# Timing of surgery for sciatica

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# 8

## GENDER & SCIATICA

**Influence of gender and other prognostic factors on outcome of sciatica; a post-hoc analysis of a randomized trial**

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## ABSTRACT

*Background:* Sciatica caused by a lumbar disk herniation is a frequently diagnosed disorder with a favourable natural course. While most prognostic studies focus on good outcome, patients might experience unsatisfactory results. Female gender has been found to be associated with chronic pain in other musculoskeletal disorders. Our aim is to quantify the relationship between gender and (1) rate of recovery and (2) outcome at one year.

*Methods:* Recovery was registered on a 7-point Likert scale for 283 patients with 6 to 12 weeks of persistent sciatica who participated in a randomized trial to investigate timing of surgery. Complete and near complete recovery were considered good outcomes. Function and pain were registered by the Roland Disability Questionnaire (RDQ) and a visual analogue scale (VAS). An univariate Cox model was used to study the influence of variables on rate of recovery while a univariate and multivariate logistic regression analysis evaluated variables predicting unsatisfactory outcome at 12 months.

*Results:* At one year unsatisfactory outcome was registered for 17 % of patients, 11 % of all males and 28 % of all females ($p<0.001$). Patients with an unsatisfactory outcome had worse RDQ and VAS scores compared to those who recovered satisfactorily ($p<0.001$). Women had a slower rate of recovery: HR 0.76 (95 % CI 0.59-0.99) and were associated with an unsatisfactory outcome represented by an unadjusted odds ratio of 3.3 (95 % CI 1.7-6.3) compared to males.

*Conclusions:* Besides a slower recovery rate, female gender was a strong predictor of unsatisfactory outcome at one year for patients with sciatica.

## Introduction

The total impact of lumbar spinal disorders on society is high, since they constitute the fifth most expensive disease category as far as hospital care is concerned and are even the most expensive disorder with respect to work absenteeism and disability[77]. Within this group of musculoskeletal disorders sciatica is an important subcategory. The literal translation of the Greek word 'sciatica' is hip pain , which leaves room for dispute about today's use of the word 'sciatica' in scientific communications. Undoubtedly "lumbosacral radicular syndrome" (LSRS) or sciatic neuralgia is a better description of the disease but it is not frequently used in peer-reviewed manuscripts. For this study sciatica is defined as intense leg pain in an area served by one or more spinal nerve roots and is occasionally accompanied by neurological deficit. The natural course of sciatica is generally favourable, since the radiating ache disappears in the majority of cases within 8 weeks of onset[51;79]. Prognostic studies usually focus on "excellent" outcomes at one year. The high indirect costs, however, due to absenteeism from work and disability are mainly caused by patients experiencing a slower pace of recovery and those with an unsatisfactory outcome in the long term. Insight into determinants of outcome is important in order to be able to inform patients and to guide management decisions.

Interestingly, some early studies[169;170] did show gender to be one of the few variables influencing the outcome of sciatica. Female gender compared to male appeared to predict worse outcomes. For unknown reasons this finding seems to have escaped the attention of studies on spinal disorders in the past two decades. Outcome studies of chronic pain management in general have reported that women experience more pain in more parts of the body, with greater frequency and for longer periods compared to men[171;172]. Explanations for such gender differences have included differences in emotional and coping responses to pain between men and women. Women not only report greater emotional distress, but may also use more emotion-focused problem-solving which may cause the less beneficial long-term outcomes[173;174].

Based upon the findings reported in early studies and recent pain intervention effectiveness trials in general, we hypothesized that female patients with sciatica would show (1) a slower rate of recovery in the short term and (2) experience a higher rate of unsatisfactory outcome in the long term compared to males with sciatica. Besides gender we analysed the influence of other demographic, neurological and radiological determinants on rate of recovery from sciatica and estimated the effect of the unsatisfactory outcomes at one year.

**Table 1 a.** Gender related demographic and clinical characteristics *

| Variable | *n* | Gender | | |
|---|---|---|---|---|
| | | Male (n=186) | Female (n=97) | p value |
| Age (yrs) | 283 | 42.4 ± 9.6 | 42.9 ± 10.1 | 0.66 |
| Duration sciatica (w) | 283 | 9.4 ± 2.0 | 9.6 ± 2.5 | 0.49 |
| Time intake to randomization (w) | 283 | 2.3 ± 1.0 | 2.4 ± 1.4 | 0.45 |
| Randomization (%) | 283 | | | 0.38 |
| Surgery | 142 | 48 | 54 | |
| Conservative | 141 | 52 | 46 | |
| Timing of surgery n(%) | | | | 0.35 |
| Operated < 4 weeks | 116 | 71(40) | 45 (49) | |
| Operated between 4-26 weeks | 44 | 32(17) | 12(12) | |
| Not operated or later than 26 weeks | 123 | 83(43) | 40 (39) | |
| Absence from work (%) | 220 | 88 | 84 | 0.45 |
| Mentally demanding job (%) | 167 | 73 | 46 | <0.001 |
| Physical job (%) | 100 | 41 | 33 | 0.13 |
| Spouse/partner | | | | |
| Yes (%) | 215 | 77 | 74 | 0.66 |
| Children | | | | |
| Yes (%) | 193 | 69 | 67 | 0.68 |
| Smoking | | | | |
| Yes (%) | 117 | 41 | 42 | 0.47 |
| Body mass index (kg/m2) † | 283 | 26.0± 3.7 | 25.1 ± 3.8 | 0.05 |
| Sciatica provoked by ….. | | | | |
| Sitting (%) | 215 | 80 | 81 | 0.74 |
| Coughing, sneeze (%) | 206 | 69 | 79 | 0.24 |
| Straight leg raising (degrees) | 283 | 75. ± 24.4 | 74.9 ± 23.9 | 0.94 |
| Positive < 60 degrees (%) ‡ | 207 | 77 | 70 | 0.15 |
| Crossed leg raising positive (%) | 167 | 58 | 62 | 0.53 |
| Bragard test positive (%) | 83 | 22 | 46 | <0.001 |
| Preference for surgery (%) | | | | |
| Strong | 111 | 39 | 39 | 0.97 |
| Roland Disability § | | | | |
| Baseline | 283 | 15.9 ± 4.2 | 17.3 ± 3.9 | 0.009 |
| Outcome at one year | | 2.7± 4.3 | 5.0 ± 7.0 | 0.001 |
| VAS legpain in mm ¶ | | | | |
| Baseline | 283 | 63 ± 19.9 | 72 ± 20.1 | <0.001 |
| Outcome at one year | | 8.0 ± 13.9 | 16.6± 26.3 | <0.001 |
| VAS backpain in mm | | | | |
| Baseline | | 29.9 ± 27.4 | 37.1 ± 30.3 | 0.042 |
| Outcome at one year | | 12.7 ± 17.4 | 20.5 ± 28.4 | 0.006 |
| Recovery at one year, n (%) | | | | 0.001 |
| Good outcome | 235 | 165 (89) | 70 (72) | |
| Unsatisfactory outcome | 47 | 20 (11) | 27 (28) | |

**Table 1b.** Pain and disability characteristics per outcome group at 12 months *

| | Outcome | | |
|---|---|---|---|
| | **Good (n=235)** | **Unsatisfactory (n=47)** | **p value** |
| Roland Disability § | 1.6 ± 3.1 | 12.8 ± 5.5 | <0.001 |
| VAS leg pain in mm ¶ | 5.1 ± 10.9 | 40.7± 25.5 | <0.001 |
| VAS back pain | 9.3 ± 14.5 | 45.8 ± 27.9 | <0.001 |

* Plus-minus value are means ± SD.
† Quetelet Index or Body Mass Index is calculated by dividing the weight in kilograms by the squared of the height in meters. Higher scores define overweight.
‡ Lasègue's sign is positive if the examiner observes a typically dermatomal area of pain reproduction and pelvic muscle resistance when the unilateral straight leg is raised below an angle of 60 degrees; it is called crossed positive if the same is noted when the other leg is raised below 90 degrees.
§ The Roland Disability Questionnaire for Sciatica is a disease-specific disability scale that measures the functional status of patients with pain in the leg or back. Scores range from 0 to 23, with higher scores indicating worse functional status.
¶ The intensity of pain is indicated on a horizontal 100 mm visual analogue scale, with 0 representing no pain and 100 the worst pain ever experienced.

## METHODS

### *Patients*

The Sciatica Trial provided extensive one year follow-up data on 283 patients after one year of follow-up who had suffered a period of 6 to 12 weeks of severe sciatica[129]. Eligible patients were 18-65 years of age, had a radiologically 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 with complaints was confirmed 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 had identical complaints in the past twelve months, a history of spinal surgery, bony stenosis, spondylolisthesis, pregnancy or severe comorbidity.

This randomized multicentre trial assessed the effect on outcome during the first year by varying the timing of surgery. Patients aged 18 to 65 years old were allocated randomly to either a strategy of prolonged conservative care, possibly with late surgery or early surgery preferably within two weeks. Independent academic research nurses assessed and recorded baseline sociodemographic factors, clinical symptoms and neurological nerve stretch signs. The individual interviews and physical examinations were performed in a standardized fashion and repeated at each visit to the research nurse.

**Table 2**. Univariate analysis of variables for rate of recovery by an unadjusted Cox proportional hazard model

| Variable | *n* | Univariate Cox Proportional Hazard analysis | | |
|---|---|---|---|---|
| | | HR | 95 % CI | p value |
| Randomization | | | | |
| Surgery | 141 | 1.97 | 1.72-2.22 | < 0.001 |
| Conservative | 141 | 1.00 | - | |
| Gender | | | | |
| Female | 97 | 0.76 | 0.58-0.99 | 0.04 |
| Male | 185 | 1.00 | - | |
| Age | | | | |
| <40 | 116 | 1.00 | - | |
| ≥ 40 | 166 | 0.87 | 0.68-1.12 | 0.28 |
| Mentally demanding job | | | | |
| No | 92 | 1.00 | - | |
| Yes | 166 | 1.17 | 0.90-1.53 | 0.25 |
| Physical job | | | | |
| No | 158 | 1.00 | - | |
| Yes | 100 | 1.03 | 0.80-1.34 | 0.80 |
| Housewife | | | | |
| Yes | 21 | 0.78 | 0.47-1.30 | 0.34 |
| No | 255 | 1.00 | - | |
| Start sciatica | | | | |
| Acute | 170 | 1.00 | - | |
| Slow increase | 111 | 1.10 | 0.86-1.42 | 0.43 |
| Sciatica provoked by ….. | | | | |
| Sitting | | | | |
| Yes | 215 | 0.72 | 0.48-1.06 | 0.098 |
| No | 67 | 1.00 | - | |
| Coughing, sneeze | | | | |
| Yes | 205 | 1.14 | 0.86-1.50 | 0.36 |
| No | 77 | 1.00 | - | |
| VAS leg pain | | | | |
| < 70 mm | 151 | 1.00 | - | |
| ≥ 70 mm | 130 | 1.00 | 0.79-1.28 | 0.97 |
| Straight leg raising | | | | |
| Negative ≥ 60 ° | 69 | 1.00 | - | |
| Positive <60° | 206 | 0.96 | 0.73-1.28 | 0.80 |
| Crossed leg raising | | | | |
| Negative | 116 | 1.00 | - | |
| Positive | 166 | 0.78 | 0.61-1.00 | 0.047 |
| Kemp's sign | | | | |
| Positive | 121 | 0.89 | 0.66-1.10 | 0.23 |
| Negative | 141 | 1.00 | - | |

**Table 2**. *continued*

| Variable | *n* | Univariate Cox Proportional Hazard analysis | | |
|---|---|---|---|---|
| Finger-ground in cm | | | | |
| >30 | 156 | 1.10 | 0.86-1.42 | 0.45 |
| ≤30 | 119 | 1.00 | - | |
| Bragard's test | | | | |
| Positive | 83 | 0.65 | 0.49-0.86 | 0.002 |
| Negative | 186 | 1.00 | - | |
| Sensory disturbance | | | | |
| No | 28 | 1.00 | - | |
| Yes | 251 | 0.95 | 0.63-1.41 | 0.79 |
| MRI-level herniation | | | | |
| L4L5 (and L3L4) | 105 | 1.00 | - | |
| L5S1 | 166 | 0.88 | 0.68-1.11 | 0.34 |
| MRI-sequester | | | | |
| No | 154 | 1.00 | - | |
| Yes | 107 | 1.16 | 0.90-1.50 | 0.26 |
| MRI-Gadolinium | | | | |
| No enhancement | 71 | 1.00 | - | |
| Enhancement | 138 | 0.83 | 0.61-1.11 | 0.21 |
| Preference surgery | | | | |
| Strong | 111 | 1.00 | - | |
| Mild | 171 | 0.95 | 0.74-1.22 | 0.70 |

***Interventions***

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

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 disc 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 disc herniation by an annular

**Table 3**. Univariate and multivariate log rank analysis of predicting factors for unsatisfactory outcome of sciatica.

| Variable | *n* | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|
| | | OR | 95 % CI | p value | OR | 95% CI | p value |
| Randomization | | | | 0.27 | | | 0.05 |
| Surgery | 141 | 0.70 | 0.37-1.31 | | 0.49 | 0.24-1.00 | |
| Conservative | 141 | 1.00 | - | | 1.00 | - | |
| Timing surgery after randomization | | | | | | | - |
| No surgery or later than 26 weeks | 116 | 1.00 | - | - | - | - | |
| < 4 weeks) | 121 | 0.78 | 0.08-1.48 | 0.49 | - | - | |
| 4-26 weeks | 43 | 1.05 | 0.13-1.97 | 0.92 | - | - | |
| Gender | | | | | | | |
| Female | 97 | 3.29 | 1.72-6.28 | <0.001 | 2.81 | 1.38-5.74 | 0.006 |
| Male | 185 | 1.00 | - | - | 1.00 | - | - |
| Age | | | | 0.10 | | | - |
| <40 | 116 | 1.00 | - | | - | - | |
| ≥ 40 | 166 | 1.76 | 0.89-3.47 | | - | - | |
| Mentally demanding job | | | | 0.09 | | | 0.89 |
| No | 92 | 1.00 | - | | 1.00 | - | |
| Yes | 166 | 0.56 | 0.29-1.09 | | 1.06 | 0.44-2.53 | |
| Physical job | | | | 0.67 | | | - |
| No | 158 | 1.00 | - | | - | - | |
| Yes | 100 | 1.16 | 0.59-2.29 | | - | - | |
| Housewife | | | | 0.015 | | | 0.37 |
| Yes | 21 | 3.26 | 1.26-8.44 | | 1.72 | 0.52-5.65 | |
| No | 255 | 1.00 | - | | 1.00 | - | |
| Spouse/partner | | | | | | | |
| Yes | 214 | 0.69 | 0.34-1.38 | 0.29 | - | - | - |
| No | 68 | 1.00 | - | | - | - | - |
| Children | | | | | | | |
| Yes | 193 | 1.26 | 0.63-2.52 | 0.52 | - | - | - |
| No | 89 | 1.00 | - | | - | - | - |
| Smoking | | | | 0.07 | | | 0.05 |
| Yes | 117 | 1.81 | 0.96-3.41 | | 2.01 | 0.99-4.1 | |
| No | 165 | 1.00 | - | | 1.00 | - | |
| Quetelet index | 282 | 1.03 | 0.95-1.12 | 0.50 | - | - | - |
| Start sciatica | | | | 0.79 | | | - |
| Acute | 170 | 1.00 | - | | - | - | |
| Slow increase | 111 | 0.91 | 0.47-1.77 | | - | - | |

**Table 3**. *continued*

| Variable | *n* | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|
| | | OR | 95 % CI | p value | OR | 95% CI | p value |
| Sciatica provoked by ….. | | | | | | | |
| Sitting | | | | 0.22 | | | 0.63 |
| Yes | 215 | 1.67 | 0.74-3.78 | | 1.26 | 0.50-3.20 | |
| No | 67 | 1.00 | - | | 1.00 | - | |
| coughing, sneeze | | | | 0.45 | | | - |
| Yes | 205 | 0.77 | 0.39-1.52 | | - | - | |
| No | 77 | 1.00 | - | | - | - | |
| VAS leg pain | | | | 0.32 | | | - |
| < 70 mm | 151 | 1.00 | - | | - | - | |
| ≥ 70 mm | 129 | 1.39 | 0.73-2.62 | | - | - | |
| Straight leg raising | | | | 0.81 | | | - |
| Negative ≥ 60 ° | 69 | 1.00 | - | | - | - | |
| Positive < 60° | 206 | 0.91 | 0.44-1.89 | | - | - | |
| Crossed leg raising | | | | 0.15 | | | 0.15 |
| Negative | 116 | 1.00 | - | | 1.00 | - | |
| Positive | 166 | 1.64 | 0.84-3.20 | | 1.75 | 0.82-3.77 | |
| Kemp's sign | | | | 0.70 | | | |
| Positive | 121 | 1.15 | 0.58-2.27 | | - | - | |
| Negative | 141 | 1.00 | | | - | - | |
| Finger-ground in cm | | | | 0.38 | | | - |
| >30 | 156 | 0.75 | 0.39-1.42 | | - | - | |
| ≤ 30 | 119 | 1.00 | - | | - | - | |
| Bragard's test | | | | <0.001 | | | 0.006 |
| Positive | 83 | 3.80 | 1.92-7.50 | | 2.72 | 1.33-5.58 | |
| Negative | 186 | 1.00 | - | | 1.00 | - | |
| Sensory disturbance | | | | 0.39 | | | - |
| No | 28 | 1.00 | - | | - | - | |
| Yes | 251 | 1.73 | 0.50-6.00 | | - | - | |
| MRI-level herniation | | | | 0.88 | | | - |
| L4L5 (and L3L4) | 105 | 1.00 | - | | - | - | |
| L5S1 | 166 | 0.95 | 0.49-1.83 | | - | - | |
| MRI-sequester | | | | 0.61 | | | - |
| No | 154 | 1.00 | - | | - | - | |
| Yes | 107 | 0.84 | 0.43-1.63 | | - | - | |
| MRI-Gadolinium | | | | 0.04 | | | 0.04 |
| No enhancement | 71 | 1.00 | - | | 1.00 | - | |
| Enhancement | 138 | 2.94 | 1.07-8.06 | 0.04 | 2.88 | 0.98-8.45 | 0.05 |
| No gadolinium | 73 | 5.57 | 1.68-18.4 | 0.005 | 4.49 | 1.44-14.0 | 0.01 |
| Preference surgery | | | | 0.77 | | | - |
| Strong | 111 | 1.00 | | | - | - | |
| Mild | 171 | 0.91 | 0.48-1.73 | | - | - | |

fenestration, curettage and removal of loose degenerated disc material out of the disc space using a rongeur, without any attempt to perform a subtotal diskectomy. The duration of hospitalization depended on the patient's functional ability to mobilize. Normal 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.

Follow-up of patients at 2, 4, 8, 12, 26, 38 weeks and at one year was recorded according to the trial protocol[109] and included perceived recovery measured by a 7-point Likert scale, a VAS 100 millimetres intensity of leg pain scale, VAS back pain and disease-specific functional status measured by the Roland Disability Questionnaire for Sciatica (RDQ). The study was approved by all participating institutes and central and local ethics committees. All patients gave informed consent.

The present study included all patients from both groups of this randomized trial. Patients with 6 to 12 weeks of persistent sciatica, with an indication for surgery and eligible for trial participation were included in this analysis, irrespective of their randomization status. Except for the actual procedure and the moment of surgical intervention as a possible determinant, all baseline socio-demographic, neurological and radiological variables were collected shortly before randomization. In order to study the effect of baseline variables on speed of recovery the prescheduled moments of outcome registration during the first year were used, while the one year outcome was used to estimate the performance of these variables as predictors of an unsatisfactory result at one year.

***Statistical analysis***

Data were analysed with the SPSS package (version 14.0 for Windows; SPSS Inc, Chicago, IL, USA). Fisher's exact test for categorical variables or the t test for continuous variables was used to assess differences between baseline and outcome variables. To analyse time to recovery and the actual state of recovery at one year the 7 point Likert scale was dichotomized. "Complete" and "Near complete" recovery, considered to be indicative of good or favourable outcome, were defined as "recovery", while a score in the remaining 5 categories was concluded to be a poor or unsatisfactory outcome and thus defined as "no recovery".

Descriptive statistics describe the basic properties of "recovered" and "not recovered" patients as well as those of both genders. To answer the first hypothesis a univariate Cox Proportional Hazard model was used to study the influence of each variable on the short-term rate of recovery. The predictive effect of gender and other variables was analysed by univariate logistic regression analysis with "no recovery"

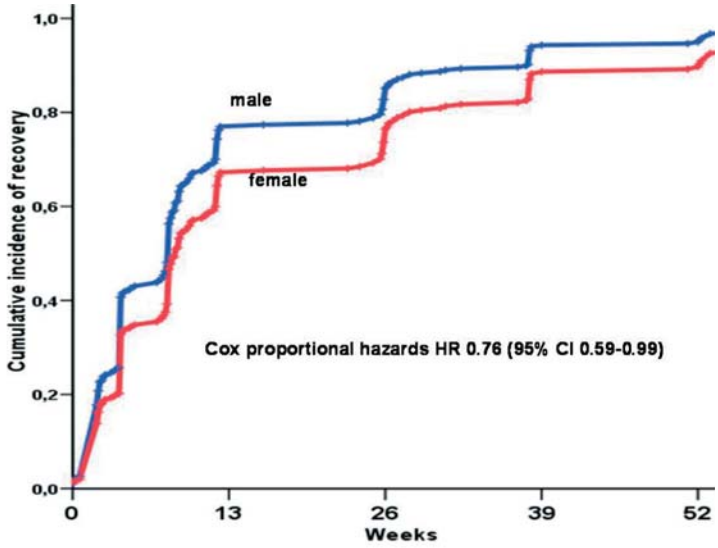



*Figure 1. Cox proportional hazard analysis of rate of recovery comparing females to males (p=0.04)*

at twelve months as the outcome of interest. The initial list of prognostic factors, chosen in advance by the investigators, was based on potential clinical importance, based on earlier published results[153;163] or current neurological textbooks. Variables were used for multivariate analysis if the univariate effects (Cox Proportional Hazard models and logistic regression, respectively) were significant with a p-value $<0.10$. The multivariate modelling process itself was a stepwise backward approach starting with the above-mentioned variables, retaining those for which the two-sided p value in the multivariate model remained $\leq 0.05$. The result of randomization was always included in the multivariate model, regardless of significance since this factor is the original allocated treatment strategy itself. Repeated measurement analysis of variance was applied in case of continuous outcome measures (disability and pain) with both gender and randomization group as the main effects, while their interaction was assessed and possibly added to the model in a stepwise forward way.

### *Role of funding source*

The sponsor did not influence the study design and had no role in data collection, data analysis or writing of the report. The corresponding author had full access to the data and had final responsibility for the decision to submit for publication.

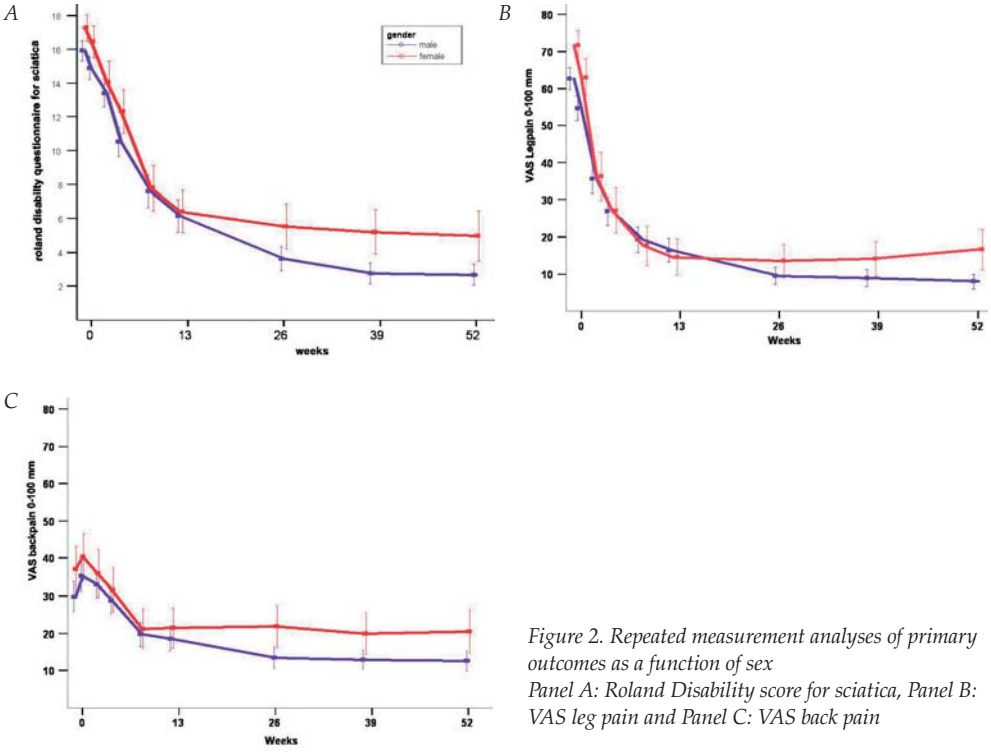



*Figure 2. Repeated measurement analyses of primary outcomes as a function of sex*
*Panel A: Roland Disability score for sciatica, Panel B: VAS leg pain and Panel C: VAS back pain*

## RESULTS

Allocation of an early surgical strategy resulted in 125 of 141 (89 %) patients who actually underwent lumbar diskectomy after a median period of 1.9 weeks, while of the 142 conservatively managed patients surgery could not be evaded in 55 (39 %) after a median time of 14.6 weeks. At different follow-up moments during the first year 269 of 283 (95 %) patients registered complete recovery. At exactly 12 months, however, 83 % of patients reported complete recovery. The patients with a good outcome at 12 months of follow-up showed a mean RDQ score of 1.6, VAS-leg of 5.1 mm and VAS-back 9.3 mm, while the 17 % of patients with an unsatisfactory outcome had a mean RDQ score of 12.8, VAS-leg 40.7 mm and VAS-back 45.8 mm at 12 months ($p<0.001$) (Table 1b). At intake 97 (34 %) of 283 patients were female. Demographic characteristics of male and female patients were not different at baseline, except for mentally demanding work rated by the patient (Table 1a). Clinical variables, such as disability and pain, showed significantly different baseline values, such that females experienced somewhat worse sciatica at intake. For the patients allocated to conservative treatment, no proportional difference

was noted between genders as far as patients who crossed over to delayed surgery is concerned. Results at 12 months showed a significantly different outcome between genders with 28 % of females exhibiting an unsatisfactory perceived outcome versus 11 % of males (Table 1). The result of the perceived recovery score was consistent with other outcomes such as the mean VAS leg pain, back pain and RDQ functioning scores (Table 1 and Figure 2).

Cox proportional hazard analysis showed a slower rate, HR 0.76 (95 % CI 0.59-0.99) to complete recovery for females as compared to males (Table 2; Figure 1), while interaction with timing of surgery did not influence the result[129]. Other variables with a negative influence on speed of recovery were a positive Bragard's sign and crossed leg raising test.

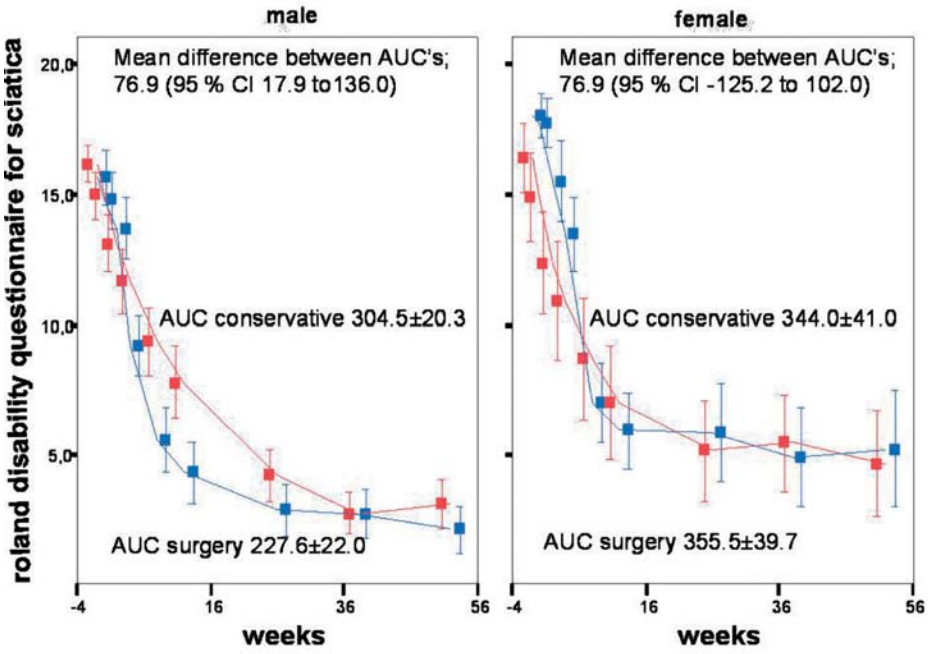
Table 3 shows the results of univariate and multivariate logistic regression analyses of prognostic variables for "no recovery" at 12 months, irrespective of intermediate recovery. In the univariate logistic regression analysis, a clear association between gender and outcome was found. Compared to males, females had a univariate Odds Ratio of 3.29 (95 % CI 1.72-6.28) for an unsatisfactory outcome ($p<0.001$). A positive Bragard test, MRI enhancement by gadolinium, and smoking rendered a significantly higher chance of an unsatisfactory outcome. Likewise did the variable "type of work" after dichotomizing into housewife and other jobs.

Only gender and Bragard's sign were expressed consistently across both analyses. In both logistic regression models and the Cox regression models timing of surgery and neurological, radiological and intensity of pain variables did not have any predictive value for outcome at 12 months, while the effect of gender on outcome was unequivocal.

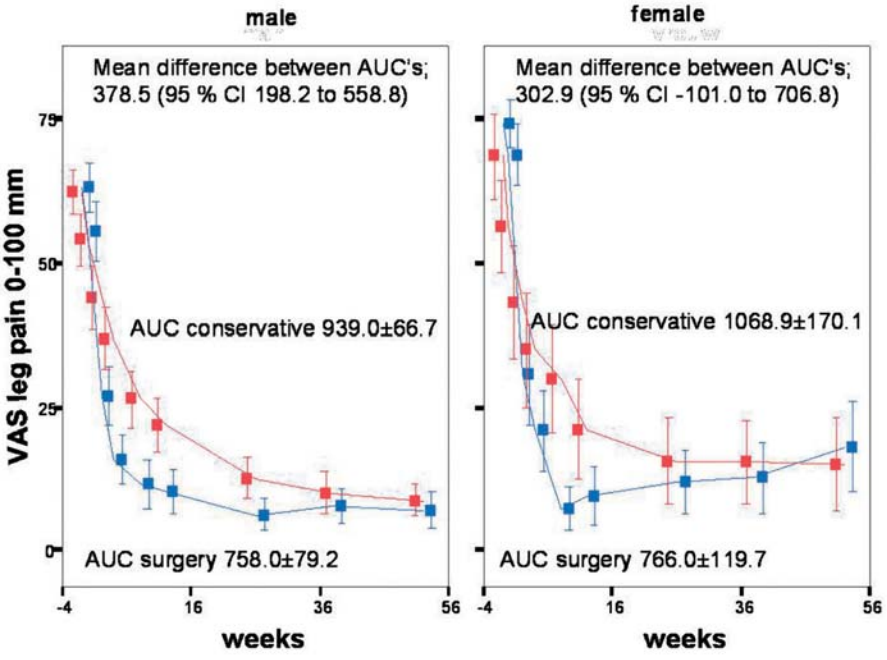
Multivariate analyses showed consistent findings for gender, but also for Bragard sign, gadolinium contrast enhancement and smoking (table 3). Furthermore the risk of unsatisfactory outcome was influenced significantly ($p=0.05$) by the allotted treatment strategy with an odds ratio of 0.49 (95 % CI 0.24-1.00) when corrected for gender in favour of early surgery. The estimated risks for an unsatisfactory outcome for the variables retained by multivariate analysis, vary substantially on specific combinations of risk factor values (Table 4). Figure 3, which illustrates the repeated measurement analysis results for the primary outcomes of the randomized trial stratified for gender, displays a smaller and not significant short-term effect of early surgery on early functional recovery in females. Differences between areas under the curves of all three primary outcomes over the first year after randomization are statistically significant for men in favor of early surgery and not for women.

With regard to experienced relief of disability, leg-pain and back-pain, the early surgery strategy does not seem to be as effective for females compared to men.

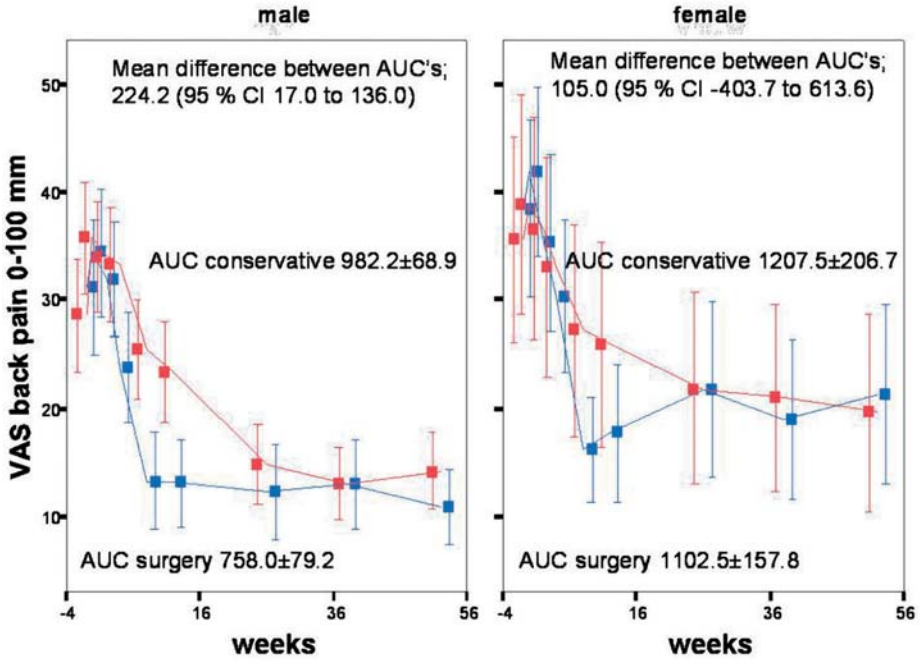
Those males and females who reported recovery at 12 months had similar RDQ




*Panel A*




*Panel B*




***Panel C***

*Figure 3. 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. Areas under the curve (AUC) are described by their means (SE).*

***Panel A** represents the mean disability scores at consecutive moments of measurement stratified by gender.*

*The overall difference between the areas under the curves over 12 months is not significant for females ($p=0.84$) and significant for males ($p=0.01$) in favor of early surgery.*

***Panel B** represents mean visual analogue scores for intensity of leg pain in mm. The difference between the mean AUC's is not significant for females ($p=0.14$) and significant for males ($p<0.001$) in favor of early surgery.*

***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 for females ($p=0.68$) and significant for males ($p=0.03$)*

** The mean difference between areas under the curves are expressed by the corresponding 95 percent confidence interval*

**Table 4.** Estimated risks of unsatisfactory outcome at 12 months, based on a logistic regression model using gender, smoking, Bragard and randomization as main effects.

| Variable | Randomization | Gender | |
|---|---|---|---|
| | | Male (n=186) | Female (n=97) |
| **Smoking Yes** | | | |
| Bragard; Positive | Surgery | 18 % | 38 % |
| | Conservative | 31 % | 55 % |
| Negative | Surgery | 7 % | 18 % |
| | Conservative | 14 % | 31 % |
| **Smoking No** | | | |
| Bragard; Positive | Surgery | 10 % | 23 % |
| | Conservative | 18 % | 38 % |
| Negative | Surgery | 4 % | 10 % |
| | Conservative | 7 % | 19 % |

and VAS scores (Table 5). Under the unsatisfactory circumstances of not being recovered at one year, however, females scored significantly worse on both the pain and disability scales compared to males. The interaction between gender and perceived recovery on all three symptom outcome scores was significant, implying that the difference between males and females in any of these outcome scores depends significantly on whether they recovered or not.

## DISCUSSION

Our study showed unequivocally that female gender is an independent predictive determinant for an unsatisfactory outcome at one year after 6 to 12 weeks of severe sciatica. The estimated unadjusted (crude) odds for a long-term poor outcome was 3.3 higher for female patients with sciatica than for males and this finding was statistically highly significant. In addition females showed a slower perceived recovery from sciatica, but compared to conservative care it was still significantly faster after early surgery. Notwithstanding this important treatment result the early surgery strategy failed to yield any early treatment effects on intensity of leg pain in females compared to the original repeated measurement analysis of the non-stratified study population. Males, however, presented more pronounced early treatment effects which were significantly different in favor of early surgery for all three outcomes scales (Figure 3). Besides a worse initial value on all pain and disability scales for females, the latter also presented with higher pain and disability scores when they

**Table 5.** Mean disability pain scores according to outcome group and gender at 12 months *

| | Gender | | |
|---|---|---|---|
| **Outcomes** | **Male** | **Female** | **p-value †** |
| **Roland Disability** | | | <0.001 |
| Recovered | 1.7 (1.2 to 2.3) | 1.8 (1.0 to 2.7) | |
| No recovery | 10.6 (9.1 to 12.2) | 15.2 (13.9 to 16.6) | |
| **VAS leg pain in mm** | | | <0.001 |
| Recovered | 5.4 (3.3 to 7.4) | 5.0 (1.8 to 8.2) | |
| No recovery | 27.6 (21.6 to 33.5) | 55.9 (50.7 to 61.0) | |
| **VAS back pain in mm** | | | <0.001 |
| Recovered | 9.3 (6.7 to 12.0) | 8.8 (4.7 to 12.9) | |
| No recovery | 37.1 (29.5 to 44.6) | 53.7 (47.2 to 60.2) | |

* 12 months mean scores are described with their corresponding 95 % confidence interval (CI)

† P value interaction effect between gender and perceived outcome on Roland and VAS scores.

recorded unsatisfactory perceived recovery in contrast to males with unsatisfactory recovery.

In addition to gender, smoking and Bragard's sign seemed to be predictive of an unsatisfactory outcome too. When adjusted for gender, multivariate analysis resulted in a considerable treatment effect of the early surgery strategy compared to prolonged conservative treatment, such that the odds ratio for unsatisfactory outcome at one year was halved.

Irrespective of treatment the proportion of patients with a good outcome was 83 % at one year. Since this is the actual state of the patients at 12 months, this proportion is lower than the apparently high proportion of 95 % perceived recovery during the first year as indicated by survival analysis[129]. The explanation for this discrepancy is that a considerable proportion of patients had recurrent back or leg pain after initial recovery, which could not be taken into account during Kaplan Meier calculations, since the survival model measures the time until a good outcome occurs for the first time, ignoring any later deterioration of the patient. The results of this trial are comparable to previous prognostic studies[113;151]. Most of these studies focus on good outcome and not on predictions of unsatisfactory outcome. Since prolonged absence from work is influenced by persistent high RDQ scores and VAS pain scores, the mean RDQ and VAS pain scores of patients with an unsatisfactory outcome at one year in this trial represent painful and disabling suffering. Quantification of the degree of failure has not yet been reported.

Notwithstanding the unequivocal findings reported here one must interpret these results carefully. Since this study was not designed primarily to analyse gender influ-

ences on outcome, one might argue that the high odds ratio for poor outcome could be the result of multiple testing. The latter mechanism is quite certainly responsible for the fact that Bragard's sign was also indicated by the analyses as a predictive factor. Although this test was standardized and performed independently by trained research nurses, these positive neurological nerve stretch signs were found previously to be quite unreliable in diagnostic studies. However earlier studies[40;170] also showed less favourable outcomes of treatment of sciatica for females, but these were not quantified and supported by pain and disability scores. Furthermore Kosteljanetz[169] in his famous diagnostic placebo-controlled trial found a good outcome for 90 % of males, compared to only 60 % of females. A good result for 89 % of our males one year after treatment for sciatica is in agreement with information provided by general physicians and spine surgeons for all of their patients, irrespective of gender. The fact that only 72 % of the females in our study and even less in Kosteljantetz's study perceived a good outcome should be taken into account when aiming at the prevention of unsatisfactory outcomes and when informing patients.

In our study population a proportional gender difference was noted with a preponderance of male patients. This is remarkable since extramural epidemiological studies and conservative treatment trials could not detect differences in incidence and prevalence between genders. The baseline characteristics of patients, seeking surgical help in most hospital care intervention trials show a minority for females compared to men. Since utilization of health care sources for sciatica seems to vary between genders, females in surgical populations might differ in baseline characteristics from females in conservative treatment studies and males in surgical series. Although eligibility for surgery, as defined by the general practitioner and medical specialist, is supposed to be the same, female patients might be less willing to request surgery and may only consult the spine surgeon at a higher threshold of pain and disability compared to males. In surgical studies similar to the current trial, this hypothesis is supported by the fact that compared to males females present with higher baseline pain intensity and disability scores. This consistent observation suggests that the differences in perceiving pain severity between genders might be an important factor. Additional investigation is warranted to characterize the nature and practical impact of these effects. During the retrieval of patients, who opted for surgery for sciatica, differential selection bias might have occurred.

In several studies female gender appeared to be a risk factor for chronic pain and disability caused by other musculoskeletal pain disorders as well[175]. Recent basic and clinical research showed biological[176;177], social and behavioural[178;179] factors to contribute to the risk of pain-induced chronic disability in females. Most factors involved are difficult to influence with therapeutic procedures, whereas catastrophizing, more prevalent among females, forms an important prognostic variable for developing

chronic pain disorders and seems to be susceptible to treatment intervention[171;172]. There may be various reasons why females do worse in terms of pain relief. As stated above females in our study as in other surgical trials registered higher baseline values for pain and disability, suggesting a worse start when compared to males. However, baseline pain intensity and disability did not predict outcome at all and the analyses failed to show any confounding or interaction effects with the registered variables.

Minor differences in the low back disability questionnaire reporting as a function of gender have been described before[180;181].

The design of this randomized trial did not allow the investigators to perform an elaborate observational prognostic study. Preferably social-, psychological factors, somatization scores, co-morbidities more prevalent in females (e.g. irritable bowel syndrome and fibromyalgia) and hormone differences should have been registered to account for interaction and confounding effects while estimating the prognostic effect of gender on outcome. Furthermore variables to support the difference in the prevalence of catastrophizing between genders and the theory of social and cognitive behavioural effects were not measured. Despite the prospective nature of a randomized trial, this study has to be considered as a post-hoc subgroup analysis with all the inherent disadvantages, such as lacking registered baseline variables to control for in multivariable regression analyses and possible over-estimation of treatment effects. The findings however concur with some previous sciatica studies and recent biological and social pain theories, but the results of our repeated measurement analyses, with special regard to the randomization effect, need further confirmation by future studies. To improve care for sciatica patients a gender-specific approach might be necessary but these treatment modalities have not been studied yet. Observational studies, starting in an extramural setting, are needed to specify possible gender-specific factors, responsible for differences between utilization of health care services and worse outcomes. Until these data become available discussion about targeted treatment strategies remains highly speculative.

Classical predictive neurological signs and the site or morphology of the disk herniation did not influence results, whereas an unsatisfactory outcome at one year was influenced markedly by gender and smoking, but modified by early surgery in a favourable direction.

Prognosis and treatment of sciatica depend strongly on patient preferences and realistic expectations. The fact that female gender is with a slower rate of perceived recovery and a higher likelihood of unsatisfactory outcome must not be neglected and should be taken into account when informing patients individually.