BMJ open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002534.R2
Article Type:	Research
Date Submitted by the Author:	05-Apr-2013
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Primary Subject Heading:	Neurology
Secondary Subject Heading:	Surgery, General practice / Family practice, Evidence based practice
Keywords:	NEUROSURGERY, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Neurological pain < NEUROLOGY, Pain management < ANAESTHETICS, Neurosurgery < SURGERY, Clinical trials < THERAPEUTICS

Surgery versus prolonged conservative treatment for sciatica: 5-year results of a randomised controlled trial

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ARTICLE SUMMARY

Article Focus

- The sciatica trial, a randomised controlled trial, showed no significant differences after one and two years of follow-up in disability and pain between patients with severe sciatica for six to eight weeks, allocated for either early surgery or six months of prolonged conservative care
- 20% of all patients reported an unsatisfactory recovery after two years. In this study the five years' follow-up is described and predictors for unsatisfactory recovery are identified

Key Messages

- 8% of all patients never showed any recovery
- In 23% of all patients sciatica results in ongoing complaints, which fluctuate over time, irrespective of treatment
- A strategy of prolonged conservative care with eventually delayed surgery gives a high chance of pain and disability to resolve, although 46% of these patients needed surgery after a few more months of prolonged suffering
- Age over 40 years, severe leg pain at baseline and a higher affective McGill pain score were predictors for an unsatisfactory recovery

Strengths and Limitations

- Five years' follow-up results of a randomised controlled trial
- 18% of the patients were lost to follow-up at five years
- No difference in baseline characteristics between dropouts and patients providing the five years' data

Abstract:

Objective

This study describes the five years' results of the Sciatica trial focused on pain, disability, (un)satisfactory recovery, and predictors for unsatisfactory recovery.

Design

A randomised controlled trial.

Setting

Nine Dutch hospitals

Participants

Five years' follow-up data from 231 of 283 patients (82%) were collected.

Intervention

Early surgery or an intended six months of conservative treatment

Main Outcome measures

Scores from Roland disability questionnaire, visual analogue scale for leg and back pain and a Likert self rating scale of global perceived recovery were analysed.

Results

There were no significant differences between groups on the five years' primary outcome scores. Despite at least six months of conservative treatment 46% of the conservatively allocated patients were treated surgically because of severe leg pain and disability. Fourty-nine (21%) patients had an unsatisfactory recovery at five years and the recovery pattern showed that there was a variable group of 66 patients (31%) with at least one unsatisfactory outcome at one, two or five years of follow-up. Multivariate logistic regression showed that age (>40; OR: 2.42 (95% CI: 1.16-5.02)), severity of leg pain (VAS>70; OR: 3.32 (95% CI: 1.69-6.54)), and the Mc Gill affective score (score>3; OR: 6.23 (95% CI: 2.23-17.38)) were the only significant predictors for an unsatisfactory outcome at five years.

Conclusions

In the long term, 8% of the patients with sciatica never showed any recovery and in at least 23%, sciatica appears to result in ongoing complaints, which fluctuate over time, irrespective of treatment. Prolonged conservative care might give patients a fair chance for pain and disability to resolve without surgery, but with the risk to receive delayed surgery after prolonged suffering of sciatica. Age above 40 years, severe leg pain at baseline and a higher affective Mc Gill pain score were predictors for unsatisfactory recovery. Trial Registry ISRCT No 26872154.

Introduction

The lumbosacral radicular syndrome (LSRS), caused by a herniated lumbar disc, is one of the most expensive disorders for society in terms of work absenteeism and disability[1]. In 2007, the Sciatica Trial showed that the clinical outcome after one year was not different from prolonged conservative treatment, although recovery within the first year was better with early surgery[2]. In the prolonged conservative treatment group however, 39% of patients crossed over to surgical treatment because of intractable pain within one year, and 44% within two years of follow-up[3]. Despite the fact that this study showed, along with other randomised controlled trials[4, 5-7], that a strategy of prolonged conservative care is safe and reduces the risk for patients of undergoing surgery, the optimal timing of surgery with regard to long-term outcome has still not been defined.

Although LSRS is described in the literature as having a quite favourable course, one might question this assumption as the two years' follow-up showed that about twenty percent of patients report an unsatisfactory outcome on all outcome scales and that the risk to suffer prolonged disability is higher than expected beforehand[2;3].

The primary aim of the present study is to compare the pain and disability scores at five years' follow-up between patients in the Sciatica Trial randomised for surgery or randomised for prolonged conservative treatment. The second aim is to evaluate the proportion of patients with an unsatisfactory recovery at five years' follow-up and to identify factors contributing to these unsatisfactory results.

Material and Methods

Design

The study is part of the Sciatica Trial, a multicentre, prospective randomised trial among patients with 6 to 12 weeks of sciatica to determine whether a strategy of early surgery leads to better outcomes during the first year than does a strategy of prolonged conservative treatment for an additional six months followed by surgery for those patients who do not improve.

In summary, patients, 18-65 years of age, with an LSRS with a concomitant disc herniation confirmed by MRI, were eligible for participation. A computer-generated permuted-block scheme was used for randomisation stratified by centre. In the

surgical intervention group, a disc herniation removal through a unilateral transflaval approach using optical magnification was performed. Prolonged conservative treatment regimen was defined by general practitioners and treatment was mainly aimed at resuming daily activities. Patients were notified beforehand that they were participating in a study comparing two different strategies for the timing of intervention rather than comparing surgery with non-surgical treatment.
The design and study protocol have been published previously[2;8]. Baseline characteristics from the Sciatica Trial have been published previously[2;3] and were combined with the findings obtained from the five years' follow-up of the participants.

Procedures

As a standard procedure, the participants received the same study questionnaires as used for the one and two- year follow-up every year. At approximately five years after study inclusion, the participants were contacted once again by mail but now with an accompanied letter and asked to fill out the study questionnaires as used for the one and two-years' follow-up with extra questions about re-operations. Patients who did not respond initially, were contacted by telephone by a research nurse and asked once again to participate in the study by filling out the questionnaires. The additional 5 years' assessment was approved by the local medical ethics committee.

Primary and secondary outcomes

Primary outcome measures consisted of the Roland disability questionnaire (RDQ) for sciatica[9], a 100 mm visual analogue scale (VAS) for leg pain[10],and a seven-point Likert score of global perceived recovery. Higher RDQ and VAS scores were indicative of the experience of worse disability or greater intensity of pain, respectively. Global perceived recovery was measured with a 7-point Likert self-rating scale. Complete or almost complete disappearance of complaints (Likert scores 1-2) was defined as "satisfactory recovery", whereas Likert scores 3-7 were defined as "unsatisfactory recovery"[2;8].
Secondary outcomes were a 100 mm VAS for back pain and the number of (re)operations for severe sciatica in the interval between two and five years. The number of (re)operations for severe sciatica was evaluated by asking patients whether there had been any new operations for severe sciatica in the interval

between two and five years. Additionally, in all participating centres it was checked whether patients had had a treatment because of sciatica in the intervening period.

Potential prognostic factors

The prognostic value of demographic and clinical baseline variables for unsatisfactory recovery at five years was evaluated. The initial list of prognostic factors, chosen in advance by the investigators, was based on potential clinical importance, as indicated by earlier clinical results[11-13] The following potential prognostic demographic variables were included in the analysis: age (dichotomised <40/≥ 40), gender, smoking status, BMI (dichotomised <25/≥ 25), physical job (yes/no), or mentally demanding job (yes/no).

The following clinical baseline variables were included in the analysis: level of herniation at the MRI, the presence of a sequester on MRI (yes/no), sciatica provoked by sitting (yes/no), sciatica provoked by coughing/sneezing (yes/no), outcome of Bragard's test (positive/negative), sensory disturbance (yes/no).

Furthermore, the following measurement instruments for general health, mental health, affective score and pain were included: the VAS scores for leg pain, back pain and general health, the Mental Health subscore of the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36)[14], and the McGill affective score[2]. The VAS score range from 0-100, with higher scores indicating more severe symptoms. For this analysis, dichotomised VAS scores were used (<70/≥70), as described in an earlier study[2]. The SF-36 Mental Health score ranges from 0 to 100, with higher scores indicating less severe symptoms. For this analysis, dichotomised SF-36 Mental Health subscores were used (scores below one standard deviation of the dutch reference population[1] were defined as impaired). The McGill affective score measures the qualitative perception of pain by the patient and ranges from 0-5 where a high score (3-5) is correlated with a more depressed and anxious mood. For this analysis, dichotomised McGill affective scores were used (<3/≥3)[2].

Statistical analysis

The original sample size calculation was based on a difference in RDQ outcome during and in a different speed to recovery during the first year. The main endpoint "recovery" is in principle time-dependent in the sense that it reflects the situation of a patient at a particular moment in time and the situation may also deteriorate

afterwards, so it can change from recovered to non-recovered and back to recovered again, therefore actually being a time-varying dichotomous outcome which should be taken into account when interpreting the results of the analyses. Differences between randomisation groups at baseline and after five years of follow-up were assessed by comparing means, medians, or percentages, depending on the type of variable. Baseline values of variables were used as covariates in the main analyses whenever appropriate to adjust for possible differences between the randomised groups and to increase the power of the analyses. Outcomes of function and pain over the entire follow-up period were analysed using a repeated measurements analysis of variance with a first order autoregressive covariance matrix. Estimated consecutive scores were expressed as means and 95% confidence intervals. Pointwise estimates were obtained using models with time as a categorical covariate to allow assessment of systematic patterns. Differences between groups in the dichotomised Likert score at five years were evaluated with Fisher's exact test (randomisation group) or Mann-Whitney U (disability and pain scores).

The analyses were done according the intention-to-treat principle, except the comparison of groups with a satisfactory or unsatisfactory recovery.

Univariate and multivariate analyses were performed to evaluate the prognostic value of baseline variables for an unsatisfactory outcome at five years. The results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Chi-square tests were used to perform the univariate analyses. Potential predictors with a $p<0.10$ in the univariate analysis were included in the multivariate logistic regression. The multivariate logistic regression model was performed in a backward approach and included randomisation group irrespective of its significance in the univariate analysis, to control for its influence on the dependent variable.

For all other analyses, $p<0.05$ was considered significant. Data collection and quality checks were performed with the ProMISe web-based secure data management system of the Department of Medical Statistics and Bioinformatics of Leiden University Medical Centre. For all statistical analyses, SPSS version 18.0 was used.

Results

Fifty-two of the 283 patients (18%) were lost to follow-up, among them one patient who died after a cardiac bypass operation and 19 patients who refused to participate. The baseline characteristics age, gender, BMI, randomization group, RDQ, and VAS-

scores were not significantly different between the dropouts and those patients providing the five years' follow-up data. Twenty-six of the dropouts were randomised for early surgery. Among the 26 dropouts in the prolonged conservative group, 11 (42%) had surgery for sciatica during follow-up.

At five years' follow-up, 66 of the 142 patients (46%) assigned to conservative treatment had had surgery because of intractable sciatica (table 1). Within the first year this was 55 (39%) and after two years 62 (44%). Of the 141 patients allocated for early surgery, 16 (11%) recovered before surgery and were not operated on during the five years of follow-up. Within this five years' period, nine patients (7%) in the early surgery group and eight of the conservatively allocated patients who had surgery (12%), needed recurrent disc surgery. Three patients in the conservative group needed two re-operations or more (table 1).

The primary and secondary outcome scores concerning disability, leg pain and back pain at five years were slightly higher in the early surgery group compared to the prolonged conservative group, however, there were no significant differences (table 2, fig 1a-c).

In the total group, after five years, 49 (21%) patients still had an unsatisfactory recovery, defined as not having a complete or almost complete recovery on the dichotomised Likert scale, irrespective of their allocated treatment group (25 patients in the prolonged conservative group, 24 patients in the early surgery group, p=1.00). Patients with an unsatisfactory recovery had a significantly higher amount of leg pain, back pain and disability (all p-values <0.01) compared to the group with a satisfactory recovery (table 3). At five years' follow-up, 93 patients (62 men and 31 women, mean age 43.7, SD 9.8) had not had surgery (76 from the conservative group and 16 from the early surgery group) and the percentage recovered (77%) or not-recovered at five years (23%) was not different from the total group.

In the period of five years, 66 of the 213 patients (31%) with collected data at one, two and five years of follow-up had at least one period of unsatisfactory recovery. The pattern of recovery showed 16 patients who did not report any recovery at one, two and five years of follow-up. Twenty-four patients switched from 'not recovered' in the first or second year to 'recovered' at the five-years' analysis. Sixteen of these patients were from the prolonged conservative group. Six of these patients needed an operation of whom four needed a re-operation before they recovered, compared to two of the eight patients in the early surgery group needing a re-operation. Twenty-

six patients showed a good recovery at one and/or two years but not at five years of follow-up (fig 2).

Univariate logistic regression evaluating the relationship between possible prognostic variables and unsatisfactory recovery at five years, irrespective of intermediate recovery, showed that a high McGill affective score (score > 3; OR 6.23 (95% CI: 2.23-17.38)) was a significant predictor, as were severe leg pain at baseline (VAS > 70; OR 2.95 (95% CI: 1.54-5.64), an impaired score on the SF-36 Mental Health subscale (OR 2.25 (95% CI: 1.16-4.35)), higher age (age > 40; OR 2.22 (95% CI: 1.11-4.47)), and a positive Bragard test (OR 1.91(95% CI: 0.97-3.74)) (table 4). The multivariate analysis included all variables that were related to unsatisfactory outcome in the univariate analysis ($p < 0.10$), as well as randomisation group. This analysis showed that a high McGill affective score (score > 3; OR: 4.48 (95% CI: 1.43-14.08)), severity of leg pain (VAS > 70; OR: 2.80 (95% CI: 1.39-5.62)), and age (age > 40 years; OR: 2.36 (95% CI: 1.12-5.00)) were the only significant predictors for an unsatisfactory outcome at five years.

Discussion

This long-term follow-up study of the same patient cohort corroborates with earlier 1 and 2 year results as no significant differences between randomisation groups in disability, leg pain or back pain are found after five years of follow-up[2;3]. Eighteen percent of the initial cohort of 283 patients was lost to follow-up after five years. This reduced the power of our latest analysis to some extent. However, the baseline characteristics showed no differences between the included group and the dropouts. The allocated strategy of an extra six months of wait-and-see resulted in a large proportion of delayed surgical treatment (46%) for persistent intense leg pain causing severe disability, despite all kinds of conservative treatment. This means that patients should be informed that prolonged conservative care gives them quite a high chance for resolution of pain and disability without the need of a surgical intervention, but that this strategy also carries a fair chance (46%) that this waiting for the pain to resolve will still end with them needing disc surgery.

The question however, is whether this conclusion is completely accurate. The design of the original study was a comparison of early surgery versus prolonged conservative care for six months, after which surgery was offered when there still were severe complaints. This means that we do not know the precise percentage of

patients who would have become pain free with even longer conservative care, because the majority of these patients was operated on after six months. But on the other hand one might question whether such a proposed long conservative regimen is in proportion with the small risk of a surgical intervention, which provides a better outcome in the first six months, rather than being disabled in daily life during this long period of conservative care. Furthermore, the proportion of patients who were not operated after five years with a satisfactory or unsatisfactory recovery was the same as in the total population, showing that also in the non-operated patients there was a rather high amount of unsatisfactory recovery.

Twenty-one percent of patients experienced unsatisfactory recovery at five years, while 31% of the patients with complete data at one, two and five years of follow-up noted at least once an unsatisfactory recovery during this five years' follow-up period, irrespective of their allocated group. So the optimal timing of surgery is still on debate, as is the question which patients would benefit from surgery and which from prolonged conservative care.

The study design of this five year analysis did not permit us to look properly for the causes of an unsatisfactory recovery. A shortcoming of this study is the fact that there was no permission in the present study to retrieve new MR-images, but a recent study with the same patient population did not show any correlation between MR-images and satisfactory or unsatisfactory recovery at one year[15].

The patterns of recovery show that 8% of all patients with collected data, had never had any recovery during the follow-up period, showing that there are not that many non-responders of conservative or surgical treatment. The other 50 patients (23%) with an unsatisfactory recovery showed a switch over time from recovered to not-recovered, or vice versa. This is in line with the idea that sciatica is caused by chronic disc disease with intermittent nerve compression or inflammation and that pain can thus re-occur despite any earlier treatment [16;17]. In the 24 patients who switched from 'not-recovered' in the first or second year to 'recovered' at the five-years' analysis, there was a higher amount of patients who needed a re-operation before recovery occurred in the prolonged conservative group compared to the early surgery group. This may be caused by less effectiveness of late surgery, although this could not be proven. This less effectiveness of late surgery compared to early surgery could be caused by more chronic changes around the disc protrusion or sequester, causing more difficulty in freeing the nerve from compression.

In our study we could not estimate the effect of early versus late surgery, or surgery versus conservative treatment in an unbiased way since that would require a per protocol analysis. This would ignore the randomised allocation and compare patients who by definition would be incomparable since the design of our study did not envisage a randomisation between early and late surgery but merely allowed for the time of surgery being determined by the assessment of both patient and physician after initial randomisation. The impossibility to capture completely the condition of the patient and the selection mechanism which leads to the decision to operate, or not, at any given point in (follow-up) time, renders any multivariate analysis that attempts to make the groups of early and late operations comparable, biased. This bias has occurred in other randomised studies where this “per protocol” analysis was used and patients who were operated on after a prolonged duration of symptoms from a herniated lumbar disk have been shown to have a worse outcome than patients who were operated on relatively early[18-21]. As a consequence of this “per protocol analysis both groups differed in baseline characteristics such as type of disc herniation, neurological deficit and reported depression, rendering comparison of both groups fallacious[21].

In this five-years’ analysis the independent prognostic factors for an unsatisfactory outcome were a high McGill affective score, a high amount of leg pain, and age over 40 years at baseline. A high McGill affective score correlates with a more depressed and anxious mood[2], and mental stress, depression or other psychological factors have been widely described as risk factors for development of chronic pain[22]. Although a high amount of pain at baseline can also be caused by psychological factors, it is an independent prognostic factor for an unsatisfactory outcome in this study. Perhaps the severity of nerve root compression at intake predicts the overall outcome, but a correlation between amount of pain and amount of root compression has not been proven[23]. In our study, other factors concerning the severity of nerve root damage, such as severe sensibility disturbance, showed no association. In a systematic review of non-surgically treated sciatica none of the three studies that investigated baseline leg pain severity showed a clear prognostic influence on outcome. Age was also not found to be a prognostic factor in six out of seven studies[24]. The reason for age over 40 years being a prognostic indicator for a unsatisfactory outcome could be because disc herniation is part of a degenerative disease which seems to worsen in time. A study of prognostic factors for

unsatisfactory recovery among operated and unoperated patients did not show leg pain severity and age to be a prognostic factor, but found the variables severe back pain and male gender as predictors for a bad outcome at the one year follow-up[24;25]. This was in contrast with our one year study where being female was a prognostic factor for a bad outcome, but in this five years' analysis this also disappeared. The possible prognostic role of gender might be over-estimated in the past.

Conclusion

After five years of follow-up there were still no differences in pain and disability between the patients randomised for early surgery or prolonged conservative care. Signs of pain quality associated with depression and a more anxious mood, the age of the patient and the severity of leg pain at baseline were predictive of an unsatisfactory outcome.

In general, patients must be informed that prolonged conservative care might give them a fair chance for pain and disability to resolve without surgery, but with the risk for delayed surgery in the end after a prolonged period of suffering from sciatica.

Furthermore, although the total number of disabled patients without pain free periods in this study seems to be low, in almost one fourth of the patients, sciatica appears to be an ongoing disease with variable complaints in time, irrespective of treatment. These patients need our full attention, and further investigation at 10 years' follow-up is being planned, because this patient category has the highest burden on society concerning work absenteeism and general health costs.

Data sharing: No additional data available.

Contributors: The participants in the Leiden-The Hague Spine Intervention Prognostic Study Group were: protocol committee, WCP, BWK, and RTWMT; steering committee, BWK, RTWMT, JAH Eekhof, JTJ Tans, WBvdH, WCP, RB, and HC van Houwelingen; statistical analysis, WBvdH; research nurses and data collection and management, M Nuyten, P Bergman, G Holtkamp, S Dukker, A Mast, L Smakman, C Waanders, L Polak, A Nieborg; coordinating physicians of participating hospitals, JTJ Tans, R Walchenbach (Medical Center Haaglanden, The Hague), J van Rossum, P Schutte, RTWMT (Diaconessen Hospital,

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Competing Interests: None

Funding: None

Reference List

(1) van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. *Pain* 1995; 62(2):233-240.

(2) Peul WC, Van Houwelingen HC, van den Hout WB, et al. Surgery versus prolonged conservative treatment for sciatica. *N Engl J Med* 2007; 356(22):2245-2256.

(3) Peul WC, van den Hout WB, Brand R, et al. Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial. *BMJ* 2008; 336(7657):1355-1358.

(4) Jacobs WC, van TM, Arts M, Rubinstein SM, et al. Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review. *Eur Spine J* 2011; 20(4):513-522.

(5) Weinstein JN, Lurie JD, Tosteson TD, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort. *JAMA* 2006; 296(20):2451-2459.

(6) Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA* 2006; 296(20):2441-2450.

(7) Weinstein JN, Lurie JD, Tosteson TD, et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). *Spine (Phila Pa 1976)* 2008; 33(25):2789-2800.

(8) Peul WC, Van Houwelingen HC, van der Hout WB, et al. 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* 2005; 6:8.

(9) Patrick DL, Deyo RA, Atlas SJ, et al. Assessing health-related quality of life in patients with sciatica. *Spine (Phila Pa 1976)* 1995; 20(17):1899-1908.

(10) Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimetres? *Pain* 1997; 72(1-2):95-97.

(11) Hurme M, Alaranta H. Factors predicting the result of surgery for lumbar intervertebral disc herniation. *Spine (Phila Pa 1976)* 1987; 12(9):933-938.

(12) Peul WC, Brand R, Thomeer RT, et al. Influence of gender and other prognostic factors on outcome of sciatica. *Pain* 2008; 138(1):180-191.

(13) Vroomen PC, de Krom MC, Knottnerus JA. Predicting the outcome of sciatica at short-term follow-up. *Br J Gen Pract* 2002; 52(475):119-123.

(14) Brazier JE, Harper R, Jones NM, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ* 1992; 305(6846):160-164.

(15) el BA, Vleggeert-Lankamp CL, Nijeholt GJ, et al. Magnetic resonance imaging in follow-up assessment of sciatica. *N Engl J Med* 2013; 368(11):999-1007.

(16) Omarker K, Myers RR. Pathogenesis of sciatic pain: role of herniated nucleus pulposus and deformation of spinal nerve root and dorsal root ganglion. *Pain* 1998; 78(2):99-105.

(17) Mulleman D, Mammou S, Griffoul I, et al. Pathophysiology of disk-related sciatica. I.--Evidence supporting a chemical component. *Joint Bone Spine* 2006; 73(2):151-158.

(18) Jonsson B. Patient-related factors predicting the outcome of decompressive surgery. *Acta Orthop Scand Suppl* 1993; 251:69-70.

(19) Ng LC, Sell P. Predictive value of the duration of sciatica for lumbar discectomy. A prospective cohort study. *J Bone Joint Surg Br* 2004; 86(4):546-549.

(20) Nygaard OP, Kloster R, Solberg T. Duration of leg pain as a predictor of outcome after surgery for lumbar disc herniation: a prospective cohort study with 1-year follow up.[see comment]. *J Neurosurg Pediatrics* 2000; 92(2 Suppl):131-134.

(21) Rihn JA, Hilibrand AS, Radcliff K, et al. Duration of symptoms resulting from lumbar disc herniation: effect on treatment outcomes: analysis of the Spine Patient Outcomes Research Trial (SPORT). *J Bone Joint Surg Am* 2011; 93(20):1906-1914.

(22) Pincus T, Burton AK, Vogel S, et al. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine (Phila Pa 1976)* 2002; 27(5):E109-E120.

(23) Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. *J Clin Epidemiol* 1998; 51(11):1055-1068.

(24) Ashworth J, Konstantinou K, Dunn KM. Prognostic factors in non-surgically treated sciatica: a systematic review. *BMC Musculoskelet Disord* 2011; 12:208.

(25) Haugen AJ, Brox JI, Grovle L, et al. Prognostic factors for non-success in patients with sciatica and disc herniation. *BMC Musculoskelet Disord* 2012; 13:183.

Table 1: Baseline and follow-up characteristics of patients with sciatica

Patient characteristics	Early surgery (n=141)	Conservative treatment (n=142)
Baseline characteristics		
Mean (SD) age (years)	41.6 (10.0)	43.3 (9.6)
Male sex	89 (63)	97 (68)
Mean (SD) BMI	25.9 (4.1)	25.5 (3.3)
Mean (SD) duration of sciatica (weeks)	9.43 (2.37)	9.48 (2.11)
Took sick leave from work	107 (76)	116 (82)
Mean (SD) duration of sick leave (weeks)	5.32 (2.78)	5.28 (2.62)
Left sided leg pain	67 (48)	73 (51)
Positive straight leg raising test (SLR)	100 (71)	104 (73)
Positive crossed SLR	71 (50)	70 (49)
Dermatomal sensory loss	123 (87)	128 (90)
Dermatomal anaesthesia	31 (22)	33 (23)
Dermatomal muscle weakness	93 (66)	99 (70)
Knee tendon reflex difference	54 (38)	51 (36)
Ankle tendon reflex difference	75 (53)	107 (75)
Clinically suspected level of herniated disc	-	-
L3-L4	6 (4)	4 (3)
L4-L5	65 (46)	52 (37)
L5-S1	70 (50)	86 (61)
Preference for conservative treatment	42 (30)	43 (30)
Mean (SD) RD score	16.5 (4.4)	16.3 (3.9)

Mean (SD) VAS score	-	-
Leg pain	67.3 (19.6)	64.3 (21.2)
Back pain	34.0 (29.6)	30.8 (27.7)
Mean (SD) SF-36 scores	-	-
Bodily pain	21.9 (16.6)	23.9 (18.1)
Physical functioning	33.9 (19.6)	34.6 (19.0)
Surgical treatment during follow-up		
Surgery performed in first year	125 (89)	55 (39)
Surgery performed during 2 years	125 (89)	62 (44)
Surgery performed during 5 years	125 (89)	66 (46)
Recurrent disc surgery after 5 years	9 (6)	8 (6)
follow-up	9 of 125 (7)	8 of 66 (12)
Patients requiring two re-operations or more	0	3
Patients who dropped out during 5 year	26 (18)	26 (18)

Values are numbers (percentages) unless stated otherwise.

Table 2: Primary and secondary outcomes from early surgery (ES) versus prolonged conservative treatment (CT) for patients with sciatica

	8 weeks			52 weeks			104 weeks			260 weeks		
Outcomes	ES	PCT	Difference [95% CI]	ES	PCT	Difference [95% CI]	ES	PCT	Difference [95% CI]	ES	PCT	Difference [95% CI]
Disability*	6.1 (0.5)	9.2 (0.5)	3.2 [1.9-4.4]	3.3 (0.5)	3.7 (0.5)	0.4 [-0.8-1.7]	3.4 (0.5)	2.6 (0.5)	-0.8 [-2.1-0.5]	3.5 (0.5)	3.4 (0.5)	-0.1[-1.4-1.3]
Leg pain**	10.2 (1.9)	27.9 (1.9)	17.7[12.5-22.9]	11.0 (1.9)	10.9 (1.9)	-0.1 [-5.3-5.1]	10.9 (2.0)	8.8 (2.0)	-2.0 [-7.5-3.4]	15.6 (2.0)	12.8 (2.0)	-2.7 [-8.4-2.9]
Back pain**	14.4 (2.4)	25.7 (2.4)	11.3 [4.6-18.0]	14.6 (2.4)	16.0 (2.4)	1.4 [-5.3-8.2]	16.0 (2.6)	17.0 (2.5)	1.0[-6.0-8.1]	20.0 (2.6)	17.0 (2.6)	-3.1[-10.3-4.2]

* Roland disability questionnaire for sciatica. Score ranges from 0 to 23, with higher scores representing worse disability

** Measured on a 100 mm visual analogue scale, with 0 representing no pain and 100 the worst pain ever experienced

Values are means (SE) unless stated otherwise and are based on intention to treat, confidence interval [CI] assessed with repeated measurements analysis

Table 3: Primary and secondary outcome scores among patients treated for sciatica according to perceived recovery at five years

	Disability*		Leg pain†		Back pain†	
Outcome	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**	**Mean (SD)**	**Median (IQR)**
Unsatisfactory recovery (n=49) ‡	11.3 (5.6)	11.0 (6.5-15.5)	42.8 (27.9)	46.0 (17.5-66.0)	48.6 (49.5)	49.5 (32.0-66.75)
Satisfactory recovery (n=182) ‡	1.3 (2.3)	0.0 (0.0-2.0)	6.5 (13.7)	1.0 (0.0-6.0)	10.2 (14.6)	4.0 (0.0-15.0)

IQR=interquartile range
* Roland disability questionnaire for sciatica
† measured on a 100 mm analogue scale
‡The 7-point Likert scale of global perceived recovery was dichotomised to satisfactory outcome (“complete” and “nearly complete” recovery) and unsatisfactory outcome (the other 5 scores ranging from “some recovery” to “severe worsening of complaints”).

Table 4: Univariate and multivariate logistic analysis of predicting factors for unsatisfactory outcome of sciatica

Variable	n	Univariate analysis		p-value	Multivariate analysis		p-value
		OR	95% CI		OR	95% CI	
Randomization							
Surgery	115	0.96	0.51-1.80	0.899			
Conservative	116	1.00	-				
Gender							
Female	75	1.27	0.66-2.46	0.472			
Male	156	1.00	-				
Age							
>/= 40	137	2.22	1.11-4.47	0.023	2.36	1.11-5.00	0.024
< 40	94	1.00	-				
Mentally demanding job							
Yes	139	1.17	0.57-2.37	0.669			
No	76	1.00	-				

Physical job				
Yes	85	1.39	0.71-2.70	0.339
No	132	1.00	-	
Smoking				
Yes	84	1.09	0.57-2.09	0.792
No	142	1.00	-	
BMI				
>/= 25	125	1.19	0.62-2.29	0.605
< 25	101	1.00	-	
Sciatica provoked by sitting				
Yes	180	0.73	0.35-1.51	0.397
No	51	1.00	-	
Coughing, sneezing				
Yes	163	1.06	0.53-2.12	0.881
No	68	1.00	-	

Bragard's test							
Positive	62	1.91	0.97-3.74	0.059			
Negative	154	1.00	-				
Sensory disturbance							
Yes	200	1.45	0.47-4.47	0.514			
No	24	1.00	-				
VAS leg pain							
>/= 70	89	2.95	1.54-5.64	0.001	2.80	1.39-5.62	0.004
< 70	142	1.00	-				
VAS back pain							
>/= 70	34	1.68	0.74-3.80	0.211			
< 70	196	1.00	-				
McGill affective score							
High (3-5)	17	6.227	2.23-17.38	<0.001	4.48	1.43-14.08	0.010
Low (0-2)	209	1.00	-				
MRI-level herniation							

L5S1	125	0.69	0.37-1.31	0.256
L3L4/L4L5	106	1.00	-	
MRI-sequester				
Yes	84	0.85	0.43-1.68	0.643
No	122	1.00	-	
SF-36 Mental Health*				
Impaired	66	2.25	1.16-4.35	0.014
Not impaired	163	1.00	-	
VAS General Health				
>/= 70	60	1.36	0.68-2.74	0.382
< 70	168	1.00	-	

Only the numbers of the potential predictors with a p<0.10 in the univariate analysis were shown in the multivariate logistic regression.
*The scores on the SF-36 Mental Health subscale were dichotomised using one standard deviation below the dutch reference population.

Surgery versus prolonged conservative treatment for sciatica: 5-year results of a randomised controlled trial

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Article Focus

- The sciatica trial, a randomised controlled trial, showed no significant differences after one and two years of follow-up in disability and pain between patients with severe sciatica for six to eight weeks, allocated for either early surgery or six months of prolonged conservative care
- 20% of all patients reported an unsatisfactory recovery after two years. In this study the five years' follow-up is described and predictors for unsatisfactory recovery are identified

Key Messages

- 8% of all patients never showed any recovery
- In 23% of all patients sciatica results in ongoing complaints, which fluctuate over time, irrespective of treatment
- A strategy of prolonged conservative care with eventually delayed surgery gives a high chance of pain and disability to resolve, although 46% of these patients needed surgery after a few more months of prolonged suffering
- Age over 40 years, severe leg pain at baseline and a higher affective McGill pain score were predictors for an unsatisfactory recovery

Strengths and Limitations

- Five years' follow-up results of a randomised controlled trial
- 18% of the patients were lost to follow-up at five years
- No difference in baseline characteristics between dropouts and patients providing the five years' data

Introduction

The lumbosacral radicular syndrome (LSRS), caused by a herniated lumbar disc, is one of the most expensive disorders for society in terms of work absenteeism and disability[21]. In 2007, the Sciatica Trial showed that the clinical outcome after one year was not different from prolonged conservative treatment, although recovery within the first year was better with early surgery[17]. In the prolonged conservative treatment group however, 39% of patients crossed over to surgical treatment because of intractable pain within one year, and 44% within two years of follow-up[16]. Despite the fact that this study showed, along with other randomised controlled trials[8, 23-25], that a strategy of prolonged conservative care is safe and reduces the risk for patients of undergoing surgery, the optimal timing of surgery with regard to long-term outcome has still not been defined.

Although LSRS is described in the literature as having a quite favourable course, one might question this assumption as the two years' follow-up showed that about twenty percent of patients report an unsatisfactory outcome on all outcome scales and that the risk to suffer prolonged disability is higher than expected beforehand[16, 17].

The primary aim of the present study is to compare the pain and disability scores at five years' follow-up between patients in the Sciatica Trial randomised for surgery or randomised for prolonged conservative treatment. The second aim is to evaluate the proportion of patients with an unsatisfactory recovery at five years' follow-up and to identify factors contributing to these unsatisfactory results.

Material and Methods

Design

The study is part of the Sciatica Trial, a multicentre, prospective randomised trial among patients with 6 to 12 weeks of sciatica to determine whether a strategy of early surgery leads to better outcomes during the first year than does a strategy of

prolonged conservative treatment for an additional six months followed by surgery for those patients who do not improve.

In summary, patients, 18-65 years of age, with an LSRS with a concomitant disc herniation confirmed by MRI, were eligible for participation. A computer-generated permuted-block scheme was used for randomisation stratified by centre. In the surgical intervention group, a disc herniation removal through a unilateral transflaval approach using optical magnification was performed. Prolonged conservative treatment regimen was defined by general practitioners and treatment was mainly aimed at resuming daily activities. Patients were notified beforehand that they were participating in a study comparing two different strategies for the timing of intervention rather than comparing surgery with non-surgical treatment.

The design and study protocol have been published previously[17, 18]. Baseline characteristics from the Sciatica Trial have been published previously[16, 17] and were combined with the findings obtained from the five years' follow-up of the participants.

Procedures

As a standard procedure, the participants received the same study questionnaires as used for the one and two- year follow-up every year. At approximately five years after study inclusion, the participants were contacted once again by mail but now with an accompanied letter and asked to fill out the study questionnaires as used for the one and two-years' follow-up with extra questions about re-operations. Patients who did not respond initially, were contacted by telephone by a research nurse and asked once again to participate in the study by filling out the questionnaires. The additional 5 years' assessment was approved by the local medical ethics committee.

Primary and secondary outcomes

Primary outcome measures consisted of the Roland disability questionnaire (RDQ) for sciatica[14], a 100 mm visual analogue scale (VAS) for leg pain[4],and a seven-point Likert score of global perceived recovery. Higher RDQ and VAS scores were indicative of the experience of worse disability or greater intensity of pain, respectively. Global perceived recovery was measured with a 7-point Likert self-rating scale. Complete or almost complete disappearance of complaints (Likert scores 1-2) was defined as "satisfactory recovery", whereas Likert scores 3-7 were defined as "unsatisfactory recovery"[17, 18].

Secondary outcomes were a 100 mm VAS for back pain and the number of (re)operations for severe sciatica in the interval between two and five years. The number of (re)operations for severe sciatica was evaluated by asking patients whether there had been any new operations for severe sciatica in the interval between two and five years. Additionally, in all participating centres it was checked whether patients had had a treatment because of sciatica in the intervening period.

Potential prognostic factors

The prognostic value of demographic and clinical baseline variables for unsatisfactory recovery at five years was evaluated. The initial list of prognostic factors, chosen in advance by the investigators, was based on potential clinical importance, as indicated by earlier clinical results[7, 15, 22] The following potential prognostic demographic variables were included in the analysis: age (dichotomised <40/≥ 40), gender, smoking status, BMI (dichotomised <25/≥ 25), physical job (yes/no), or mentally demanding job (yes/no).

The following clinical baseline variables were included in the analysis: level of herniation at the MRI, the presence of a sequester on MRI (yes/no), sciatica provoked by sitting (yes/no), sciatica provoked by coughing/sneezing (yes/no), outcome of Bragard's test (positive/negative), sensory disturbance (yes/no). Furthermore, the following measurement instruments for general health, mental health, affective score and pain were included: the VAS scores for leg pain, back pain and general health, the Mental Health subscore of the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36)[3], and the McGill affective score[17]. The VAS score range from 0-100, with higher scores indicating more severe symptoms. For this analysis, dichotomised VAS scores were used (<70/≥70), as described in an earlier study[17]. The SF-36 Mental Health score ranges from 0 to 100, with higher scores indicating less severe symptoms. For this analysis, dichotomised SF-36 Mental Health subscores were used (scores below one standard deviation of the dutch reference population[1] were defined as impaired). The McGill affective score measures the qualitative perception of pain by the patient and ranges from 0-5 where a high score (3-5) is correlated with a more depressed and anxious mood. For this analysis, dichotomised McGill affective scores were used (<3/≥3)[17].

Statistical analysis

The original sample size calculation was based on a difference in RDQ outcome during and in a different speed to recovery during the first year. The main endpoint "recovery" is in principle time-dependent in the sense that it reflects the situation of a patient at a particular moment in time and the situation may also deteriorate afterwards, so it can change from recovered to non-recovered and back to recovered again, therefore actually being a time-varying dichotomous outcome which should be taken into account when interpreting the results of the analyses. Differences between randomisation groups at baseline and after five years of follow-up were assessed by comparing means, medians, or percentages, depending on the type of variable. Baseline values of variables were used as covariates in the main analyses whenever appropriate to adjust for possible differences between the randomised groups and to increase the power of the analyses. Outcomes of function and pain over the entire follow-up period were analysed using a repeated measurements analysis of variance with a first order autoregressive covariance matrix. Estimated consecutive scores were expressed as means and 95% confidence intervals. Pointwise estimates were obtained using models with time as a categorical covariate to allow assessment of systematic patterns. Differences between groups in the dichotomised Likert score at five years were evaluated with Fisher's exact test (randomisation group) or Mann-Whitney U (disability and pain scores).

The analyses were done according the intention-to-treat principle, except the comparison of groups with a satisfactory or unsatisfactory recovery.

Univariate and multivariate analyses were performed to evaluate the prognostic value of baseline variables for an unsatisfactory outcome at five years. The results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). Chi-square tests were used to perform the univariate analyses. Potential predictors with a $p<0.10$ in the univariate analysis were included in the multivariate logistic regression. The multivariate logistic regression model was performed in a backward approach and included randomisation group irrespective of its significance in the univariate analysis, to control for its influence on the dependent variable.

For all other analyses, $p<0.05$ was considered significant. Data collection and quality checks were performed with the ProMISe web-based secure data management system of the Department of Medical Statistics and Bioinformatics of Leiden University Medical Centre. For all statistical analyses, SPSS version 18.0 was used.

Results

Fifty-two of the 283 patients (18%) were lost to follow-up, among them one patient who died after a cardiac bypass operation and 19 patients who refused to participate. The baseline characteristics age, gender, BMI, randomization group, RDQ, and VAS-scores were not significantly different between the dropouts and those patients providing the five years' follow-up data. Twenty-six of the dropouts were randomised for early surgery. Among the 26 dropouts in the prolonged conservative group, 11 (42%) had surgery for sciatica during follow-up.

At five years' follow-up, 66 of the 142 patients (46%) assigned to conservative treatment had had surgery because of intractable sciatica (table 1). Within the first year this was 55 (39%) and after two years 62 (44%). Of the 141 patients allocated for early surgery, 16 (11%) recovered before surgery and were not operated on during the five years of follow-up. Within this five years' period, nine patients (7%) in the early surgery group and eight of the conservatively allocated patients who had surgery (12%), needed recurrent disc surgery. Three patients in the conservative group needed two re-operations or more (table 1).

The primary and secondary outcome scores concerning disability, leg pain and back pain at five years were slightly higher in the early surgery group compared to the prolonged conservative group, however, there were no significant differences (table 2, fig 1a-c).

In the total group, after five years, 49 (21%) patients still had an unsatisfactory recovery, defined as not having a complete or almost complete recovery on the dichotomised Likert scale, irrespective of their allocated treatment group (25 patients in the prolonged conservative group, 24 patients in the early surgery group, p=1.00). Patients with an unsatisfactory recovery had a significantly higher amount of leg pain, back pain and disability (all p-values <0.01) compared to the group with a satisfactory recovery (table 3). At five years' follow-up, 93 patients (62 men and 31 women, mean age 43.7, SD 9.8) had not had surgery (76 from the conservative group and 16 from the early surgery group) and the percentage recovered (77%) or not-recovered at five years (23%) was not different from the total group.

In the period of five years, 66 of the 213 patients (31%) with collected data at one, two and five years of follow-up had at least one period of unsatisfactory recovery. The pattern of recovery showed 16 patients who did not report any recovery at one, two and five years of follow-up. Twenty-four patients switched from 'not recovered' in

the first or second year to 'recovered' at the five-years' analysis. Sixteen of these patients were from the prolonged conservative group. Six of these patients needed an operation of whom four needed a re-operation before they recovered, compared to two of the eight patients in the early surgery group needing a re-operation. Twenty-six patients showed a good recovery at one and/or two years but not at five years of follow-up (fig 2).

Univariate logistic regression evaluating the relationship between possible prognostic variables and unsatisfactory recovery at five years, irrespective of intermediate recovery, showed that a high McGill affective score (score > 3; OR 6.23 (95% CI: 2.23-17.38)) was a significant predictor, as were severe leg pain at baseline (VAS > 70; OR 2.95 (95% CI: 1.54-5.64), an impaired score on the SF-36 Mental Health subscale (OR 2.25 (95% CI: 1.16-4.35)), higher age (age > 40; OR 2.22 (95% CI: 1.11-4.47)), and a positive Bragard test (OR 1.91(95% CI: 0.97-3.74)) (table 4). The multivariate analysis included all variables that were related to unsatisfactory outcome in the univariate analysis ($p < 0.10$), as well as randomisation group. This analysis showed that a high McGill affective score (score > 3; OR: 4.48 (95% CI: 1.43-14.08)), severity of leg pain (VAS > 70; OR: 2.80 (95% CI: 1.39-5.62)), and age (age > 40 years; OR: 2.36 (95% CI: 1.12-5.00)) were the only significant predictors for an unsatisfactory outcome at five years.

Discussion

This long-term follow-up study of the same patient cohort corroborates with earlier 1 and 2 year results as no significant differences between randomisation groups in disability, leg pain or back pain are found after five years of follow-up[16, 17]. Eighteen percent of the initial cohort of 283 patients was lost to follow-up after five years. This reduced the power of our latest analysis to some extent. However, the baseline characteristics showed no differences between the included group and the dropouts. The allocated strategy of an extra six months of wait-and-see resulted in a large proportion of delayed surgical treatment (46%) for persistent intense leg pain causing severe disability, despite all kinds of conservative treatment. This means that patients should be informed that prolonged conservative care gives them quite a high chance for resolution of pain and disability without the need of a surgical intervention, but that this strategy also carries a fair chance (46%) that this waiting for the pain to resolve will still end with them needing disc surgery.

The question however, is whether this conclusion is completely accurate. The design of the original study was a comparison of early surgery versus prolonged conservative care for six months, after which surgery was offered when there still were severe complaints. This means that we do not know the precise percentage of patients who would have become pain free with even longer conservative care, because the majority of these patients was operated on after six months. But on the other hand one might question whether such a proposed long conservative regimen is in proportion with the small risk of a surgical intervention, which provides a better outcome in the first six months, rather than being disabled in daily life during this long period of conservative care. Furthermore, the proportion of patients who were not operated after five years with a satisfactory or unsatisfactory recovery was the same as in the total population, showing that also in the non-operated patients there was a rather high amount of unsatisfactory recovery.

Twenty-one percent of patients experienced unsatisfactory recovery at five years, while 31% of the patients with complete data at one, two and five years of follow-up noted at least once an unsatisfactory recovery during this five years' follow-up period, irrespective of their allocated group. So the optimal timing of surgery is still on debate, as is the question which patients would benefit from surgery and which from prolonged conservative care.

The study design of this five year analysis did not permit us to look properly for the causes of an unsatisfactory recovery. A shortcoming of this study is the fact that there was no permission in the present study to retrieve new MR-images, but a recent study with the same patient population did not show any correlation between MR-images and satisfactory or unsatisfactory recovery at one year[5].

The patterns of recovery show that 8% of all patients with collected data, had never had any recovery during the follow-up period, showing that there are not that many non-responders of conservative or surgical treatment. The other 50 patients (23%) with an unsatisfactory recovery showed a switch over time from recovered to not-recovered, or vice versa. This is in line with the idea that sciatica is caused by chronic disc disease with intermittent nerve compression or inflammation and that pain can thus re-occur despite any earlier treatment [10, 13]. In the 24 patients who switched from 'not-recovered' in the first or second year to 'recovered' at the five-years' analysis, there was a higher amount of patients who needed a re-operation before recovery occurred in the prolonged conservative group compared to the early

surgery group. This may be caused by less effectiveness of late surgery, although this could not be proven. This less effectiveness of late surgery compared to early surgery could be caused by more chronic changes around the disc protrusion or sequester, causing more difficulty in freeing the nerve from compression.

In our study we could not estimate the effect of early versus late surgery, or surgery versus conservative treatment in an unbiased way since that would require a per protocol analysis. This would ignore the randomised allocation and compare patients who by definition would be incomparable since the design of our study did not envisage a randomisation between early and late surgery but merely allowed for the time of surgery being determined by the assessment of both patient and physician after initial randomisation. The impossibility to capture completely the condition of the patient and the selection mechanism which leads to the decision to operate, or not, at any given point in (follow-up) time, renders any multivariate analysis that attempts to make the groups of early and late operations comparable, biased. This bias has occurred in other randomised studies where this “per protocol” analysis was used and patients who were operated on after a prolonged duration of symptoms from a herniated lumbar disk have been shown to have a worse outcome than patients who were operated on relatively early[9, 11, 12, 20]. As a consequence of this “per protocol analysis both groups differed in baseline characteristics such as type of disc herniation, neurological deficit and reported depression, rendering comparison of both groups fallacious[20].

In this five-years’ analysis the independent prognostic factors for an unsatisfactory outcome were a high McGill affective score, a high amount of leg pain, and age over 40 years at baseline. A high McGill affective score correlates with a more depressed and anxious mood[17], and mental stress, depression or other psychological factors have been widely described as risk factors for development of chronic pain[19]. Although a high amount of pain at baseline can also be caused by psychological factors, it is an independent prognostic factor for an unsatisfactory outcome in this study. Perhaps the severity of nerve root compression at intake predicts the overall outcome, but a correlation between amount of pain and amount of root compression has not been proven[1]. In our study, other factors concerning the severity of nerve root damage, such as severe sensibility disturbance, showed no association. In a systematic review of non-surgically treated sciatica none of the three studies that investigated baseline leg pain severity showed a clear prognostic influence on

outcome. Age was also not found to be a prognostic factor in six out of seven studies[2]. The reason for age over 40 years being a prognostic indicator for a unsatisfactory outcome could be because disc herniation is part of a degenerative disease which seems to worsen in time. A study of prognostic factors for unsatisfactory recovery among operated and unoperated patients did not show leg pain severity and age to be a prognostic factor, but found the variables severe back pain and male gender as predictors for a bad outcome at the one year follow-up[2, 6]. This was in contrast with our one year study where being female was a prognostic factor for a bad outcome, but in this five years' analysis this also disappeared. The possible prognostic role of gender might be over-estimated in the past.

Conclusion

After five years of follow-up there were still no differences in pain and disability between the patients randomised for early surgery or prolonged conservative care. Signs of pain quality associated with depression and a more anxious mood, the age of the patient and the severity of leg pain at baseline were predictive of an unsatisfactory outcome.

In general, patients must be informed that prolonged conservative care might give them a fair chance for pain and disability to resolve without surgery, but with the risk for delayed surgery in the end after a prolonged period of suffering from sciatica.

Furthermore, although the total number of disabled patients without pain free periods in this study seems to be low, in almost one fourth of the patients, sciatica appears to be an ongoing disease with variable complaints in time, irrespective of treatment. These patients need our full attention, and further investigation at 10 years' follow-up is being planned, because this patient category has the highest burden on society concerning work absenteeism and general health costs.

Extra data is available by emailing the first author.

- Contributors: The participants in the Leiden-The Hague Spine Intervention Prognostic Study Group were: protocol committee, WCP, BWK, and RTWMT; steering committee, BWK, RTWMT, JAH Eekhof, JTJ Tans, WBvdH, WCP, RB, and HC van Houwelingen; statistical analysis, WBvdH; research nurses and data collection and management, M Nuyten, P Bergman, G Holtkamp, S Dukker, A Mast, L Smakman, C Waanders, L Polak, A Nieborg; coordinating physicians of participating hospitals, JTJ Tans, R Walchenbach (Medical Center Haaglanden, The Hague), J van Rossum, P Schutte, RTWMT (Diaconessen Hospital, Leiden), GAM Verheul, JE Dalman, JAL Wurzer (Groene Hart Hospital, Gouda), JWA Sven, A Kloet (Reinier de Graaf Hospital, Delft/Voorburg), ISJ Merkies, H van Dulken (Spaarne Hospital, Heemstede/Haarlem), PCLA Lambrechts, JAL Wurzer (Bronovo Hospital, The Hague), RWM Keunen, CFE Hoffmann (Haga Hospital, The Hague), J Haan, H van Dulken (Rijnland Hospital, Leiderdorp/Alphen ad Rijn), R Groen, RRF Kuiters (Lange Land Hospital, Zoetermeer), RAC Roos, JHC Voormolen (Leiden University Medical Center, Leiden), JAH Eekhof (Public Health and Primary Care, Leiden University, Leiden). WCP is guarantor for the study.

Reference List

1. Aaronson NK, Muller M, Cohen PD, et al: Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. **J Clin Epidemiol 51**:1055-1068, 1998

2. Ashworth J, Konstantinou K, Dunn KM: Prognostic factors in non-surgically treated sciatica: a systematic review. **BMC Musculoskelet Disord 12**:208, 2011

3. Brazier JE, Harper R, Jones NM, et al: Validating the SF-36 health survey questionnaire: new outcome measure for primary care. **BMJ 305**:160-164, 1992

4. Collins SL, Moore RA, McQuay HJ: The visual analogue pain intensity scale: what is moderate pain in millimetres? **Pain 72**:95-97, 1997

5. el BA, Vleggeert-Lankamp CL, Nijeholt GJ, et al: Magnetic resonance imaging in follow-up assessment of sciatica. **N Engl J Med 368**:999-1007, 2013

6. Haugen AJ, Brox JI, Grovle L, et al: Prognostic factors for non-success in patients with sciatica and disc herniation. **BMC Musculoskelet Disord 13**:183, 2012

7. Hurme M, Alaranta H: Factors predicting the result of surgery for lumbar intervertebral disc herniation. **Spine (Phila Pa 1976) 12**:933-938, 1987

8. Jacobs WC, van TM, Arts M, et al: Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review. **Eur Spine J 20**:513-522, 2011

9. Jonsson B: Patient-related factors predicting the outcome of decompressive surgery. **Acta Orthop Scand Suppl 251**:69-70, 1993

10. Mulleman D, Mammou S, Griffoul I, et al: Pathophysiology of disk-related sciatica. I.--Evidence supporting a chemical component. **Joint Bone Spine 73**:151-158, 2006

11. Ng LC, Sell P: Predictive value of the duration of sciatica for lumbar discectomy. A prospective cohort study. **J Bone Joint Surg Br 86**:546-549, 2004

12. Nygaard OP, Kloster R, Solberg T: Duration of leg pain as a predictor of outcome after surgery for lumbar disc herniation: a prospective cohort study with 1-year follow up.[see comment]. **J Neurosurg Pediatrics 92**:131-134, 2000

13. Omarker K, Myers RR: Pathogenesis of sciatic pain: role of herniated nucleus pulposus and deformation of spinal nerve root and dorsal root ganglion. **Pain 78**:99-105, 1998

14. Patrick DL, Deyo RA, Atlas SJ, et al: Assessing health-related quality of life in patients with sciatica. **Spine (Phila Pa 1976) 20**:1899-1908, 1995

15. Peul WC, Brand R, Thomeer RT, et al: Influence of gender and other prognostic factors on outcome of sciatica. **Pain 138**:180-191, 2008

16. Peul WC, van den Hout WB, Brand R, et al: 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, 2008

17. Peul WC, Van Houwelingen HC, van den Hout WB, et al: Surgery versus prolonged conservative treatment for sciatica. **N Engl J Med 356**:2245-2256, 2007

18. Peul WC, Van Houwelingen HC, van der Hout WB, et al: 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, 2005

19. Pincus T, Burton AK, Vogel S, et al: A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. **Spine (Phila Pa 1976) 27**:E109-E120, 2002

20. Rihn JA, Hilibrand AS, Radcliff K, et al: Duration of symptoms resulting from lumbar disc herniation: effect on treatment outcomes: analysis of the Spine Patient Outcomes Research Trial (SPORT). **J Bone Joint Surg Am 93**:1906-1914, 2011

21. van Tulder MW, Koes BW, Bouter LM: A cost-of-illness study of back pain in The Netherlands. **Pain 62**:233-240, 1995

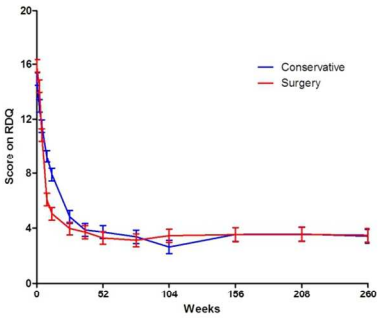
22. Vroomen PC, de Krom MC, Knottnerus JA: Predicting the outcome of sciatica at short-term follow-up. **Br J Gen Pract 52**:119-123, 2002

23. Weinstein JN, Lurie JD, Tosteson TD, et al: Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort. **JAMA 296**:2451-2459, 2006

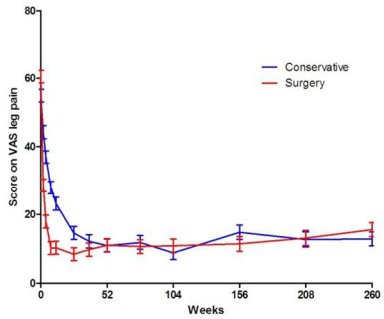
24. Weinstein JN, Lurie JD, Tosteson TD, et al: Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). **Spine (Phila Pa 1976) 33**:2789-2800, 2008

25. Weinstein JN, Tosteson TD, Lurie JD, et al: Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. **JAMA 296**:2441-2450, 2006

Figure 1a.



1b.



1c.

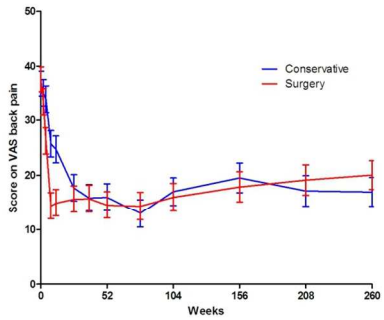


Fig 1a-c: Repeated measurement analysis curves of mean scores for Roland disability questionnaire (top panel) and visual analogue scales for leg pain and back pain (lower panels).
90x146mm (300 x 300 DPI)

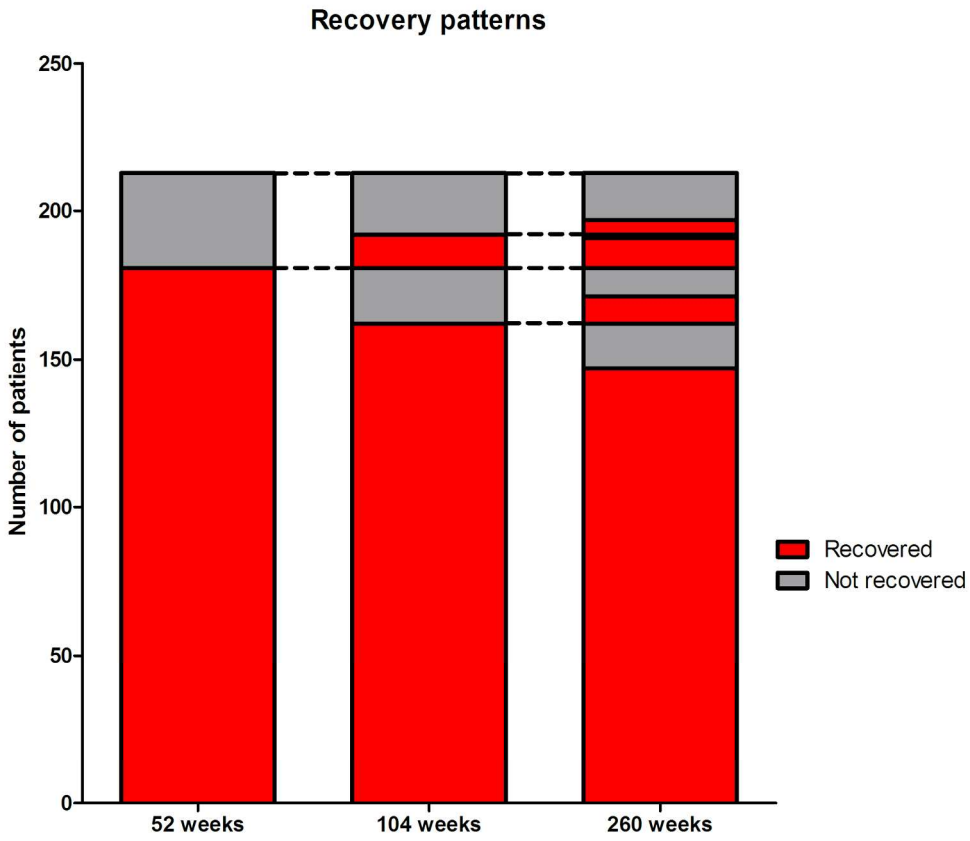
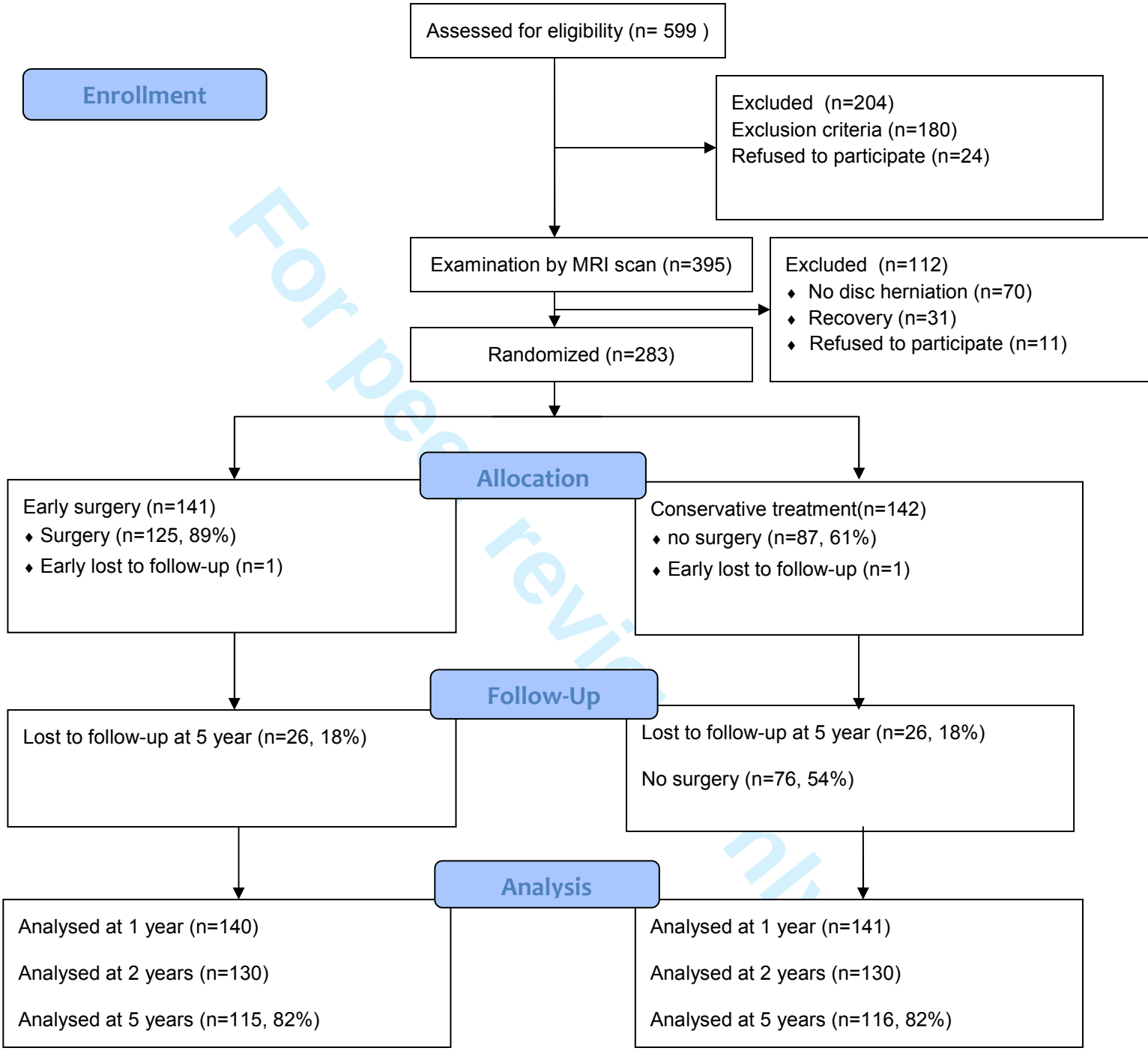


Fig 2 patterns of recovery between results of the one, two and five years' analysis with a dichotomized Likert score for perceived recovery.
182x158mm (300 x 300 DPI)

CONSORT 2010 Flow Diagram



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	3
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	3
	4b	Settings and locations where the data were collected	3
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	3
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	4
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	See previous article **BMJ**. **2008** Jun 14;336(7657): 1355-8. doi: 10.1136/**bmj**. a143. Epub **2008** May 23.
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Non applicable

Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	See the remark above
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	See above
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	See above
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	See above
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	5
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5 plus 6
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Table 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	Page 6
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Page 3
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Included table1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Table 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Page 6 and 7
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	none
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 7-10
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	7-10

Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	yes
Other information			
Registration	23	Registration number and name of trial registry	In the abstract
Protocol	24	Where the full trial protocol can be accessed, if available	BMC Musculoskelet Disord. 2005 Feb 11;6:8.
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	none

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.