Surgical management of degenerative disorders of the lumbar spine, with a focus on patients' perceptions

Ph.D. thesis

Tamás Fülöp Fekete

Semmelweis University
János Szentágothai Doctoral School of Neurosciences

Thesis supervisors: Péter Banczerowski, MD, Ph.D., DSc.
Dezső Jeszenszky, MD, Ph.D.

Official opponents: Tibor Kovács, MD, Ph.D.
László Novák, MD, Ph.D.

Head of Ph.D. Examination Committee:
Dániel Bereczki, MD, D.Sc.

Members of Complex Examination Committee:
Alán Alpár, MD, D.Sc.
Árpád Dobolyi, MD, D. Sc.
Emília Madarász, MD, D. Sc.

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1. Introduction

Most people will experience back pain at some point in their life. Low back pain (LBP) has become the number one cause of disability, globally. Interestingly enough, the prevalence of LBP across different age groups shows less variability than previously suspected. Teenagers seem to have a similar prevalence to adults, although the pain is less disabling in this young age group. In contrast, elderly individuals are more disabled by the pain condition, rendering it a more relevant problem from the management point of view.

The other common condition affecting millions of people is sciatica, which was first described in ancient times. Sciatica refers to pain radiating from the buttock downwards, along the sciatic nerve. It is a less frequent condition than low back pain, but it is more frequently specific, i.e. an underlying morphological cause for it can be identified. In fact, the most common cause of radicular pain is related to an abnormality of the intervertebral disc. Both conditions are frequently the result of degenerative changes of the spine.

Advanced age is associated with increasing symptomatic degeneration of the musculoskeletal system. For the first time in human history there soon will be more people in the world over age 65 than under age 5. This profound population transformation will affect society in many fundamental ways, not least in relation to the health-care costs associated with the treatment of degenerative spinal diseases.

The most common degenerative disorders of the spine are lumbar spinal stenosis, disc herniation, degenerative spondylolisthesis, degenerative deformity and a heterogeneous group of segment degeneration including disc degeneration, facet joint arthrosis or synovial cyst formation. The majority of patients with these conditions are treated non-operatively. A small proportion

will develop a chronic condition or become so disabled that surgical treatment becomes necessary. The time-point over the course of the degenerative disease at which a more invasive therapeutic method (i.e. surgical intervention) should be implemented very much depends on the level of symptoms and the risk/benefit ratio of the planned intervention. Both the symptoms and the benefit are best assessed by applying patient reported outcome measures (PROM). There are many PROMs available, with various scopes (general health-related quality of life instruments and various disease or condition specific questionnaires). Many years of development resulted in the creation of an instrument known as the Core Outcome Measures Index (COMI), first described by Mannion et al. in 2005. This core set of questions comprises a single item per domain and has been translated into more than 15 languages including Hungarian.

One of the most frequent conditions encountered in the elderly population is symptomatic lumbar spinal stenosis. Patients with spinal stenosis typically, but not necessarily, have symptoms of neurogenic claudication, i.e. symptoms that are aggravated by walking. To alleviate the symptoms of spinal stenosis, epidural steroid injections into the lumbar spine can be applied. However, a study by Radcliff et al. published in 2013, evaluating clinical outcome after ESIs reported disquieting results: those patients treated with ESIs were less likely to benefit from subsequent surgical or non-operative treatment compared with patients who had not received ESIs. This result was unexpected and contradicted the clinical experience of many specialists treating degenerative spinal disorders. The study was criticized for various reasons, including the failure to use a condition-specific instrument such as the Spinal

Stenosis Measure (SSM) as the primary outcome measure. Hence, a study to further investigate the issue, which included disease-specific outcome measures, was carried out.

The goal of spinal interventions is to improve patients' complaints, and the improvement is measured with PROMs. Such measurements allow for comparison amongst various treatment methods or amongst diagnostic groups. However, it is not always clear to what extent the quantitatively measured score-changes reflect a notable benefit to the patient. The concept of the patient acceptable symptom state (PASS) was introduced into the field of rheumatology some years ago. Whether the same concept was applicable in patients undergoing spine surgery remained to be elucidated.

Surgery always causes bodily harm, in terms of the tissue damage sustained due to the invasiveness of the procedure. Thus, even if the cause of the painful condition for which the surgery was indicated has been eliminated, the patient still needs time to recover. The length of this convalescence period depends on the preoperative condition of the patient, the underlying pathology and the invasiveness of the surgery, amongst other factors. The use of PROMs has become the gold standard for assessing the success of elective spine surgery, but there are marked differences across treatment centres in the time intervals and frequency of administration of such assessments. Standards are lacking, as to when, how often, and — importantly — for how long such measurements of patients' health related quality of life (HRQL) should be made.

2. Objectives

- The objective of the first study in this dissertation was to evaluate, within a multicentre study (the Lumbar Spinal Stenosis Outcome Study – LSOS),

the influence of prior ESI on the clinical outcome of patients treated either surgically or non-surgically for spinal stenosis. Outcomes were compared in two groups of patients who either did or did not receive an ESI in the 12 months prior to enrolment. The aim was to examine whether previous ESIs would result in inferior treatment outcome.

- Pain is the most common reason that patients seek treatment for degenerative spinal disorders. Surgical interventions aim to tackle the problem and relieve the pain, but rarely can they eliminate it completely. The benefit for the patient, i.e. the success of surgery, is dependent on the extent of pain reduction and the degree of residual pain. The objective of this second study was to determine the pain level that patients consider to be acceptable (referred to as the Patient Acceptable Symptom State, PASS) after surgery.
- There is a gradual improvement in the patient's symptoms over time following a surgical intervention. The third study sought to establish the time-point at which the effect of surgery plateaued. To this end, the changes in patient-rated outcome over time were monitored for the most common lumbar degenerative conditions

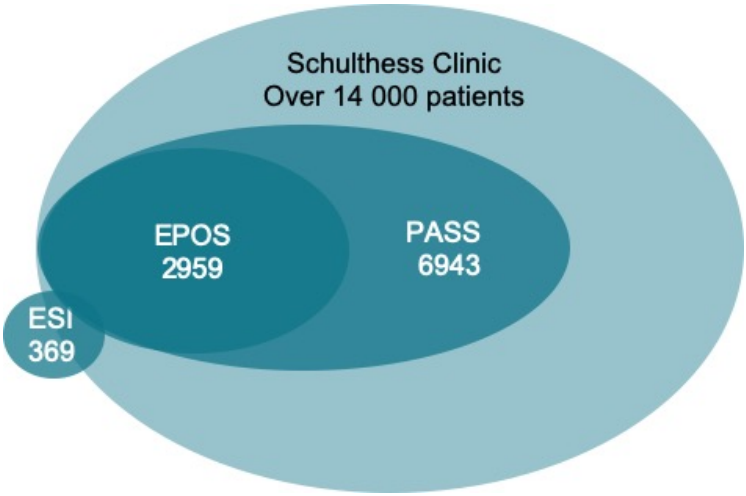
3. Methods

The indication for a diagnostic or surgical intervention and the selection of the corresponding surgical technique was chosen at the discretion of the treating spine specialist (physician or surgeon). The studies described in this dissertation report on the retrospective analysis of prospectively collected data. The single centre studies about PASS and the changes in outcome over time (EPOS) were carried out using the framework of the Spine Society of Europe

(SSE) Spine Tango Surgery Registry together with our own local patient-rated outcomes database. To be included in the above mentioned two studies, patients had to have undergone spine surgery for degenerative disorders of the thoracolumbar spine between 2005 and 2011 for EPOS and between 2005 and 2013 for PASS and have had no previous spine surgery at the same segment of the spine. The patients were further categorized in relation to their main diagnosis based on the fields ticked on the Spine Tango form, according to the Spine Tango diagnostic groups algorithm.

The study investigating the effect of prior epidural steroid injection (ESI) on treatment outcome was performed using data from a prospective, observational, multicentre study called the Lumbar Stenosis Outcome Study (LSOS).

The sample sizes in the different studies were very different, and varied depending on the disorder under investigation, the extensiveness of the investigations carried out and the complexity of participation for the patients. In the ESI study, a very specific degenerative disorder, namely spinal stenosis with neurogenic claudication, was closely and comprehensively analysed. Hence, even though a relatively short follow-up period of 6 months was used, and it was a multicentre study, the patient group comprised just 369 individuals.



For the PASS study, all types of degenerative disorder were investigated, using a simple outcome instrument and a follow-up period of up to 24 months. It was therefore possible to include a large number of patients (6943 patients). For the EPOS study, however, a much longer follow-up period of 5 years was chosen, and only patients with degenerative spine disorders who returned questionnaires at all of the five time points (preop; 3, 12, 24, 60 months postop) were included. As such, the number of patients that could be included was reduced to less than half (in total 2'959 patients).

In the ESI study, the Spinal Stenosis Measure (SSM) was distributed to patients at all participating centres. The SSM is a disease specific questionnaire with three subscales assessing the severity of symptoms (SSM symptom severity scale), physical function (SSM physical function), and satisfaction with treatment results (SSM satisfaction). The SSM symptom severity scale comprises a pain subdomain and a neuroischemic subdomain. Each item is rated on a scale with ordered responses.

For the PASS and the EPOS studies, patients completed the Core Outcome Measures Index (COMI) preoperatively and at 3, 12, 24 and 60 months' follow-up. The COMI is a short, validated, multidimensional outcome instrument. The questionnaire contains one question on each of the following: intensity of axial pain (back), intensity of peripheral pain (leg/buttock), back-related function, symptom-specific well-being, general quality-of-life, work-disability, and social disability.

Descriptive data are presented as means ± standard deviations (SD) or percentages, as appropriate.

3.1. Data analysis of the effect of epidural injections (ESI)

The primary analyses comprised comparisons of the change in the SSM score and its subscale scores from baseline to 6 months' follow-up between those with and without previous epidural steroid injections, for each of the two treatment groups (surgical and non-surgical treatment). The Wilcoxon rank sum test was used to evaluate raw differences between the groups. Additionally, multiple linear regression models controlled for covariates were fitted separately to the 6-month scores for the two SSM subscales, Physical Function and Symptom Severity, and to the two subdomains of the Symptom severity scale, Pain and Neuroischemic. The independent variables were surgical treatment (yes / no) and epidural steroid injection prior to baseline (yes / no).

3.2. Data analysis in the PASS study

The differences between groups were analysed using analysis of variance (ANOVA) (with posthoc Fisher's PLSD tests) for continuous data and contingency analyses with Chi-squared/Fisher's exact P test for categorical variables. The follow-up data collected 12 months postoperatively were used

for the main analysis of PASS for pain in the whole group of patients with degenerative spinal disorders. Receiver Operating Characteristics (ROC) curves were used to describe the probability of the pain score (the higher of leg pain and back pain) correctly classifying patients in PASS (sensitivity) and not in PASS (specificity) according to the external criterion –dichotomised response on the symptom-specific well-being (SSWB) scale. ROC is considered analogous to evaluating a diagnostic test, in which the pain score itself is the diagnostic test and the dichotomised SSWB response is the ground truth.

3.3. Data analysis in the evolution of patient-rated outcome after surgery for the degenerative disorders of the lumbar spine (EPOS)

Two-way repeated measures analysis of variance (ANOVA) with one between factor (either diagnostic group or treatment) and one within factor (time of assessment) was used to examine differences in mean scores between groups and over time (and their interaction) from preoperative to 3, 12, 24 and 60 months postoperatively. Pearson-product moment correlation coefficients were used to evaluate the relationship between the change scores from preoperative to each of the follow-up periods. The proportion of patients achieving the MCIC for the COMI at each time-point was compared at the different follow-up time-points using contingency analyses.

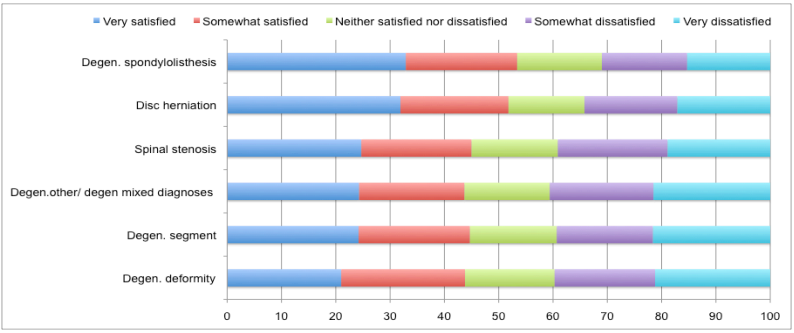
4. Results

From 2009 until 2014, 369 patients from 8 centres were enrolled into the ESI study. After applying the exclusion criteria, 281 patients were included in the analysis. A total of 229 patients were treated surgically between baseline and

6 months' follow-up: 111 of these had received an ESI in the 12 months prior to surgery and 118 had not. Fifty-two patients were treated non-operatively: 29 had received an ESI in the 12 months before study entry and 23 had not. The non-operative therapy consisted of physical therapy with or without oral analgesics. Seventy-nine % of the surgically treated patients received decompression only and 21% received additional instrumented fusion. In about two thirds of the patients, symptoms of lumbar spinal stenosis had been present for more than one year. The baseline scores of the SSM (all subdomains) and the Roland Morris disability questionnaire as well as the intensity of pain were all higher in patients undergoing surgery compared with patients in the non-operative treatment group. Changes in the unadjusted SSM scores between baseline and 6 months' follow-up were not statistically significantly different between patients with and without prior ESI, in either the surgical or non-operative patient groups. The adjusted effect of surgery versus non-operative treatment (negative values indicate greater improvement with surgery) was -0.41 ($p<0.001$) for SSM Symptoms, and -0.34 ($p=0.002$) for SSM Neuroischemic Pain. The adjusted effect of ESI prior to study entry (versus no prior ESI; negative values indicate greater improvement with ESI) was -0.08 ($p=0.40$) for SSM Symptoms, and -0.10 ($p=0.24$) for SSM Neuroischemic Pain. There was just one significant interaction between treatment group and ESI/no ESI prior to study entry, for SSM Function: the interaction effect was -0.46 ($p=0.01$) (having had an ESI (vs no ESI) led to less improvement in the non-operative group but not in the surgical group). This can probably be explained by the ongoing positive effect of ESI prior to inclusion into the study in the conservative group. This difference can be

measured only in the conservatively treated patients, where the changes over time are much smaller compared to the surgically treated patients.

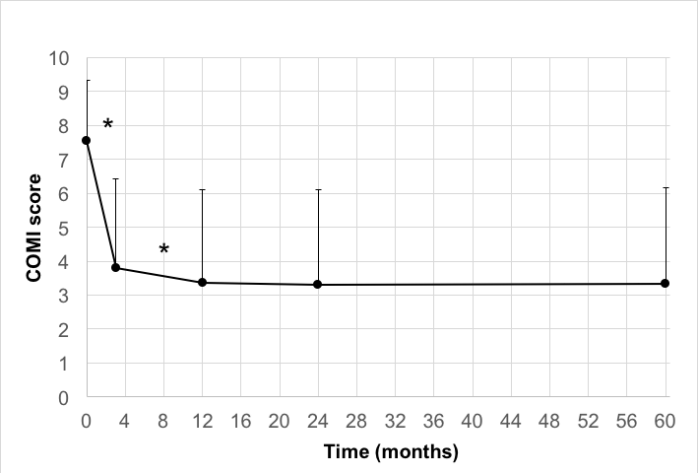
Extending the study sample to include all patients with degenerative disorders of the lumbar (thoracolumbar) spine yielded a larger patient population. We identified 6'248 out of 6943 patients who returned their 12 months' follow up questionnaire after surgery. The distribution of ratings for symptom-specific well-being (i.e. satisfaction with the current symptom-state) at 12 months' postoperatively, for each diagnostic group, is shown below.



The ROCs showed a cut-off value for an acceptable (satisfactory) symptom state of ≤2 points out of 10 on the pain scale for disc herniation and ≤3 points for all other pathologies. In other words, if a patient with lumbar disc herniation has a pain level of 2 or less, 12 months after surgery, he or she is expected to be satisfied with his/her symptom state; for any other type of degenerative disorder, the corresponding acceptable pain level would be 3 or less out of 10.

We also evaluated the how the patient-reported outcome changed over time after surgery for degenerative disorders of the lumbar spine (EPOS). Out of

the identified 4’287 patients without previous surgery at the same level of the lumbar spine, 2’959 patients sent back questionnaire at all five timepoints (1 preop and 4 postop questionnaires up to 5 years' follow-up). The COMI score of the whole group decreased significantly from pre-op to 3 months’ (by 3.6 ± 2.8 points, $p<0.05$), and from 3 months' to 12 months' follow-up (by 0.30 ± 2.4 points, $p<0.05$), then levelled off up to 60 months' follow-up (0.04-0.05 point-change; $p>0.05$).



There was a slight difference in the pattern of change, depending on the treatment modality. In patients undergoing decompression only, the COMI score did not change significantly beyond 3 months. In contrast, patients with fusion surgery showed further improvements up to 12 months after surgery, after which they achieved a stable value up to 5 years ($p<0.05$ for the interaction between treatment group and time of measurement).

5. Conclusions

- The analysis of patient-rated outcome in the multicentre LSOS cohort provided no evidence that the prior administration of an ESI had a negative effect on the 6-month result of surgery treatment, in patients with neurogenic claudication due to lumbar spinal stenosis.
- A new concept, the patient acceptable symptom-state, was applied for the first time in patients undergoing spine surgery. Using this concept, the "acceptable pain level" in patients after surgery for degenerative spinal disorders was determined. For most degenerative disorders, this is a score of ≤3 out of 10.
- The identified pain-threshold can be used as a criterion for denoting the presence or otherwise of "notable pain" when designing pain studies or epidemiological studies. Having a clear and measurable value provides a more valid basis for dichotomising patients into those with or without significant pain and this finding will hence contribute to better study design in future.
- The identified cut-off value for pain can also be used as a more stringent criterion to determine whether a treatment has been successful. Instead of determining how much improvement occurred following a given treatment (by measuring the change in pain score), the proportion of patients achieving an acceptable symptom (pain) state (i.e. achieving a score ≤3) can be determined. In other words, the target will be ensuring that patients feel good rather than just better, following an intervention.
- It has been shown for the first time that the greatest improvement in patient-rated outcome after surgery for degenerative disorders of the thoracolumbar

spine is seen in the first 3 months' postoperative, independent of the pathology and type of surgery.

- Simple decompression shows the fastest improvement. Fusion patients need somewhat longer to recover, and significant but not substantial improvement can still be seen between 3 months and 12 months postoperatively. A prudent recommendation for the minimum follow up for the procedures discussed in this thesis, and with the given inclusion criteria, would therefore be 3 months for simple decompression and 12 months for fusion. These findings can be taken into consideration when planning the follow-up schedule in everyday clinical practice or in clinical studies involving these patient populations.
- As the early postoperative results appear to herald the longer-term outcome, a ‘wait and see policy’ in patients with a poor initial outcome is not advocated. Instead, analysis of reasons for the failure to achieve a substantial improvement should begin at 3 months’ postoperatively, even in patients undergoing fusion surgery. This may avoid unnecessary suffering on the part of the patient.

6. List of own publications

6.1. Publications related to this dissertation

1. **Fekete TF**, Woernle C, Mannion AF, Held U, Min K, Kleinstuck F, Ulrich N, Haschtmann D, Becker HJ, Porchet F, Theiler R, Steurer J, Group LW. The Effect of Epidural Steroid Injection on Postoperative Outcome in Patients From the Lumbar Spinal Stenosis Outcome Study. Spine (Phila Pa 1976). 2015;40(16):1303-10. Epub 2015/05/07. doi: 10.1097/BRS.0000000000000969. PubMed PMID: 25943085.
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