\hline
\textbf{Subgroups according to back pain and presence of disc herniation on MRI at baseline} & & & & \\
\hline
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 \\
\hline
\end{tabular}
\end{table}

\textsuperscript{0} Perceived recovery was defined as complete or nearly complete disappearance of symptoms according to the Likert-7 point scale.

\textsuperscript{‡} 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.

\textsuperscript{¶} 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.
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, and between sciatica patients compared to low back pain patients. 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. 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. 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.

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. 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. Back in time, Cotugnio, an 18th Century Italian physician, explained the sciatic complaints as a consequence of neuritis or edema of the sciatic nerve. 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. 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.

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 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.
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**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 cranial and caudal 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 against 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 |
| Separate for every end plate from level L2-L3 through L5-S1 | Presence of vertebral endplate signal changes (VESC) |
| Presence of Schmorl's nodes (herniation of the disc into the vertebral-body end plate) | Presence of Schmorl's nodes (herniation of the disc into the vertebral-body end plate) |

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  

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  

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

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

\¶ 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.

\ö 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).

| Characteristic                                                                 | A vs B | A vs C | B vs C | All observers |
|--------------------------------------------------------------------------------|--------|--------|--------|---------------|
| Disc level with the most severe nerve root compression ¶                       | 92.0   | 88.4   | 90.5   | 86.4          |
| Probability of disc herniation (2 categories) ‡                               | 93.6   | 91.8   | 90.0   | 87.7          |
| Probability of nerve root compression (2 categories) ‡                         | 94.1   | 85.4   | 84.6   | 82.0          |
| Presence of vertebral end plate changes ó                                      | 73.8   | 83.4   | 81.0   | 69.1          |
| Presence of Schmorl’s nodes ó                                                  | 80.3   | 81.6   | 82.6   | 72.2          |
| Characteristics disc herniation                                                |        |        |        |               |
| Location axial view ¶                                                          | 94.2   | 95.5   | 96.7   | 95.6          |
| Size disc herniation in relation to spinal canal (2 categories) ¶              | 82.1   | 76.3   | 86.3   | 71.5          |
| Protrusion versus extrusion                                                    | 77.4   | 75.0   | 73.7   | 63.2          |
| Loss of disc height of the disc level ó                                        | 97.9   | 72.2   | 72.4   | 71.5          |
| Signal intensity of nucleus pulposus on T2 images ¶                            | 95.3   | 90.4   | 90.7   | 88.6          |

¶ 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.

ó 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 recovery | 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 |

ó 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

| Subgroups according to back pain and presence of nerve root compression on MRI at baseline | Perceived recovery| Roland Disability‡ | VAS-Leg pain¶ | VAS-back pain¶ |
|---|---|---|---|---|
| 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 | Perceived recovery| Roland Disability‡ | VAS-Leg pain¶ | VAS-back pain¶ |
|---|---|---|---|---|
| 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 |

* 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.
Figure 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.