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

Ph.D. thesis

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List of abbreviations

ANOVA	-	ANalasys Of Variance
ap view	-	antero-posterior view
AUC	-	Area Under the Curve
COMI	-	Core Outcome Measures Index
DegDef	-	Degenerative Deformity
DegSeg	-	Degenerative Segment
DegSpondy	-	Degenerative Spondylolisthesis
DH	-	Disc Herniation
EMG	-	ElectroMyoGraphy
EPOS	-	Evolution of Patient-rated Outcome following Spinal surgery
ESI	-	Epidural Steroid Injection
HRQL		Health Related Quality of Life
LBP	-	Low Back Pain
LSOS	-	Lumbar Stenosis Outcome Study
LSS	-	Lumbar Spinal Stenosis
MCIC	-	Minimal Clinically Important Change
$MCIC_{imp}$	-	Minimal Clinically Important Change improvement score
MEP	-	Motor Evoked Potentials
MIONM	-	Multimodal Intraoperative Neuromonitoring
MRI	-	Magnetic Resonance Imaging
NPRS	-	Numeric Pain Rating Scale
PASS	-	Patient Acceptable Symptom State
PLIF	-	Posterior Lumbar Interbody Fusion
PROM	-	Patient Rated Outcome Measure
ROC	-	Receiver Operating Characteristics
SCB	-	Substantial Clinical Benefit
SD	-	Standard Deviation
SEP	-	Sensory Evoked Potentials
SSWB	-	Symptom-Specific Well-Being
SS	-	Spinal Stenosis

SSM	-	(Swiss) Spinal Stenosis Measure questionnaire
TLIF	-	Transforaminal Lumbar Interbody Fusion
TNFα	-	Tumor Necrosis Factor alpha
VAS	-	Visual Analog Scale

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1 Introduction (literature overview)

1.1 Epidemiology of low back pain (LBP) and sciatica

The majority of people will experience back pain at some point in their life. The lifetime prevalence has been estimated to range from 11% to as high as 84%, and the point prevalence, from 12% to 33% (1). The wide range of values is partly explained by differences in the definitions of LBP used in epidemiological surveys. The prevalence is lower if LBP is defined as pain requiring sick leave, and is higher if a less stringent criterion is used, such as pain lasting for at least 1 day (2). In the last few decades, LBP has been recognised as a major problem throughout the world, and, with the ageing of society and increasing world population, the situation is getting worse (3). The most frequent reason for office visits to physicians used to be upper respiratory illness, with back pain ranking second (4). But now LBP has become the number one cause of disability, globally (5). This data is even more striking when considering that only a limited proportion (23% to 1/3) of individuals with LBP seek medical attention (6, 7). The number of physician visits due to LBP has not increased substantially over the last decade, but the associated expenditure has increased markedly, such that LBP now presents a major problem for most public healthcare systems (8).

An episode of LBP is usually self-limiting and transient, but 10-15% individuals go on to develop a chronic pain condition. According to an inception cohort study in Australia, about one third of patients will still have LBP 1 year after the onset of the initial pain episode (9). More worrying is the fact that 1 in 4 patients will have a recurrence of LBP within 12 months of a resolved pain episode, and having a history of low back pain is a risk factor for recurrence (10, 11).

Interestingly enough, the prevalence of LBP across different age groups shows less variability than previously expected. Teenagers seem to have a similar prevalence to adults, although the pain is less disabling in this young age group (12). In contrast, elderly individuals are more disabled by the pain condition, rendering it a more relevant problem from the management point of view (13). Furthermore, advanced age is associated with increasing symptomatic degeneration of the musculoskeletal system.

The other common condition affecting millions of people is sciatica, which was first described in ancient times (14). Sciatica refers to pain radiating from the buttock downwards, along the sciatic nerve. It is a much 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 (15, 16). The incidence of sciatica is reported to be around 10 per 1000 person per year, although this value varies depending on the definition and its relation to LBP (17). Women and individuals above the age of 45 years are affected more often (17).

The United Nations Population Division reported that in mid-2010 there were 523 million people in the world who were aged 65 years or more (18). It has been estimated that this will rise to 714 million in 2020, such that for the first time in human history there 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.

1.2 Low back pain, sciatica and degenerative disorders of the lumbar spine

The pathomechanism of painful spinal disorders is not completely understood. LBP is thought to be most commonly elicited by mechanical overload and/or degenerative processes, but the presence of tumor necrosis factor alpha (TNFα) (19) and nerve growth factor (20) may also play a role. Instability, spinal stenosis, intervertebral disc alterations, deformity or a combination of these may also underlie back pain. Two types of LBP are often described, namely specific and non-specific LBP, depending on whether the cause of the pain can be identified. Non-specific LBP is, by definition, a symptom of unknown origin (8). Ideally, with the advancement of medical science, the term non-specific low back pain will disappear. However, for now, it is a diagnosis of exclusion of a known origin for the pain. A relationship between the symptoms and clinical and radiological findings is more frequently found in sciatica than in LBP.

The major challenge in everyday clinical practice is to identify a causal relationship between radiological findings of spinal degeneration and pain, since such findings are

not symptomatic per se. Degenerative changes are encountered more frequently in patients of advanced age. Radiological imaging shows degenerative changes of the spine in a high proportion of asymptomatic individuals, increasingly so with age. Possibly, many of these degenerative changes are part of normal aging and not necessarily associated with pain (21). The imaging findings must therefore be interpreted with caution, within the context of the patient's clinical condition and in relation to the prevailing signs and symptoms. With the increasing size of the population and growing proportion of elderly individuals, symptomatic musculoskeletal degeneration is likely to increase rapidly in years to come. Such trends will necessitate a greater importance being placed on diagnostics, to be able to differentiate between physiological aging with asymptomatic degenerative changes and symptomatic degeneration of the spine.

1.3 Diagnostic workup – clinical diagnosis

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. Taking a careful history and performing a thorough physical examination of the patient have an important role in the diagnostic armamentarium of the physician.

The diagnosis of degenerative spondylolisthesis, degenerative deformity or other combinations of degenerative processes are difficult to establish solely based on the findings of a clinical examination. However, a combination of symptoms, such as mechanical low back pain and pain worsening during physical activity, are typical, and help to establish the appropriate treatment plan along with the imaging findings. In the case of LBP, it is sometimes difficult to categorize it as specific (with known cause) or non-specific (unknown cause). Examining the causal relationship between the radiological and clinical findings is a crucial step in the diagnostic workup of LBP. Depending on the severity of the symptoms, the neurological status and the amount of disability, further investigation by means of conventional standing X-rays or MRI scans can be considered, generally after a period of 6 weeks to 3 months. Disabling pain, severe and progressive neurological disturbances, or the presence of so-called red flags indicating a significant pathology (neoplasm, pathological fracture, etc.) might

necessitate imaging on first presentation, independent of the duration of pain history. If no specific cause can be found at the start of the diagnostic workup, after a series of consultations, diagnostic injections may be required. The latter include image-guided (ultrasound-, CT- or fluoroscopy-guided) interventions, where a drug is administered at or near the site of the suspected origin of pain and the change in the patient's pain is recorded. If the pain generator is thought to be the facet joint, then a facet joint or medial branch block can alleviate the symptoms (22).

In another group of degenerative conditions, the history and clinical examination alone typically shed some light on the underlying radiological entity. Patients with lumbar disc herniation usually present with unilateral radiating leg pain. On clinical examination, the sciatica can be reproduced by the ipsilateral straight-leg-raising test (Lasegue sign is positive). The sensitivity of this clinical test is high, but the specificity is low. In contrast, the contralateral straight-leg-raising test (crossed-Lasegue sign) has a high specificity but low sensitivity for disc herniation (23). A small proportion of patients with lumbar disc herniation continue to have debilitating symptoms and need a surgical intervention. The outcome is likely to be better if the preoperative symptoms are worsened by sitting (24). Predominating leg pain and lower levels of concomitant back pain are also associated with a better outcome (25).

In the elderly population, one of the most frequent conditions is symptomatic lumbar spinal stenosis. Patients with spinal stenosis often complain of radiating pain into the buttocks or legs. This symptom has a sensitivity of 88% but a specificity of only 34% according to a study by Katz et al. The same study found that, even in the absence of radiating pain, the low back pain relieved by sitting and elicited by standing had a sensitivity of 93% and a specificity of 46% (26). Spinal stenosis patients typically, but not necessarily, have claudication symptoms, i.e. worsening of the symptoms by walking (27, 28).

1.4 The role of epidural injections

The diagnostic value of injections into spinal structures is the subject of much discussion among spinal specialists. It is, however, an additional tool in the diagnostic and therapeutic armamentarium of physicians managing back pain and degenerative spinal disorders (22). A classic example of an indication for epidural steroid injection in

the lumbar spine is spinal stenosis. Epidural injections can be administered via transforaminal or interlaminar routes or via the sacral hiatus. Although the efficacy of epidural steroid injections (ESIs) in patients with lumbar stenosis is still a matter of debate, the number of injections in such patients tripled in the Medicare population from 1994 to 2001 (29). Some trial results indicate a short-term (3- to 6-month) benefit of ESIs in patients with lumbar spinal stenosis (30), but the majority of studies evaluating the longer-term efficacy (six months to two years) show no clinically relevant improvement compared with physical therapy (31) and the Guideline of the "North American Spine Society" recommends ESIs with some reluctance in patients with lumbar stenosis (32). Done in the correct manner, under contrast-enhanced fluoroscopy or CT-guided, ESIs are considered safe. The complication rate, including infection and bleeding, is very low. However, a recent study 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 (33). In both surgical and non-surgical treatment groups, pain and physical function were worse in the subsequent 4-year follow-up period in patients who had undergone ESIs in the three months prior to treatment. This result was unexpected, and the study was criticized for various reasons (34, 35), including the failure to use a condition-specific instrument such as the Spinal Stenosis Measure (SSM) as the primary outcome measure. Further studies were recommended in order to establish whether the findings could be reproduced.

1.5 Variation of indications for surgical treatment

Only a small proportion of patients treated conservatively 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 risk/benefit ratio of the planned intervention. The risks (chance of complication) have been discussed in many studies (36, 37) and will not be discussed here in detail. The benefit, i.e. the outcome can be measured in various ways and will be discussed in the next section.

The boundary at which a conservative patient should proceed to surgical treatment is ill-defined and so too is the indication for surgery. There are huge regional variations in the

rate and types of indication for spinal surgery (38, 39). In the early 1990's, the use of back surgery in the US was reported to vary from one area to another by as much as 15-fold (40). Medicare data from the Dartmouth Atlas Project showed that from 1992 to 2003 lumbar surgery rates in the USA increased markedly, especially for fusion (4-fold increase), and in 2003 there was an almost 20-fold variation in rates of fusion among geographical regions with demographically similar populations (41). In 2011, the rate of spinal fusion operations for stenosis had increased 67% to 52.7 per 100,000 Medicare beneficiaries, up from 31.6 per 100,000 in 2001 (42). Recent studies comparing France, Britain and the US have also shown substantial geographic variation (5-6 fold) for age- and sex-adjusted utilisation rates of spine surgery (43). Regional variations and an increasing use of spine surgical procedures (especially decompression combined with fusion) have also been reported for Switzerland (44). One of the most recent reports from the SPORT trial revealed that significant differences were found between its various study centres with regard to the enrolled patients' neurological deficit, stenosis location, severity and number of stenotic levels at baseline, as well as their functional outcome up to 4 years after surgery for lumbar degenerative spondylolisthesis (45). All this variation in thresholds for surgery and surgical rates is considered by some to — at least in part — represent evidence of medical uncertainty about the appropriateness of care (46, 47).

1.6 Measuring Outcome – the concept of acceptable symptom state

The uncertainty with respect to the appropriateness of care partly results from uncertainties regarding the likely outcome of surgical treatment. Treatment methods often rely on common sense, experience and tradition. In years gone by, surgeons recommended and performed surgery without involving the patients in the decision-making process. In recent decades there has been an evolution with regards to consenting patients for surgery, and informed consent of patients has now become routine. This was a major step forward, but the information delivered was mainly based on information delivered by the surgeon according to his/her own subjective perception. An example of such an outcome measure is the Macnab criterion recorded by the treating surgeon (48). This is a four-grade scale: excellent, good, fair and poor. The patient may well be asked for their impression of the outcome during the postoperative consultation, but the score is primarily intended to reflect the surgeon's rating. The item

became popular due to its simplicity and tendency to show good or excellent results. Other outcome measures based primarily on radiological results or technical success might have helped to improve and refine surgical techniques, but they probably created an overly rosy picture of the results and the success rate of surgical interventions. A more realistic type of outcome measure, based on the unbiased self-reporting of the result by the patient, evolved in the 90's (49). Such measures have become known as patient rated/reported outcome measures (PROM) and they are gaining increasing recognition. 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 (50). This core set of questions has been translated into more than 15 languages including Hungarian (51).

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 individual patient. For these reasons, the concepts of the "minimal clinically important change score (MCICimp)" (52) or score reflecting "substantial clinical benefit" (SCB) (53) have been introduced for quantifying the achievement of "relevant" improvement. Using terms such as "clinically important change" or "substantial benefit" may appear to tackle the essence of the problem, but there is no consensus on the interpretation of these expressions, since it is not defined "to whom" or "for what" they are important (54). To circumvent this seemingly semantic but very substantial question, the concept of the patient acceptable symptom state (PASS) was introduced in the field of rheumatology (55). Whether this same concept was applicable in patients undergoing spine surgery remained to be elucidated.

1.7 Evolution of patients' state over time following surgery

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 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.

Spinal fusion for various spinal pathologies is a common surgical procedure and radiological evaluation of the fusion status has long been considered the gold standard method for assessing the technical success of the treatment. As such, and in order to reliably assess fusion status, 2 years' follow-up has grown to become the accepted minimum time-frame for publication of outcome studies related to fusion. Possibly as a result of this, some journals continue to demand that reports on outcome after spinal surgery should include a minimum 2-year follow-up. However, the indiscriminate application of this principle to all types of spine surgery may not be appropriate.

As discussed above, 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 measures (56). There are no standards 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

1. The first line of treatment for lumbar spinal stenosis is conservative therapy, which is often enhanced and complemented by applying ESIs. If conservative therapy fails, surgical treatment is considered, and the latter seems to be more effective than conservative treatment (57). The objective of the first study in this dissertation was to evaluate the influence of prior ESI on the clinical outcome of patients treated either surgically or non-surgically in the Lumbar Spinal Stenosis Outcome Study (LSOS) (58). 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 surgical outcome.
2. 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 PASS) after surgery.
3. There is a gradual improvement in the patient's symptoms over time following a surgical intervention. This third study sought to establish the time-point at which the effect plateaued. To this end, the changes in patient-rated outcome over time were monitored for the most common lumbar degenerative conditions such as disc herniation, spinal stenosis, degenerative spondylolisthesis and lumbar degenerative deformity. From here-on in, this study will be referred to as the Evolution of patient-rated Outcome following Spine surgery (EPOS).

3 Materials and methods

3.1 Description of diagnostic workup, surgical techniques and intraoperative neuromonitoring

The results and conclusions presented in the second half of this thesis apply to the patient population treated mainly at the Schulthess Clinic. Whilst this limits the generalisability of the findings, the large number of treating physicians and spine surgeons working at the hospital over the years provides some diversity of treatment methods. There is a vast array of spinal interventions, techniques and implants available globally. Even the most common spinal conditions, such as lumbar disc herniation, can be managed in many different ways. A variety of conservative therapy regimes can be offered, and these can be supplemented by epidural steroid injections via the transforaminal, interlaminar route or via the hiatus sacralis. If an indication for surgery has been established, many different techniques can be used, such as microsurgical discectomy (described by Caspar (59)), discectomy through a tubular retractor (60), conventional (historical) discectomy through a laminectomy (61), or endoscopic discectomy (interlaminar, transforaminal, mono- or biportal) (62), to mention just the most common. The technique chosen is more likely to depend on the tradition of the hospital and region, and the education of the surgeon, than on hard scientific evidence. Because of this diversity of treatment methods, it is considered of importance to describe some of the interventions and techniques applied in the study population presented here. There are, of course, certain variations among surgeons; however, the similarities among them, when contrasted with other centres, outweigh the differences.
The background, rationale and technical details of the applied interventions will be described in this section. There are some surgeon or patient specific variations in the techniques described below, but the concept and the majority of the interventions are relatively homogeneous amongst the treating physicians/surgeons. A combination of interventions (i.e. epidural infiltration, and, later, decompression with or without fusion) was possible and the potential interaction between them was investigated in a study of the effect of ESIs on the outcome of patients undergoing subsequent lumbar spine surgery or non-operative treatment. The indication for a diagnostic or surgical

intervention and the selection of the corresponding surgical technique was decided by the treating physician or surgeon.

3.1.1 Lumbar epidural infiltration

The lumbar epidural space is a narrow space between the dural sac and the osteoligamentous boundaries of the spinal canal.

The pain generators in many painful degenerative spine conditions are believed to be located within the epidural space. This space is filled with a thin layer of areolar connective tissue (63). Some authors refer to this as the epidural membrane (64). Within this areolar tissue are the pronounced anterior and the less extensive posterior internal vertebral venous plexuses. Within this collection of veins is located the epidural fat. The latter is concentrated around the exiting nerve roots, i.e. in the intervertebral foramen and posterior to the dural sac in the midline recess between the dural sac and the interior surface of the ligamentum flavum. This epidural fat not only serves to provide thermal and mechanical insulation but also ensures a fine gliding of the neural elements within the osseous spinal canal. Previously, if this epidural fat tissue was present at the involved segment it was considered to be an indication that there was no significant neural compression (65). However, this seems not to be the case, as removal of excessive amounts of epidural fat has similarly good results to conventional lumbar decompression (66). It seems that the configuration of the dural sac on axial and sagittal MRIs and the relation of the epidural fat to the dural sac gives more information regarding the possibility of a clinically relevant compression of neural elements as seen in “Schizas Grade C” lumbar stenosis (67). The Schizas grading of spinal stenosis was published in 2010 and it describes the severity of the stenosis based on the relation of the rootlets of the cauda equine. If CSF around the rootlets is still visible at the level of the intervertebral disc on the axial T2 weighted images, it is graded as “A”, hardly any stenosis, or as “B”, mild stenosis. If the stenosis is more severe, but epidural fat is still visible on that level, it is called grade “C” stenosis. The most severe form of stenosis is the grade “D” where the individual structures of the spinal canal cannot be differentiated (68).

The most common conditions leading to spinal stenosis are facet joint hypertrophy due to osteoarthritis, spondylolisthesis, disc herniation, epidural fat accumulation or a combination of these conditions. The majority evolve slowly over a long period of time.

At the start, symptoms are mild, but they usually progress insidiously, often leading to a significant decrease in quality of life and pain if left untreated. As the pathoanatomical structures leading to stenosis have no tendency to spontaneously regress (except for disc herniation), physical therapy and exercise have a limited role in treatment in the acute phase. Oral analgesics and muscle relaxants are recommended as first line treatments. Alternatively, epidural injection of corticosteroids or local anesthetics can be applied to alleviate symptoms. As described above, the epidural space contains many (potential) pain generators. Applying drugs to this space can reduce oedema and thus decrease the intraspinal pressure, and can also directly alleviate pain by inhibiting the C-fibers (69). Hence, it not only serves as a treatment modality but also helps in the diagnostic work-up, as patients who respond well to an epidural injection are more likely to benefit from surgical decompression (70). In fact, historically, the diagnostic potential of nerve root blocks was first identified in the 1960s, at a time when the radiological workup consisted solely of radiographs and myelography, with limited diagnostic value. Response to diagnostic nerve root blocks and reproduction of the pain pattern deliver valuable information regarding the possible source of pain (71, 72). We still use this diagnostic modality today although the role and the interpretation has evolved in the past 5 or 6 decades.

There are three main routes for epidural infiltration of the lumbar spine: via hiatus sacralis (Figure 3-1), the interlaminar approach (Figure 3-2), and the transforaminal approach (Figure 3-3). Each of these has its own features rendering them more suitable in a specific case. The basic principle is to deliver the drug(s) as close to the suspected source of pain as possible. Administration via the sacral hiatus is technically easy: the entry point into the spinal canal is close to the skin surface and is in the majority of cases easily palpable.

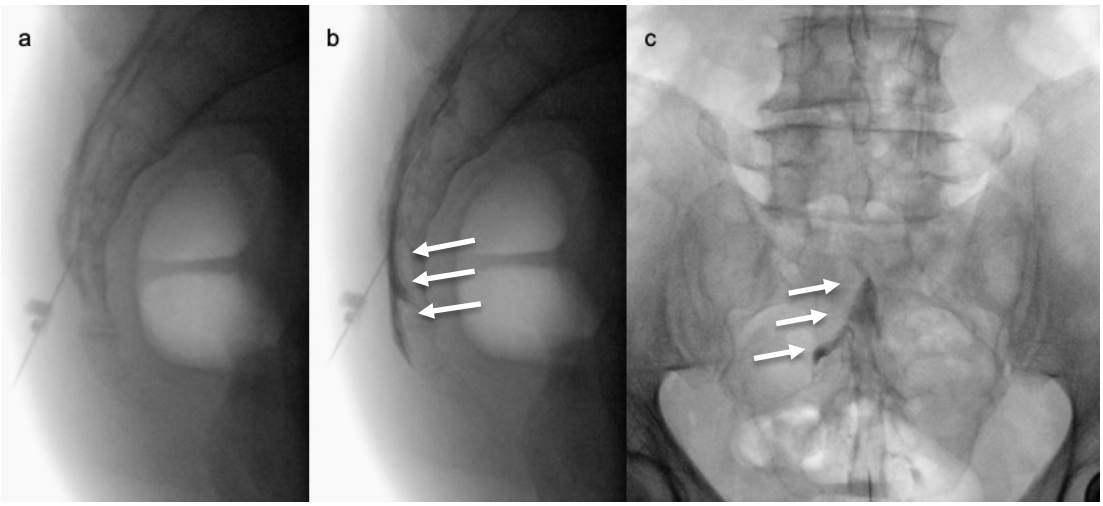


Figure 3-1: Epidural injection through the sacral hiatus with fluoroscopy. a; and b; lateral view (before and after injection of contrast agent). c; antero-posterior (ap) view after injection of contrast agent (white arrows).

A possible drawback is that various amounts of the applied drug can exit the caudal end of the spinal canal towards the sacral nerve roots and decrease the amount of drug available to exert the desired effect at the site of the pathology, usually the caudal most lumbar segments. If the spinal stenosis is located more cranially within the lumbar spine, or severe adhesions (e.g. postoperative scarring) are suspected caudally, then an interlaminar route allows for more efficient drug-delivery.

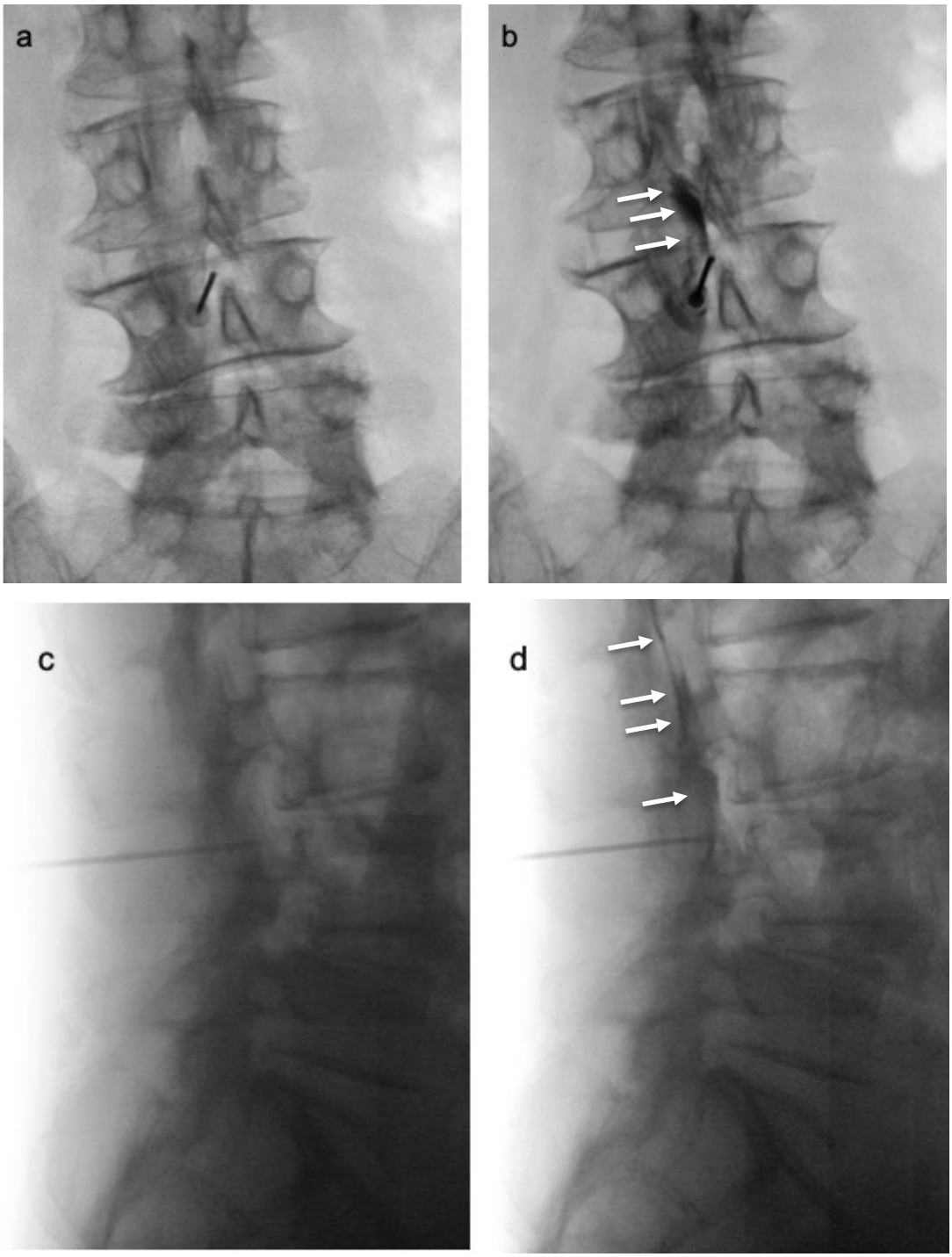


Figure 3-2: Lumbar epidural injection through the interlaminar space under fluoroscopy. a; and b; ap view. c; and d; lateral view. Note the distribution of the contrast agent in the epidural space (white arrows).

In some cases, where there is a a clear side-dominance to the pathology (disc herniation, foraminal stenosis), a transforaminal approach might offer the most accurate form of diagnostic application of local anaesthetics with or without corticosteroids.

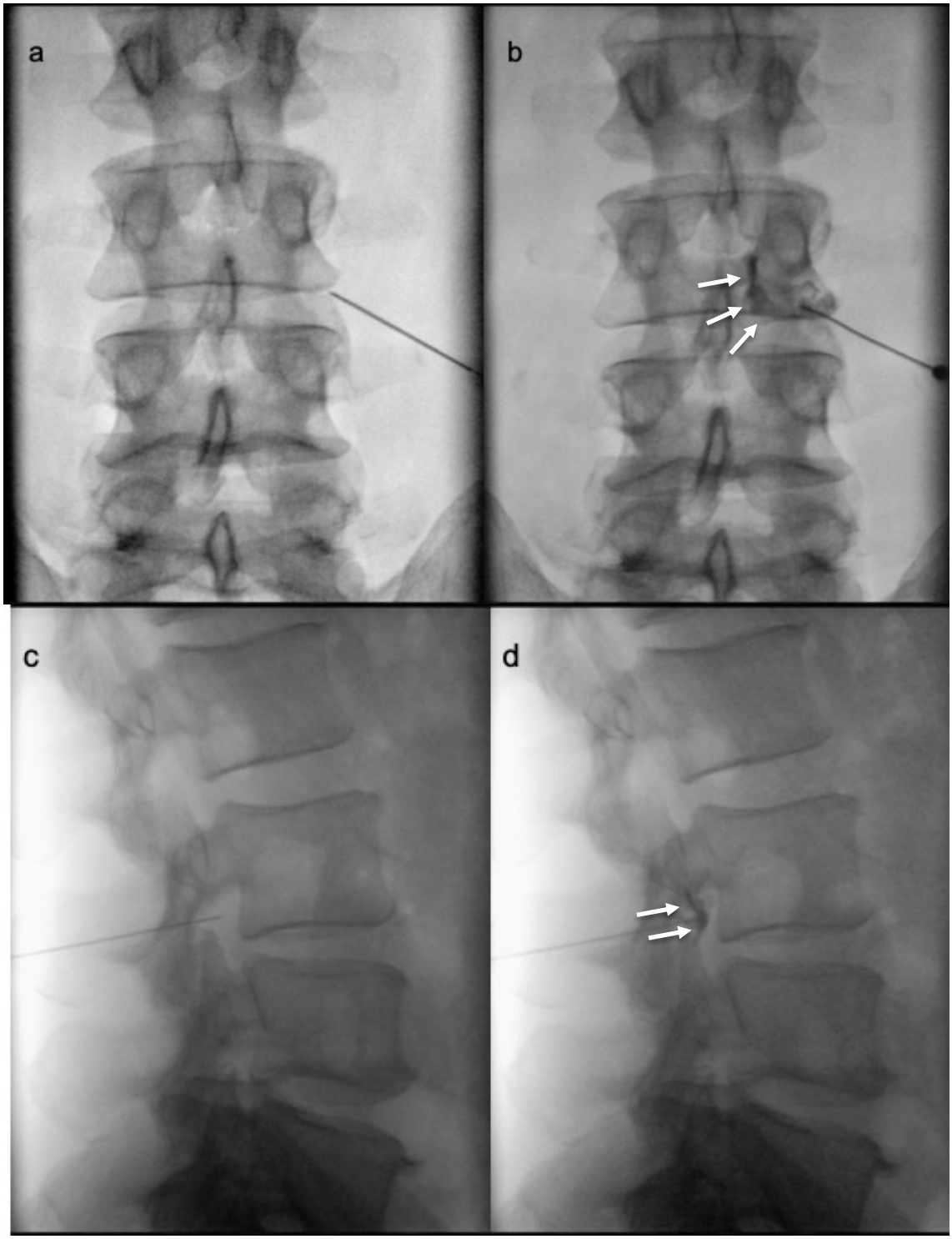


Figure 3-3: Transforaminal epidural injection. a; and b; ap-view. c; and d; lateral fluoroscopic images. Note again the distribution of the contrast agent in the epidural space (white arrows).

3.1.2 Lumbar microdiscectomy

The technique presented in the most cited report about surgical removal of the disc by Mixter and Barr in 1934 (61) was the gold standard for many decades. The introduction of the operating microscope in spine surgery was reported by Caspar in 1977 (59). Nowadays, this microdiscectomy technique, or modifications thereof, constitute the most popular technique for the surgical removal of the herniated disc.

The patient is positioned prone, although some surgeons prefer the modified "knee-elbow" position (Mecca-positioning) in order to open up the interlaminar space by reducing the lumbar lordosis. Following verification of the correct vertebral level by means of fluoroscopy, a midline or paramedian incision is made in the thoracolumbar fascia. A paramedian incision of the fascia, as originally described by W. Caspar, allows for a shorter incision. After placing the retractors, the interlaminar space is exposed and the caudal aspect of the cranial hemilamina (hemilaminotomy) is removed using Kerrison rongeurs or a high-speed burr. In some instances, especially at the lumbosacral level, the interlaminar space is sufficiently wide that it is not necessary to perform a hemilaminotomy or hemilaminectomy. In such cases, a U-shaped incision or resection of the yellow ligament (ligamentum flavum) is performed.

Once access to the spinal canal has been gained, the thecal sac and nerve root under compression can be mobilized and retracted medially. The protruding or sequestered disc material, the disc herniation, is then removed, thereby decompressing the nerve root.

3.1.3 Lumbar decompression

In the case of symptomatic central or lateral recess stenosis, a decompression of neural elements can be performed. Patient positioning is similar to the positioning for lumbar discectomy. The decompression can be performed through a midline approach exposing the interlaminar space bilaterally or unilaterally. When a bilateral approach is performed, the caudal third of the spinous process along with the caudal portion of the lamina is removed using a high-speed burr or Kerrison rongeur. The yellow ligament is detached and removed as part of the decompression. The medial aspect of the usually hypertrophic facet joint along with a portion of the facet joint is then removed until the neural elements are decompressed sufficiently.

An alternative to the above is the unilateral approach (Figure 3-4 and 3-5), which can be especially advantageous in patients with some scoliotic deformity of the lumbar spine. As scoliosis is inherently associated with a rotatory component, the lamina on the convex side of the curve faces more posteriorly than does that on the contralateral (concave) side and offers easier access to the spinal canal~~.~~ Accordingly, the decision regarding the approach depends mainly on the configuration of the curve, although other aspects may be considered as well. Right-handed surgeons prefer to approach from the left side. If the stenosis is further aggravated by a herniated disc, the side of the herniation should be chosen. This unilateral (monoportal, or over-the-top) decompression is carried out using a technique similar to that described by Matsumura et al (73). For a single level decompression, a midline incision is made to expose the posterior elements up to the medial part of the facet joint on one side. Using a high-speed burr (usually with a 4-mm diamond-tip) and a microscope, the caudal portion of the cranial lamina is removed until the cranial end of the yellow ligament and, laterally (on both sides), the medial aspects of the joint capsules are reached.

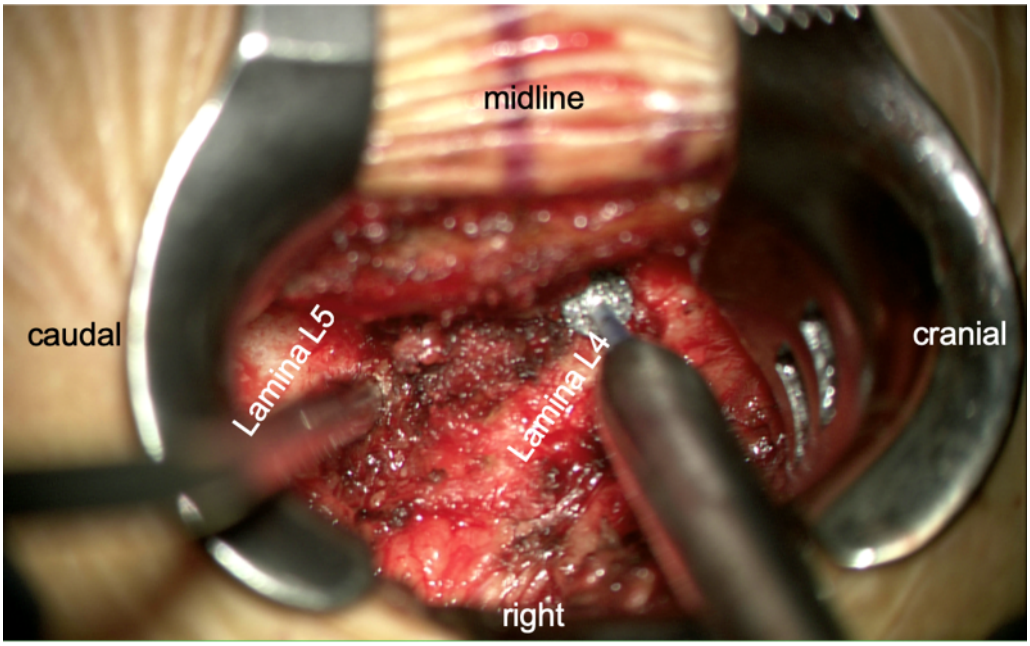


Figure 3-4: View through the operating microscope. The blades of the Caspar retractor are visible on the right (cranial) and left side of the image. The diamond-tip burr is placed on the transition of the lamina L4 and the ligamentum flavum.

Using a Kerrison rongeur and microcurette, the medial (on both sides), cranial, and caudal margins of the ligamentum flavum are detached. For working on the contralateral side, the operating table can be tilted approximately 20° away from the surgeon. Visualization of the contralateral side is enhanced by removal of the caudal base of the spinous process at that level.

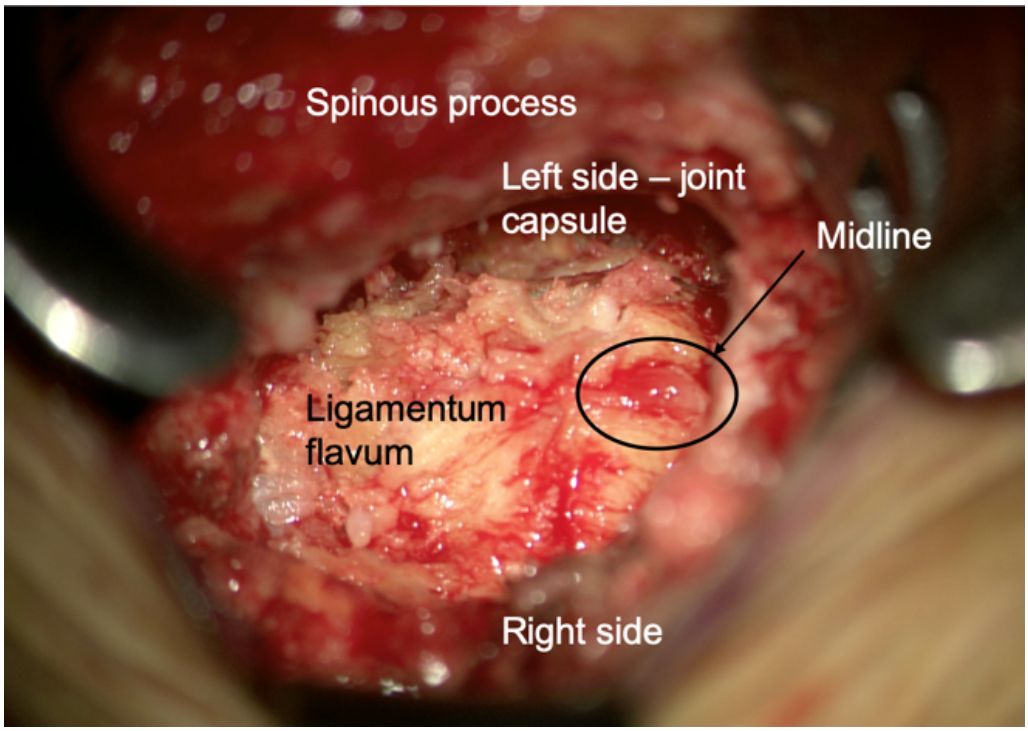


Figure 3-5: Microscopic view after bony decompression. The ligamentum flavum is exposed on both sides. Epidural fat is protruding in the midline.

Finally, the ligamentum flavum can be removed. As the bony decompression is done first, the dural sac is protected by the yellow ligament while using the burr. Another advantage of this technique is that the preparation between the inner part of the yellow ligament and the dural sac is easier, as the yellow ligament can be mobilized away from the dura, since the bony decompression is already done.

The final step of this procedure is to make sure that the neural elements are sufficiently decompressed.

A third advantage of this unilateral approach is that the facet joint on the concave side is preserved to a greater extent than is that on the convex side (73). This offers the theoretical advantage of reducing the risk of destabilizing the spine during

decompression. The concave (preserved) side bears a greater load, for biomechanical reasons, and therefore it is more important to preserve all the strategically relevant structures on this side.

3.1.4 Lumbar interbody fusion

Interbody fusion of the lumbar spine was introduced to improve on the results of simple posterior spinal fusion by aiming for fusion of the biomechanically more important anterior structures. The posterior lumbar interbody fusion (PLIF) technique, historically the first interbody fusion, is a simple extension of the approach used for lumbar discectomy. Later, an approach with a more lateral trajectory through the intervertebral foramen was developed, to decrease the complication rate by limiting exposure of the spinal canal and the fibres of the cauda equina. A detailed description of this technique with application of the load-sharing concept (anterior support with structural graft or intervertebral cage) and segmental instrumentation with pedicle screws was published by Harms and Jeszenszky in 1998 (74). They coined the term “transforaminal lumbar interbody fusion; TLIF” for the technique they had used since 1993. In the last two decades, TLIF has become the workhorse of spinal surgery, especially for degenerative lumbar spine disorders. In contrast to PLIF, TLIF can be applied also at the thoracolumbar junction, or even, with some minor adaptations, in the thoracic region. Further advantages of TLIF over PLIF include better restoration of segmental lumbar lordosis and the inherent benefits of a unilateral approach: preservation of the contralateral posterior elements allows for preparation of a greater fusion site including the lamina and the almost complete contralateral facet joint. Even though the use of anterior and lateral lumbar interbody fusion with additional posterior instrumentation has become increasingly popular, TLIF is probably still the most frequently used circumferential fusion technique nowadays due to its excellent risk profile. The vast majority of lumbar fusions studied in this dissertation were performed using the TLIF technique, and somewhat less frequently, the PLIF, although the boundaries between the two techniques are ill-defined and the transition is smooth. Therefore, no explicit distinction between the two has been aimed for in the present work. A brief description of the technique of interbody fusion is presented below.

3.1.5 Transforaminal Lumbar Interbody Fusion (TLIF) – surgical technique

There are different options to access the transforaminal space from a posterior approach. Only the conventional open and the bilateral transmuscular approach, also known as the mini-open approach, are described here. The type of approach affects the way in which the transpedicular screws are inserted, but the differences are only slight and will not be discussed here. In the case of the conventional open approach, the paravertebral muscles are detached from the posterior elements of the spine (Figure 3-6).

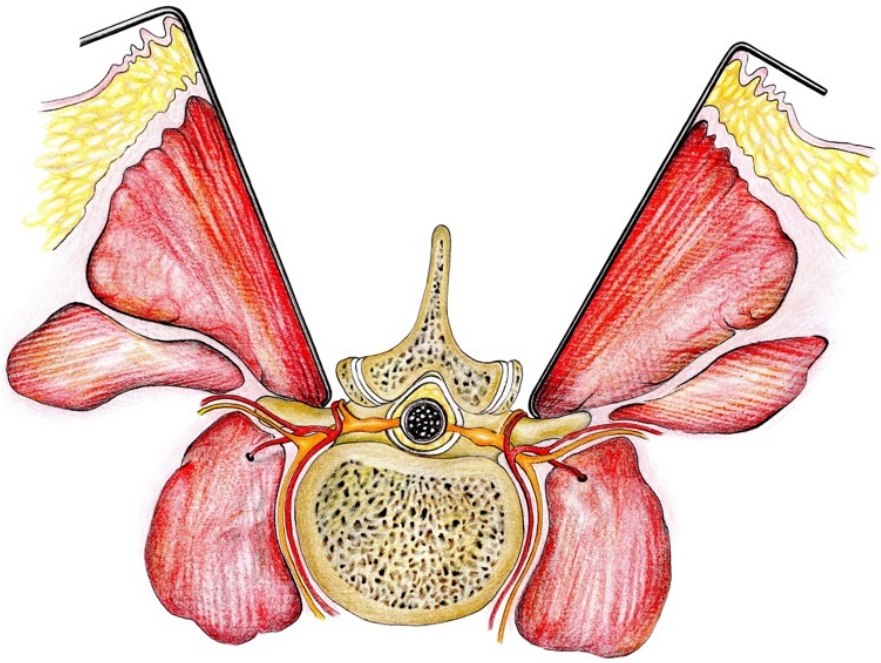


Figure 3-6: Conventional open posterior approach. both the medial and lateral tract of the erector spinae muscles are detached.

In contrast, the mini-open approach starts with a bilateral paraspinal skin incision and blunt dissection between the medial and lateral tracts of the erector spinae muscles as described originally by Watkins (75) and later by Wiltse (76). (Figure 3-7)

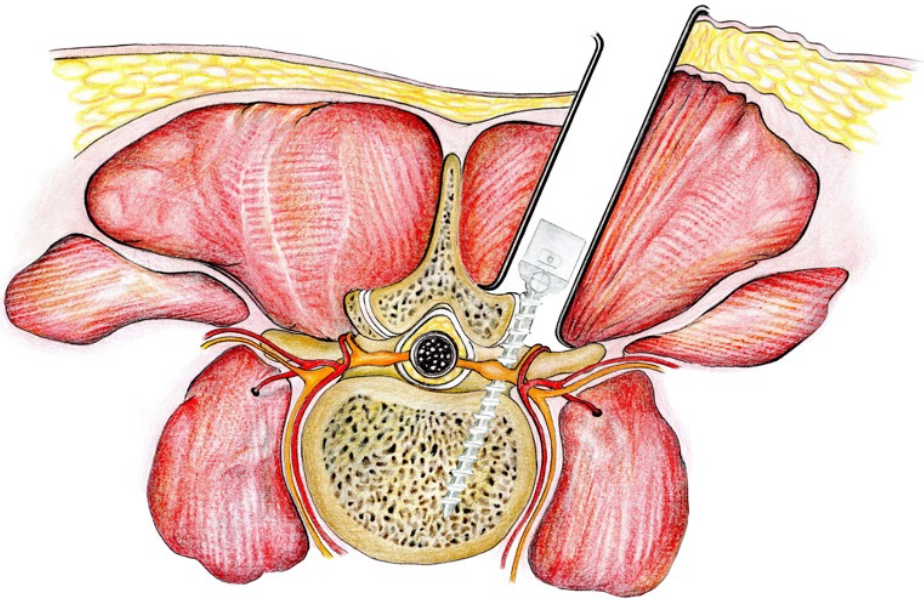


Figure 3-7: Transmuscular (mini-open) posterior approach. The illustration shows a retractor placed between the medial and lateral tracts of the erector spinae muscles. This limited approach opens solely the relevant area and allows for transpedicular screw insertion and for a transforaminal approach to the intervertebral disc.

The patient is in prone position, care must be taken to minimize abdominal pressure, which in turn reduces the epidural venous pressure and thus intraoperative blood loss.

The TLIF procedure itself is regarded as technically demanding, but many clinical studies have shown it to be a safe and effective way of achieving circumferential fusion (77, 78). In order to keep it safe and effective, the procedure of TLIF can be split into standardized steps. The order of the steps is important and leads to a smooth and secure workflow.

Midline skin incision centered at the disc space to be operated. Expose the facet joints bilaterally, and the proximal portion of the transverse processes of the vertebrae to be fused. Mark the entry points and prepare the screw holes, preferably using a free-hand technique. After placement of the pedicle screws, the facet joints to be fused are osteotomised on both sides. Opening the foramen starting medially. and create a sufficiently sized working corridor to the intervertebral space.

Incise the annulus in a rectangular fashion using a scalpel. Removal of disc can be accomplished by using ring and cup curettes or other sharp tools. Aim for complete

removal to enhance the chances of fusion and to mobilize the segment. Interbody distraction in addition to interlaminar (or screw-based) distraction facilitates discectomy and insertion of the cage in the next step. Insertion of fusion material into the intervertebral space and an intervertebral cage packed with bone or bone substitute.
Compression over the screws and rods. Finally, following verification of segmental alignment and implant position with fluoroscopy, tighten the screws. Decortication of the lamina on the contralateral side and placement of bone graft for posterior fusion. Wound closure. Application of a wound drain is usually necessary.

3.1.6 Postoperative rehabilitation

Patients are mobilised on the first postoperative day. A physiotherapy program starts 3 weeks after decompression and 6 to 12 weeks following a lumbar fusion procedure. There is a scheme applied to all patients treated at the Schulthess Clinic, but it is difficult to assess and account for the differences in external physiotherapy regimes. However, a randomized controlled study conducted in our hospital some years ago showed no difference in outcomes between structured physiotherapy and self-management (no physiotherapy) two years following lumbar decompression (79). As such, we did not aim to document every detail of the postoperative rehabilitation in the various patient groups.

3.1.7 Intraoperative neuromonitoring – indications and relevance

In this section, the intraoperative neuromonitoring procedures used at the Schulthess Clinic will be presented.
Over the last century, intraoperative monitoring of blood pressure, oxygenation and many other parameters has become standard practice for every spine surgical intervention. Intraoperative neuromonitoring, however, is still in its early phase and is only used in select cases where the risk of neural injury is expected to be high. The most feared complication of spinal surgery is spinal cord or nerve injury. To reduce the risk of injury to these structures, intraoperative measurement of their function is necessary. Multimodal intra-operative neuro-monitoring (MIONM) provides information about the physiological integrity of the spinal cord and nerves. It is important to mention that it does not give direct information about anatomical integrity.

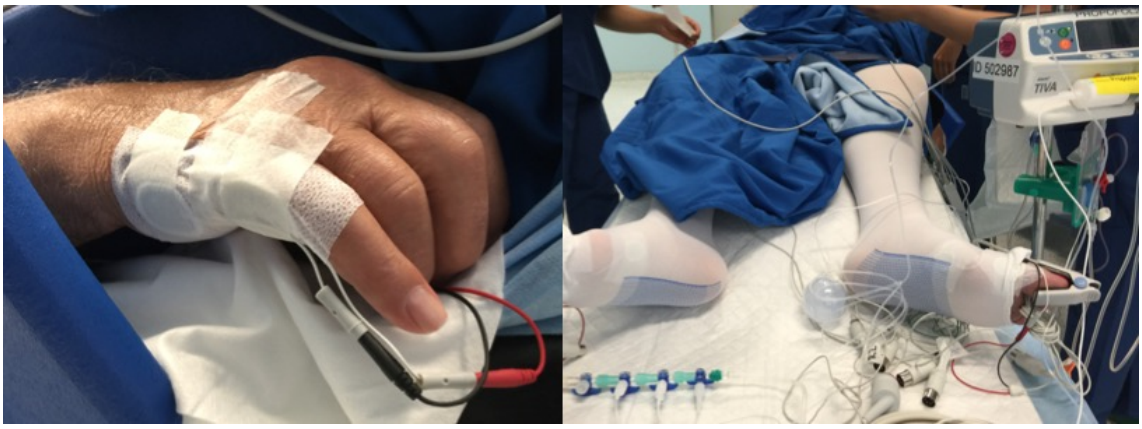


Figure 3-8: Placement of electrodes on the hand and the feet. The same electrodes are used to stimulate and to record signals.

When a large mixed nerve is stimulated at the periphery, the sensory impulses travel within the dorsal column to the sensory cortex. A single stimulation is not detectable due to the background noise of the brain, but the averaging of several hundred stimulations can be measured as a Sensory Evoked Potential (SEP).

Motor Evoked Potentials (MEP) can be elicited by applying a train of stimuli close to the motor cortex (via needles, surface electrodes or transcranial magnetic stimulation), which is required to activate the motor cortex (or the sub-cortical white matter) and in turn, the corticospinal tract. A train of stimuli usually consists of 5 stimuli within a few milliseconds. This train results in a compound muscle action potential, which can be recorded at the muscle level by appropriately mounted electrodes (Figure 3-8). These stimuli can be described by the stimulus intensity, the number of pulses in the train of stimulation (Figure 3-9), the duration of each stimulus and the inter-stimulus interval.

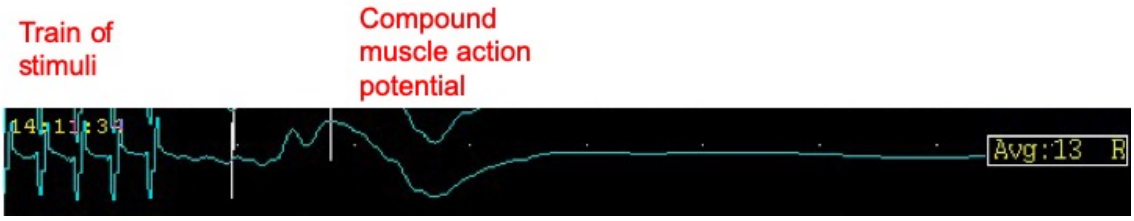


Figure 3-9: Motor evoked potential. Train of transcranial stimuli. Potentials recorded as compound muscle action potentials

Transcranial motor evoked potentials can also be recorded at the spinal cord level. To this end, one can also use epidural electrodes instead of measuring muscle action potentials. That way, the cortically elicited impulses can be detected as they propagate along the corticospinal tract. This is also called D-Wave monitoring.

The surface electrodes can be used to stimulate the peripheral nerves (SEP) but they can also be used to record EMG. This can be used for nerve root monitoring. One form of EMG is continuous (free running) EMG. This can alert the surgeon to nerve root compression or distraction. Another form is the so-called neurography, also known as triggered EMG. With this, the surgeon can confirm that for example the pedicle screw is not compromising the nerve root. A threshold value of 5mA or less indicates that the nerve-root is at least being touched by the pedicle screw (Figure 3-10).

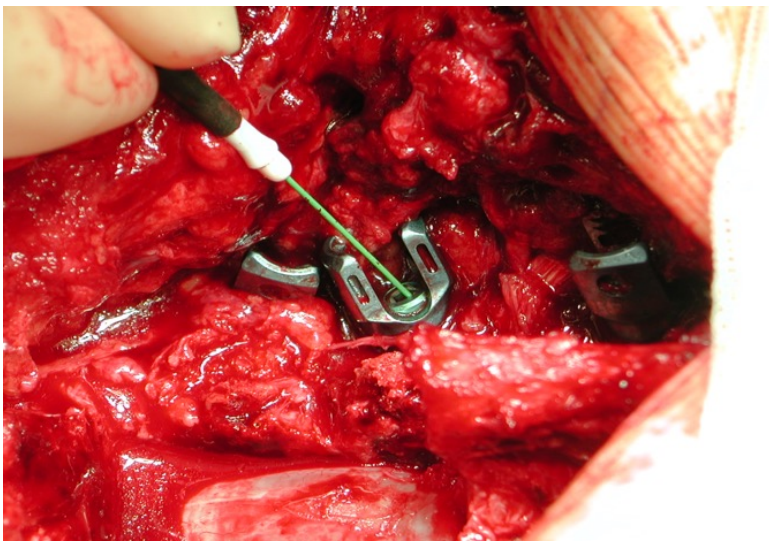


Figure 3-10: Stimulating a transpedicular screw to measure the threshold of eliciting a compound muscle action potential (triggered EMG)

The most reliable measurements can be made if the modalities described above are combined. This is the so called multimodal IONM. The indications for MIONM used during the surgeries evaluated in this thesis were as follows:

- pre-existing or imminent neurological damage
- correction of moderate to severe deformities of the lumbar spine
- spondylolisthesis
- long operating time
- patients with severe comorbidities

The vast majority of patients in the ESI study were operated without neuromonitoring. The policy at the Schulthess Clinic is that surgical interventions with increased risk of neural injury, such as those carried out for spinal deformity (scoliosis, kyphosis, high grade spondylolisthesis), cervical myelopathy, and conditions with preexisting neurological abnormality, are performed under continuous multimodal intraoperative neuromonitoring. Also, the removal of extradural and intradural spinal tumors is usually accompanied by neuromonitoring. In addition, if a long surgical time is expected, during which slightly inadequate patient positioning can result in neurological injury such as brachial plexus compression injury, neuromonitoring is performed. Accordingly, the more complex cases in the PASS and EPOS studies were operated under multimodal neurological monitoring. The indication for monitoring was at the discretion of the operating surgeon and the type of monitoring was individualized, based on discussion with one of the senior neurologists specialized in intraoperative monitoring.

3.2 Ambispective data collection (LSOS, PASS, EPOS)

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. The latter, which was introduced in 2005, documents surgical and patient-rated outcome data from all patients undergoing surgery for spinal disorders in our institution. 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 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 unique main diagnosis as herniated disc, spinal stenosis without spondylolisthesis, degenerative spondylolisthesis, degenerative deformity, or degenerative disc/segment disease, based on the fields ticked on the Spine Tango form, according to the Spine Tango diagnostic groups algorithm[1] (80).

[1] http://www.eurospine.org/cm_data/def_of_degen_patho.pdf

The study investigating the effect of prior epidural steroid injection on treatment outcome was performed using data from a prospective, observational, multicentre study called the Lumbar Stenosis Outcome Study (LSOS) (58).

Table 3-1: Inclusion and exclusion criteria for the LSOS.

Inclusion criteria	**Exclusion criteria**
Age ≥ 50 years	Cauda equina syndrome requiring urgent surgery
Neurogenic claudication (uni- or bilateral)	Current fracture, infection or significant deformity (> 15° lumbar scoliosis)
Radiological diagnosis of lumbar stenosis (MRI, or CT if MRI not possible)	Current enrolment in another spine related treatment study
Able to give informed consent	Clinically relevant peripheral arterial disease

The patients were recruited from 8 centres in the county of Zürich, Switzerland. All the participating centres used the same inclusion and exclusion criteria in patients with radiologically verified lumbar spinal stenosis (Table 3-1) (LSS). A unified set of questionnaires (see below) and predefined follow up schedule was used. The study included both surgically and conservatively treated patients.

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 narrow spectrum of degenerative disorders, 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 (Figure 3-11). The PASS study investigated all types of degenerative disorders with a simple outcome instrument and a relatively short (12 to 24 months) follow-up period, and hence included a large number of patients (6943 patients). In contrast, the EPOS study had a follow up of 5 years, and only patients who returned questionnaires at multiple time points up to 5 years were

included, such that a somewhat lower total number of patients could be included (2959 patients).

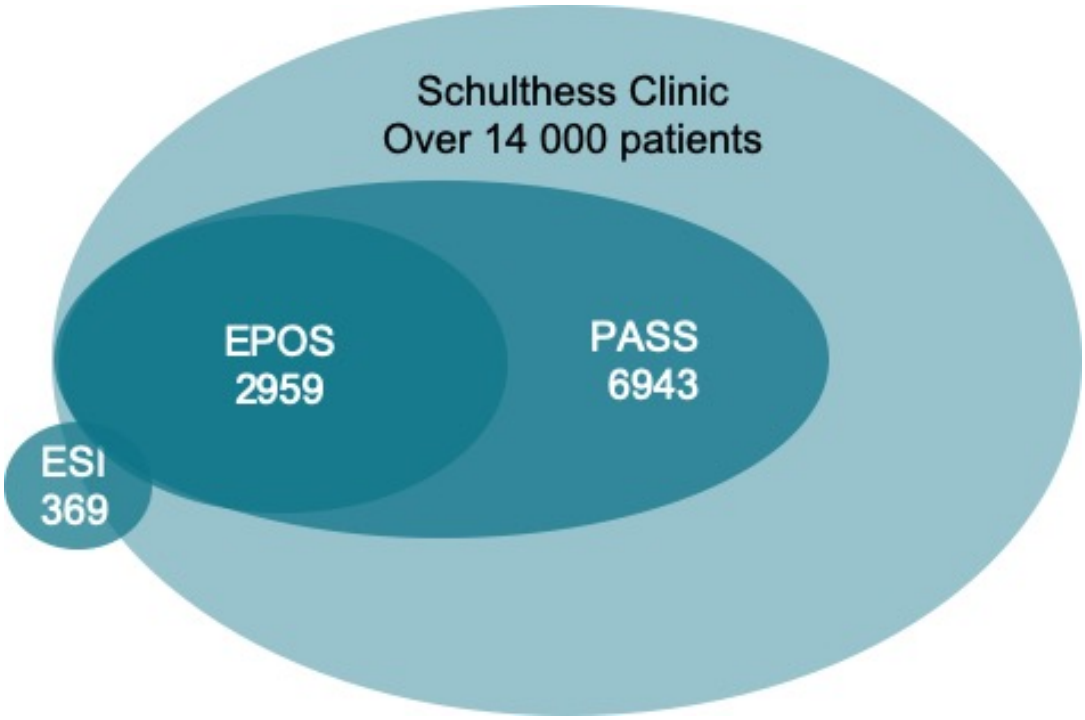


Figure 3-11: The database of the Schulthess Clinic contains perioperative information on more than 14000 patients treated surgically. This diagram shows the relationship among the patient cohorts in the studies presented here. The patient cohorts of the multicentric ESI study (LSOS) showed a small overlap with those of the other two studies (EPOS and PASS).

3.3 Patient questionnaires

In the study investigating the effect of prior epidural steroid injection (ESI) on outcome, several questionnaires were distributed to the patients at all participating centres. Demographic data and information about the duration of symptoms and previous epidural injections were collected at baseline. At baseline and 6 months' follow-up, the following questionnaires (validated German language versions) were used to gather information about the patients' complaints:

1) the Spinal Stenosis Measure (SSM), a disease specific questionnaire (81) 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. Response options on the SSM symptom severity scale range from [1] (best status, no symptoms) to [5] (worst status); on the SSM function scale, from [1] (best function) to [4] (worst function), and on the SSM satisfaction scale, from [1] (very satisfied) to [4] (very dissatisfied);

2) the Roland Morris Disability Questionnaire, assessing back pain related functional disability (score 0 (no disability) to 24 (severe disability)) (82);
3) pain intensity scale (numeric rating scale NRS), quantifying the average intensity of the back-problem-related pain (back or leg pain) within the last seven days (score 0 (no pain) to 10 (extreme pain)) (83);
4) EuroQol-5D (EQ-5D) for the measurement of quality of life (sum score 0 to 100; higher values indicate higher quality of life) (84).
5) The Hospital Anxiety and Depression Score (HADS) at baseline only (sum score for anxiety 0 to 21, and sum score for depression 0 to 21; 21 indicates severe anxiety or severe depression) (85)
6) Chronic Illness Rating Scale for the measurement of comorbidities (sum score 0 to 56; higher values indicate a higher number of and/or more severe comorbidities) (86).

In addition, detailed information was recorded about treatments received between baseline and six months' follow-up.

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 (87-89) (50). The questionnaire contains one question on each of the following: intensity of axial pain (back), intensity of peripheral pain (leg/buttock), (Fig 3-12) back-related function, symptom-specific well-being, general quality-of-life, work-disability, and social disability.

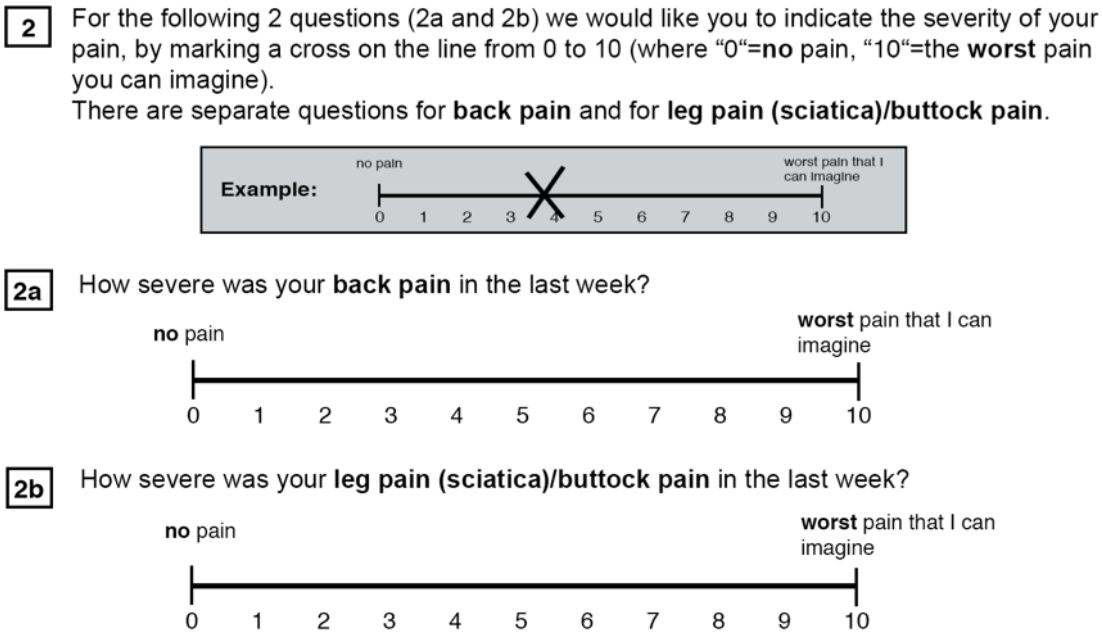
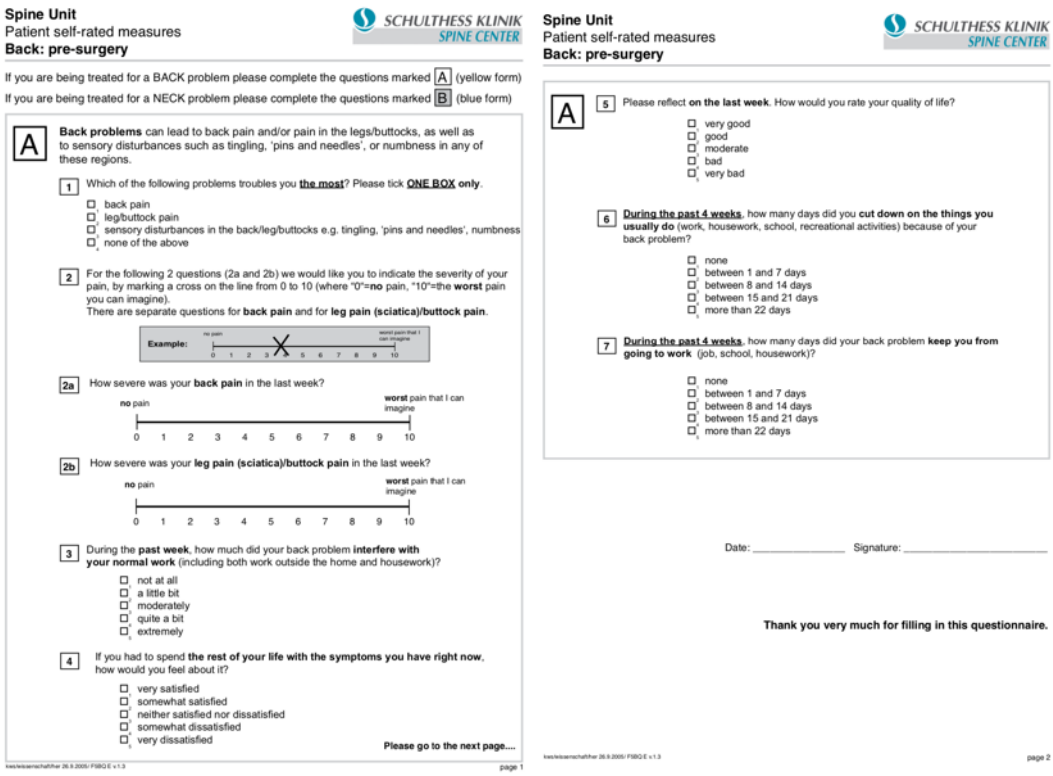


Figure 3-12: Question Nr.2 on the COMI questionnaire asks about pain intensity (0-10 graphic rating scales).

The pre-operative questionnaire was sent to the patient at home, along with the information about their forthcoming hospital stay. They were asked to complete it and hand it in at admission. Completion of the questionnaire at home ensured that the answers given by the patient were free of any potential influence of the care-provider. For the same reasons, the follow-up questionnaires were sent by post, and the patients returned them directly to the hospital's spine research unit. The COMI sum score was calculated as previously described (50, 90). Briefly, the items originally scored 1 to 5 (function, symptom-specific well-being, general quality of life, disability (average of social and work disability)) were firstly re-scored on a 0-10 scale (raw score minus 1, multiplied by 2.5). These items and the higher of the two pain scores (leg pain and back pain; already scored 0-10) were then averaged to provide a COMI index score ranging from 0 to 10 (a higher score indicates a worse status). The Minimum Clinically Important Change (MCIC) score for the COMI, indicating relevant improvement to the individual patient, was considered to be 2.2 points (91).

The COMI (Fig 3-13) contains an item ("symptom specific well-being") concerning the acceptability of the current symptoms: "if you had to spend the rest of your life with the

symptoms you have now, how would feel about it?", answered on a 5-point scale from "very satisfied" to "very dissatisfied". The answers on the latter were dichotomised and used as the external criterion in receiver operating characteristics (ROC) analyses to derive the cut-off score for pain that best indicated a satisfactory or "acceptable" state.



Spine Unit
Patient self-rated measures
Back: pre-surgery

SCHULTHESS KLINIK SPINE CENTER

If you are being treated for a BACK problem please complete the questions marked A (yellow form)
If you are being treated for a NECK problem please complete the questions marked B (blue form)

A

Back problems can lead to back pain and/or pain in the legs/buttocks, as well as to sensory disturbances such as tingling, 'pins and needles', or numbness in any of these regions.

1 Which of the following problems troubles you **the most**? Please tick **ONE BOX only**.

- ☐ back pain
- ☐ leg/buttock pain
- ☐ sensory disturbances in the back/leg/buttocks e.g. tingling, 'pins and needles', numbness
- ☐ none of the above

2 For the following 2 questions (2a and 2b) we would like you to indicate the severity of your pain, by marking a cross on the line from 0 to 10 (where "0"=**no** pain, "10"=the **worst** pain you can imagine).
There are separate questions for **back pain** and for **leg pain (sciatica)/buttock pain**.

Example: no pain — worst pain that I can imagine: 0 1 2 3 X 5 6 7 8 9 10

2a How severe was your **back pain** in the last week?

no pain — **worst** pain that I can imagine: 0 1 2 3 4 5 6 7 8 9 10

2b How severe was your **leg pain (sciatica)/buttock pain** in the last week?

no pain — **worst** pain that I can imagine: 0 1 2 3 4 5 6 7 8 9 10

3 During the **past week**, how much did your back problem **interfere with your normal work** (including both work outside the home and housework)?

- ☐ not at all
- ☐ a little bit
- ☐ moderately
- ☐ quite a bit
- ☐ extremely

4 If you had to spend **the rest of your life with the symptoms you have right now**, how would you feel about it?

- ☐ very satisfied
- ☐ somewhat satisfied
- ☐ neither satisfied nor dissatisfied
- ☐ somewhat dissatisfied
- ☐ very dissatisfied

Please go to the next page....

page 1

Spine Unit
Patient self-rated measures
Back: pre-surgery

SCHULTHESS KLINIK SPINE CENTER

A

5 Please reflect **on the last week**. How would you rate your quality of life?

- ☐ very good
- ☐ good
- ☐ moderate
- ☐ bad
- ☐ very bad

6 **During the past 4 weeks**, how many days did you **cut down on the things you usually do** (work, housework, school, recreational activities) because of your back problem?

- ☐ none
- ☐ between 1 and 7 days
- ☐ between 8 and 14 days
- ☐ between 15 and 21 days
- ☐ more than 22 days

7 **During the past 4 weeks**, how many days did your back problem **keep you from going to work** (job, school, housework)?

- ☐ none
- ☐ between 1 and 7 days
- ☐ between 8 and 14 days
- ☐ between 15 and 21 days
- ☐ more than 22 days

Date: _____ Signature: _____

Thank you very much for filling in this questionnaire.

page 2

Figure 3-13: COMI questionnaire filled in preoperatively

The top two categories (very satisfied and somewhat satisfied) were considered to indicate that the patient was in an acceptable symptom state (in PASS), whilst all others (neither satisfied nor dissatisfied, somewhat dissatisfied, dissatisfied) indicated they were not (not in PASS).

3.4 Data analysis - Effect of epidural steroid injection on outcome[2]

All data were collected on paper forms and were entered independently by two persons into a Filemaker® database (FileMaker Inc) and checked for inconsistencies. Descriptive statistics are presented as means and standard deviations for continuous variables and as numbers and percentages of total for categorical variables. 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 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). Additionally, the respective SSM sub-scale baseline score, age, gender, HADS anxiety score, HADS depression score, pain duration > 6 months (yes/no), and the CIRS comorbidity score were included in the regression model to adjust for potential confounding. We also included an interaction term between surgical treatment and ESI, to determine whether any effect of ESI might differ between the treatment groups. If the p-value for the interaction effect was ≥ 0.05, the interaction term was removed from the model. P-values < 0.05 were considered statistically significant. All analyses were conducted with R for Windows (R Core Team (2014). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.)

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[2] Statistical methods as described in Fekete et al 2015, Spine (Phila Pa 1976) 92. Fekete T, Woernle C, Mannion AF, Held U, Min K, Kleinstuck F, Ulrich N, Haschtmann D, Becker HJ, Porchet F, Theiler R, Steurer J, Group LW. (2015) The Effect of Epidural Steroid Injection on Postoperative Outcome in Patients From the Lumbar Spinal Stenosis Outcome Study. Spine (Phila Pa 1976). 40(16):1303-1310. Epub 2015/05/07. doi: 10.1097/BRS.0000000000000969. PubMed PMID: 25943085.. The statistical analyses were performed in cooperation with the statistician of the Horten Center Zürich (Ulrike Held) and with the scientific head of the Spine Unit Research Group at the Schulthess Clinic (Anne F Mannion).

3.5 Data analysis – Patient acceptable symptom state [3]

Descriptive data are presented as means ± standard deviations (SD) or % distributions of responses in each outcome category for SSWB. 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 SSWB scale, see earlier). This is considered analogous to evaluating a diagnostic test, in which the pain score is the diagnostic test and the dichotomised SSWB response is the gold standard. The ROC curve combines information on sensitivity and specificity for detecting PASS and comprises a plot of 'true-positive rate' (sensitivity) versus 'false positive rate' (1-specificity) for each of several possible cut-off points in pain score (Figure 3-14).

[3] Statistical methods as described in Fekete et al 2016, Spine J 93. Fekete TF, Haschtmann D, Kleinstuck FS, Porchet F, Jeszenszky D, Mannion AF. (2016) What level of pain are patients happy to live with after surgery for lumbar degenerative disorders? Spine J. 16(4 Suppl):S12-18. Epub 2016/02/07. doi: 10.1016/j.spinee.2016.01.180. PubMed PMID: 26850172.. The statistical analysis were done with Anne F Mannion.

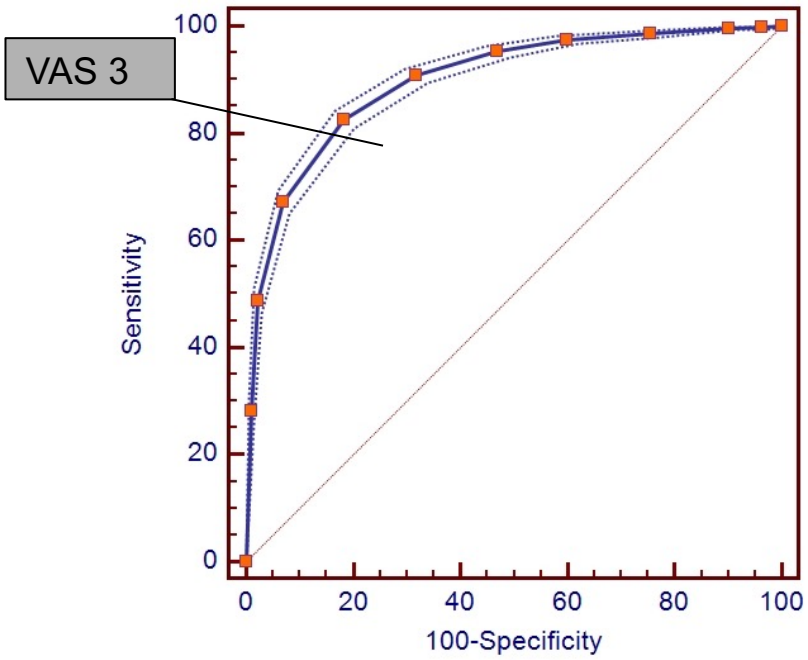

Figure 3-14: Receiver Operating Characteristics (ROC) curve: for a range of cut-off thresholds for the highest (back or leg) pain score at 12 months the true positives (sensitivity) vs. false positives (100 − specificity) are plotted, in terms of predicting whether the patient declares being in an "acceptable symptom state" or not. Each point represents a sensitivity and 100-specificity value corresponding to a number on the pain scale ranging from 0 to 10. The sensitivity and (100-specificity) for the pain score of 3 is indicated as an example, and this also corresponds to the best cut-off value for indicating "being in an acceptable symptom state" (=point on the curve that is closest to the top left corner)

The area under the ROC curve (AUC; with exact binomial confidence intervals) was used to indicate the probability of correctly discriminating between the dichotomised outcomes (i.e. being in PASS or not) based on the pain score. An AUC of 0.5 indicates discrimination no better than chance and an AUC of 1.0 indicates perfect discrimination (100% sensitivity and 100% specificity). The cut-off giving the best combination of sensitivity and specificity was used to indicate the PASS for pain.

Various "sensitivity" analyses were carried out for subgroups, based on information derived from the Spine Tango surgery form or the baseline COMI form: diagnostic group (herniated disc, spinal stenosis without spondylolisthesis, degenerative

spondylolisthesis, degenerative deformity, and degenerative disc/segment disease); previous surgery at the same level (yes/no); smoking status (yes/no); comorbidity status (American Society of Anaesthesiologists Physical Status grade 1-5, dichotomised as ASA <3, and ≥ 3 for further analyses); age-group (<50, ≥50-70, ≥ 70 yrs old); sex (male, female); baseline pain intensity (mild, ≤3; moderate, 4-6; high, 7-8; extreme, 9-10); and health insurance category (private, semi-private, basic obligatory). Sensitivity analyses were also carried out for the additional follow-up periods of 3 months and 24 months (in patients who had reached 24 months' postoperative).

The analyses were carried out using Statview 5.0 (SAS Institute Inc, San Francisco, USA) and Medcalc (MedCalc Statistical Software, Mariakerke, Belgium). P values<0.05 were considered to be statistically significant.

3.6 Data analysis - Evolution of patient-rated outcome after surgery [4]

Descriptive data are presented as means ± standard deviations (SD) or percentages, as appropriate. 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 the 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. The analyses were conducted using Statview 5.0 (SAS Institute Inc, San Francisco, CA, USA) and statistical significance was accepted at the p<0.05 level.

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[4] Statistical methods as described in Fekete et al 2018, Eur Spine J 94. Fekete TF, Loibl M, Jeszenszky D, Haschtmann D, Banczerowski P, Kleinstuck FS, Becker HJ, Porchet F, Mannion AF. (2018) How does patient-rated outcome change over time following the surgical treatment of degenerative disorders of the thoracolumbar spine? Eur Spine J. 27(3):700-708. Epub 2017/10/29. doi: 10.1007/s00586-017-5358-2. PubMed PMID: 29080002.. The statistical analysis have been done with Anne F Mannion.

4 Results

4.1 Results - Effect of epidural steroid injection on outcome (ESI study)

From 1st January 2009 until 1st June 2014, 415 patients were enrolled in the study. The non-operative therapy consisted of physical therapy with or without oral analgesics. Data at baseline and 6 months' follow-up were available for 369 patients (Figure 4-1). Of these, 88 had received one or more ESIs between baseline and 6 months' follow up and were excluded from further analyses. The remaining 281 were included in the present study. 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. Seventy-nine % of the surgically treated patients received decompression only and 21% received additional instrumented fusion.

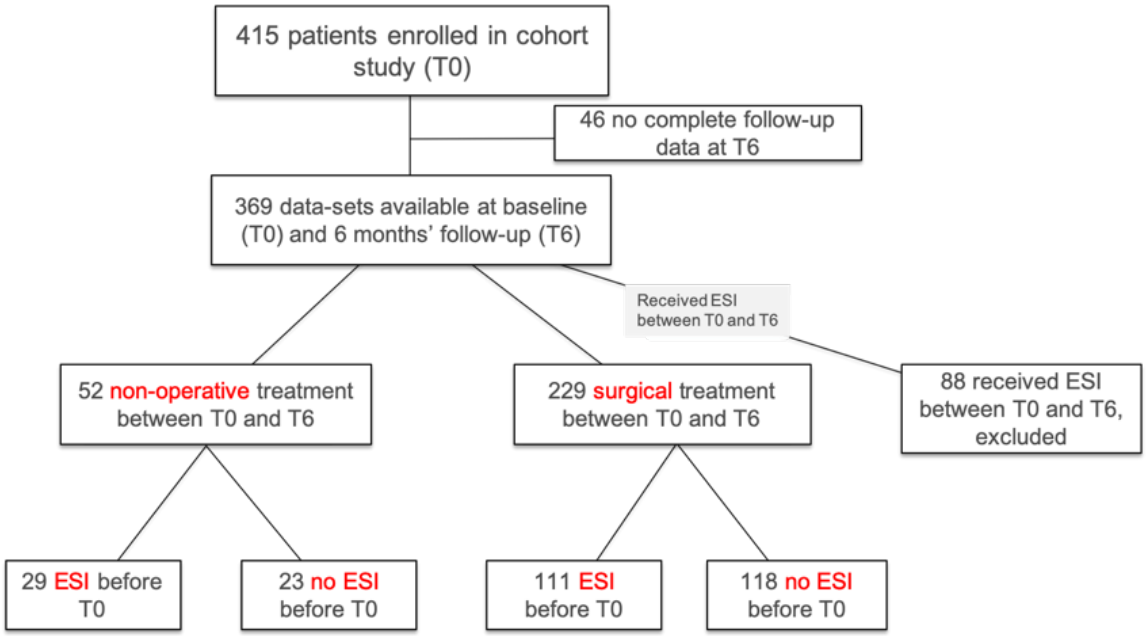


Figure 4-1: Patient flow in the multicentre study about the effect of epidural steroid injections on outcome.

The patients' demographic details and other baseline data are shown in Table 4-1.

The mean age of the patients was 75 (SD 8.7) years. In the non-operative treatment arm, 60% were female, and in the surgical group, 50%. In about two thirds of the patients, symptoms of lumbar spinal stenosis had been present for more than one year and in about 10%, less than three months. More than 80% of the patients were retired.

Table 4-1: Baseline characteristics of the patients in the ESI study

	Non-operative treatment group		Surgical treatment group	
	ESI (n=29)	No-ESI (n=23)	ESI (n= 111)	No-ESI (n= 118)
Age, mean (SD), yr	76.2 ± 10.1	74.1 ± 8.3	74.2 ± 9.2	75.4 ± 8.0
Female, no. (%)	17 (59%)	14 (61%)	55 (50%)	59 (50%)
Educational level, no. (%)				
Compulsory education	6 (21%)	6 (26%)	21 (19%)	26 (22%)
Baccalaureate/Apprenticeship	22 (76%)	16 (70%)	76 (68%)	78 (66%)
University degree	1 (3%)	1 (4%)	14 (13%)	14 (12%)
Employment status, no. (%)				
Employed full or part time	5 (17%)	3 (13%)	23 (21%)	16 (14%)
Retired	24 (83%)	20 (87%)	88 (79%)	102 (86%)
Comorbidities, no. (%)				
Osteoarthritis of the hip	4 (14%)	2 (9%)	15 (14%)	17 (14%)
Gonarthrosis	8 (28%)	3 (10%)	16 (14%)	17 (14%)
Peripheral neuropathy	3 (10%)	1 (3%)	8 (7%)	11 (9%)
Obstructive lung disease	3 (10%)	2 (9%)	5 (5%)	6 (5%)
Heart failure	3 (10%)	1 (3%)	3 (3%)	7 (6%)
Coronary heart disease	2 (7%)	0	6 (6%)	8 /7%)
M. Parkinson	1 (3%)	0	1 (1%)	2 (2%)
Duration of symptoms, no. (%)				
< 3 mo	4 (14%)	3 (10%)	10 (9%)	14 (12%)
3-6 mo	2 (7%)	2 (9%)	16 (14%)	17 (14%)
6-12 mo	2 (7%)	4 (17%)	19 (17%)	13 (11%)
> 12mo	21 (72%)	14 (61%)	65 (59%)	72 (61%)

The surgical interventions comprised posterior lumbar decompression with or without additional fusion, depending on the surgeon's assessment of the individual pathology. Seven patients were re-operated between baseline and 6 months' follow-up; three were in the group with prior ESI, and four in the group with no prior ESI. The type of surgical interventions were similar in the ESI and No-ESI groups (Table 4-2).

Table 4-2: Surgical procedures performed in patients with (ESI) and without (No-ESI) prior epidural injections.

Surgical procedure, n (%)	**ESI (n=118)**	**No-ESI (n=111)**
Decompression only	94 (80%)	85 (77%)
Decompression and non-instrumented fusion	0	1 (1%)
Decompression and instrumented fusion	24 (20%)	25 (22%)
Multilevel fusion, n(%)	12 (10%)	15 (14%)
Levels decompressed, n(%)		
1	41 (35%)	41 (37%)
2	44 (37%)	50 (45%)
3	29 (25%)	17 (15%)
4	4 (3%)	3 (3%)

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 (Table 4-3). The quality of life at baseline, was lower in the group undergoing surgery as measured by the EQ-5D questionnaire (Table 4-4).

Table 4-3: Differences in the Swiss Spinal Stenosis Measure (SSM) scores (mean ± SD) between baseline (T0) and 6 months' follow-up (T6) in patients with lumbar spinal stenosis treated surgically or non-operatively, with and without prior epidural steroid injections (ESI).

	Time of assessment			Time of assessment			
	ESI (n=29)			No ESI (n=23)			ESI vs no ESI
Conservative	T_0	T_6	Improvement	T_0	T_6	Improvement	p-value
SSM-Symptom	2.9 ± 0.7	2.6 ± 0.7	0.3	2.9 ± 0.9	2.6 ± 1.0	0.3	0.847
SSM-Function	2.4 ± 0.9	2.1 ± 0.8	0.3	2.3 ± 0.9	1.8 ± 0.7	0.5	0.241
SSM-Pain	3.6 ± 0.8	3.2 ± 0.9	0.4	3.5 ± 1.1	2.9 ± 1.1	0.6	0.589
SSM-Neuroischemic	2.4 ± 0.9	2.2 ± 0.8	0.2	2.4 ± 1.0	2.4 ± 1.2	0.0	0.584
SSM-Satisfaction		2.0 ± 0.7			2.0 ± 0.8		
	ESI (n=111)			No ESI (n=118)			
Surgical	T_0	T_6	Improvement	T_0	T_6	Improvement	p-value
SSM-Symptom	3.2 ± 0.5	2.3 ± 0.8	0.9	3.1 ± 0.6	2.3 ± 0.8	0.8	0.148
SSM-Function	2.3 ± 0.7	1.6 ± 0.6	0.7	2.3 ± 0.7	1.7 ± 0.6	0.6	0.450
SSM-Pain	3.8 ± 0.7	2.5 ± 1.0	1.3	3.7 ± 0.7	2.6 ± 1.1	1.1	0.517
SSM-Neuroischemic	2.8 ± 0.7	2.1 ± 0.8	0.7	2.6 ± 0.8	2.1 ± 0.9	0.5	0.179
SSM-Satisfaction		1.7 ± 0.6			1.8 ± 0.7		

At 6 months' follow-up, improvements in unadjusted SSM scores, Roland Morris and EQ-5D were more pronounced in the surgical group compared with the non-operative group (Table 4-4).

Table 4-4: Differences in the Numeric Rating Scale, Roland Morris Disability Questionnaire, and EQ-5D (mean ± SD) between baseline (T0) and 6 months' follow-up (T6) in patients with lumbar spinal stenosis treated surgically or non-operatively, with and without prior epidural steroid injections

Non-operative treatment	**ESI (n= 29)**			**No ESI (n= 23)**			**ESI vs no ESI p-value***
	T_0	T_6	Improve-ment	T_0	T_6	Improve-ment	
NRS	4.9 ± 2.4	5.4 ± 2.8	-0.5	5.1 ± 3.0	4.4 ± 2.9	0.7	0.316
Roland Morris	10.6 ± 6.2	8.9 ± 5.7	1.7	10.1 ± 6.7	8.8 ± 5.9	1.3	0.283
EQ-5D	72.8 ± 21.7	70.0 ± 20.0	- 2.8	68.7 ± 20.1	77.0 ± 15.2	8.3	0.047
Surgical treatment	**ESI** (n= 111)			**No ESI** (n= 118)			
	T_0	T_6		T_0	T_6		
NRS	6.8 ± 1.8	3.7 ± 4.6	3.1	6.3 ± 2.1	3.2 ± 2.6	3.1	0.656
Roland Morris	12.7 ± 4.9	8.2 ±5.9	4.5	12.2 ± 5.1	8.1 ± 5.4	4.2	0.592
EQ-5D	65.4 ± 15.5	81.2 ± 15.0	15.8	66.6 ± 14.5	80.6 ± 16.8	14.0	0.337

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 (Table 4-3). Adjusted mean change scores from baseline in SSM Symptoms, SSM Function, SSM Pain Domain and SSM Neuroischemic Pain in relation to the treatment modality (surgery yes/no, epidural steroid injection yes/no) are displayed in Figure 4-2.

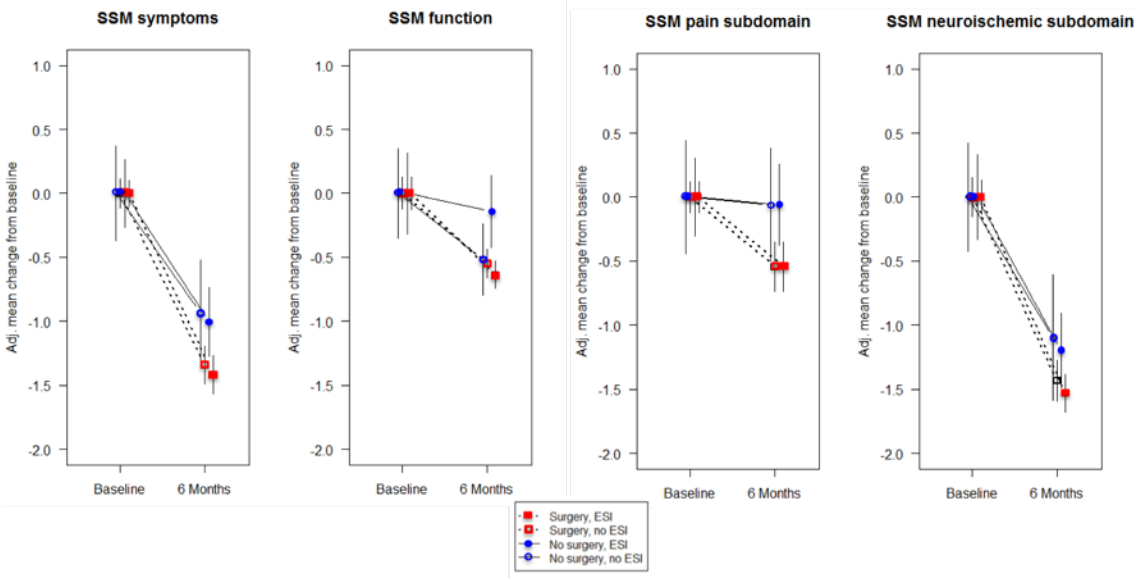


Figure 4-2: Adjusted mean changes (+- SD) from baseline at 6 months' follow-up for the SSM domains and subdomains. Note that surgery with or without previous ESI showed a greater improvement (negative values) compared to conservative treatment.

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, -0.03 ($p=0.81$) for SSM Function, -0.48 ($p=0.002$) for SSM Pain, 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, 0.37 ($p=0.02$) for SSM Function, 0.0003 ($p=0.99$) for SSM Pain, and -0.10 ($p=0.24$) for SSM Neuroischemic Pain. There was just one significant interaction between surgery and ESI prior to study entry, for SSM Function: the interaction effect was -0.46 ($p=0.01$) (having had an ESI led to less improvement in the non-operative group but not the surgical group).

The change-scores for the NRS, Roland Morris, and EQ-5D followed the same pattern as the SSM, with two exceptions: compared with no prior ESI, non-operative patients who had received a prior ESI showed a reduced quality of life (EQ-5D) and a slight increase of NRS values between baseline and 6 months' follow-up, indicating a worsening of the symptom state (Table 4-4).

4.2 Results – Patient acceptable symptom state

4.2.1 Patients and follow-up rates

The average compliance rate for the surgeons' completion of the Spine Tango Surgery Forms was 98% percent from 2005 to 2013. Hence, theoretically, the proportion of eligible patients that were not included in the present study could have ranged from 0% (if none of the patients without a Surgery Form would have qualified for this study) to 2% (if all patients without a Surgery Form would have qualified).

Of all the patients in our local spine surgery database, 6'943 satisfied the study's admission criteria. A COMI questionnaire was completed by 6'467 (93%) of these at baseline, 6'453 (93%) at 3 months' follow-up, 6'248 (90%) at 12 months' follow-up, and 5'666 (86%) at 24 months' follow-up. The baseline data of the patients are shown in Table 4-5.

Table 4-5: Baseline demographic, comorbidity, and self-reported clinical data (means ± SD, or % values) for the study group (N=6'943 patients)

Variable	Mean ± SD or N (%)
Age, mean (SD), yrs	76.2 ± 10.1
Female, no. (%)	3'692 (53%)
Comorbidities, ASA grade (%)	
ASA 1	1'720 (24.8%)
ASA 2	3'387 (48.8%)
ASA 3	1'732 (25.0%)
ASA 4	35 (0.5%)
unknown	63 (0.9%)
Back pain intensity (0-10 scale)	5.6 ± 2.9
Leg pain intensity (0-10 scale)	6.4 ± 2.7
Intensity of **worst pain**, back/leg (0-10 scale)	7.3 ± 2.0
Diagnosis	
Disc herniation (DH)	1'608 (23.2%)
Spinal stenosis (SS)	1'782 (25.7%)
Degenerative spondylolisthesis (DS),	1'000 (14.4%)
Degenerative deformity (DegDef)	612 (8.8%)
Degenerative disc/segment disease (DegSeg)	473 (6.8%)
Degenerative other/mixed diagnoses	1'468 (21.1%)

4.2.2 PASS 12 months postoperatively

The distribution of ratings for satisfaction with the current symptom-state at 12 months' postoperatively, for each diagnostic group, is shown in Figure 4-3. For the whole group the distribution was: very satisfied, 25.1%; somewhat satisfied, 20.3%; neither satisfied nor dissatisfied, 15.4%; somewhat dissatisfied, 18.3%; very dissatisfied, 18.9%. Hence, an acceptable state was achieved by 47.3%.

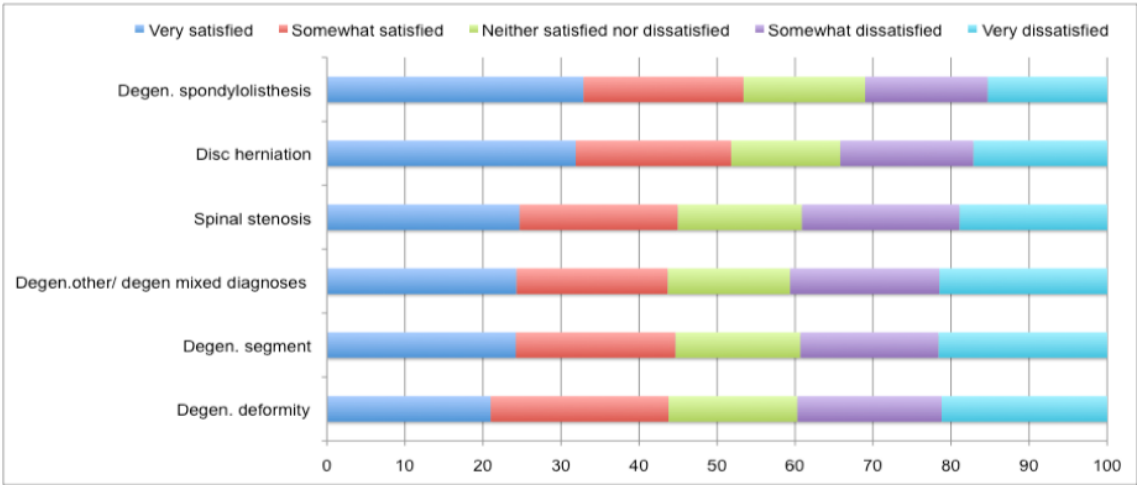


Figure 4-3: Distribution of responses to symptom-specific well-being item ("spending rest of one's life with current symptom state") at 12 months postoperatively, for the different degenerative pathologies.

The mean pain scores (higher of back or leg) corresponding to each of the categories of "satisfaction with state" at 12 months' FU are shown in Figure 4-4. There was a steady increase in the mean score from "very satisfied" down to "very dissatisfied", with significant differences ($p<0.0001$) between each step. The Spearman Rank correlation coefficient between the "satisfaction with state" ratings and the pain scores was 0.79, indicating that the symptom-specific well-being item was a valid external criterion (or "anchor") for use in the ROC analyses (95).

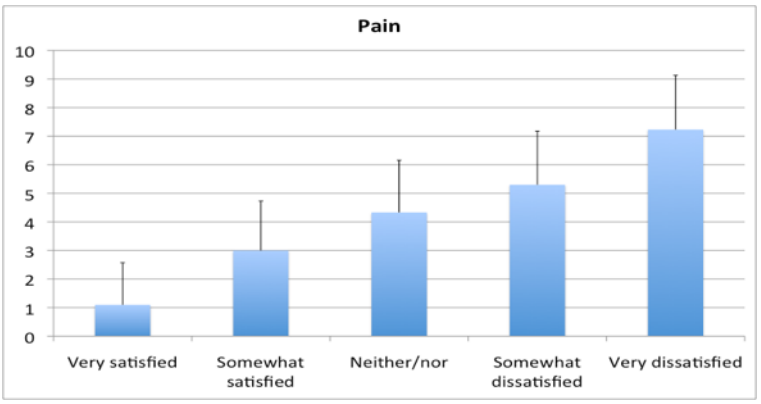


Figure 4-4: Pain score (higher of back or leg) at 12 months in relation to symptom-specific well-being category. P<0.0001 between each step from "very satisfied" to "very dissatisfied". (The y axis shows the pain intensity on the NPRS)

4.2.3 Receiver operating characteristics analysis at 12 months postoperatively

The areas under the curve (AUC) for the ROCs were 0.89-0.91 (Table 4-6) for the different pathologies, indicating a very good ability of the pain score to discriminate between being in an acceptable state or not at 12 months postoperatively. The cut-off indicating a satisfactory symptom state was ≤2 points for DH (sensitivity 76%, specificity 88%), and ≤3 points for all other pathologies (sensitivity 79-84%, specificity 81-85%). The sensitivity analyses revealed ≤3 points to be the most common cut off for the various sub-groups.

Only for the different baseline pain groups and comorbidity did the cut-off differ from ≤ 3 points: for extreme baseline pain and high comorbidity, it was in each case ≤4 points; and for low and medium baseline pain it was ≤ 2 points.

Table 4-6: PASS analyses for subgroups of patients. PASS, patient acceptable symptom state - answers 'very satisfied' and 'somewhat satisfied' on symptom-specific well-being item; Sens-sensitivity; Spec-specificity (next page).

	N	% in PASS	AUC	95% CI	Pain threshold for being in PASS	Sens %	Spec %
All patients							
12 mo FU	6248	47%	0.90	0.89-0.91	≤ 3	82.7	81.6
Diagnosis							
Disc Herniation	1430	52%	0.90	0.89-0.92	≤ 2	75.8	87.8
Spinal stenosis	1625	45%	0.90	0.89-0.92	≤ 3	80.9	83.8
Degen. spondy.	910	53%	0.89	0.87-0.91	≤ 3	81.9	81.1
Degen. deformity	557	44%	0.89	0.86-0.91	≤ 3	78.7	84.0
Degen. segment	425	45%	0.91	0.88-0.93	≤ 3	84.2	84.7
Baseline pain							
Low (0-3)	341	63%	0.83	0.79-0.87	≤ 2	76.7	73.8
Medium (4-6)	1285	54%	0.89	0.87-0.90	≤ 2	72.7	89.2
High (7-8)	2683	45%	0.90	0.89-0.92	≤ 3	82.1	84.2
Extreme (9-10)	1588	42%	0.92	0.90-0.93	≤ 4	88.1	78.8
ASA grade							
< 3	4621	50%	0.90	0.89-0.91	≤ 3	84.7	80.2
≥ 3	1564	40%	0.89	0.87-0.90	≤ 4	86.2	75.8
Age							
< 50 yrs	1362	49%	0.91	0.90-0.93	≤ 3	87.8	78.6
50 to ≤ 70 yrs	2673	47%	0.90	0.89-0.91	≤ 3	82.4	81.2
> 70 yrs	2213	47%	0.89	0.87-0.90	≤ 3	79.8	83.9
Smoker							
Yes	1280	44%	0.91	0.89-0.93	≤ 3	85.1	82.4
No	3906	49%	0.90	0.89-0.91	≤ 3	82.4	81.0
Sex							
Men	2903	49%	0.91	0.89-0.92	≤ 3	85.9	78.3
Women	3345	46%	0.89	0.88-0.90	≤ 3	79.7	84.4
Previous surgery at the same level							
Yes	1489	37%	0.89	0.87-0.91	≤ 3	77.0	85.3
No	4751	51%	0.90	0.89-0.91	≤ 3	84.0	80.2
Insurance							
General	2881	43%	0.90	0.89-0.91	≤ 3	80.2	83.8
Semi-private	1605	52%	0.90	0.89-0.92	≤ 3	85.5	81.5
Private	1759	51%	0.89	0.88-0.91	≤ 3	83.3	77.8
Time of followup							
3 mo FU	6453	43%	0.86	0.85-0.87	≤ 3	82.0	75.1
24 mo FU	5666	49%	0.91	0.90-0.92	≤ 3	84.3	83.7

4.3 Results – Evolution of patient-rated outcome after surgery (EPOS) study

Figure 4-5 summarises the formation of the final study group in the EPOS study. In total, 8'653 patients were identified who had been operated on between 01.01.2005 and 31.12.2011. Of these, 8'474 (98%) had a Spine Tango surgery form allowing us to determine whether they met the surgical inclusion criteria for the present study. In total, 7'118 of these patients had undergone surgery of the thoracolumbar spine, 5'668 of whom for a degenerative disorder as main pathology.

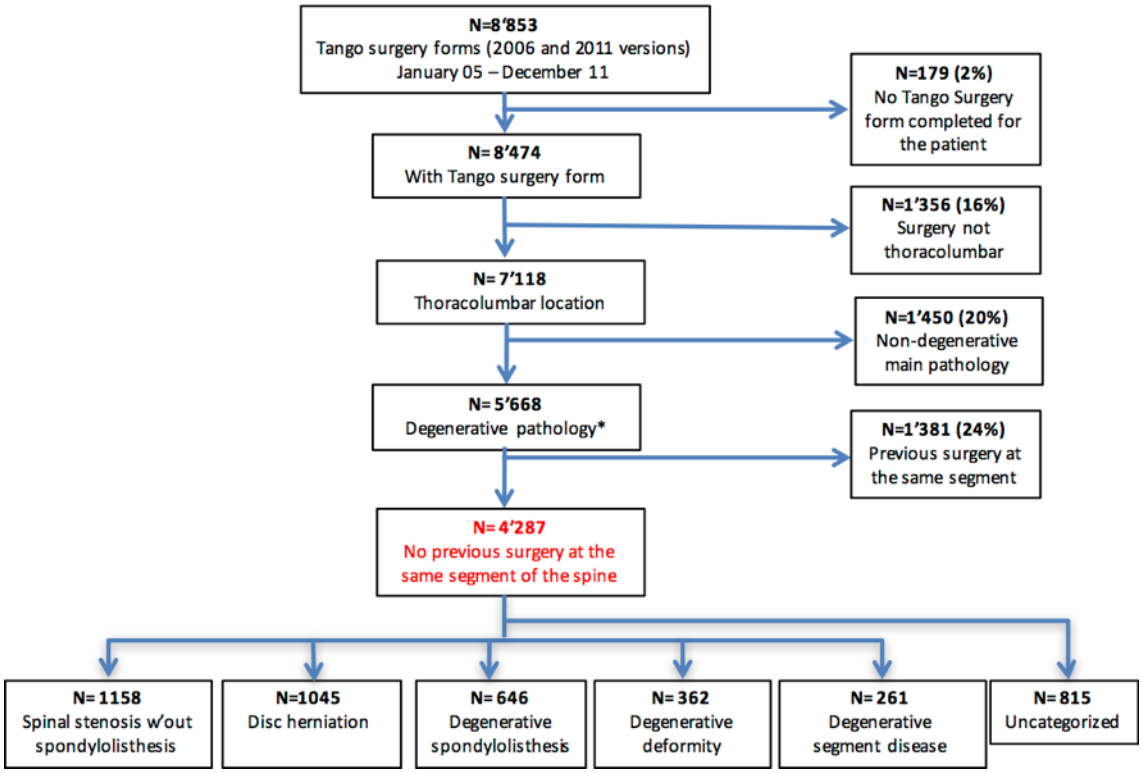


Figure 4-5: Flow chart showing the formation of the study group

A subgroup of 1'381 patients had undergone previous surgery at the same level of the spine and were hence excluded, leaving 4'287 who satisfied the inclusion criteria for the present study (2'287 women, 2'000 men; aged 62 ± 15 years). Of the 4'287 patients, 1'158 (27.0%) had stenosis without spondylolisthesis; 1'045 (24.4%), disc herniation; 646 (15.1%), degenerative spondylolisthesis; 362 (8.4%), degenerative deformity; 261 (6.1%), degenerative segment disease (degenerative disc, spondylarthrosis, etc.); and 815 (19.0%) of the patients were not further categorized, as they did not fit the criteria

for a distinct diagnostic group (i.e., although degenerative disease was the leading cause of their surgical treatment, they had multiple types or combinations of degenerative pathology and/or had additional pathologies combined with the main degenerative pathology, preventing categorisation into a unique sub-group based on the fields endorsed on the Tango form). In total, 33.5% of the patients had undergone instrumented fusion. Table 4-6 shows the baseline characteristics of the patients in each diagnostic group.

Table 4-7: Baseline characteristics of the patients.

	Diagnosis						
	SS	DH	Deg Spondy	DegDef	DegSeg	No cat	**ALL**
N	1158	1045	617	362	261	815	4287
Age, y	70 ± 10	48 ± 14	69 ± 11	69 ± 11	51 ± 14	63 ± 13	62 ± 15
% male	56 %	57 %	30 %	33 %	38 %	42 %	47 %
BMI, kg/m2*	28 ± 5	26 ± 5	27 ± 5	27 ± 5	26 ± 4	26 ± 5	27 ± 5
% smokers**	21 %	33 %	12 %	6 %	9 %	19 %	26 %
Months of prior conservative treatment							
<3 months	19 %	42 %	13 %	16 %	18 %	19 %	23 %
3-12 months	36 %	39 %	36 %	29 %	33 %	36 %	36 %
> 12 months	45 %	19 %	51 %	54 %	49 %	45 %	41 %
% ≥ASA3 (severe)	47 %	11 %	40 %	42 %	14 %	32 %	32 %
% mono-segmental	28 %	84 %	43 %	19 %	58 %	49 %	49 %
Baseline COMI	7.4 ± 1.8	7.8 ± 1.7	7.6 ± 1.8	7.8 ± 1.7	7.7 ± 1.8	7.6 ± 1.7	7.6 ± 1.8
% receiving instrumented fusion	22%	2%	70%	51%	62%	46%	33.5%

4'012/4'287 (94%) patients completed a questionnaire preoperatively, 4'008 (93%) at 3 months' follow-up, 3'897 (91%) at 1-year follow-up, 3'736 (87%) at 2 years' follow-up, and 3'387 (79%) at 5 years' follow-up. The main reasons for the relatively infrequent (6% preoperatively, up to 21% at 5 years' follow-up) non-return of the questionnaire at the given time-point included: language difficulties; having been re-operated and not able to complete questionnaires for both the previous and the repeat operation; administrative errors; living abroad; death; and unwillingness to complete questionnaires. In total, 2'959/4'287 (69%) patients completed a questionnaire at every single one of the five time-points.

The group mean COMI scores decreased significantly from pre-op to 3 months' follow-up (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; $p>0.05$) (Figure 4-6).

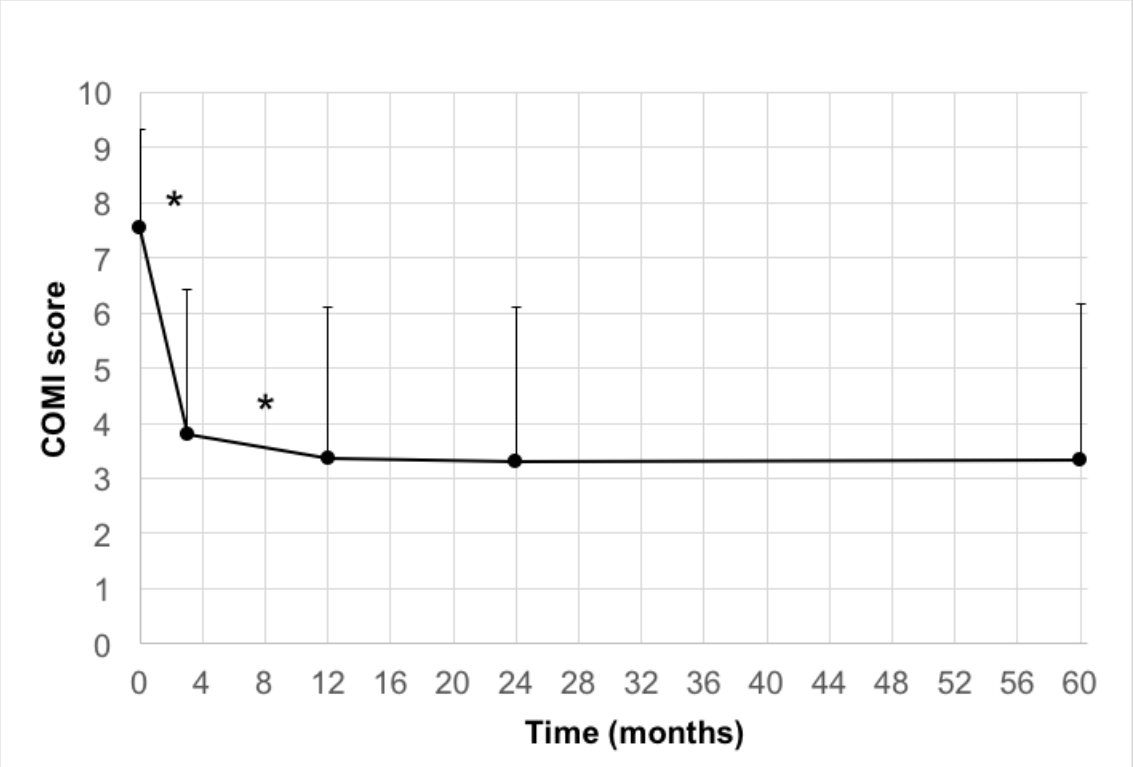
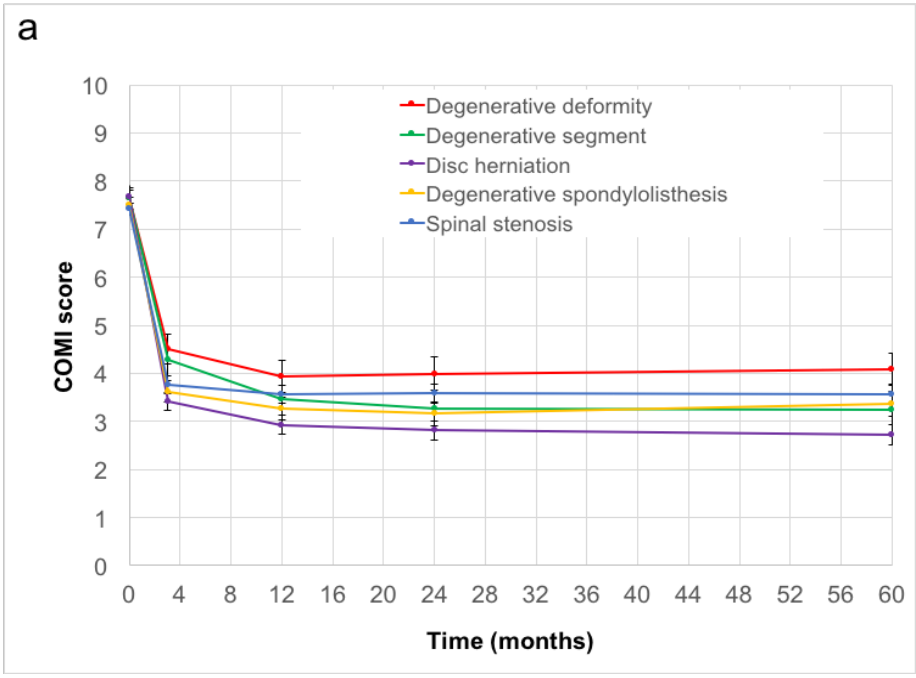


*Figure 4-6: Group mean (SD) COMI scores over time (N=2'959 patients with data at every timepoint). * p<0.05, significant difference between the adjacent time-points*

The course of change up to 12 months' follow-up differed slightly depending on pathology: patients with DH consistently showed the greatest improvement in COMI score and those with degenerative deformity, the worst (Figure 4-7 a).



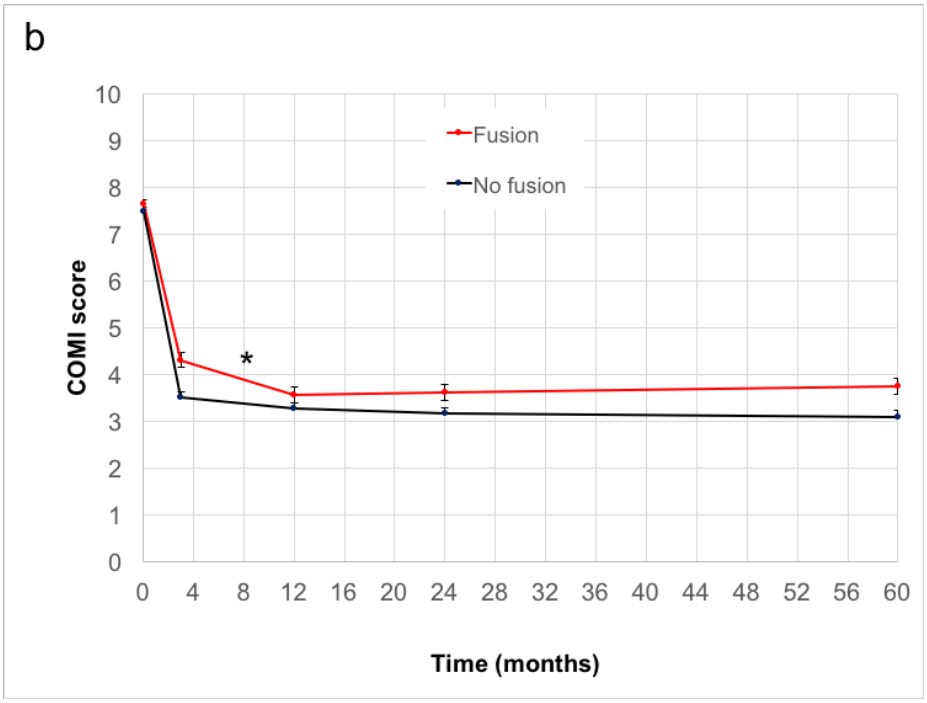


Figure 4-7: Group mean (95%CI) COMI score over time by: (a) pathology and (b) fusion/no fusion procedure (p<0.05 for the difference between fusion and no fusion for the pattern of change between 3 and 12 months' follow-up). N=2'959 patients with data at every time-point.*

Whether fusion had been carried out or not also had a significant influence on the course and extent of change in the COMI score: when no fusion had been carried out, the mean score plateaued out after just 3 months, whereas fusion patients did not achieve a stable value until 12 months' follow-up ($p<0.05$ for the interaction between group and time of measurement; Figure 4-7 b) and their final values remained slightly but significantly ($p<0.05$) worse than those of the non-fusion patients. The changes in mean COMI scores were also reflected in the results for the proportion of patients achieving the minimum clinically important change (MCIC; a 2.2-point reduction) for the COMI: for the whole group, the % achieving MCIC increased over time, being 69% at 3 months' follow-up then rising to 73% at 12 months and staying at a similar level (73-74%) up to 60 months' postoperatively (Table 4-8).

*Table 4-8: Proportion of patients achieving the minimal clinically important change score (MCIC) for the COMI at each time-point for each of the pathologies and for fusion/no fusion groups (N=2959 patients with data at every time-point). *Significant difference between the groups at all time-points (p < 0.001) ** Significant difference between the groups at 3- and 60-month follow-up*

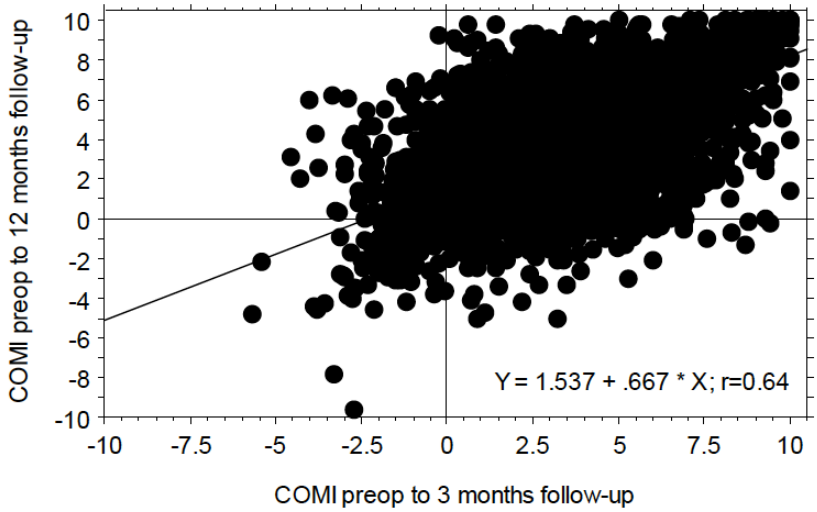
Achievement of MCIC				
Pathology*	3 mo FU	12 mo FU	24 mo	60 mo
SS	68.0%	70.2%	69.2%	68.2%
DH	74.8%	79.4%	79.8%	81.1%
Deg Spondy	72.5%	75.1%	77.6%	72.1%
Deg Def	61.3%	68.4%	68.8%	66.0%
Deg Seg	60.0%	74.7%	75.3%	73.7%
No cat	65.5%	70.4%	72.0%	73.3%
ALL	**68.8%**	**73.3%**	**73.9%**	**73.0%**
Treatment**				
Fusion	63.5%	72.5%	71.9%	69.7%
No fusion	71.6%	73.7%	75.0%	74.7%

The group differences (with respect to pathology and fusion) for the % achieving MCIC also reflected those for the mean COMI scores, with DH patients consistently showing the highest and degenerative deformity generally the lowest proportion achieving MCIC over the course of follow-up. At 3 months' follow-up, significantly fewer fusion patients than decompression-only patients achieved the MCIC (64% vs 72%, respectively; $p<0.0001$), but at 12 months' follow-up the difference was no longer significant ($p=0.46$) (Table 4-8).

The individual COMI change-scores from pre-operatively to the various follow-up time-points showed significant correlations ranging from $r=0.50$ (for the change-score at the earliest versus the latest follow-up) to $r=0.75$ (for the change-score at 12 months' versus 24 months' follow-up) (Table 4-9 and Figure 4-8).

Table 4-9: Pearson correlation coefficients showing the relationship between COMI change-scores from preoperative to follow-up at different time-points (all $p<0.0001$)

	Time period over which COMI change score calculated		
Time period	**Preop to 12 mo FU**	**Preop to 24 mo FU**	**Preop to 60 mo FU**
	r	r	r
Preop to 3 mo FU	0.64	0.57	0.50
Preop to 12 mo FU	-	0.75	0.65
Preop to 24 mo FU	-		0.71



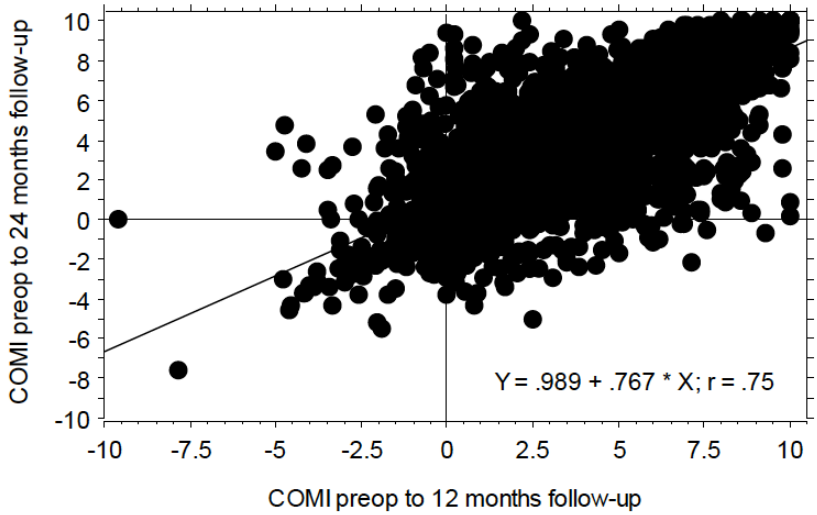


Figure 4-8: Correlation between COMI change-scores preoperative to follow-up at different time-points (top: preoperative to 3 months' follow-up vs to 12 months' follow-up; bottom: preoperative to 12 months' follow-up vs 24 months' follow-up). The graphs show that the vast majority of the patients (right upper quadrant) improved after surgery and remained so at the next follow up point. In the upper left quadrant, there are patients who showed an initial worsening after the surgery, but who finally improved.

Similarly, the proportion of individuals with exactly the same outcome status over time in relation to whether they had or had not achieved the MCIC was relatively stable, especially between consecutive time-points of assessment and beyond 12 months'

follow-up (Table 4-10). After 12 months, approximately 80% stayed in the same category at subsequent follow-ups, with the remainder changing category and showing discordant outcomes over time (first achieving MCIC and then no longer; or vice versa).

Table 4-10 - Percent of individuals with same status regarding whether they had or had not achieved MCIC when comparing subsequent time-points

	Time-point 2		
Time-point 1	**12 mo FU**	**24 mo FU**	**5y FU**
3 mo FU	76%	73%	70%
12 mo FU	-	82%	78%
24 mo FU	-	-	81%

5 Discussion

5.1 Main findings in relation to the literature

A series of studies were performed to better understand the changes in patient-rated outcome scores associated with the surgical treatment of degenerative disorders of the lumbar spine. In many cases of symptomatic degeneration of the lumbar spine, especially if spinal stenosis is present, an epidural injection is performed if oral pain medication and physical therapy fail to alleviate the symptoms. If the patient continues to be symptomatic, a surgical intervention — decompression with or without additional fusion — can be carried out with the aim of achieving a long-lasting improvement.

The results of the ESI study concerning the effect of epidural steroid injections in the year before surgery indicated no relevant impact on outcome after surgical decompression (with or without additional fusion) in patients with lumbar spinal stenosis causing neurogenic claudication. The EPOS study showed that the majority of improvement occurs by three months postoperatively. Hence, a follow up length of 6 months for the ESI study proved to be appropriate. The changes in the disease-specific Spinal Stenosis Measure (SSM) scores between baseline and six months' follow-up were not significantly different between patients with and without prior ESI.

The only difference to this pattern was seen in the group of non-operatively treated patients with prior ESI, who had a worsening of quality of life and pain after 6 months' follow up. Possibly, this might partly be explained by the prior ESI patients still experiencing some positive effect at the time of enrolment (even if this was several months back, theoretically between 0 to 12 months), such that the baseline values indicated a better status: with time, the status quo prior to the ESI would return and be reflected as an apparent worsening of the measured scores. Another explanation for the ESI-group differences in the change in pain and quality of life could be the higher proportion of patients with the two comorbidities, gonarthritis and heart failure in the group of patients with prior ESIs (28% and 10%, respectively) compared with the group without ESIs (10% and 3%, respectively; see Table 4-1).

Although there are studies reporting complications with detrimental consequences following epidural injections, such as bleeding, infection or permanent neurological

injury, their incidence is very low (96, 97). The first (and only) study on a large patient population that showed less improvement in patient-rated outcomes over four years' follow up in patients with spinal stenosis and a prior ESI was published in 2013 as a subgroup analysis of the Spine Patient Outcomes Research Trial (SPORT) (33). Less improvement was observed in both the operative and non-operative patient populations, which raises the suspicion that the results are simply reflecting the natural history of the condition rather than the effect of epidural steroids. Other concerns regarding the validity of the conclusions of the SPORT trial, based on objections to some of the methodology, have been raised as well (34, 35).

As the number of patients treated with ESIs has increased enormously in the last two decades (98), we considered it relevant to analyse the effect of epidural steroids in the large group of patients participating in the LSOS multicentre study. Our results showed that ESIs had no notable negative impact on short-term outcome in patients with lumbar spinal stenosis and claudication symptoms, regardless of whether they were subsequently treated operatively or non-operatively. This concurs with the empirical findings and summary of evidence compiled by the experts of insurance companies financing the treatment of painful spinal disorders. Some of these insurance companies in the United States only reimburse costs for surgery if a trial of treatment with epidural steroids has failed (99). However, even if surgery provides a superior and longer lasting improvement of neurogenic claudication than does conservative therapy, a complete resolution of the pain rarely occurs (89). This holds true, in fact, for the treatment of many kinds of symptomatic degeneration of the lumbar spine. In many patients, symptoms remain and vary from relatively minor and non-bothersome through to severe and debilitating. Since achievement of a pain-free state is the exception rather than the norm, we considered it of interest to measure the level of pain that patients believed they could at least live with, which we then considered to be the "patient acceptable symptom state".

The assessment of treatment outcome has changed considerably in recent decades, shifting from the surgeon's impression of his/her own work towards patient reported measures (100). However, there is little consensus on how success should be defined in relation to these patient reported outcomes. Intuitively, the success of treatment should be measured in relation to its goals; if the goal is pain relief, then a simple measure of

pain may represent the best measure of success. The sole use of a pain visual analogue scale as an outcome measure was criticized in the past for not being comprehensive enough, and other multidimensional aspects of the patient's condition were deemed important to consider as well. As such, more extensive questionnaires or questionnaire-batteries were introduced to evaluate the impact of the patient's problem on many different domains (101). However, a recent survey showed that for both spine surgeons and patients, pain relief was considered to be the most important parameter for a good outcome (102). A prospective study of expectations in patients with spinal stenosis showed that, preoperatively, most patients stated that an improvement in pain would be the single most important change in their condition that would lead them to say that the operation had helped; and, consistent with this, improvements in pain after surgery were most frequently declared to be *the* most important change experienced as a result of surgery (103).

Pain — as subjective as it is — can still be assessed relatively reliably using various types of pain scale, in both research and clinical practice (104, 105); knowing the level of pain that most patients could live with, and the likelihood of achieving this, may provide a useful reference frame when discussing with the patient realistic expectations regarding the potential outcome of treatment.

In the PASS study presented in this doctoral thesis, just 47% of the whole group of patients with degenerative spinal disorders achieved an acceptable symptom state. In a similar patient group, success rates based on achievement of the MCICimp or a global outcome measure were notably higher (approx 75%), whilst those based on satisfaction with the care process (rather than the treatment outcome *per se*) were higher still (85%)(89). The literature typically reports a wide range of spine surgical success rates, from 50% up to 95%(106). To a large extent, this discrepancy reflects differences in the definition and measurement of "success", as first discussed by Howe and Frymoyer (107) some 30 years ago. These authors analysed outcome data on 207 patients after discectomy with or without fusion, using 14 different published questionnaires. They showed that, depending on which questionnaire was used, the percentage of patients with satisfactory results varied from 60% to 97%. Since they included patients who had all undergone one and the same surgical intervention, the results represent the best-case rather than the worst-case scenario in terms of the potential variability. More recently

Copay et al (108) reported that fewer than half (40.5%) of all patients reported consistent changes on four different outcome measures after lumbar spine surgery.

Dichotomising patients' outcome scores as "successful" and "not successful" can sometimes be arbitrary and the proportions in each group depend very much on where the line is drawn regarding the cut-off indicating "success". In this paper we considered patients to be in an acceptable symptom state if they had declared that they were very satisfied or somewhat satisfied with their current symptom state (the top two answers on the 5-point scale). We could have been less stringent and considered "neither satisfied nor dissatisfied" to also be an acceptable state; however, given that patients were undergoing elective surgical procedures, with pain relief as the goal of surgery, we felt that an indeterminate response, in which the patient failed to endorse that (s)he was "satisfied", should not be deemed "success".

Interestingly, the low proportion of 47% of patients declaring their state as acceptable in the PASS study presented here fits reasonably well with previous data reported for a large and heterogeneous group of patients undergoing lumbar surgery, where 46.8% reported having "tolerable" pain at 1 year postoperative (108). If these levels of pain can be considered to represent "normal", i.e., the kind of level that is acceptable, is within the error of measurement, and would not normally be associated with disability and care-seeking, then a figure of approximately half of all patients experiencing pain of this intensity after surgery may not be quite as disheartening as it first appears. Furthermore, this figure should not necessarily discourage patients from having surgery, as the vast majority have already failed the alternative treatment method, i.e. having no surgery, contributing to the subsequent indication for surgery. In other words, all patients undergoing elective surgery for a painful degenerative disorder have already failed to improve with conservative treatment over a certain period of time prior to surgery. Nonetheless, about half of the patients in this challenging diagnostic group could be helped by the surgery.

The acceptable pain level was lower in the group of patients undergoing surgery for disc herniation (≤2) than it was in patients with spinal stenosis, degenerative disc disease, and degenerative spondylolisthesis (≤3). It was also lower in the small group of patients (a quarter of the whole group) with just low (VAS 0-3/10)/medium (VAS 4-6/10) levels of pain preoperatively. In contrast, patients with high levels of comorbidity or severe

(extreme) pain (VAS 9 or 10/10) at baseline tended to show higher values for the acceptable level of pain (≤4). Previous reports have shown that, in chronic conditions, patients find it possible to live with a higher level of pain than in acute conditions (109). The inability of patients with disc herniation to tolerate a higher level of pain might be explained in different ways. If pain arises suddenly, as it does in most cases of disc herniation, patients still remember their condition without pain, and may expect to get back to this state, being less willing to tolerate the restricted function imposed by pain. Studies show that patients with herniated disc and those with symptoms for less than 6 months more frequently expect complete pain-relief from surgery compared with those with other degenerative conditions or a longer duration of symptoms (102). Patients with lumbar disc herniation are also younger, which may make them less willing to live "the rest of their life" with a high level of pain, since the absolute length of time living this way is much longer. Nonetheless, age per se appeared to have no influence on the level of pain considered acceptable, confirming some previous studies in other musculoskeletal disorders (55, 110) and conflicting with others (111). Interestingly, gender, previous surgery and insurance status also had no influence on the PASS threshold and neither did the time of follow-up suggesting that — even if the proportion of patients in PASS might differ between the subgroups, with e.g. considerably fewer successes in those who have had previous surgery (Table 2) — the threshold considered to be acceptable is relatively robust. The stability of the PASS over time has also been reported in patients with ankylosing spondylitis (112). The finding that patients with worse baseline symptoms had a higher threshold for PASS (≤ 4) conflicts somewhat with the notion that the PASS is not influenced by the severity of the pre-treatment pain/disability, a criticism often levelled at the $MCIC_{imp}$(113). Nonetheless, even if there are remaining limitations to the use of PASS, the findings of the present study can help to improve future study designs.

When designing studies focusing on pain, it is essential to have a knowledge of what constitutes an "acceptable pain level". Having a cut-off value for indicating "notable/significant pain" may be of use when dichotomising patients in relation to the presence/absence of concomitant back pain in studies where the surgical indication is radiating/radicular pain or the other way around (low back pain studies with concomitant leg pain). Similarly, it may be useful when deciding who is considered to

have relevant residual pain after surgery (114); using a cut-off of zero is likely not valid, and does not allow for "normal" levels or the bounds of measurement error. Other implications of the study include the use of a PASS of ≤3 as a minimum pain level for entry to pain trials, so as to be sure of being able to assess whether treatment helped. If patients are below this threshold to start with, then the detection (and relevance) of any improvement is questionable. The use of the cut-off may also help in epidemiological studies when attempting to define what constitutes "pain" when evaluating its incidence and prevalence within a population. And finally, in terms of its use as an indicator of success after surgery, having such a stringent target may help to improve healthcare; differences in treatment methods may be more easily detected than when using outcome measures that yield very high success rates, with their concomitant ceiling effects. In striving to continuously improve the quality of care in spine surgery, a more critical objective may be the achievement of a state considered acceptable by the patient. It has been shown that feeling well is more important to patients than just feeling better (109).

The question naturally arises, as to when the time has arrived to say the maximum level of improvement has been achieved and no further improvement following the surgery can be expected. To this end, we analysed the evolution of patient rated outcome over time in the most common diagnostic groups and in two major categories of surgical intervention.

With our ever more hurried lifestyles, there is an increasing demand on the part of the patient to know as soon as possible whether the surgery has been successful. The literature to date tends to suggest that most of the improvement occurs in the first 3 months postoperatively, regardless of the pathology being treated, and the improved condition remains relatively stable between 3-6 months' and 2 years' follow-up (115, 116, 91, 117). However, the findings are not invariable (118, 119) and overarching conclusions are made difficult by the different outcome instruments, patient populations and diagnostic definitions used. Our study confirmed that, overall, there was minimal change in mean scores after 3 months; however, it also suggested that there are subtle differences amongst the diagnostic groups and, in particular, between treatments (instrumented fusion versus decompression only) for the course and extent of improvement after surgery. In terms of performing further diagnostic work-ups or

considering revision if the therapeutic goals are not reached, we need to know when the time has come to make such decisions.

For patients who underwent simple decompression without fusion for spinal stenosis/disc herniation, after 3 months the mean COMI score had already reached its approximate final value. Patients who had undergone fusion, in contrast, showed slightly less improvement in COMI up to 3 months postoperatively but a further slight improvement up to 12 months, with the best symptom state achieved being less favourable than that of patients undergoing decompression only. However, the extent of the differences between treatment groups in their improvement over time were relatively small, rarely exceeding half a point on the COMI or a difference of 7% with respect to the proportion achieving the MCIC for the COMI.

The differences between the degenerative diagnoses tended to follow a similar pattern to that dictated by the type of treatment: patients with pathologies that are typically treated with simple decompression (e.g. herniated disc and spinal stenosis) showed a reduction in COMI score after 3 months that remained pretty stable from thereon in; in contrast, patients with pathologies in which the pain is typically treated with fusion (e.g. degenerative segment disease) showed a lesser improvement after 3 months but a further slight decline in COMI score up to 12 months' postoperatively, after which things stabilised.

Even though some improvement was typically seen over the longer duration of follow-up, there were good correlations between the early and late results suggesting that the early postoperative results were good predictors of the longer term outcome. Within a 3-month time-frame, one should be able to ascertain whether the immediate goal of surgery — usually the relief of pain — has been achieved or not. If it has not, then we would argue that the situation is unlikely to improve substantially of its own accord. The functional capacity that was specifically impaired due to pain would be expected to show the same rapid recovery as pain after 3 months, with the remaining improvement (possibly the reversal of disuse and general "re-conditioning") taking a slightly slower and less dramatic course. This would be especially so in the case of fusion, and might explain the further slight improvement up to 12 months' follow-up. In terms of decision-making, this all means that massive improvement would be unlikely beyond 3 months, unless further intervention occurred.

The time course of change in HRQL after the treatment of different degenerative spinal disorders using different surgical procedures and assessed with one and the same outcome instrument has not been widely researched. To our knowledge, no studies have been published in the spine literature giving recommendations for the ideal or minimum length and timing of follow up. Nonetheless, these things are important to consider when establishing what might represent the "optimal" follow-up procedure. The frequency with which patient self-rated outcome questionnaires are administered, and the length of the outcome instrument used, most likely affect the patients' compliance with completion. Theoretically, the more often the measurements are made, and the longer the questionnaire battery, the more precise is our understanding regarding the course of change in outcome over time. However, the frequency and comprehensiveness of the assessment cannot be increased endlessly; instead, it should be restricted to the lowest level necessary to obtain reliable estimates, keeping the respondent burden to a minimum. Knowledge of the time-course of change in HRQL postoperatively should help to optimise the administration of questionnaires whilst maximising the information received.

In the Spine Patient Outcomes Research Trial (SPORT), repeated measurements were made over time: short-term follow up was at 6 weeks and 3 months, and longer-term at 6, 12, and 24 months; if time permitted, further assessments were made at 36 and 48 months from the time of enrolment (120). Studies on patients with adult spinal deformity have involved longitudinal assessments made preoperatively and then at 6, 12 and 24 months postoperatively (116). In both these studies, a levelling off of group mean values for the given outcome was seen at 12 months. In some instances, such as with total disc replacement devices used for the treatment of low back pain, a more rigorous scheme has been applied. For example, Siepe et al. published a follow up schedule of decreasing frequency in the first year (3 months, 6 months, 12months) with yearly follow-ups thereafter (121). The authors concluded that patient-reported outcome measures (VAS, ODI, and patient satisfaction rates) recorded at 6 months postoperatively were strongly correlated with the results at the 4-year follow up. For simple decompression for spinal stenosis, Grob et al (122) reported a strong correlation between 2-month and 2-year outcomes. Whilst some patients with a "good" initial

global treatment outcome showed a worsening over time, only few patients with a "poor" short-term outcome showed notable improvement after 2 years.

Some authors have been more skeptical as to whether the 3-month results are a good predictor of the 12-month outcome in patients with lumbar degenerative disorders. Parker et al (118) reported that, whilst the correlation between 3-month and 12-month ODI scores was good (r=0.71), on an individual patient level there was a "sizable discrepancy" (22%) in achievement of the MCIC at 3 versus 12 months. The same group reached a similar conclusion in a later paper (119). They suggested that predictive methods for functional outcome based on early patient experience can be used to help evaluate effectiveness in patient populations but not serve as a proxy for long-term individual patient experience (119). Our own data describing the predictive power of the early outcomes were almost identical to those of the above two studies — i.e., our achievement (or not) of MCIC at 3 months had a positive (or negative) predictive value for continued achievement (or not) at 12 months of 86% and 56%, respectively, compared with their 86% and 60% (118, 119) — yet we choose to interpret them somewhat more positively, for the following reasons. Firstly, as long as there is still slight improvement occurring between 3 and 12 months, as there was in all three studies, it is logical that the proportion achieving MCIC (i.e., achieving a given "absolute" score change) will increase from 3 to 12 months and hence the negative predictive value of the 3-month score will be relatively low. The positive predictive value, in contrast, at around 86% in all studies, was most acceptable. Further, like us, Parker et al (118) and Asher et al (119) both reported that approximately 22% patients had discordant data for achievement of MCIC at 3 and 12 months. However, when analysing such data, one should not forget that there is always some measurement error in assessments made at any two time-points. For COMI, the intraclass correlation coefficient for test-retest reliability within a "no clinical change" context is approximately 0.9. Hence, finding a correlation of approximately 0.70-0.75 between consecutive measurements over a longer time-period reflects reasonable predictive power. The standard error of measurement for the COMI is about 0.7 points (50). Given this degree of measurement error, and the threshold nature of the "achievement of MCIC or not", it is easy to imagine how a patient could fall into different categories on two occasions, especially if he/she is close to the 2.2 cut-off on one of the occasions.

Such measurement error would likely account for some of the up to 18%-30% shift in categories over time (Table 5 – 1) and doesn't necessarily indicate that all these cases are showing clinically relevant change between the assessment time-points.

Interestingly, in the study of Parker et al (118), the same proportions of patients continued to improve between time-points as worsen between time-points suggesting that this may reflect to some extent random error in the repeated measurements.

5.2 Limitations and weaknesses

Certain weaknesses and limitations of the studies presented in this thesis must be acknowledged in order to provide an honest and realistic picture to the reader when applying the conclusions in daily clinical practice.

Such limitations include the consequences of their being observational in nature, even if much of the data were collected prospectively. In the ESI study, patients were not randomly assigned to the four treatment groups (with or without ESI combined with non-operative or surgical treatment) and possibly selection bias was an issue. The administration of a specific treatment was in each case at the discretion of the physicians and their patients. The conclusions drawn here can only be applied to a specific patient population, i.e. lumbar stenosis patients with neurogenic claudication and without significant coronal deformity. The follow up of just six months might appear to be short. However, the effect of ESIs is much shorter than that (2-4 weeks), and hence any difference they would make should be apparent within six months of follow up, and the main benefit of surgery for spinal stenosis is usually evident within 3 months' postoperatively (see results of EPOS study; Figure 4-7). A further limitation of the ESI study is the relatively small number of non-operatively treated patients, limiting the precision of the results and potentially leading to a type II error (failure to reject a false null hypothesis).

A further limitation is that we did not consider the specific effects of treatment modality (e.g. route of administration of epidural injections, type of decompression, presence of fusion, conventional or minimal invasive techniques) in the analyses. However, whilst these may have shown an influence on, for example, the % of patients in PASS, there is no reason to expect them to influence the cut-off associated with *being* in PASS. In

addition, subdividing the patient cohort according to the type of treatment would have resulted in smaller group sizes and hence less statistical power when comparing groups in any of the presented studies. Our definition of success (PASS) was somewhat arbitrary; if we had taken only very satisfied patients, then the cut-off would have yielded a lower pain level (see Figure 4-4).

In the PASS and EPOS studies some of the patients were not able to be characterised into a distinct degenerative pathology sub-group. This was the result of: (1) some patients having additional "non-degenerative" pathologies that would have led to too many sub-groups being formed, and may have confused the overall picture; and (2) the "multiple option" approach used in the current Spine Tango documentation form, which allows the presentation of multiple degenerative pathologies to be indicated. A new iteration of the Spine Tango form (version 2017, in use from 2018) addresses this limitation by forcing the surgeon to indicate the primary degenerative problem being treated (herniated disc, degenerative disc disease, etc) and then document any other types of degeneration diagnosed. Another limitation is that we excluded patients who had had previous surgery at the same segment of the spine, which has been shown to have an influence on outcome (80). Hence the outcomes are only applicable to those undergoing first-time surgery.

In the EPOS study, a certain number of patients (4% at 12 months, 7% at 24 months and 11% at 60 months' follow-up) who still completed a questionnaire at the requisite time intervals after their index surgery declared having had another operation after that index surgery, either on the same or a different segment of the spine. Others still were re-operated and subsequently dropped out of the regular reporting schedule. It is not known how this might have influenced the outcomes reported over the period of study. Nonetheless, the items in the COMI enquire about the "current state" not "how have things changed"; hence, even if a revision occurred subsequent to the index surgery, we were still able to use the preoperative data from the index operation, and any available follow-up data to provide a valid change score in relation to the course of change after the index surgery. We have no specific data on how patients with an initially poor outcome were managed and the various treatment strategies employed (conservative or surgical) that might have influenced the outcome.

There was no assessment between 3 months and 12 months, so we cannot know when, exactly, improvement plateaued off after fusion surgery. And finally, a proportion of the patients dropped out and could not therefore be included in the repeated measures analysis, since this was intended to evaluate the same group of individuals over time. Often the patients' dropping-out was for reasons unlikely to bias our analyses of outcome (death, moving abroad, etc.) but sometimes it was due to dissatisfaction with the result and/or further treatment having been carried out. This would likely have caused a slightly positive bias to the results reported here. Nonetheless, we can still say that the majority of the patients had a regular recovery pattern (approximately 70% completed all assessments up to 5 years' postoperatively) and demonstrated the presented course of improvement.

6 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 in patients with neurogenic claudication due to lumbar spinal stenosis.
- Epidural steroid injections can be offered to patients as a non-surgical intervention before more invasive surgical options are offered, without fear of ramifications for the subsequent surgical outcome.
- 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 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, although even in patients undergoing fusion most of the improvement has occurred by 3 months' postoperative. 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.

7 Összefoglalás

Az ágyéki gerinc degeneratív megbetegedései egyre nagyobb egészségügyi kiadásokat okoznak, így a kezelési eredmények mérésének jelentősége megnőtt. Az elmúlt években fokozatosan változott a sikeres kezelés definíciója. Míg korábban a kezelő orvos maga állapította meg az eredményesség mértékét, manapság a beteg teszi ezt szubjektív és független önértékelő kérdőívek kitöltésével. Ez utóbbit Patient rated outcome measures-nek hívják. Dolgozatomban ismertetett ambispektív tanulmányok ilyen kérdőívek elemzésén alapulnak.

Időskorban gyakori a lumbális stenosis. Gyógytorna és fájdalomcsillapítás sikertelensége esetén az epidurális szteroid infiltráció a következő lépcsőfok a műtéti kezelés előtt. Kétszáznyolcvanegy betegen elvégzett vizsgálatunkkal megállapítottuk, hogy az epidurális kortikoszetroid infiltráció nem rontja a későbbi műtéti kezelés eredményességét azokhoz a betegekhez viszonyítva, akik ilyen kezelést nem kaptak.

A degeneratív gerincbetegségek többsége fájdalommal jár, mely az ehhez társuló lecsökkent életminőséggel együtt képezi a műtéti kezelés indikációját. A gerincsebészetben eddig nem alkalmazott koncepciót, „a beteg számára elfogadható tüneti szint” koncepcióját vezettük be. Egy bizonyos fájdalomszint alatt a betegek még elégedetten tudnak élni. Ahhoz, hogy ezt meghatározzuk, a következő kérdésre adott választ viszonyítottuk a fájdalom intenzitásához: „Mennyire lenne elégedett, ha az élete hátralévő részét a jelenlegi állapotában kéne leélnie?”. Az intézetünkben lumbális gerincműtéten átesett 6943 beteg anyagának tanulmányozásával megállapítottuk, hogy ágyéki porckorongsérv esetén az elfogadható fájdalomszint ≤2 (0-10-es skálán), az összes többi diagnózis esetén ≤3.

Egy másik fontos és még megválaszolatlan kérdés volt, hogyan alakul a betegek állapota ágyéki gerincműtét után. Milyen hosszú ideig tart a lábadozás? Mennyi idő elteltével lehet egy beavatkozás eredményét megállapítani? Ehhez 4287 betegünk műtét előtti és a műtét után négy különböző időpontban kitöltött kérdőíveit elemeztük ki. Azt találtuk, hogy egy év elteltével már nem várható további javulás, sőt, egyszerű dekompressziós műtéteket követően már 3 hónap után kialakul a végleges eredmény. Ez azt jelenti, hogy ha ezen idő alatt nem érte a beteg el a kívánt javulást, a sikertelenség okának keresését haladéktalanul meg kell kezdeni.

8 Summary

Degenerative disorders of the lumbar spine are becoming an increasingly costly problem for healthcare systems worldwide. The importance of measuring patient outcomes has hence never been greater. The definition of treatment success has evolved in the past decades. Previously, it was the surgeon who judged whether an intervention was successful, whereas nowadays patients complete questionnaires and self-report their outcome, resulting in a subjective and independent appraisal of the result. Such questionnaires are referred to as patient rated outcome measures. The ambispective studies presented in this thesis rely on the analysis of data collected using such measures. One of the most common disorders in the aging patient is spinal stenosis. If the first line of treatment fails, epidural steroid injections are the next step before a surgical intervention is considered. We analysed the outcome of 281 patients enrolled in a multicentre study and found that the outcome of surgery was not inferior in those treated with previous epidural steroid injections as compared to those without.

The majority of degenerative disorders of the lumbar spine are associated with pain and decreased health-related quality of life, which in turn can become an indication for surgery. A new concept was introduced into spinal surgery, which determines the highest level of pain that is considered an "acceptable symptom state" by the patient. To this end, a question was asked “If you had to spend the rest of your life with the symptoms you have right now, how would you feel about it?“, and the responses were analysed in relation to the corresponding pain intensity. Using the outcome data of 6943 patients operated on in our spine centre, we found that the acceptable level of pain was ≤2 (on a scale from 0 to 10) for disc herniation and ≤3 for all other degenerative pathologies.

Another important and as yet unanswered question concerned how outcome changed over time following lumbar spine surgery. How long does it take to recover? How long should we wait to judge the final outcome? To answer these questions, we analysed the questionnaires completed by 4287 patients preoperatively and at four time-points up to 5 years postoperatively. We found that there is no further improvement to be expected beyond one year, and for patients undergoing simple decompression, beyond just 3 months. As a consequence, if improvement is not seen by one year at most, the search for possible causes of treatment failure should be initiated without further delay.

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10 Publications related to this dissertation

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