Timing of surgery for sciatica

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SYNTHESIS & GENERAL DISCUSSION

"The art of medicine consists of comforting the patient for a few months while nature cures the sciatica. "
(Adaptation of Voltaire)

The majority of patients with sciatica recover in 2-3 months. After this period general practitioners refer patients with persistent leg pain to the neurologist or rheumatologist. A considerable proportion of these patients however are not diagnosed with a radicular syndrome or, if diagnosed, do not have a lumbar disk herniation. The exact course of natural recovery from sciatica over the first year is not known.

Several conclusions can be drawn from the randomized controlled trial, presented in this thesis. Undoubtedly early surgery for sciatica more quickly relieved the excruciating leg pain compared to the prolonged 'wait and see' strategy. The positive effect of early surgery on the speed of recovery was present for all subgroups except for patients without 'leg-pain provoked by sitting'. After one and two years the results of early surgery and prolonged 'wait and see' were not different. Female gender was a strong predictor of unsatisfactory outcome, but this finding resulted from post-hoc analysis and therefore affirmation of this finding and its possible implications on an individual and societal level needs future studies.

Timing of surgery was based on today's guidelines. Although not specifically designed for this purpose, one may question to what degree this thesis produces scientific support for the current guideline strategy for the timing of disk surgery. One unequivocal answer is hard to give.

This thesis assesses the efficacy of different timing strategies for surgical treatment of sciatica, caused by a lumbar disk herniation. In the first part of this chapter the implications of the results for patients with 6 to 12 weeks of persistent sciatica are discussed. Is this the appropriate time frame to consider disk surgery? Or is it better to await a finally favorable natural course?

By reviewing the literature (Chapter 2) and conducting a randomized controlled trial (RCT) we now have more knowledge about the results of the current guideline regarding efficient timing of surgery. Did we find the optimal period for 'wait-and-see' before surgery?

In the second part of this chapter new steps to optimize the treatment strategy for sciatica are discussed: comparison in an international context and implementation of a new strategy for timing of surgery based on patient preferences.

The optimal timing of surgery

Although the execution of the classical guideline recommending early surgery after 6 weeks of sciatica resulted in quicker relief of leg pain and gave a feeling of complete recovery sooner, it did not result in a higher proportion of recovery at 1-year follow-up compared to prolonged conservative care[129]. Furthermore our RCT (Chapter 4)

could not detect an overall difference in functional disability at 1 year between those receiving early surgery after a short period of sciatica on the one hand and those who had the intention to delay the execution of surgery on the other. A strong argument for the majority of patients to consider 'early' surgery was the fear of the sciatic pain to become chronic. This fear appears not to be justified, since our search to factors predictive of unsatisfactory outcome (Chapter 8) and the 2-year follow-up analysis (Chapter 9) did not show differences in chronic pain between the two strategies.

Probably surgery after 6 to 12 weeks of sciatica is optimal for those with sciatica provoked by sitting (Chapter 6) and for those with intense pain and high disease-specific disability scores, the baseline values of which predicted a higher probability on late surgery in the conservative treatment cohort (Chapter 7). However, since these results were derived from subgroup analyses these findings have to be addressed carefully. From a societal point of view surgery can be considered to be cost-effective over the first year, when a threshold of $ 50,000 per Quality Adjusted Life Year (QALY) is acceptable and definitely is cost-effective when $ 100,000 is deemed acceptable (Chapter 5). Although significantly different, the overall one-year difference in QALY's was quite low between groups, and early surgery did not yield a more favorable long-term effect on direct and indirect costs compared to prolonged conservative care. Early surgery did not result in the expected benefit in indirect costs.

Early surgery may be preferred by individuals who outweigh the gain of quick recovery against the favorable natural course, which in fact includes a substantial chance of late surgery. Sufficiently informed patients are now able to choose, and based on the new knowledge physicians and certainly society should not 'decide' for them [161].

WAS THE STUDY APPROPRIATELY DESIGNED TO DEFINE THE OPTIMAL WAITING PERIOD BEFORE SURGERY?

We conducted this trial to evaluate the effectiveness of the current guideline recommendation. The major arguments were the varying rates of low back surgery in Western society, with a relatively high one in The Netherlands and combined with doubt regarding the evidence underlying the internationally well accepted 6-week threshold, before surgery is considered. Since previous comparative studies[163;186;187] promoting early surgery had a non-randomized design and the landmark randomized study by Weber[40], advocating prolonged conservative care, did not include patients with severe sciatica, there was a scientific need to study a more representative

population. Since the main advantage of surgery compared to prolonged conservative care was expected to be the gain in time to recovery and prevention of chronic disability, power and design of the study were focused on short-term results of the current guideline and not on a comparison between surgery and non-surgical treatment per se. To evaluate the effect of surgical timing on chronic disability a longer follow-up period is necessary.

In some observational cohort studies delayed surgery after 8 weeks resulted in less favorable outcomes compared to surgery before this period[163;184]. Other studies with a comparable design but another time frame provided data that this threshold might be 8 or 12 months of persistent sciatica after which period the risk of an unfavourable outcome rises significantly[186;187]. Our trial results are not in conflict with the latter conclusions, but do reject the former. Surgical treatment of every patient with 6 weeks of persistent sciatica, with the goal to prevent unfavorable outcome or chronic pain, will result in an unacceptable high rate of interventions for a disease with a favorable natural course. Since our trial does not have the disadvantage of incomparable baseline groups of these observational studies, our results are of a higher level of evidence and support the conclusion that the optimal period of "wait-and-see" can be defined as longer than this attractively clear-cut 6 to 8 weeks period.

For defining the optimal period of 'wait and see' before surgery another study design has to be considered. In order to estimate the specific effects of surgery, theoretically sham surgery for the control group would definitely give the final answer. Obviously execution of such a trial is hampered by ethical objections. In addition only patients with moderate complaints might opt to be included in such a trial, leading to selection bias and a non-representative study population.

On the basis of our study we cannot answer the question: is the optimal period of waiting for surgery 6 weeks or should it be longer? Arguments are lacking to reject the current Dutch guideline recommendation about the timing of surgery. The data of our study, however, do support an "informed" decision strategy for patients and physicians to individually outweigh the advantages and disadvantages of both timing-of-surgery choices. In patients with severe sciatica one would expect individual preferences to present influence on surgical decision making and outcomes, like has been established in other diseases and low back related disorders. With regard to the short-term speed of recovery or 1-year outcomes this trial did not reveal any predictive or interaction effects between personal preferences on the one hand and the randomized treatment strategy on the other. Most patients accrued for participation in this study, however, wanted very urgently to undergo surgery. Patients, who preferred non surgical treatment were not included or hypothetically did not visit the general practitioners or neurologists at all. This variable selection bias inevitably influenced the results of both subgroup analyses of this study. Since ample evidence

presents for the high impact of preferences on surgical strategies and outcome we advise to reject our conflicting finding and to develop shared informed patient decision programs which incorporates individual preferences[168].

RESTRICTIONS IN PERFORMANCE

Although the over-all results of our study are unequivocal, some points of attention need to be highlighted and which may have some implications for future research and the daily care of sciatica patients.

- Since patients were referred by family physicians to neurologists, the eligibility criteria were checked. In order to exactly define how many patients were excluded, all patients should have been registered and reasons for exclusion given by the neurologist. However, compliance to this procedure was not optimal despite repeated requests from the research team. Although the baseline data of our sample of patients does represent severe sciatica, patients might have been excluded selectively.
- Research nurses guided the trial patients included in the randomized trial. Although this affected both randomized groups in the same direction, one might object that the conservative treatment group received more attention, which is not the case in usual care. We do not know what the effect size of this extra attention might be. To reassure future patients about the favorable natural course, attention should be given to sufficient counselling and education.
- Surgery was performed by the conventional microdiskectomy approach, with partial removal of degenerated disk material. Recent data show conflicting evidence regarding minimal conservative removal of the sequestrated protrusion only[123;188]. This might have affected the post-operative course in an unfavorable direction. We intentionally chose for this conventional approach because it involved usual care, and maintains to be the golden standard[64]. So far, microdiskectomy as an effective treatment method has not yet been overshadowed by other approaches.
- Generally it was advised to resume work 6 to 8 weeks postoperatively. As this was regular post surgical care during the execution of the trial, this might have resulted in a relatively small contrast in working disability between the two groups. Thus in favor of the conservative treatment arm during cost-effectiveness analysis since these patients started working again despite their pain (Chapter 5). In contrast during recent years the period of rehabilitation after surgery has been reduced to 2 weeks in most primary care settings.
- Some patients, assigned to the conservative treatment group, received conflicting information, regarding the 'necessity' for surgery, and this might have caused

them to request for surgery sooner. This could have been prevented by better cooperation with physiotherapists and primary care physicians. Hypothetically this may have resulted in a larger proportion of patients who underwent surgery in the conservative treatment arm than reasonably would have been the case if the protocol had been followed strictly.

Variations in outcome definitions

These are perhaps the most important points of concern

- When designing the study, early surgery was deemed to be superior if the Roland disability questionnaire resulted in at least an 3-point average difference during all follow-up moments during the first year[81;114]. Furthermore a perceived recovery difference of more than 20 % at one year would strongly support an early surgery strategy. Both null hypotheses were not rejected and despite this evidence in favor of prolonged conservative care, most reviewers and readers highlighted the difference in quicker recovery rates in favor of early surgery.
- Another hypothesis was time until complete recovery. However, the actual measurement of complete recovery was performed at pre-scheduled visits leading to interval censoring. Indeed it would have been more appropriate, if registration of recovery had been done at the actual (though difficult to observe) moment of perceived recovery. Again, this affected both groups, but hypothetically the prolonged conservative care group had a disadvantage because meetings with research nurses were scheduled at longer intervals in time after 3 months of follow-up, and delayed recovery might have occurred during these intervals.
- Furthermore the methodology of survival analysis does not take into account recurrent sciatica or other low back related complaints. After perceived recovery patients are excluded from analysis and if recurrence of complaints is experienced these patients cannot be re-enrolled. This is a major drawback of pragmatic studies investigating the effectiveness of treatments for disorders which might recur after recovery. For example in both randomization arms 95 % of perceived recovery was registered during the first year according to survival analysis, but at exactly 1 year and 2 years of follow-up 87 % and 80 % of all patients, respectively, reported that they had recovered. Some individuals reported complete recovery but later these same individuals, apparently suffering recurrent symptoms of leg or back pain, experienced no improvement or even deterioration compared to the pre-randomization status. To solve this problem, it may be necessary to redefine “recovery” by absence of symptoms for at least a well demarcated period of time. Unfortunately there are no simple statistical solutions to this problem that

affects not only spinal pathology, but rheumatologic and neurological disorders as well; however the theory of multi state models, currently becoming "popular" as an extension of survival analysis, for example in the framework of bone marrow transplants, may offer a perspective here too. In these (complex) models, the patient may enter a state of "recovery" but then leave that state again and return to it later; the transitions between various states describe the process of falling ill and recovery. It is worthwhile to investigate the application of multi state models in the context of the before mentioned disorders.

Despite these methodological drawbacks "The Sciatica Trial" irrefutably showed that the major advantage of early surgery for patients after 6 to 12 weeks of sciatica is quick recovery of leg pain and quality of life but the outcomes at one year are nearly equivalent to a strategy of prolonged conservative care with delayed surgery.

DOES OPTIMAL SURGICAL TIMING EXIST?

We designed this RCT (Chapter 3) to evaluate the current recommendation to carry out surgery early, i.e. after 6 weeks of sciatica. Previous reports showed a high incidence of low back surgery in the United States and The Netherlands[46]. Since medical opinions from other Western countries do not differ as to in the recommendations to consider surgery after an initial period of 6 weeks of persistent sciatica, it can be assumed that incidences reported in Cherkin's study apparently underreport the surgical prevalence from neighbouring European countries.

A recently published randomized trial by Weinstein et al. comparing surgery with non surgical treatment per se[48;49], included patients with highly variable duration of complaints. Their trial results support a rather conservative approach. A surgical strategy did not lead to significant differences compared to conservative care in the intent-to-treat analysis. In contrast to the main study, their observational cohort study did present some short term advantages of surgery over conservative care. Obviously this finding carries a lower level of evidence than their randomized controlled trial in which they could not reveal any short term superiority of surgery. As in our trial there was considerable cross-over from the conservative treatment arm to the surgical one. In the early surgical treatment arm of "The Sciatica Trial" this intervention was planned prompt after randomization, leading to a mean time of less than 12 weeks of complaints before surgery was executed. The timing of surgery in the Weinstein study, however, was left to the participating hospitals and patients, which resulted in varying periods in time during the first year before surgery was

executed. A substantial part of the patients did not undergo surgery at all, while they were assigned to this intervention. This lack of contrast between treatment groups might have resulted in the absence of differences. Besides the seemingly at random scheduling of surgery after allocation of treatment, patients were amply informed about both strategies by a video which might have changed the preferences of patients and caused them to be reluctant to undergo surgery. Moreover, the choice for primary outcomes of the SPORT study differed from our trial. While relief of pain and speed of global perceived recovery are of primary concern to patients and both issues are quite susceptible to treatment, the SPORT study designers decided to evaluate general perceived quality of life, measured by the Short-Form 36. Furthermore a substantial proportion of their patients had baseline sciatica for at least 6 months, resulting in quite variable duration of complaints as compared to our trial, which, because of the primary objective to evaluate early timing of surgery, only included patients with complaints for less than 12 weeks. In conclusion the apparently similar designs of both trials did have different objectives, analysis methods and patient populations and thus resulted in a more demarcated early treatment effect in "The Sciatica Trial". But the long term results of their trial[49], the Weber trial[40], the smaller Ostermann's study[66]and the present study provide no evidence in favor of surgery at 2 year follow-up. Apart from an early gain in recovery in Ostermann's and our study surgery did not prevent an unsatisfactory outcome better than the control group. This conclusion raises doubts about the role of surgery in the seemingly unaffected natural course of sciatica. One may concur that a RCT is needed to compare microdiskectomy with placebo or sham surgery. At least all these arguments raise doubt on the very existence of an optimal timing for surgery in the disease course applicable to all sufferers from it.

In addition the question arises whether the study offers data supporting an individualized optimal timing of surgery. Our trial protocol (Chapter 3) chose surgery delayed until 6 months after randomization for the conservative treatment arm. Since baseline complaints lasted on average 9 weeks (2 months) this period of 8 months of conservative care was expected. Despite strenuous efforts of patients, research team and physicians, most of the 55 surgical patients of the conservative arm were operated on well before this period resulting in a mean of 27 weeks of sciatica complaints before surgery was performed in the prolonged conservative care group. Therefore our trial results do not contradict the observational study of Nygaard[187], who described worse results for patients with at least 8 months of complaints compared with those experiencing shorter durations of sciatica before surgery was executed. Furthermore in view of the observed difficulties of conservative treatment for this very painful group it might be a hard job to perform a future

randomized trial in this group. However, we cannot state in general that the optimal period is 8 months.

For example, high leg pain intensity and the inability to sit and a confirmed disk herniation, might be good arguments for an individual patient to time surgery early which preference should not be disregarded because of the opinion of treating physicians. On the basis of patient preferences and good information about the alternative natural course combined with registered pain and disability scores (Chapter 7), we can at present conclude that the optimal timing of surgery is an individual question, which cannot be generalized to cover all primary or secondary care patients.

Current status and future research

Implementation of a shared health decision program for sciatica is necessary to improve health care for this specific group of low back disorder patients. Surgery is a safe and cost-effective method to conquer sciatic pain quickly. Most neurological and radiological signs do not predict the course of sciatica. Since pain and disability scores reflect the individual situation, exhibit a predictive value for surgery and can be used to monitor the patient with sciatica, there is a need for implementation of these scores in daily care to improve the quality of treatment. The occurrence of chronic disabling disease after a period of sciatica needs further study. At least early surgery does not prevent its development. More elaborate survival models are designed to evaluate recurrence of disease complaints (Chapter 10). For the purpose of future intervention prognostic spine studies these sophisticated but complex epidemiological calculations will be executed in close cooperation with the Department of Medical Statistics. The baseline data of the present study will be analysed using these multi-state models with the goal to predict unsatisfactory outcome at 2 and 5 years. Finally, in our quest to evaluate invasive treatments for spine disorders by comparative cost-effectiveness studies we have to search for novel more rigorous research methods to be better able to answer clinically important research questions.

Conclusion

The results of this thesis do not contradict, nor do they support the current strategy of early disk surgery after 6 weeks of sciatica. A hypothetical future study to describe the natural course of sciatica during the first year in detail will not change the discussion about the timing of surgery.

Compared to prolonged conservative care, early surgery quickly relieves sciatica,

especially for those unable to sit as a consequence of provoked leg pain. Furthermore those with higher VAS leg-pain en RDQS scores are at a greater risk to suffer prolonged disability and delayed surgery when treated conservatively. On the basis of the information acquired individual patients now are better able to decide for themselves since they can be informed about the expected outcomes of both treatment modalities.