Timing of surgery for sciatica

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ONE-YEAR RESULTS RANDOMIZED TRIAL

Surgery versus prolonged conservative treatment for Sciatica

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ABSTRACT

Background: Lumbar disk surgery is often performed in patients who have sciatica that does not resolve within 6 weeks, but the optimal timing of surgery is not known.

Methods: We randomized 283 patients with 6-12 weeks of severe sciatica to early surgery or continued conservative treatment, with delayed surgery if needed. Primary outcome measurements were the Roland Disability Questionnaire, visual analogue scale for leg pain and patient's report of perceived recovery during the first year after randomization. Repeated measurement analysis by intention-to-treat was used to estimate the outcome curves for both groups.

Results: Of 141 patients assigned to undergo early surgery, 125 (89 percent) underwent microdiskectomy after a mean of 2.2 weeks; of 142 patients designated for conservative treatment, 55 (39 percent) were treated surgically after 18.7 weeks. There was no significant overall difference in disability scores during the first year ($p=0.13$) Improvement in the intensity of leg pain was faster for patients randomized to early surgery ($p<.001$). Early surgery also achieved a faster rate of perceived recovery hazard ratio (CI) of 1.97 (1.72-2.22), $p<.001$). In both groups, however, the probability of perceived recovery after one year of follow-up was 95 percent.

Conclusions: The strategies of early surgery and of conservative treatment with delayed surgery if needed resulted in similar outcomes at one year, but early surgery achieved more rapid recovery and pain relief.

Sciatica is characterized by radiating pain in an area of the leg typically served by one lumbar or sacral spinal nerve root; sciatica is sometimes associated with sensory and motor deficit. The most common cause of sciatica is a herniated disk. The estimated annual incidence of sciatica is 5 per 1000 adults[46]. The economic impact of lumbar spine disorders is high, ranking the fifth most expensive disease category for hospital care. It is the most expensive category as far as work absenteeism and disablement are concerned[77]. The natural history of sciatica is favorable, with resolution of leg pain within 8 weeks from onset in the majority of patients[57;79;116]. Starting from the first successful surgical treatment in 1934[4] international consensus has been that surgery should be offered only if symptoms persist after a period of conservative treatment[117]. There is however no consensus on how long conservative therapy should be tried before surgery is considered. Sociocultural preferences account for a wide variation[46] in the rates of surgery. For example in the US and the Netherlands surgery rates are relatively high. Dutch guidelines[44] recommend offering the patient the option of surgery if symptoms do not improve after 6 weeks of conservative treatment. However, the optimal timing of disk surgery has not been established. This report describes the efficacy of early surgical intervention compared to a strategy of prolonged conservative care and delayed surgery, if needed, for patients with disabling sciatica.

Methods

We conducted a multicenter prospective randomized trial among patients with 6-12 weeks of severe sciatica to determine whether a strategy of early surgery leads to better outcomes during the first year than a strategy of conservative treatment for an additional 6 months and performing delayed surgery for patients who had not improved. The medical ethics committee at each of 9 participating hospitals approved the protocol. Written informed consent was obtained from all patients. Details of the design and study protocol have been published previously[118] (Figure 1).

Eligibility and Randomization

Eligible patients were between 18-65 years of age, had a radiological confirmed disk herniation, and had been diagnosed by an attending neurologist with an incapacitating lumbosacral radicular syndrome lasting between 6 and 12 weeks. Correlation of MRI to complaints was registered by the neurosurgeon. At the time of enrolment an independent research nurse verified persistence of complaints. Patients presenting with a cauda equina syndrome, muscle paralysis or insufficient strength to move against gravity were excluded. Patients were also excluded if they had identical com-

Table 1. Base-line and Follow-up Characteristics of Patients with Sciatica*

	Early Surgery (N=141)	Conservative (N=142)
Age (yr)	41.7 ± 9,9	43.4 ± 9,6
Male sex –no (%)	89 (63)	97 (68)
Quetelet-index†	25.9 ± 4.1	25.8 ± 4.0
Duration of sciatica in weeks	9.43 ± 2.37	9.48 ± 2.11
Took sick leave from work, no (%)	107 (76)	116 (82)
Duration sick leave in weeks	5.32 ± 2.78	5.28 ± 2.62
Radiating pain left leg-no (%)	67 (48)	73 (51)
Positive straight leg-raising test % ‡	100 (71)	104 (73)
Positive crossed straight leg-raising test % ‡	71 (50)	70 (49)
Sensory loss, no (%)	123 (87)	128 (90)
Dermatome anaesthesia, no (%)	31 (22)	33 (23)
Muscle weakness, no (%)	93 (66)	99 (70)
Knee tendon reflex difference, no (%)	54 (38)	51 (36)
Ankle tendon reflex difference, no (%)	75 (53)	107 (75)
Clinical suspected level herniated disk		
Clinical suspected disk level L3-L4 no (%)	6 (4)	5 (4)
Clinical suspected disk level L4-L5 no (%)	69 (49)	57 (40)
Clinical suspected disk level L5-S1 no (%)	66 (47)	83 (58)
Roland Disabilty Questionnaire Score §	16.5 ± 4.4	16.3 ± 3.9
Score on visual analogue scale ¶		
VAS leg pain	67.2 ± 27.7	64.4 ± 21.2
VAS back pain	33.8 ± 29.6	30.8 ±27.7
VAS leg and back pain	61.0 ± 22.3	58.2 ± 20.0
VAS general health #	47.8 ± 24.5	46.0 ± 24.5
Short Form-36 Scores **		
SF-36 bodily pain	21.9 ± 16.6	23.9± 18.1
SF-36 physical functioning	33.9 ± 19.6	34.6 ± 19.0
SF-36 social functioning	44.6 ± 30.1	43.3 ± 27.1
SF-36 role-physical functioning	8.2 ± 20.7	8.3 ± 21.0
SF-36 role-emotional functioning	51.0 ± 46.0	52.4 ± 46.0
SF-36 mental health index	67.8 ± 19.7	67.7 ± 19.5
SF-36 vitality	47.5 ± 21.3	47.9 ± 21.3
SF-36 general health perception	64.6 ± 20.3	64.1 ± 20.3
Sciatica Frequency/ Bothersome Index ††		
Frequency index	16.0 ± 4.6	16,2 ± 4.2
Bothersome index	14.6 ± 5.1	14.5 ± 4.1
Preference conservative treatment-no (%)	42 (30)	43 (30)

Table 1. Continued

	Early Surgery (N=141)	Conservative (N=142)
Surgical Treatment during follow-up	**Early Surgery**	**Conservative**
Surgery actually performed (%)	125 (89)	55 (39)
Mean time to surgery in weeks (CI)	2.2 (1.9-2.5)	18.7 (14.3-23.0)
Median time in weeks (Interquartile Range)	1.9 (1.1-2.4)	14.6 (6.4-26.0)
Recurrent disk surgery (%)	4 (3.8)	1 (2)

* Plus-minus value are means ± SD. There were no significant differences among the two groups on any of the baseline characteristics.

† Quetelet-Index or Body-Mass Index is calculated by dividing the weight in kilograms by the squared length in meters. Higher scores define overweight.

‡ Lasègue's sign was defined positive if the examiner observed a typically dermatomal area of pain reproduction and pelvic muscle resistance during unilateral provocative straight leg raising below an angle of 60 degrees, and crossed positive if the same experience was noted raising the other leg below 90 degrees.

§ 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.

\# General Health perception was indicated on a visual analogue scale, on a 100 millimeter line with 0 representing the worst and 100 the best health perception a patient can imagine.

** SF-36 is the abbreviation of Medical Outcomes Study 36-Item Short Form Health Survey (Range 0-100) and is a generic health status questionnaire consisting of 36 items on physical and social functioning delineating 8 domains of quality . Higher score indicates less severe symptoms.

†† The Sciatica Frequency and Bothersome Index (SFBI) is a scale from 0 to 6, which assesses the frequency (0=not at all to 6=always) and bothersomeness (0=not bothersome to 6=extreme bothersome) of back and leg symptoms. The sum of the results of four symptom questions yields both indexes, ranging from 0 to 24: leg pain; numbness and/or tingling in the leg; weakness in the leg or foot; pain in the back or leg while sitting.

plaints in the past twelve months, a history of spine surgery, bony stenosis, spondylolisthesis, pregnancy or severe comorbidity.

A computer-generated permuted-block scheme was used for randomization, stratified according to center (n=9). One hour before randomization patients were again evaluated. If at that moment, eligibility criteria were no longer met due to recovery, patients were excluded. Otherwise they were included and the next numbered opaque envelope containing the assigned strategy was opened. Patients could not be blinded to treatment arm.

Treatment

Early surgery was scheduled within 2 weeks of assignment and only cancelled if spontaneous recovery occurred before the date of surgery. Under either general or spinal anesthesia the symptomatic disk herniation was removed by a minimal unilateral transflaval approach with magnification. The goal of surgery was to decompress the nerve root and reduce the risk of recurrent disk herniation by an annular fen-

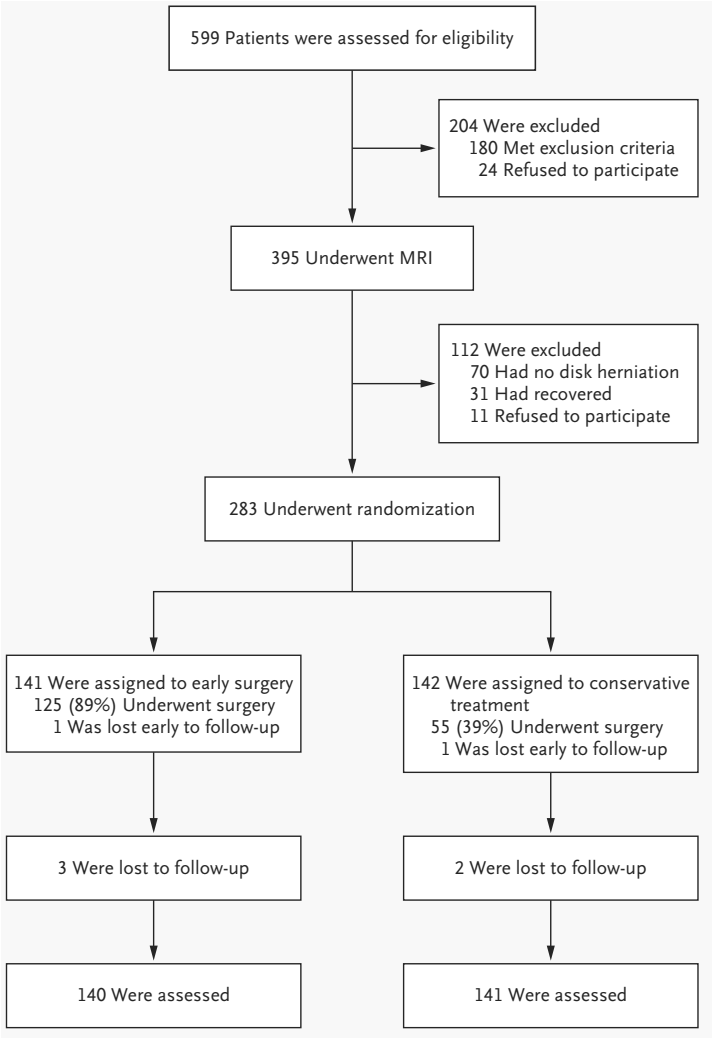

Figure 1. Flow-diagram

estration, curettage and removal of loose degenerated disk material out of the disk space using a rongeur, without any attempt to perform a subtotal diskectomy. The duration of the hospital stay depended on the patient's functional ability to mobilize. Usual care was provided according to the protocols of the participating surgical departments. At home the rehabilitation process was supervised by the physiotherapist who used a standardized exercise protocol. Patients were advised to resume their regular jobs when able, depending on the nature of the work.

Prolonged conservative management was provided by the general practitioner. Ample information was provided about the favorable prognosis. Study participants were offered to visit our trial website, exclusively designed to inform patients about their successfully natural course irrespective of the initial pain intensity. Treatment was mainly aimed at resuming daily activities. If necessary the prescription of pain medication was adjusted according to existing clinical guidelines[118]. Patients who had considerable fear of movement were referred to a physiotherapist. If sciatica persisted 6 months after randomization microdiskectomy was offered. Increasing leg pain not responsive to medications or progressive neurological deficit were reasons for performing surgery earlier than 6 months.

Outcomes

Patients were assessed by means of the Roland Disability Questionnaire for Sciatica (RDQ)[114], 100 mm visual analogue scale for leg pain (VAS-leg)[109] and a 7-point Likert self-rating scale of global perceived recovery. Functional disability, intensity of leg pain and global perceived recovery questionnaires were the primary outcomes and were assessed at 2, 4, 8, 12, 26, 38 and 52 weeks.

Secondary outcomes, such as a repeated neurological examination, functional-economic observational assessments (PROLO)[104] by the independent research nurse, as well as the Short Form-36 scale[107], Sciatica-Frequency-and-Bothersomeness Index[165] and a 100 mm visual analogue scale for health perception[118] were filled out at monitoring visits scheduled at 8, 26 and 52 weeks. Research nurses observed their own patients at the planned follow-up moments and were not blinded to the patients' treatment assignment.

Statistical analysis

The aim of this study was to estimate the difference between the two treatment groups in disease-specific disability of daily functioning measured with the RDQ, the VAS-leg pain intensity and to estimate the difference in median time to recovery, measured with dichotomized self-assessment on the Likert scale as a function of time since randomization. Assuming a mean standard deviation of 10 points[81] over the first year 140 patients were calculated to be required per treatment arm to provide a statistical power of 0.90 with a two-tailed significance level of 0.05 to detect at least three points difference on the RDQ.

Recovery was defined as complete or near complete disappearance of complaints measured with a 7-point Likert scale. Although this trial was primarily meant to study average differences in functional outcome, it was also initially estimated that this sample size would also have a statistical power of 90 percent to detect a difference of 2 months in median time to recovery using estimates from survival models.

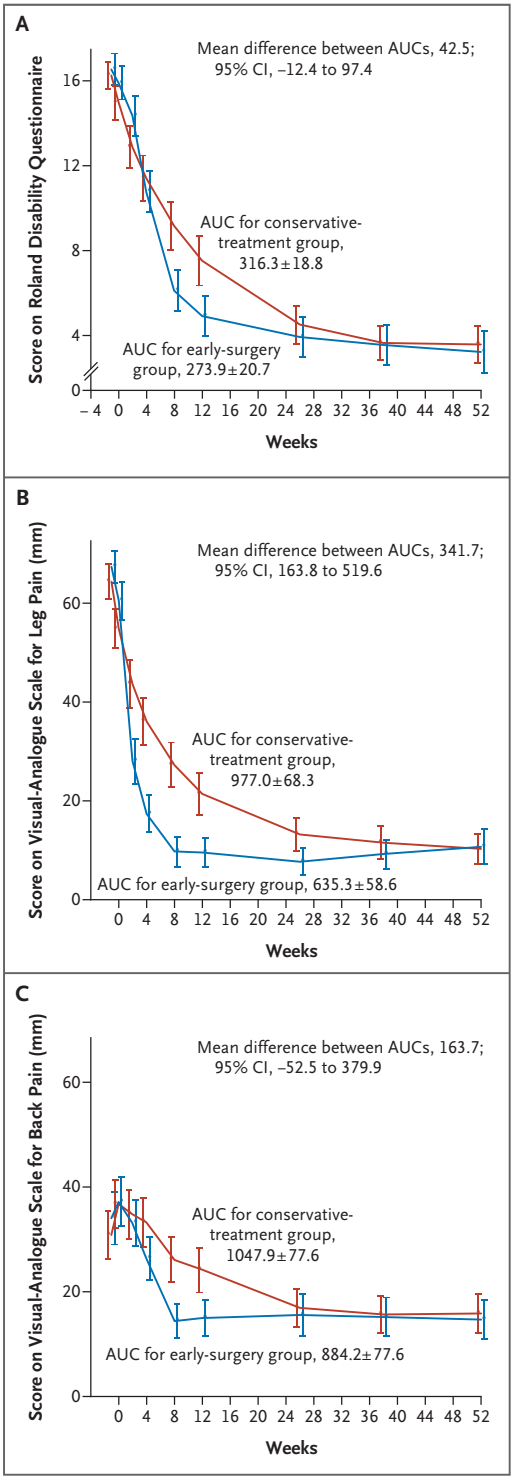

Figure 2. Repeated Measurement Analysis Curves of Mean scores for Roland Disabilty Questionnaire (Panel A), Leg Pain (Panel B) and Back Pain (Panel C) on a Visual-Analogue Scale.

All three panels show the 52-week curves with 95 percent confidence intervals represented by vertical bars at consecutive moments of measurement. Red lines represent the conservative treatment group, while the blue lines represent early surgery.

Panel A** represents the mean disability scores at consecutive moments of measurement. Although the curves differ, and the short term mean results at 8 and 12 weeks show significantly non-overlapping confidence intervals the overall difference between the areas under the curves (AUC) over 12 months is not significant **(p=0.13).

***Panel B** represents mean visual analogue scores for intensity of leg pain in mm, showing an early effect for leg pain in favor of the surgical group from 2 to 26 weeks, but with near equal scores at one year. The difference between the mean AUC's is significantly different **(p<0.001)**.*

Panel C** represents mean visual analogue scores for intensity low back pain in mm. Starting with a lower intensity score when compared to leg pain, the mean AUC's exhibit a less strong and not significant difference **(p=0.14)

** Area's under the curve are expressed by their means ± SE, while the mean difference is expressed by the corresponding 95 percent confidence interval*

Data collection and quality checking were performed with the ProMISe data management system of the Department of Medical Statistics & BioInformatics[119] of the Leiden University Medical Center . For all statistical analyses SPSS 12.0[120] was used. Differences between groups at baseline 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 randomized groups and to increase the power of the analyses. Outcomes of function and pain were analyzed using a repeated measurements analysis of variance using 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 randomization groups were assessed by either estimating the main effect of the treatment or the interaction between treatment and time. As a second approach to quantify the differences between the two groups over total follow-up time, "area under the curve" quantities (AUC) were calculated between randomization and week 52 and subsequently compared using Student t-tests. Finally a Kaplan-Meier survival analysis was used to estimate the "time elapsed from randomization until recovery" and curves were compared using a logrank test. A Cox model was used to compare speeds of recovery by calculation of a Hazard Ratio. Whether "speed of recovery" can be demonstrated to differ among subgroups[118] was assessed by testing the interaction between each subgroup variable and the randomization variable with a cutoff value of 0.10 for significance in view of the lower power of the interaction test. All analyses were performed by intention-to-treat.

RESULTS

Between November 2002 and February 2005, 599 patients meeting the criteria for a surgical indication according to their GP were contacted (Figure 1). After initial consultation with the neurologist, 395 patients who met the inclusion criteria were referred for MRI. At the second visit 283 patients continued to suffer from sciatica, the causal disk herniation had been visualized as well and subsequently were allocated to one of two treatment strategies. No significant differences were noted in baseline characteristics between patients in the two study groups (Table 1). Of 141 patients assigned to receive early surgical treatment, 16 patients recovered before surgery was actually performed. Median time to early surgery for the remaining 125 patients was 1.9 weeks (Table 1) after randomization. Of the 142 patients assigned to the conservative treatment group 55 underwent surgery during the first year (Table 1) after

Table 2. Primary and Secondary Outcomes based on Intent-to-Treat Repeated Measurements Analysis and Treatment effects*

	2 weeks			8 weeks		
Primary Outcomes	**Surgery**	**Conservative**	**Treatment effect (95% CI)**	**Surgery**	**Conservative**	**Treatment effect (95% CI)**
Roland Disabilty †	14.4 (0.5)	13.0 (0.5)	**-1.6 (-2.8 to -0.3)**	6.1 (0.5)	9.2 (0.5)	**3.1 (1.7 to 4.3)**
VAS-Legpain ‡	28.5 (1.9)	44.2 (1.9)	**15.7 (11.7 to 19.7)**	10.2 (1.9)	27.9 (1.9)	**17.7 (12.3 to 23.1)**
VAS-Backpain §	33.3 (2.1)	34.9 (2.1)	**1.5 (-4.5 to 7.4)**	14.4 (2.1)	25.7 (2.1)	**11.3 (5.6 to 17.4)**
Likert-Global ‡ ¶	3.1 (0.1)	3.5 (0.1)	**0.4 (0.1 to 0.6)**	2.2 (0.1)	3.1 (0.1)	**0.9 (0.6 to 1.2)**
Secondary Outcomes						
PROLO Functional ‖ **	1.1 (0.08)	1.1 (0.08)	**0.04 (-0.2 to 0.3)**	2.8 (0.09)	2.0 (0.09)	**-0.8 (-1.1 to 0.6)**
PROLO Economic ‖ **	1.2 (0.1)	1.3 (0.1)	**0.2 (-0.2 to 0.6)**	1.8 (0.1)	2.3 (0.1)	**0.5 (0.09 to 0.8)**
SF-36 bodily pain	-	-	**-**	62.8 (2.1)	54.4 (2.0)	**-8.4 (-13.5 to -3.2)**
SF-36 physical functioning	-	-	**-**	71.2 (1.7)	61.9 (1.9)	**-9.3 (-14.2 to -4.4)**
SF-36 social functioning	-	-	**-**	69.9 (2.3)	67.6 (2.3)	**-2.3 (-8.3 to 3.7)**
SF-36 role physical functioning	-	-	**-**	29.5 (3.1)	29.3 (3.2)	**-0.2 (-5.9 to 5.5)**
SF-36 role emotional functioning	-	-	**-**	69.3 (3.5)	66.2 (3.7)	**-3.1 (-9.3 to 3.0)**
SF-36 mental health index	-	-	**-**	82.1 (1.3)	73.0 (1.7)	**-9.1 (-13.4 to -4.8)**
SF-36 vitality	-	-	**-**	67.5 (1.7)	57.1 (1.7)	**-10.4 (-15.1 to -5.7)**
SF-36 general health perception	-	-	**-**	75.7 (1.5)	65.2 (1.6)	**-10.5 (-15.2 to -5.8)**
SFBI Frequency	-	-	**-**	5.3 (0.4)	9.3 (0.5)	**4.0 (2.7 to 5.3)**
SFBI Bothersomeness				4.0 (0.4)	7.6 (0.5)	**3.6 (2.3 to 4.9)**
VAS Health	59.8 (1.9)	55.2 (2.2)	**4.6 (-1.2 to 10.4)**	74.7 (2.3)	62.7 (2.4)	**12.0 (5.3 to 18.8)**
Cumulative Surgeries performed (%) ††	87 (62)	2 (1)	**Δ 85 (61)**	123 (87)	16 (11)	**Δ 107 (76)**

* Results are described by their mean (SE)
† Overall difference between scores not significant (p=0.12)
‡ Fixed effects significantly different in favor of early surgery ($p < 0.001$)
§ Significantly different in favor of early surgery (p =0.045)
¶ Likert global perceived recovery is defined by a 7-point scale "Worse" to "Complete" recovery. Lower scores represent recovery.
‖ PROLO is a 4-point qualitative functional-economic scale filled in by the observer; it is divided into a functional and an economic scale. A lower value represents poor functioning and decreased possibility to work
** Functional observation scores show a difference in favor of surgery ($p<0.001$) while the overall Economic scores were not significantly different (p=0.154) with an outcome at 8 weeks in favor of conservative treatment

Table 2. Continued

	26 weeks			52 weeks		
Primary Outcomes	**Surgery**	**Conservative**	**Treatment effect (95% CI)**	**Surgery**	**Conservative**	**Treatment effect (95% CI)**
Roland Disabilty †	4.0 (0.5)	4.8 (0.5)	**0.8 (-0.5 to 2.1)**	3.3 (0.5)	3.7 (0.5)	**0.4 (-0.9 to 1.7)**
VAS-Legpain ‡	8.4 (1.9)	14.5 (1.9)	**6.1 (2.2 to 10.0)**	11.0 (1.9)	11.0 (1.9)	**0 (-4.0 to 4.0)**
VAS-Backpain §	15.5 (2.2)	17.8 (2.1)	**2.3 (-3.6 to 8.2)**	14.2 (2.2)	16.5 (2.1)	**2.3 (-3.6 to 8.2)**
Likert-Global ‡ ¶	2.1 (0.1)	2.3 (0.1)	**0.2 (-0.07 to 0.5)**	1.9 (0.1)	2.1 (0.1)	**0.2 (-0.1 to 0.4)**
Secondary Outcomes						
PROLO Functional ‖**	3.4 (0.08)	2.9 (0.08)	**-0.5 (-0.7 to -0.2)**	3.3 (0.08)	3.3 (0.08)	**0. 04 (-0.19 to 0.28)**
PROLO Economic ‖**	3.0 (0.1)	2.9 (0.1)	**-0.1 (-0.5 to 0.3)**	3.2 (0.1)	3.4 (0.1)	**0.2 (-0.2 to 0.6)**
SF-36 bodily pain	76.1 (1.1)	72.8 (1.9)	**-3.3 (-8.4 to 1.8)**	81.2 (2.0)	78.5 (1.9)	**-2.7 (-7.9 to 2.6)**
SF-36 physical functioning	79.1 (1.9)	77.6 (1.7)	**-1.5 (-6.4 to 3.4)**	84.2 (1.8)	82.0 (1.9)	**-2.2 (-7.2 to 2.8)**
SF-36 social functioning	86.9 (1.8)	82.4 (1.9)	**-4.5 (-10.6 to 1.4)**	89.4 (1.6)	88.1 (1.7)	**-1.3 (-7.3 to 4.7)**
SF-36 role physical functioning	69.1 (3.5)	61.9 (3.6)	**-7.2 (-13.0 to -1.4)**	78.4 (3.2)	74.5 (3.3)	**-3.9 (-9.7 to 1.9)**
SF-36 role emotional functioning	84.9 (2.7)	81.0 (3.0)	**-3.9 (-10.1 to 2.3)**	87.2 (2.6)	88.6 (2.5)	**1.4 (-4.8 to 7.6)**
SF-36 mental health index	83.2 (1.3)	80.5 (1.5)	**-2.7 (-7.0 to 1.6)**	83.0 (1.3)	81.1 (1.4)	**-1.9 (-6.2 to 2.4)**
SF-36 vitality	71.7 (1.5)	68.5 (1.6)	**-3.2 (-7.9 to 1.3)**	72.2 (1.7)	69.9 (1.5)	**-2.3 (-7.1 to 2.5)**
SF-36 general health perception	74.1 (1.7)	71.6 (1.6)	**-2.5 (-7.2 to 2.2)**	74.2 (1.8)	74.3 (1.7)	**-0.1 (-4.8 to 4.7)**
SFBI Frequency	4.8 (0.4)	6.6 (0.4)	**1.8 (0.7 to 1.9)**	4.8 (0.5)	5.3 (0.4)	**0.5 (-0.8 to 1.8)**
SFBI Bothersomeness	3.2 (0.4)	4.4 (0.4)	**1.2 (0.1 to 1.3)**	3.1 (0.4)	3.5 (0.4)	**0.4 (-0.7 to 1.5)**
VAS Health	76.2 (2.2)	71.7 (2.4)	**4.5 (-2 to 11.0)**	79.3 (2.2)	77.9 (2.2)	1.4 (-2.0 to 11.0)
Cumulative Surgeries performed (%) ††	125 (89)	42 (30)	**Δ 83 (59)**	125 (89)	55 (39)	**Δ 70 (50)**

†† Just before crossing over to surgery, patients (n=55) assigned for conservative treatment had a mean VAS leg pain score (CI) of 54.0 mm (46.2-61.8) and RDQ score (CI) of 15.0 (13.3-16.8).

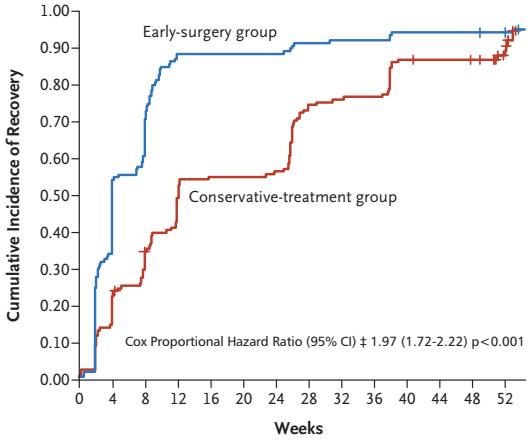

*Figure 3. Inverse Kaplan Meier Curves representing Cumulative Incidence of Recovery * † .*

Not recovered	*8w*	*26w*	*38w*	*52w*
Early Surgery	*54*	*13*	*10*	*6*
Conservative	*97*	*48*	*28*	*8*
Δ %	*36*	*22*	*9*	*6*
CI of Δ % §	*25-47*	*12-32*	*0.7-17*	*0.1-12*

Median time to recovery (CI 95 %) was 4.0 (3.7-4.3) weeks for early surgery and 12.1 (9.5-14.8) weeks for conservative treatment. The number of patients who had not yet recovered patients at each measurement are listed, with the proportion difference Δ (%) of recovered patients and 95 percent confidence interval.

** Recovery is defined as complete or near complete recovery using the Likert 7-point scale.*

† Log Rank (p< 0.001)

‡ The hazard ratio (with 95 percent confidence interval and p value) , obtained with the unadjusted Cox model, estimates the average ratio of recovery rate between patients assigned to receive a strategy of early surgery, versus the rate among those assigned to conservative treatment.

§ 95 percent Confidence Interval of Difference

a median period of 14.6 weeks, because of intractable pain expressed by a mean VAS-leg score of 54 mm and RDQ of 15.0, measured shortly before choosing surgery. In the early surgery group 3.2 percent suffered recurrent sciatica leading to a second surgical intervention, compared to 2 percent after delayed surgery. Complications occurred in 1.6 percent of all surgical patients, involving 2 dural tears and 1 wound hematoma. All complications recovered spontaneously. None of the patients developed neurological signs after surgery.

After randomization, RDQ curves (Figure 2) initially separate in favor of conservative treatment. The slopes cross at 4 weeks, indicating the moment when a better outcome was noted in the early surgery arm. The major difference in function was noted between 8 and 12 weeks. Analysis of the area under the curves (AUC) of the mean RDQ revealed no significant difference (p=0.13) over the 52-

week follow-up period. The difference between the AUC's of the mean VAS-leg pain however was significantly ($p<0.001$) in favor of early surgery. After surgery, leg and concomitant back pain diminished quickly whereas a slower and linear recovery of pain was noted in the prolonged conservative treatment group. One year after randomization the RDQ, Likert and VAS-leg pain scores however show nearly equal recovery rates for the two arms (Table 2). The subgroup of 55 patients with persistent sciatica and delayed surgery experienced identical improvement of these scores at one year, when compared those patients allocated to early surgery. The survival analysis (Figure 3; logrank $p<0.001$) highlights the influence of early surgery on the speed of recovery during the first 9 months, but the difference in cumulative incidence of recovery decreased over time with similar recovery rates of about 95 % for both groups after one year. Median time (CI) to recovery was 4.0 (3.7-4.4) weeks for early surgery and 12.1 (9.5-14.9) weeks for prolonged conservative treatment.

The Hazard Ratio as estimated in a univariable Cox model with recovery as an endpoint, was 1.97 (1.72-2.22), favoring early surgery. Analyses of treatment groups according to predefined baseline characteristics showed that surgery was beneficial in all subgroups assessed, with the possible exception of patients without sciatica provocation by sitting (Figure 4).

Discussion

Although relief of complaints was twice as fast for sciatica patients treated with early surgery, this multicenter randomized trial demonstrated that this strategy did not result in a better overall 1-year functional recovery rate when compared with a policy of prolonged conservative treatment with eventually offering delayed surgery. During one year 89 percent of patients in the early surgery group and 39 percent of the conservative treatment group were treated by microdiskectomy. At one-year follow-up no significant differences were detected in mean scores for any outcome measurement, including leg pain. Thus, the major advantage of early surgical treatment remained the faster relief of sciatica.

Slow recovery of daily functioning two weeks after early surgery may have been caused by standard microdiskectomy techniques when compared to modern micro-endoscopic or sequestrectomy methods[121-123]. This period was however followed by faster recovery during the following weeks, but without an overall significant difference over the first year. RDQ scores did not reach the minimal clinical important difference (MCID) of 4 points, required to conclude clinical relevance in favor of early surgery[114;118]. Leg pain exhibited a significantly faster recovery in the early surgery

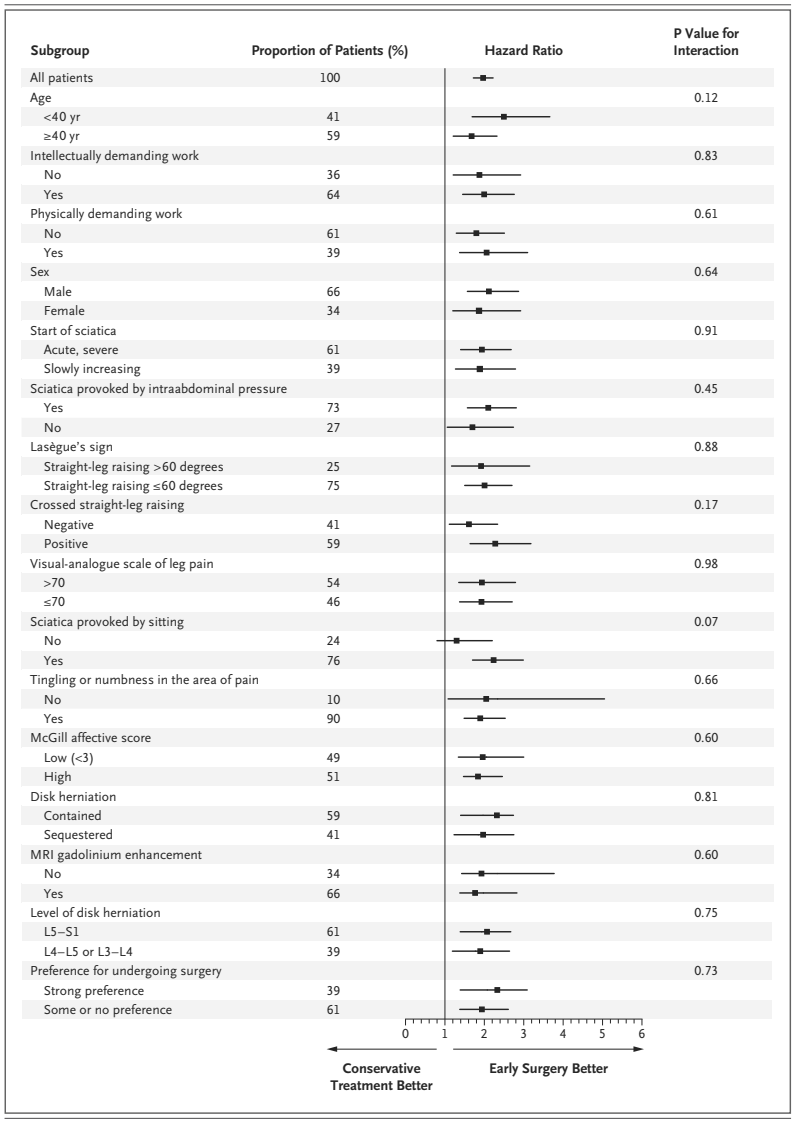

Figure 4: Time to complete recovery according to baseline patient characteristics. Hazard ratios (black squares), 95 % CI's (horizontal lines) show the effect within each subgroup. P values for the interaction between treatment effect and the predefined subgroup variables for prolonged conservative treatment versus early surgery are shown.

** These variables were dichotomized before entered in the Cox proportional hazard model. Results were comparable when analyses of continuous variables were performed.*

† Lasègue's sign was defined positive if the examiner observed a typically dermatomal area of pain reproduction and pelvic muscle resistance during unilateral provocative straight leg raising below an angle of 60 degrees, and crossed positive if the same experience was noted raising the other leg below 90 degrees.

‡ The McGill affective score measure the qualitative perception of pain by the patient. High affective dimensional scores correlate to a more depressed and anxious individual mood when compared to patients who report low affective scores.

§ Sequestrated disk herniations are defined by a defect in the annulus fibrosis and loose disk fragments in the epidural space, visualized by MRI scanning.

group but maximum differences between mean scores were less then 20 mm, on a 100 mm scale, and at one year scores approached equivalence.

The benefits of surgery on speed of recovery and pain relief were consistent among all predefined subgroups except for patients who did not have provocation of sciatica by sitting. The interaction level is however marginally significant and the majority of patients (76 %) did experience provocation of sciatica by sitting. It is however reasonable to assume that daily functioning is highly influenced by the impossibility to sit. Remarkably and unexpected were the absent interactions of Lasègue's sign, pain intensity, MRI disk sequestrations and patient preferences with treatment strategies.

Since 1934 many studies have demonstrated the success of surgical treatment of sciatica. Weber's landmark study comparing surgery with conservative care in a randomized clinical trial, excluding patients with "intolerable" pain, demonstrated surgery to be superior at one-year follow-up while after four years the results no longer differed[40;124;125]. Surgery did show some early benefit in a randomized study[126] comparing surgery to corticosteroids. Weinstein et al. recently reported the results of their carefully designed SPORT trial trying to answer the same research question but failed to show any benefit of surgery on primary outcomes in their intention-to-treat analyses[49]. Substantial cross-over, however, occurred in both treatment arms leading to only 14 % proportional difference in surgery rates at six weeks. Furthermore only 59 % actually underwent this intervention after being allotted to surgery, apparently planned at highly variable moments in time during the first year instead of an early execution. Also in contrast to our study which enrolled patients with 6-12 weeks of sciatica, in the Weinstein et al study at least 20 % of patients at baseline had complaints for at least 6 months[122]. Notwithstanding the fact that primary outcomes of our study were also strongly influenced by a substantial crossover during conservative treatment, timing of surgery was executed early in the intervention arm. While 61 % of patients recovered quickly without surgery, the remaining 39 % continued to register relatively high pain and disability scores concordant with physical suffering for a prolonged period of time until surgery was performed. Recently Österman reported results of a comparable designed trial, showing the same trend with earlier recovery of those assigned to surgery and nearly 40 % undergoing seemingly "inevitable" surgery during conservative management, but did not accrue enough patients to gain adequate statistical power[66].

Sciatica results in high direct and indirect costs[77]. Most of these costs are not generated by medical treatment but are attributed to production loss. Annually more than 1.5 million disk surgeries are performed[127] worldwide, using different time windows for treatment. Prior studies did not succeed to evaluate how timing of surgery affects outcomes. Patients need a thorough understanding of the course of symptoms to in-

form their decisions about surgery. The results of this study will help in the decision making process.

This study had several limitations, which may limit the generalizability of its findings. Patients randomized to conservative therapy were guided by research nurses who participated in pain management. Although this additional support did not prevent surgeries in 39 % of patients with severe sciatica, it does not reflect usual care. This must be kept in mind when implementing a strategy of prolonged conservative treatment for general populations. It is clearly impossible to blind patients and independent research nurses. A methodological point of attention is the fact that "time until recovery" was calculated only at predefined moments in follow-up, leading to interval censoring. The exact date of recovery was not registered, but sampled at planned follow-up moments. This leads to an underestimated speed of recovery in the interval between the sampling time points, but affects both treatment groups in the same way.

The present study provides individual patients with sciatica, who are considering disk surgery, information about how early surgery and conservative treatment affect the three separate outcome parameters, i.e. disease specific disability, intensity of leg pain and time to recovery. Patients who are not able to cope with leg pain, experience an unacceptable slow natural course of sciatica and who want to minimize time to recovery of pain are likely to choose early surgery. Patients who are achieving control of pain that is acceptable to them may decide to postpone surgery with the hope that it will not be needed, without reducing the chance on complete recovery at twelve months. Although both policies result in equilibrium after one year, early surgery remains a valid treatment option for well informed patients.