Tampere University

LEEVI TOIVONEN

Long-Term Outcome of Lumbar Spine Fusion Surgery

Tampere University Dissertations 674

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ACADEMIC DISSERTATION
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the Faculty of Medicine and Health Technology
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ACADEMIC DISSERTATION
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To Sylvi, Sanni, Alise,
and Loviisa

Ex spondylodesim potentia!

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Kangasala, September 2022

Leevi Toivonen

ABSTRACT

Lumbar spine fusion (LSF) surgery is an established method in the treatment of several spinal pathologies. Those conditions are usually encumbered with substantial pain and disability, and thus impaired quality of life, which may also result in depressive symptoms. Prior literature is ambiguous whether depressive symptoms compromise LSF outcome. Mostly, knowledge of the long-term outcome of LSF surgery is limited. A major cause of recurring spinal problems beyond LSF is adjacent segment disease (ASD). Its pathogenesis is not fully understood. Pre-existing literature is conflicting whether sagittal alignment in LSF predisposes to ASD.

Aim of this thesis was to evaluate the long-term outcome of LSF surgery. The 5-year outcome was investigated on a prospective follow-up of elective LSF patients (n=523). Outcome measures included the Oswestry disability index (ODI), and the SF-36 health-related quality of life (HRQoL) survey. Those and mortality were compared to a matched general population sample (n=682). Influence of depressive symptoms on the 5-year outcome (n=392) was scrutinized using the Depression scale (DEPS) and ODI. All spinal reoperations were explored from the hospital records to determine the 10-year rates of revision surgeries for ASD. Rates were compared across surgical indications (n=365). Postoperative lumbar sagittal alignment was determined from standing radiographs. Effect of poor balance on the risk of revision for ASD was evaluated (n=215).

Generally, the benefits of LSF on disability and HRQoL were sustained at 5 years. Mortality was not increased. Depressive patients gained similar benefits with their non-depressive counterparts. In addition, LSF relieved the depressive symptoms. Isthmic spondylolisthesis infrequently became complicated with ASD (4.8%) whereas revisions for ASD accumulated almost linearly over time after LSF for degenerative spinal disorders (21%). Effect of postoperative sagittal alignment on ASD development could not be demonstrated.

TIIVISTELMÄ

Lannerangan luudutusleikkaus on vakiintunut menetelmä usean selkäongelman hoidossa. Leikkaushoitoa harkittaessa selkäsairaus tavallisesti aiheuttaa vaikeaa kipua sekä alentaa toimintakykyä ja elämänlaatua. Tämä voi johtaa myös masennusoireisiin. Aiemman tutkimustiedon perusteella on epävarmaa, huonontavatko masennusoireet lanneselän luudutusleikkausten tuloksia. Myös luudutusleikkausten pitkäaikaishyödystä on niukasti tietoa. Yleinen syy luudutusleikkausten jälkeen ilmaantuville selkäongelmille ovat viereisen liikesegmentin ongelmat (ASD). ASD:n syntymekanismia ei täysin tunneta. Aiemmat havainnot ovat ristiriitaisia sen suhteen, vaikuttaako lannerangan ryhti ASD:n syntyyn.

Tämän tutkimuksen tavoitteena oli arvioida lannerangan luudutusleikkausten pitkäaikaistuloksia. Viiden vuoden seurannassa elektiivisten lannerangan luudutusleikkausten (n=523) tuottamaa hyötyä arvioitiin Oswestryn toimintakykyindeksillä (ODI) ja SF-36-elämänlaatumittarilla. Mittareiden tuloksia ja kuolleisuutta verrattiin kaltaistettuun väestöotokseen (n=682). Lisäksi masennusoireiden vaikutusta viisivuotistulokseen arvioitiin (n=392) käyttäen depressioseulaa (DEPS) sekä ODI:a. ASD:n takia tehtyjen uusintaleikkausten ilmaantuvuus 10 vuoden aikana määritettiin käymällä potilastiedoista läpi kaikki myöhemmät selkäleikkaukset. Uusintaleikkausriskiä verrattiin alkuperäisten luudutusleikkaukseen johtaneiden diagnoosien välillä (n=365). Luudutusleikkauksen jälkeisen lannerangan ryhdin vaikutusta uusintaleikkausriskiin arvioitiin (n=215).

Luudutusleikkausten tuottama hyöty toimintakykyyn ja elämänlaatuun pääosin säilyi viiden vuoden seurannassa. Kuolleisuus ei lisääntynyt. Leikkaukset vähensivät masennusoireita, eivätkä leikkausta edeltäneet masennusoireet heikentäneet leikkaustulosta. Kymmenen vuoden aikana ASD ilmaantui harvoin (4,8 %) potilaille, joilla oli nikamakaaren höltymästä johtuva liukuma. Sen sijaan uusintaleikkausmäärä ASD:n takia kasvoi lineaarisesti ajan myötä (21 %) potilailla, joiden alkuperäinen selkäongelma oli rappeumaperäinen. Leikkauksen jälkeisellä ryhdillä ei pystytty osoittamaan olevan vaikutusta ASD:n ilmaantumiseen.

CONTENTS

ABBREVIATIONS

AI	Artificial intelligence
ALIF	Anterior lumbar interbody fusion
ASD	Adjacent segment disease
ATP	Anterior to psoas
CLBP	Chronic low back pain
CI	Confidence interval
DDD	Degenerative disc disease
DEPS	Depression scale
DLSD	Degenerative lumbar spine disease
DS	Degenerative spondylolisthesis
HR	Hazard ratio
HRQoL	Health-related quality of life
IS	Isthmic spondylolisthesis
LBP	Low back pain
LDI	Lordosis distribution index
LL	Lumbar lordosis
LLIF	Lateral lumbar interbody fusion
LLL	Lower lumbar lordosis
LSS	Lumbar spinal stenosis
LSF	Lumbar spine fusion
MRI	Magnetic resonance imaging
MCID	Minimum clinically important difference
MCS	Mental component summary score
MISS	Mini-invasive spine surgery
NRS	Numeric rating scale
ODI	Oswestry disability index
OLIF	Oblique lumbar interbody fusion
PCS	Physical component summary score
PI	Pelvic incidence
PLF	Posterolateral fusion

PLIF	Posterior lumbar interbody fusion
PROM	Patient-reported outcome measure
PT	Pelvic tilt
RCT	Randomized controlled trial
SD	Standard deviation
SF-36	The 36-item short-form 36 health survey
SL	Segmental lordosis
SS	Sacral slope
TDR	Total disc replacement
TLIF	Transforaminal lumbar interbody fusion
VAS	Visual analogue scale
XLIF	Extreme lateral lumbar interbody fusion

ORIGINAL PUBLICATIONS

I Toivonen L*, Pekkanen L*, Neva MH, Kautiainen H, Kyrölä K, Marttinen I, Häkkinen A. Disability, Health-Related Quality of Life and Mortality in Lumbar Spine Fusion Patients-A 5-Year Follow-Up and Comparison With a Population Sample. Global Spine J. 2022;12(6):1052-1057. https://doi.org/10.1177/2192568220972977

II Toivonen L, Häkkinen A, Pekkanen L, Salonen A, Kautiainen H, Neva MH. Influence of Depressive Symptoms on the Outcome of Lumbar Spine Fusion-A 5-year Follow-up Study. Spine (Phila Pa 1976). 2021;46(6):408-412. https://doi.org/10.1097/BRS.0000000000003803

III Toivonen LA, Mäntymäki H, Häkkinen A, Kautiainen H, Neva MH. Isthmic Spondylolisthesis is Associated with Less Revisions for Adjacent Segment Disease After Lumbar Spine Fusion Than Degenerative Spinal Conditions: A 10-Year Follow-Up Study. Spine (Phila Pa 1976). 2022;47(4):303-308. https://doi.org/10.1097/BRS.0000000000004242

IV Toivonen LA, Mäntymäki H, Häkkinen A, Kautiainen H, Neva MH. Postoperative sagittal balance has only a limited role in the development of adjacent segment disease after lumbar spine fusion for degenerative lumbar spine disorders: A sub-analysis of the 10-year follow-up study. Spine (Phila Pa 1976) 2022;47(19):1357-1361. https://doi.org/10.1097/BRS.0000000000004400

*Equal contribution.

AUTHOR'S CONTRIBUTION

I Toivonen and Pekkanen drafted the manuscript, Toivonen participated in the statistical analyses, Toivonen wrote the final version of the manuscript, Toivonen submitted the manuscript.

II Toivonen participated in the statistical analyses, drafted the manuscript, wrote the final version of the manuscript, Toivonen submitted the manuscript.

III Toivonen participated in the study planning, data acquisition, analyzed all primary surgeries and reoperations, participated in the statistical analyses, drafted, and wrote the manuscript, and submitted the manuscript.

IV Toivonen participated in the study planning, data acquisition, Toivonen and Mäntymäki performed the radiological measurements, Toivonen participated in the statistical analyses, drafted, wrote, and submitted the manuscript.

1 INTRODUCTION

In recent decades, the number of lumbar spine fusion (LSF) surgeries has amplified in western countries (Deng et al., 2021, Grotle et al., 2019). After being first introduced into management of instability and deformity, use of LSF has expanded into treatment of heterogeneous spinal pathologies (Schnake et al., 2019, Reisener et al., 2020). Conditions leading to LSF are often severely disabling (Yavin et al., 2017). On the other hand, LSF operations are costly and expose patients to the risk of complications. Evolving techniques and advanced perioperative care have decreased the treatment-related morbidity and enabled surgical management of even more fragile patients. While the aging populations with elevated requirements set growing demand on healthcare systems, the limited resources, on the other hand, may increasingly restrict the succeeded surgeries.

In shorter follow-ups, benefits of LSF surgery have been established in diverse populations (Pekkanen et al., 2014, Weinstein et al., 2007, Strömqvist et al., 2013, Möller and Hedlund, 2000b). It is essential to know how those benefits are preserved in longer follow-ups. Obviously, durable benefits increase the cost-effectiveness of treatment (Glassman et al., 2012).

Second, long-lasting pain and disability burden patients mentally. Patients with depressive symptoms are reported to benefit less from spine surgery than non-depressive patients (Trief et al., 2006, Sinikallio et al., 2011). On the contrary, equal benefits also have been described (Wahlman et al., 2014, Wagner et al., 2020). Proper knowledge of the depressive patients' surgical outcomes will aid in the surgical decision-making.

A common reason for late reoperations following LSF is adjacent segment disease (ASD) (Gerling et al., 2017, Kraemer et al., 2012). Revisions for ASD are frequently heavy and costly surgeries including extension of fusion. While, on the one hand, ASD is considered a sequela of the ongoing degenerative process in the spine, LSF surgery may, on the other hand, accelerate the degeneration by increasing loading at the adjacent disc level (Hashimoto et al., 2019). Knowledge of the incidence of ASD is modest, and even less is known of the incidence with specific indications (Xia et al., 2013). If isthmic spondylolisthesis (IS) infrequently becomes

complicated with ASD as some reports suggest (Choi et al., 2014)–in contrast to degenerative pathologies–this would emphasize the role of the wide-ranging spinal degeneration in ASD pathogenesis.

Spinal sagittal balance is often considered relevant to ASD so that either loss of lordosis or failure to restore lordosis in LSF predisposes to ASD progression (Hashimoto et al., 2019, Alentado et al., 2016). Accordingly, if ASD can be prevented with adequate surgical technique, it is of paramount importance.

2 REVIEW OF THE LITERATURE

2.1 Lumbar spine fusion (LSF) surgery

Almost without exception, the goal of LSF surgery is to treat pain and disability. Pain is usually originated from neural compression or spinal degeneration. Spinal fusion may be performed to cease pathological movement between vertebrae (i.e., instability), or facilitate adequate neural decompression, and prevent the development of postsurgical instability.

2.1.1 Indications

LSF is an established method in the management of several spinal pathologies, but fusions are performed for more controversial indications, as well (Martin et al., 2019). Common indications are listed in **Table 1**. Huge variation has been reported in practices within and between countries (Yavin et al., 2017, Mäntymäki et al., 2021, Lønne et al., 2019).

Table 1. Common indications for LSF surgery.

Indication	Reference(s)
Isthmic spondylolisthesis (IS)	Saraste, 1993; Pekkanen et al., 2014
Lumbar spinal stenosis (LSS)	
with or without degenerative spondylolisthesis (DS)	Weinstein et al, 2008; Weinstein et al., 2007; Malmivaara et al. 2007; Försth et al., 2016
foraminal stenosis	Lee et al., 2010
Postoperative conditions	
postoperative instability or deformity	Iida et al., 1990; Phillips and Cunningham, 2002
recurrent disc herniations	Yoshihara et al., 2016
Degenerative disc disease (DDD)	Fritzell et al., 2001; Fairbank et al., 2005; Hedlund et al., 2016
Scoliosis or kyphosis	Bridwell et al., 2010; Kelly et al., 2019; Smith et al., 2021
Posttraumatic deformity	De Gendt et al., 2021
Fractures	Vaccaro et al., 2016; Joaquim et al., 2019
Tumors and metastases	Fanous and Fabiano, 2017; Boriani 2018
Infection	Gentile et al., 2019

Isthmic spondylolisthesis (IS) is the anterior translation of a vertebral body relative to its caudal segment resulting from spondylolysis (i.e., a stress fracture or a congenital defect in pars interarticularis) (**Figure 1**) (Saraste, 1993). In registry-based data, up to 20% of elective LSF surgeries were performed for IS (Pekkanen et al., 2014). In an RCT comparing exercise program with posterolateral fusion (with or without transpedicular fixation) in patients with symptomatic IS, the surgical treatment yielded better functional results and greater pain relief than conservative treatment in 1- and 2-year follow-ups (Möller and Hedlund, 2000b). A longer follow-up (mean 9 years) of the same cohorts revealed a partial loss of surgical benefit although the perceived overall outcome of surgery still surpassed that of conservative treatment (Ekman et al., 2005). A Swedish register-based study showed that instrumented fusions for IS resulted in better pain-relief and satisfaction to treatment than fusions in situ, although revision surgeries were more frequent after instrumented fusions (Endler et al., 2017).

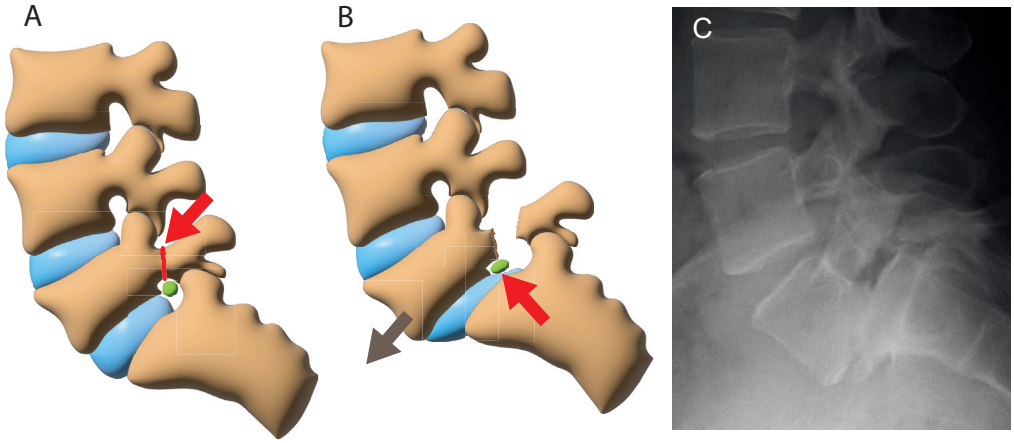


Figure 1. **A.** Spondylolysis due to fractured pars interarticularis **B.** resulting in isthmic spondylolisthesis (IS) causing foraminal compression of the exiting nerve root (green). **C.** A radiograph showing L5 spondylolysis and spondylolisthesis.

Degenerative spinal disorders are the main reason to LSF surgery. The disease entity per se is heterogeneous ranging from disc herniation to degenerative deformities. The most common manifestation of this condition is spinal stenosis (LSS, lumbar spinal stenosis) which may present with degenerative spondylolisthesis (DS). In spinal stenosis, changes from disc degeneration and facet joint arthrosis lead to compression of neural structures in spinal canal or neural foramina (Genevay and Atlas, 2010). Surgical decompression renders superior outcome over conservative treatment in spinal stenosis with moderate to severe symptoms (Weinstein et al.,

2010, Weinstein et al., 2008a, Malmivaara et al., 2007) However, a major proportion of LSS can be managed with decompression without fusion (Grob et al., 1995, Rampersaud et al., 2014, Försth et al., 2013, Lønne et al., 2019).

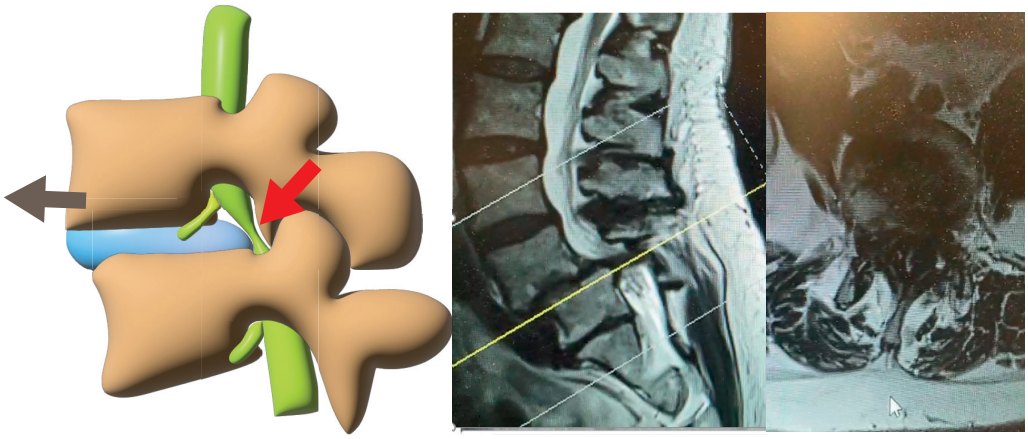


Figure 2. Degenerative spondylolisthesis (DS) resulting in severe central spinal stenosis.

Degenerative spondylolisthesis (DS) is the anterior displacement of a vertebra with intact posterior arch over the subjacent vertebra. Therefore, the condition results in the narrowing of spinal canal and foramina (**Figure 2**) (Bydon et al., 2019). 3 mm slippage has been used as a limit for DS although the definition is not universally acknowledged (Ghogawala et al., 2016, Reitman et al., 2021). Furthermore, management of LSS with DS remains controversial, as well, despite of the emerging evidence stating that LSF produces no benefit in addition to decompression surgery. In 2016, the same issue of New England Journal of Medicine released two RCTs with diverging findings on adding fusion to decompression for DS (Försth et al., 2016, Ghogawala et al., 2016). The Swedish study with looser inclusion criteria and a lower dropout rate, and therefore better external validity, found that both treatments yielded similar clinical outcomes (Försth et al., 2016). In Ghogawala et al. (2016), the physical component score (PCS) of SF-36 instrument indicated better functional mid-term outcome with LSF, in addition to that the decompression only patients ended up in revision surgery more often. The Försth study, nevertheless, influenced treatment practices in Finland, having reduced LSF surgeries relative to decompressions (Ponkilainen et al., 2021). A recent RCT from Norway demonstrated that decompression only for single level DS did not result in inferior clinical outcome as compared to LSF, even though reoperations were slightly

more frequent in the decompression group (Austevoll et al., 2021). A recent meta-analysis seconded this view (Chen et al., 2020).

Broad consensus prevails among spine surgeons that certain subgroups of DS, namely patients with instability, are best treated with LSF (Spina et al., 2019). However, there exist no agreement for the definition of instability (Leone et al., 2007). Although Austevoll et al. (2021) included patients with "dynamic instability" (by flexion-extension radiographs), they were inconclusive on this specific subgroup alone. Decisions still need to be made at the discretion of the treating surgeon.

Foraminal stenosis may be originated from horizontal (due to ligamentum flavum thickening and facet arthrosis) or vertical (due to disc space narrowing and/or spondylolisthesis) narrowing of neural foramen, or from the combination of those both (**Figure 2**) (Lee et al., 2010). Especially the vertical narrowing often warrants LSF with an interbody spacer to restore the foraminal height as indirect decompression. Austevoll and colleagues had excluded patients with foraminal stenosis given DS from their RCT (Austevoll et al., 2021).

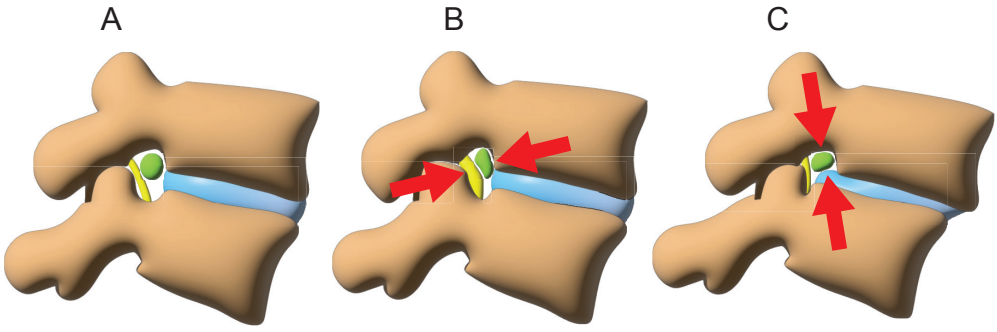


Figure 3. Foraminal stenosis. **A.** Healthy foramen harboring the exiting nerve root (green). **B.** Horizontal foraminal narrowing due to facet arthrosis and ligamentum flavum (yellow) thickening. **C.** Vertical foraminal stenosis due to disc shallowing and spondylolisthesis.

Postoperative conditions lead to LSF surgeries, as well. Persistent pain following spine surgery is a complex issue. Residual or recurrent stenosis is best addressed with meticulous decompression, but instability or deformity may indicate LSF (Iida et al., 1990, Phillips and Cunningham, 2002, Sebaaly et al., 2018). Recurring disc herniations are often managed with fusion, although re-discectomies have been reported to grant similar outcomes (Yoshihara et al., 2016). For chronic back pain after previous disc herniation surgery LSF appeared futile (Brox et al., 2006).

LSF in the management of axial pain attributed to disc degeneration is controversial. There is evidence supporting LSF with this indication, although the

benefit might be marginal (Fritzell et al., 2001, Fairbank et al., 2005, Hedlund et al., 2016). Also, contradictory findings exist (Brox et al., 2010).

Modern LSF techniques provide a powerful means to manage deformities of various origins. Patients with adult deformity (predominantly scoliosis or kyphosis) may gain long-lasting profit from fusion surgery (**Figure 4**) (Bridwell et al., 2010, Kelly et al., 2019, Smith et al., 2021). With adolescents, spinal fusion for idiopathic scoliosis may yield even better long-term clinical outcome than fusion for spondylolisthesis (Helenius et al., 2008). Posttraumatic deformity often is painful kyphosis which can be addressed with fusion under the corrective surgery (De Gendt et al., 2021).

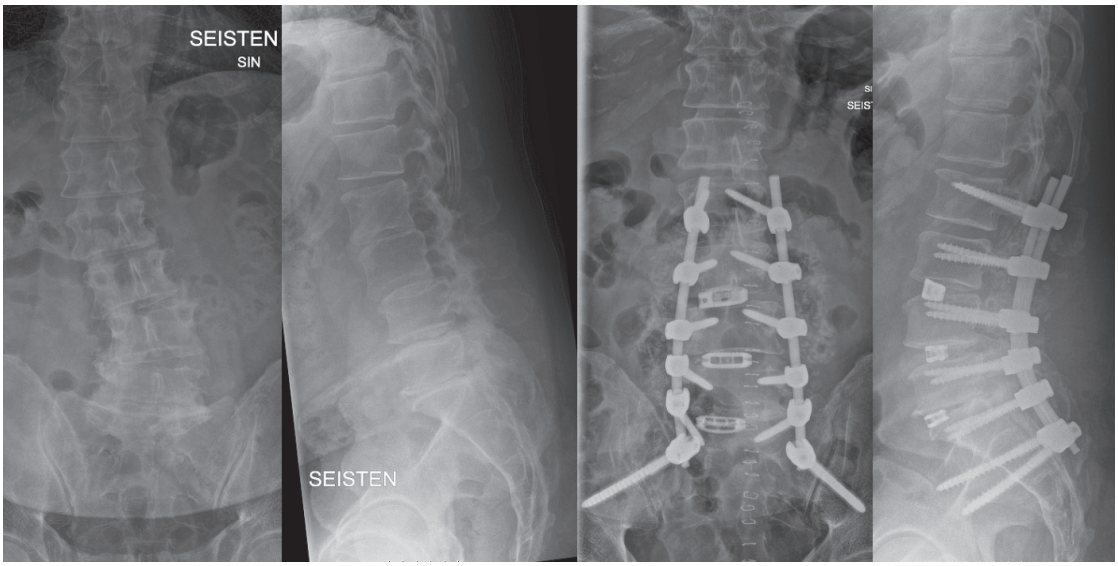


Figure 4. Radiographs demonstrating lumbar kypho-scoliosis accompanied with stenosis treated with lumbopelvic fusion.

Fractures, spinal neoplasms, and infection causing spinal instability or destruction are specific indications for fusion surgery (Vaccaro et al., 2016, Joaquim et al., 2019, Rajasekaran et al., 2017, Fanous and Fabiano, 2017, Boriani, 2018, Gentile et al., 2019).

2.1.2 Methods

In 1911, Hibbs first described a spinal fusion technique for the management of progressive tuberculotic deformity (Hibbs, 2007). Fusion was pursued by fracturing of the spinous processes and subsequent bedrest. A comparable method, (non-instrumented) posterolateral fusion (PLF), where bone graft is applied on decorticated transverse processes, pars interarticularis, and facet joints, can still be counted lege artis (Levin et al., 2018).

Introduction of pedicle screws (**Figure 5**) in 1960's revolutionized LSF surgery. Pedicle screw techniques enable rigid fixation and early mobilization of patients along with providing a means to manage deformities (Roy-Camille et al., 1986, Vaccaro and Garfin, 1995). Use of pedicle screw instrumentation in PLF may increase the fusion rate, but its advantage on the clinical outcome is not as overt (Boos and Webb, 1997, Bjarke Christensen et al., 2002, Möller and Hedlund, 2000a, Abdu et al., 2018, Poussa et al., 2006).

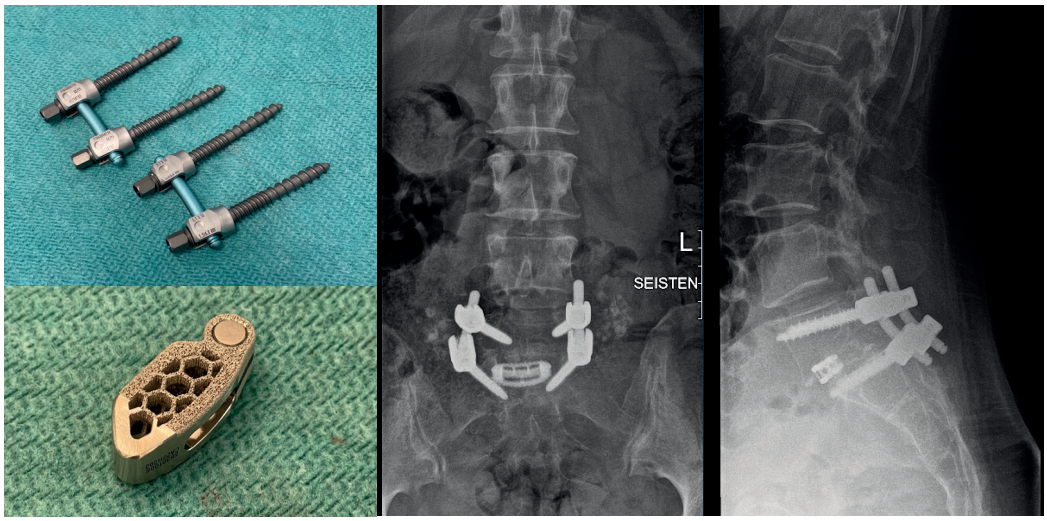


Figure 5. Example of pedicle screw instrumentation and a TLIF spacer for a single level fusion. Radiographs showing L5–S1 fusion for isthmic spondylolisthesis.

Several lumbar interbody fusion techniques (**Table 2**) have been developed to add anterior column support to bolster the posterior instrumentation, to facilitate indirect foraminal decompression, and help restore the alignment (Mobbs et al., 2015, Lenz et al., 2022, Schnake et al., 2019). After the first description of posterolateral lumbar interbody fusion (PLIF) (Briggs and Milligan, 1944), the technique has evolved remarkably, and largely it has been replaced by transforaminal lumbar interbody fusion (TLIF) technique (**Figure 5**) (Harms and Rolinger, 1982, de Kunder et al., 2017). In addition to the posterior techniques, several anterior approaches to the disc space mostly via retroperitoneal corridors have been introduced. They allow utilization of large, hyperlordotic spacers, and they help reduce the risk of neural damage (Capener, 1932, Hsieh et al., 2007, Mobbs et al., 2016, Mayer, 1997, Pimenta, 2001, Ozgur et al., 2006). Optimal approach depends on the anatomical features of the level (**Figures 6** and **7**).

Table 2. Lumbar interbody fusion techniques.

Abbreviation	Explanation	Introduction
PLIF	Posterior lumbar interbody fusion	Briggs and Milligan, 1944
TLIF	Transforaminal lumbar interbody fusion	Harms and Rolinger, 1982
ALIF	Anterior lumbar interbody fusion	Capener, 1932
OLIF/ATP	Oblique lumbar interbody fusion/Anterior to psoas	Mayer, 1997
XLIF/LLIF	Extreme lateral/lateral lumbar interbody fusion	Pimenta, 2001

The interbody spacers (either posteriorly or anteriorly implanted) are consistently used in combination with the pedicle screw instrumentation. Such a construct may be entitled circumferential or 360º fusion. However, there are options to augment the interbody spacer via single anterior approach, *e.g.*, using a standalone ALIF screw cage or an anterior plate, thus omitting the need for pedicle screws. Along with instrumentation, decent preparation of the fusion site and use of appropriate graft material are requisite for successful fusion (Boden, 2002, Scheufler and Diesing, 2015).

Further, mini-invasive techniques (MISS, mini-invasive spine surgery) have been introduced in an attempt to decrease the approach-related morbidity, mostly by avoiding extensive detachment of posterior spinal musculature. MISS can be utilized both in implanting pedicle screws and interbody spacers, and decompression. Despite the potentially faster early recovery, superior clinical outcomes of MISS over open surgery have not been established (Vazan et al., 2017, Khan et al., 2015, Phan et al., 2015, Le et al., 2021, Heemskerk et al., 2021).

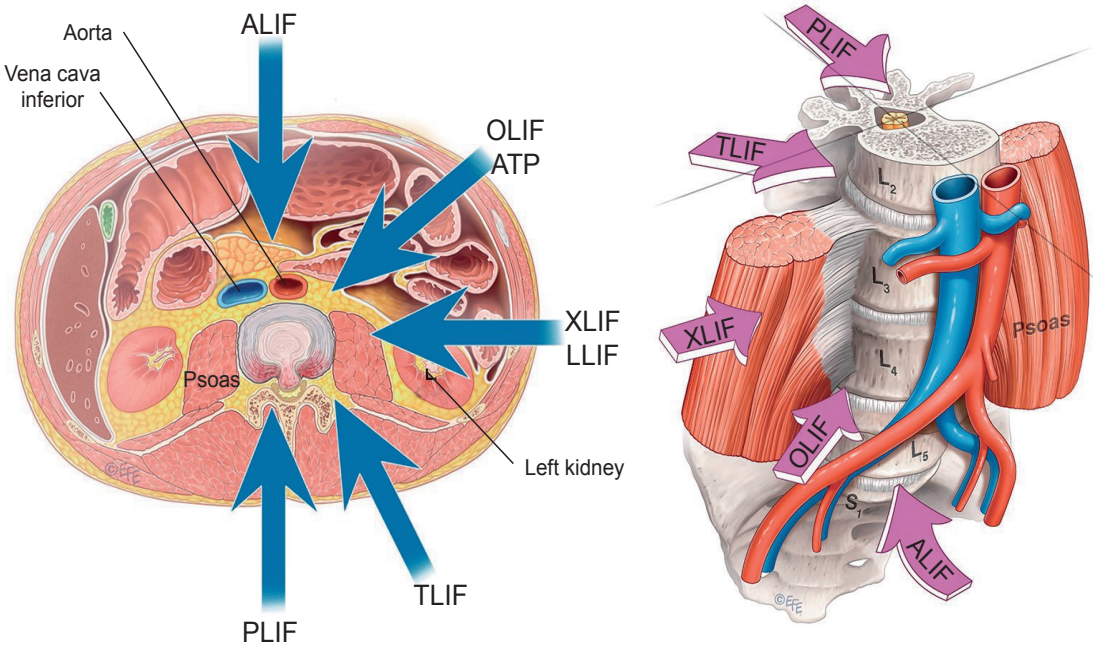


Figure 6. Different approaches for interbody fusion, adapted with permission from *Mobbs et al, 2015*.

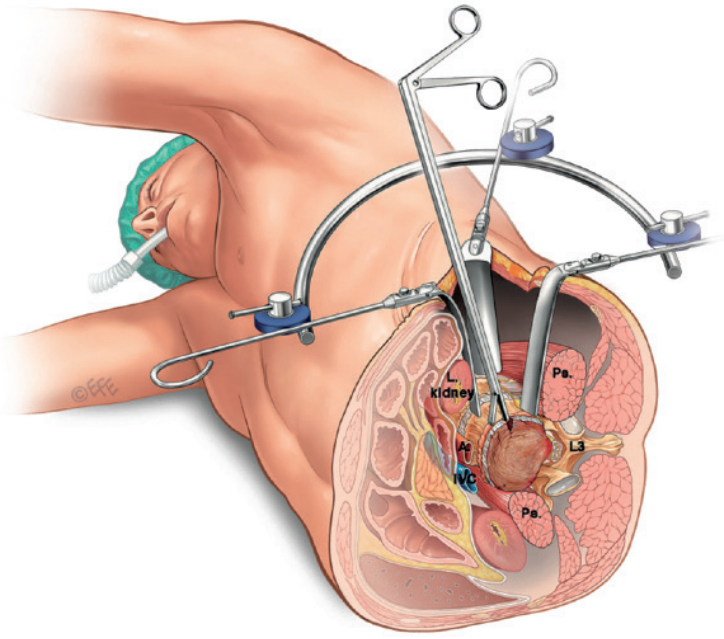


Figure 7. Lateral lumbotomy approach for oblique lumbar interbody fusion (OLIF) of L3–L4, adapted with permission from *Mobbs et al, 2015*.

Influx of computer-assisted navigation (**Figure 8**) has increased accuracy in the placement of pedicle screws, subsequently reducing the concomitant surgical complications (Van de Kelft et al., 2012, Sun et al., 2020, Driver and Groff, 2021). Emerge of robotics seems to characterize the future of spine surgery to some extent (D'Souza et al., 2019, Ahern et al., 2020).

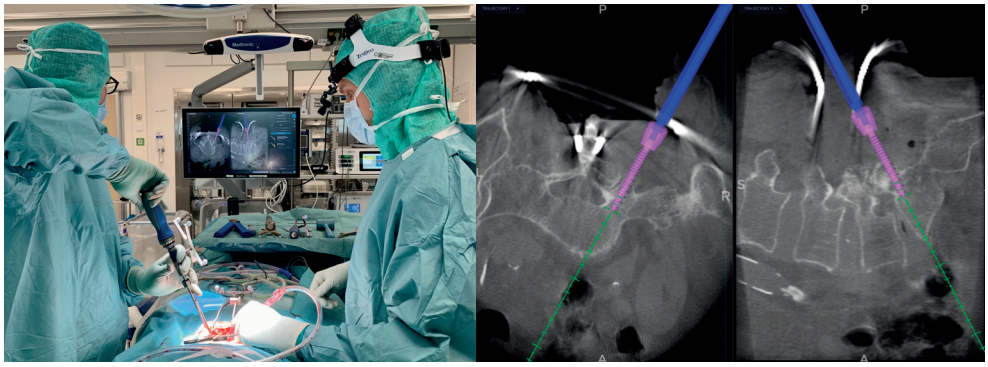


Figure 8. Pedicle screw insertion with computer assisted navigation.

2.1.3 Alignment

Spinal balance is a complex whole pursuing to minimize the muscle work needed for locomotion and posture maintenance in the gravity field (Duval-Beaupere et al., 1992, Lamartina and Berjano, 2014). Alignment of the spinal curvatures (**Figure 9**) and pelvis contribute to the dynamic balance.

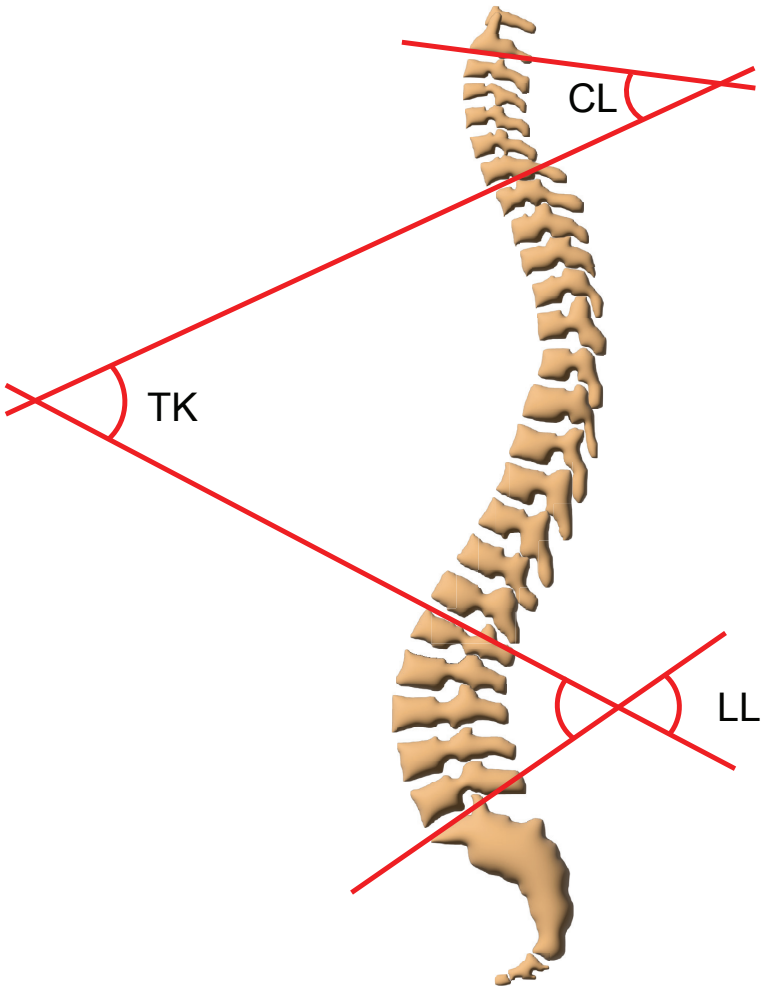


Figure 9. Anatomic spinal curvatures: CL = cervical lordosis, TK = thoracic kyphosis, LL = lumbar lordosis.

In the assessment of spinal curvatures, the Cobb angle was first introduced into measurement of coronal deviation with scoliosis (Cobb, 1948). Later, evaluation of sagittal spinal alignment with sagittal endplate angles has become routine in spine surgery. Several parameters have been established to describe both normal and pathological sagittal spinal curvatures. While coronal and rotational deviations predominate in adolescents' spinal deformities, the role of sagittal deviation prevails in adults (Weinstein et al., 2008b, Diebo et al., 2019). The impact of sagittal alignment on quality of life and disability has been acknowledged (Schwab et al., 2009, Iyer et al., 2018, Videbaek et al., 2011).

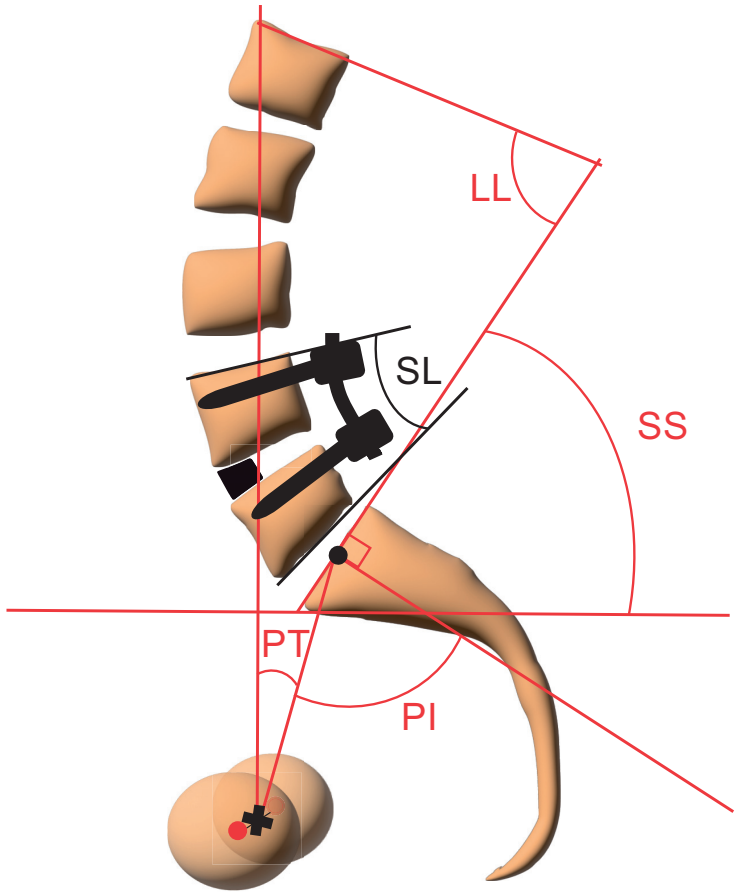


Figure 10. Lumbopelvic parameters: lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), pelvic tilt (PT) and segmental lordosis (SL) of the fusion segment.

Pelvic incidence (PI) is the angle between the line perpendicular to sacral upper endplate and the line from its center to the center of axis between femoral heads (**Figure 10**) (Legaye et al., 1998). In adulthood, it is regarded a constant value determined by individual pelvic anatomy (Mangione et al., 1997). PI determines the shape of the lumbar spine above. Substantial variation has been described in PI (33º–85º) (Vaz et al., 2002).

Sacral slope (SS) is determined as the angle between sacral upper endplate and a horizontal line. Pelvic tilt (PT) is the angle between the line from the center of upper sacral endplate to the center of axis between femoral heads and a vertical line (Legaye et al., 1998). SS and PT describe the orientation of the pelvis.

Lumbar lordosis (LL) describes the lordotic curve between sacrum and thoracic kyphosis (**Figures 9 and 10**). Anatomically, it is the angle between the upper endplates of the first lumbar vertebra and sacrum (Iyer et al., 2018). Howbeit, there is variation in thoracolumbar sagittal spinal morphology, including the true inflection point between thoracic kyphosis and lumbar lordosis. Roussouly, a pioneer of spinal balance research, proposed four basic types of thoracolumbar morphology based on measurements in an asymptomatic population (**Figure 11**). (Roussouly et al., 2003, Roussouly and Pinheiro-Franco, 2011). The classification has latterly been supplemented with a fifth type (Type 3AP) (Laouissat et al., 2018). The steepest part of lumbar lordosis ideally concentrates to the lowest lumbar spine in an elliptical fashion (Roussouly et al., 2005). Lumbar distribution index (LDI) has been introduced to describe the shape of lordosis (**Figure 12**). LDI between 50%–80% is considered normal (Yilgor et al., 2017).

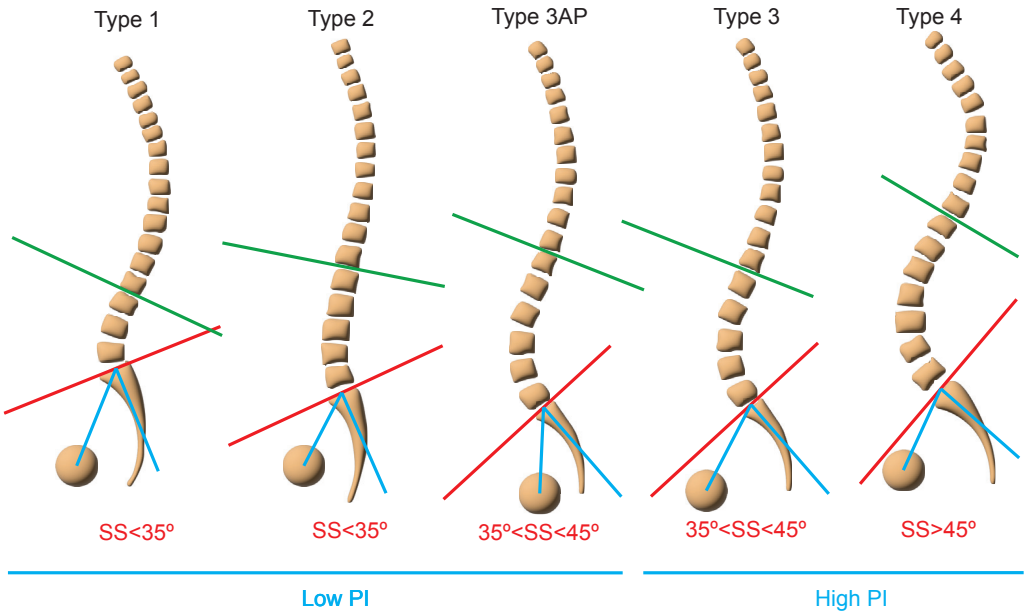


Figure 11. Updated Roussouly classification on sagittal spinal morphology. Sacral slope (SS) expressed in red, the inflection point between thoracic kyphosis and lumbar lordosis in green, and pelvic incidence (PI) in blue.

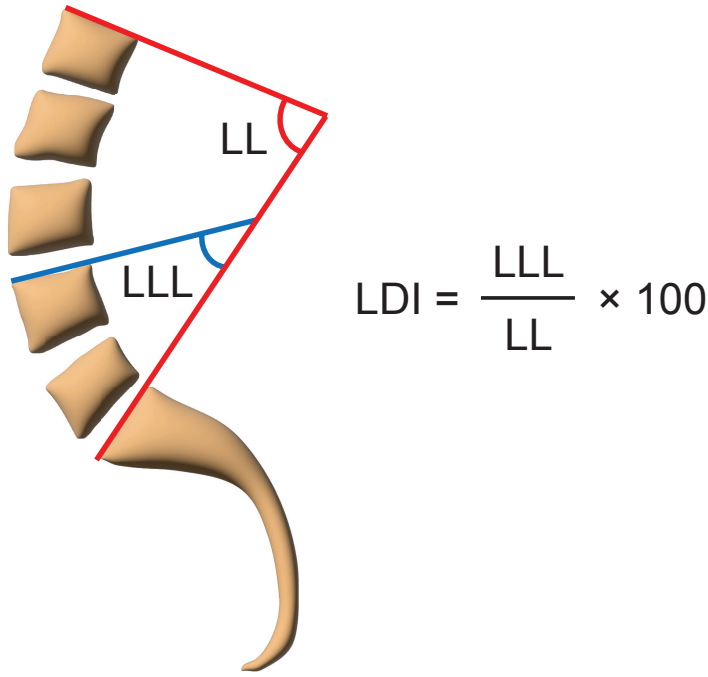


Figure 12. Lordosis distribution index (LDI) describes the ratio between lower lumbar lordosis (LLL), *i.e.*, L4–S1 lordosis, and total lumbar lordosis (LL).

With normally oriented pelvis, higher PI results in more oblique starting point to the lumbar spine, implying higher SS, and requiring higher LL to maintain an economical balance. Schwab et al. (2009) postulated a formula LL = PI ± 9° in normal population. According to this, a patient can be considered malaligned, i.e., hypolordotic, with the PI-LL mismatch of >9° (Schwab et al., 2010). However, when correcting sagittal malalignment, the optimal target for correction varies with age so that older patients need less aggressive correction (Lafage et al., 2016, Asai et al., 2022).

In patients undergoing LSF, hypolordosis is the major component of possible malalignment. In addition, failure to maintain appropriate LL may result in postoperative kyphotic malalignment, flatback. Lack of LL requires compensatory mechanisms from the patient to restore an economical posture. Main compensatory mechanisms for segmental lumbar hypolordosis are hyperextension of the mobile spine, principally upper lumbar hyperlordosis, and/or thoracic hypokyphosis, and pelvic retroversion (Di Martino et al., 2014, Lamartina and Berjano, 2014).

2.2 LSF outcome

Historically, objective tools for evaluating LSF outcome were scarce, as even solid radiological fusion does not guarantee satisfactory clinical outcome (Park et al., 2011). More recently, general and condition-specific outcome indicators, the patient-reported outcome measures (PROMs), have been introduced. They have brought the patients' perception of what is essential to the center of outcome evaluation (Lübbeke, 2018).

As pain and disability are the primary motives to LSF surgery, its success should foremost be deemed by measuring the relief for these symptoms.

2.2.1 Pain

Low back pain (LBP) contributes to tremendous global disease burden with a reported life-time prevalence of 84%, and a long-term prevalence of 23%. 11–12% of population are chronically disabled by LBP (Balague et al., 2012). While most of LBP is nonspecific, 5–10% of these patients also suffer from radicular pain which often is caused by neural compression (Jensen et al., 2019, Ropper and Zafonte, 2015). Nevertheless, the long-lasting mechanical compression of a nerve root may lead to nerve damage and neuropathic pain, which sometimes is difficult to distinguish from mechanical pain (Jensen et al., 2011). LSF surgeries are performed to treat a mechanical disorder. Consequently, uncertainty in the preoperative differential diagnostics of pain incurs uncertainty to the estimation of surgical benefit. Spinal conditions necessitating LSF surgery are usually associated with both back pain and radicular pain. Equal relief to both has been reported after surgery (Strömqvist et al., 2013).

Pain intensity can be quantified with the Visual analogue scale (VAS), or the comparable verbally administered Numeric rating scale (NRS). With VAS, the patient reports pain intensity on a 100 mm line which results in a pain score ranging from 0 to 100 (Price et al., 1983). Usually, back and leg (radicular) pain are measured separately.

2.2.2 Disability

Disability means all limitations due to a health condition, comprising physical impairment, activity limitations, and participation restrictions (WHO, 2001).

Disability from spinal disorders may be severe, extending to inability to move and maintain an upright position. Disability and pain together amply contribute to quality of life.

The Oswestry Disability Index (ODI) is the most widely used back-specific disability gauge in both clinical work and research (Fairbank et al., 1980, Fairbank and Pynsent, 2000). The questionnaire has been translated and validated into several languages (Osthus et al., 2006, Pekkanen et al., 2011). It consists of ten items measuring different aspects of physical functioning (**Table 3**). The Roland-Morris disability questionnaire is another widely used spine-specific disability indicator (Roland and Morris, 1983). It is reportedly more sensitive in low levels of disability as compared to ODI which is more sensitive with higher disability (Baker et al., 1989, Leclaire et al., 1997).

Table 3. Ten items of the Oswestry disability index (ODI) *(Fairbank et al., 1980).*

1	Pain
2	Personal care
3	Lifting
4	Walking
5	Sitting
6	Standing
7	Sleeping
8	Sex life
9	Social life
10	Traveling

2.2.3 Health-related quality of life (HRQoL)

Health-related quality of life (HRQoL) reflects patients' wellbeing with their health condition in respect of what they perceive possible or ideal (Cella and Bonomi, 1995). Acquiring paraplegia would result in lower HRQoL in a young athlete than in an old rheumatic who previously was only partially ambulatory, although the current disability was equal. The burden of spinal stenosis on HRQoL is reported to equal that of diabetes, heart disease, or stroke (Battié et al., 2012).

Many generic instruments have been developed to estimate the health-related quality of life. The 36-item short-form health survey (SF-36) is among the most widely used (Ware and Sherbourne, 1992). Others include 15D (Sintonen, 2001) and EQ-5D (Rabin and de Charro, 2001). SF-36 consists of eight dimensions (**Table 4**) that can be aggregated into two summary measures: the Physical Component Summary score (PCS) and the Mental Component Summary score (MCS) (Ware et al., 1994).

Table 4.	Eight dimensions of the 36-item short-form health survey (SF-36) for the measurement of the health-related quality of life (HRQoL) *(Ware and Sherbourne, 1992)*.
1	Limitations in physical activities because of health problems
2	Limitations in social activities because of physical or emotional problems
3	Limitations in usual role activities because of physical health problems
4	Bodily pain
5	General mental health (psychological distress and well-being)
6	Limitations in usual role activities because of emotional problems
7	Vitality (energy and fatigue)
8	General health perceptions

In a systematic review comparing changes in patient-reported pain (VAS), physical function (ODI), and HRQoL (SF-36) after spine surgery, only weak to moderate correlation was found between those instruments suggesting they measure different constructs (DeVine et al., 2011). VAS and ODI were more sensitive to treatment effect than HRQoL instruments. MCS and PCS were more sensitive than the SF-36 total score.

2.2.4 Depression and LSF outcome

Depressive symptoms are reportedly higher among those with chronic pain, especially chronic low back pain (CLBP) (Currie and Wang, 2004). Causality between depression and chronic pain is complex (Fishbain et al., 1997). Either of these conditions may precede and aggravate the other.

In some publications, depressive patients received poor outcomes from spine surgery. Sinikallio et al. (2011) reported depressive patients having gained inferior pain relief and less improvement to disability or walking ability than non-depressive patients at 2 years after lumbar spine decompression. In a retrospective study by Anderson et al. (2015), preoperatively depressive patients returned to work significantly less frequently within 2 years of LSF. Trief et al. (2006) pointed out patients' better preoperative emotional status to correlate with better pain relief and functional status up to 2 years after fusion.

Contradicting those, other studies have demonstrated comparable surgical benefits to depressive and non-depressive patients. Wagner et al. (2020) compared depressive and non-depressive patients undergoing lumbar spine surgery (74

decompression only, 106 fusion). The depression cohort had significantly poorer scores in pain, disability, and quality of life preoperatively, but the differences tapered during the 12-month follow-up. A retrospective study showed that the preoperatively depressive patients' physical function and depressive symptoms improved more, although they did not reach the level of the non-depressive patients in a 6-month follow-up (Merrill et al., 2018). In a one-year follow-up of LSF, Wahlman et al. (2014) found preoperatively depressive patients to receive remarkable relief to pain and disability, and substantial alleviation to their depressive symptoms, as well.

A cross-sectional analysis of LSF patients showed a strong influence of psychological factors on pain, disability and HRQoL (Abbott et al., 2010). In an HRQoL analysis of patients undergoing single-level LSF for discogenic CLBP, poor preoperative mental status (MCS of SF-36) correlated with poor physical outcome (PCS of SF-36) (Derby et al., 2005). In a prospective follow-up of single-level TLIFs for DS, preoperative depression predicted a less frequent return to work despite of equal benefits on pain, disability, and HRQoL (Parker et al., 2015).

2.2.5 Long-term benefit

While the short-term advantages of LSF surgery are established with diverse indications, descriptions of the long-term outcomes are required to determine the overall rationale of the method. Many LSF reports with long follow-ups compare specific interventions or focus on selected patients or definitive conditions.

Studies reporting ODI or HRQoL in a minimum 5-year follow-up of LSF are listed in **Table 5**. Most studies were retrospective descriptions demonstrating sustainment of benefits. In a comparison of non-instrumented and instrumented LSFs, Pourtaheri et al. (2015) reported significant long-term (mean 21 years) benefits in the instrumented cohort (ODI from 83 to 43). However, in 15 years, 45% of the instrumented and 64% of the non-instrumented LSF patients had undergone revision surgery. Two studies retrospectively compared different fusion techniques with DS patients (Gaffney et al., 2019, Liao et al., 2011), and one study with heterogeneous indications (Disch et al., 2008), all showing reasonable benefits at the long-term follow-up. In comparison of patients with different BMIs, all had improved at least marginally at 5 years (Owens et al., 2016). A study comparing MIS TLIF outcomes between sexes showed that, although women had greater preoperative disability and poorer HRQoL, both sexes attained similar outcomes at

5 years (Lim et al., 2020). An RCT comparing instrumented PLF with PLF+ALIF showed that patient who were well balanced independent of randomization, enjoyed superior long-term (8 to 13 years) functional outcome over the unbalanced patients (mean ODI 25 vs. 44, $p < 0.01$) (Videbaek et al., 2011).

While LSF for CLBP or DDD is controversial, corresponding long-term benefits seemed marginal, as well. Despite the perceived benefit to back pain, the 12.8-year follow-up of the Swedish RCT did not show clinically meaningful improvement in ODI (Hedlund et al., 2016). Another RCT showed a long-term improvement over the reported minimum clinically important difference (MCID) of ODI, but surgery was not superior over conservative treatment (Froholdt et al., 2012, Copay et al., 2008). A retrospective analysis of 56 LSFs for DDD showed marginally significant improvement in ODI (Luckenbill et al., 2015). A long-term follow-up of patients from three previous RCTs indicated no superiority of surgery over conservative treatment for CLBP (Mannion et al., 2013).

A long-term report of RCT on adult patients with IS showed that while some of the short-term benefit of surgery was lost over time, the long-term (mean 9 years) global clinical outcome of surgery surpassed that of conservative treatment (Ekman et al., 2005). Both surgically and conservatively treated patients remained below the general population in disability and HRQoL. One study showed comparable long-term profits from 360º fusion for DDD and IS (Schulte et al., 2007).

Some studies reported reasonable long-term outcomes of LSF as a part of comparison with disc replacement surgery (TDR) or use of an interspinous device (Sköld et al., 2013, Guyer et al., 2009, Hu et al., 2019, Bredin et al., 2017, Korovessis et al., 2009).

Generally, the mid-term benefits of LSF surgery seemed to endure at long-term follow-ups. In an RCT comparing instrumented PLF with PLF+TLIF, the 2-year disability and HRQoL benefits were preserved at 5-10 years (Høy et al., 2017). A retrospective report of standalone ALIFs showed the moderate 6.6-year outcome to last at 19.7 years, although the baseline was not reported (Kroeze et al., 2020). In contrast to those, a retrospective analysis of PLIF surgeries showed that following initial benefits of surgery, ODI was reverted to the preoperative level by 10 years (Maruenda et al., 2016). An explanation for the poor long-term outcomes of that study was the high incidence of adjacent segment disease (ASD) (radiologically 51%; 25% having undergone revision surgery by 10 years). Patients that underwent revision for ASD were functionally superior over the rest of patients more than 10 years beyond the index operation. Glassman et al. (2012) calculated that preservation of surgical benefits at 5 years turned LSF surgery cost-effective.

Table 5. Studies reporting long-term (minimum 5 years) outcomes of LSF with ODI or HRQoL instruments. From studies comparing LSF with another treatment method, LSF outcomes were retrieved.

Authors	Study design	Indication(s)	Surgical procedure(s)	n	Mean f-u	Findings
Bredin et al., 2017	Retrospective	LSS	LSF vs. Dynesys dynamic stabilization	25 (LSF)	93.6 mo	ODI from 48 to 19; SF-36 (only postoperative) PCS 37.2, MCS 50.1
Disch et al., 2008	Retrospective	Heterogeneous	LSF 1-2 levels	102	13.8 yrs	Mean ODI during f-u 26
Ekman et al., 2005	RCT	IS	LSF vs. non-instrumented LSF vs conservative treatment	111	9 yrs	ODI baseline n.a., f-u 27/30/31
Froholdt et al., 2012	RCT	CLBP	LSF vs. conservative treatment	99	9 yrs	ODI from 45 changed -16
Gaffney et al., 2019	Retrospective	L4/L5 DS	PLF vs. PLF+TLIF	31 vs 58	8.7 yrs	ODI from 43 vs. 40 to 21 vs. 22, n.s. btw groups. Reoperations 6% vs. 28%, p = 0.02
Glassman et al., 2012	Retrospective analysis of prospective date	Heterogeneous	Single level PLF	74	5 yrs	ODI from 56 to 28, SF-36 PCS 27.5 to 37.6
Guyer et al., 2009	RCT	DDD	ALIF vs. TDR	43 (ALIF)	5 yrs	Baseline n.a., ODI stayed below 30 during f-u, SF-36 PCS +12.3
Hedlund et al., 2016	RCT	CLBP	LSF vs. non-specific physiotherapy	222 vs 72	12.9 yrs	ODI from 47.3, changed -10.5
Hu et al., 2019	Retrospective	LSS	LSF vs. Dynesys dynamic stabilization	44 (LSF)	70 mo	ODI from 69 to 24, p < 0.001
Høy et al., 2017	RCT	DS or LSS or IS	TLIF vs. PLF	44 vs 44	8.6 yrs	ODI from 43 vs. 41 to 24 vs. 23; Post SF-36 PCS 49 vs. 48, MCS 51 vs. 53; n.s. btw groups
Korovessis et al., 2009	RCT	LSS or DS	LSF w/out Wallis implant	25 (LSF)	5 yrs	ODI from 31 to 13, SF-36 PCS from 12 to 44
Kroeze et al., 2020	Retrospective	DDD or grade I DS	Standalone ALIF	50	19.7 yrs	At 6.6 and 19.7 yrs: ODI 41 in both; SF-35 PCS 41.4 and 40.8, MCS 48.7 and 49.9

Liao et al., 2011	Retrospective	DS	Lumbar floating fusion vs. lumbosacral fusion for lumbar DS with L5/S1 degeneration	83 vs 24	75 mo	ODI from 49 vs. 54 to 20 vs. 31, p = 0.278 and 0.011 btw groups
Lim et al., 2020	Prospective registry study	DS	MISS TLIF, comparison btw the sexes	M/F 94/202	5 yrs	M/F ODI from 42/50 to 12/13; SF-36 PCS from 35.6/31.9 to 46.5/47.6; MCS 49.2/44.9 to 54.7/52.3; p<0.01 pre, n.s. post
Luckenbill et al., 2015	Retrospective	DDD	LSF	19	5 yrs	ODI from 25 to 13, p = 0.025
Mannion et al., 2013	Prospective follow-up from 3 RCT's	CLBP	LSF vs. conservative treatment	140 (LSF)	11.4 yrs	ODI from 45 to 30 (ITT) or 46 to 31 (AT) vs. 42 to 30 (ITT) or 40 to 27, n.s. btw groups
Maruenda et al., 2016	Retrospective	DS or DDD or LSS	PLIF	73	15 yrs	ODI from 72 to 31 at 2 yrs, gradually increased again to the preoperative level during 10 yrs in patients without revision surgery; By 10 yrs 24.6% revised
Owens et al., 2016	Propensity matched case control study	Heterogeneous	LSF: BMI 20-25/25-30/30-40	82/82/82	5 yrs	ODI baseline 49/49/51 changed -14/-10/-10.; SF-36 PCS baseline 31.15/31.40/30.15 changed 5.85/2.86/3.46; n.s. btw groups
Pourtaheri et al., 2015	Retrospective	LSS	Comparison of instrumented (23) vs. non-instrumented (11) PLF	23	21 yrs	ODI from 83 to 43; 45% and 64% underwent revision surgery.
Schulte et al., 2007	Retrospective	DDD or IS	360° fusion	27 and 13	114 mo	ODI from 58 to 35 and 54 to 23, n.s. btw groups (included only those who had not undergone reoperation during f-u)
Sköld et al., 2013	RCT	CLBP	LSF vs. TDR	72 (LSF)	5 yrs	ODI from 41 to 23, EQ-5D from 0.63 to 0.68
Videbaek et al., 2011	RCT	CLBP	ALIF+PLF vs. PLF only	48 vs 44	*8–13* yrs	At f-u ODI 29 vs. 36, SF-36 PCS 36 vs. 36, MCS 55 vs. 47; n.s. btw groups

BMI = body mass index, RCT = Randomized controlled trial

DDD = degenerative disc disease, DS = degenerative spondylolisthesis, CLBP = chronic low back pain, IS = isthmic spondylolisthesis, LSS = lumbar spinal stenosis

ALIF = anterior lumbar interbody fusion, LSF = lumbar spine fusion, MISS = mini-invasive spine surgery, PLIF = posterior lumbar interbody fusion, PLF (here) instrumented posterolateral fusion, TDR = total disc replacement, TLIF = transforaminal lumbar interbody fusion

ODI = Oswestry disability index, SF-36 = Short form 36, PCS = physical component score, MCS = mental component score

M = male, F = female, n.s. = non-significant, n.a. = not available, btw = between, yrs = years, mo = months, f-u = follow-up, ITT = intention-to-treat, AT = as-treated

When analyzing long-term treatment effects, comparisons with the general population are useful to eliminate potential bias from ageing. Even in short-term, studies comparing LSF outcome with the general population are scarce. A prospective study with a short-term follow-up (median 2 years) showed that single-level LSF for DS initiated similar benefits as total hip arthroplasty, both upraising patients to the general population level (Mokhtar et al., 2010). In a long-term follow-up (mean 9 years) of patients with IS, both surgically and conservatively treated patients remained below the general population level in disability and HRQoL (Ekman et al., 2005). Another long-term follow-up (mean 14.8 years) of adolescents with high grade IS showed that fusion in situ produced statistically better clinical outcome than fusion with reduction although both groups achieved the general population (Poussa et al., 2006).

2.2.6 Complications and reoperations

Complication reports commonly incorporate systemic complications, such as postoperative anemias, urinary tract infections, and bowel dysfunctions to total complication rates, thus raising the early complication rate of elective LSF surgery as high as 19% (Deng et al., 2021). Surgical complications are more infrequent, yet often more serious, frequently leading to reoperations (Ghobrial et al., 2015, Hadjipavlou et al., 1996).

Reported cumulative 4-year reoperation rates following instrumented LSF are presented in **Table 6** (Irmola et al., 2018). Cummins et al. (2021) reported a comparable 5-year reoperation rate (13.5%) after 1–2 level LSF surgeries. After surgeries for DS (72% instrumented fusion, 21% non-instrumented fusion, 7% decompression alone), the 8-year reoperation rate was 22% (Gerling et al., 2017).

Early complications are, in part, an inherent disadvantage of surgery, but they should be avoided by all possible means. Hematomas and infections are best prevented with standardized surgical practice (Jenis et al., 2013, Canseco et al., 2021, Sawires et al., 2021). Instrumentation misplacements and neurological complications are best averted with rigorous surgical technique (Ghobrial et al., 2015, Van de Kelft et al., 2012, Sun et al., 2020, Laratta et al., 2018). Early failures may relate to poor bone quality and insufficient stability of the construct to which suboptimal placement of instrumentation may contribute. Same factors may lead to late failures (Hadjipavlou et al., 1996). Implant loosening and pseudoarthrosis characterize late failures, which regularly lead to revision surgeries consisting of implant replacements,

use of biologics, and different interbody fusion techniques (Chun et al., 2015, Jung et al., 2021). Advances in accomplishing LSF surgeries have, however, reduced the occurrence of this complication (Chun et al., 2015).

Table 6. Cumulative 4-year reoperation rates (95% CI) following instrumented lumbar spine fusion, modified from *Irmola et al., 2018.*

Indication for reoperation	Cumulative reoperation rate		
	1 year	2 years	4 years
Acute complications (Include hematomas, surgical site infections, spinal fluid leaks, new neurologic symptoms, misplaced instrumentations	2.5% (1.4–4.5)	2.5% (1.4–4.5)	2.5% (1.4–4.5)
Early failure	3.4% (2.0–5.6)	3.9% (2.4–6.2)	4.4% (2.7–7.0)
Late failure	0	1.3% (0.5–3.6)	2.9% (1.9–7.1)
Adjacent segment pathology	0.7% (0.2–2.2)	3.5% (2.1–5.8)	8.7% (6.1–12.5)

In longer follow-ups, adjacent segment disease (ASD) becomes the leading cause of reoperations following LSF (Irmola et al., 2018, Hashimoto et al., 2019). That will be discussed more in depth at the next chapter.

Patient-related factors significantly affect the risk of complications (Schoenfeld et al., 2011). However, mortality is reportedly not a significant adverse effect of LSF surgery (Schoenfeld et al., 2011, Salmenkivi et al., 2017, Lurie et al., 2015, Yavin et al., 2017, Cummins et al., 2021).

2.2.7 Adjacent segment disease (ASD)

By definition, adjacent segment pathology is the degenerative condition that postoperatively develops to the disc level adjacent to fusion segment (Kraemer et al., 2012). Meta-analysis by Xia et al. (2013) calculated a pooled prevalence of 26.6% for radiological adjacent segment degeneration following LSF. Approximately 25–30% of radiological adjacent segment degeneration are assumed to proceed to symptomatic adjacent segment disease (ASD) (Hashimoto et al., 2019). ASD occurrence is described as linearly accumulating over time (Ghiselli et al., 2004). Consequently, ASD prevalence depends on the length of follow-up. With ASD, the degenerative changes at the adjacent segment (**Table 7**) render symptoms via instability or neural compression (**Figure 13**) (Park et al., 2004).

Key question in understanding ASD pathogenesis is that whether it is a consequence of LSF, a sequel of the altered biomechanics at the adjacent segment, or is it rather a part of the natural course of the degenerative spinal disease (Park et al., 2004, Hilibrand and Robbins, 2004).

Table 7. Degenerative changes with ASD, observed at the adjacent segment after spinal fusion, according to *Park et al., 2004.*

Disc degeneration (Loss of disc height, disc space narrowing)
Spondylolisthesis (anterolisthesis, retrolisthesis)
Instability
Herniated nucleus pulposus
Stenosis
Hypertrophic facet arthritis
Osteophyte formation
Scoliosis
Vertebral compression fracture

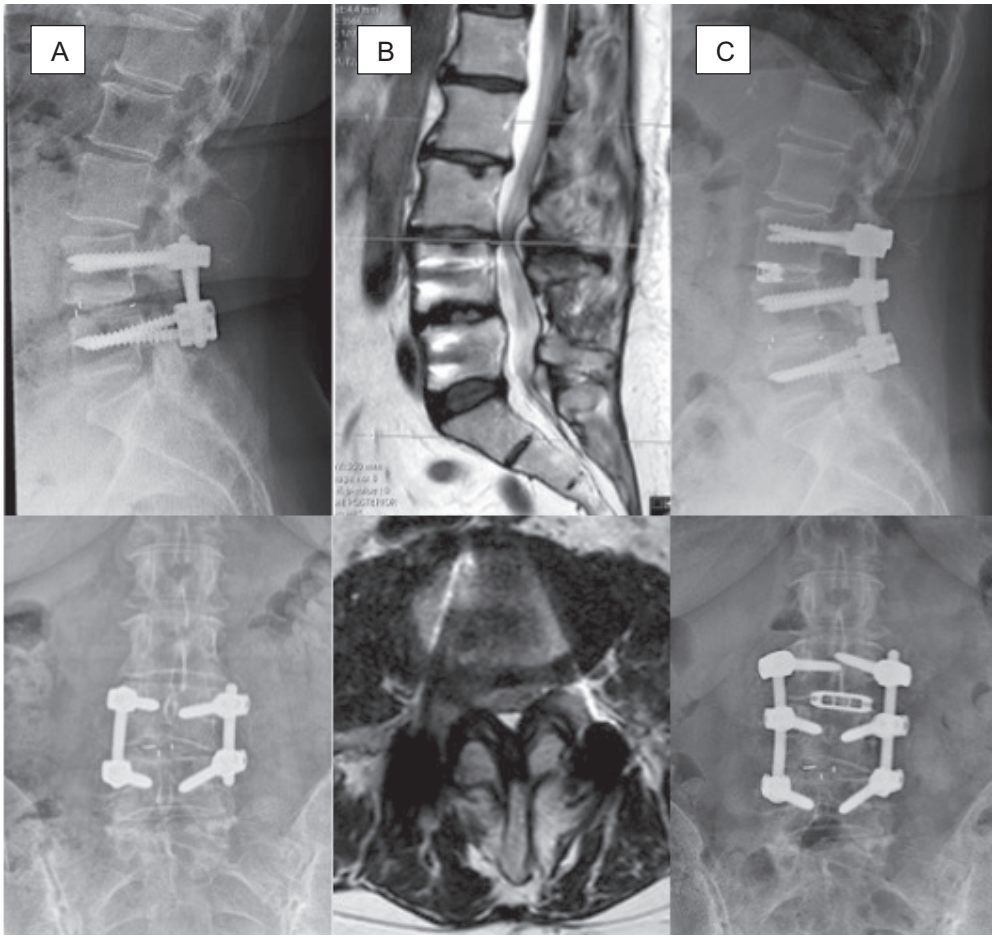


Figure 13. **A.** Prior L4–L5 fusion. **B.** Adjacent segment disease (ASD) at L3–L4 level. **C.** Revision surgery encompassing extension of fusion to L3.

Several potential risk factors have been associated with ASD development: age, genetic factors, pre-existing adjacent segment degeneration or stenosis, laminectomy to the adjacent vertebra to fusion, osteoporosis, and poor sagittal alignment (Hashimoto et al., 2019, Radcliff et al., 2013). Even the related terminology is not consistent in the literature, let alone consensus to exist on the impact of individual risk factors. Pre-existing degeneration at the adjacent level is considered both a risk factor and irrelevant to ASD propagation (Hashimoto et al., 2019, Choi et al., 2015, Ghiselli et al., 2004).

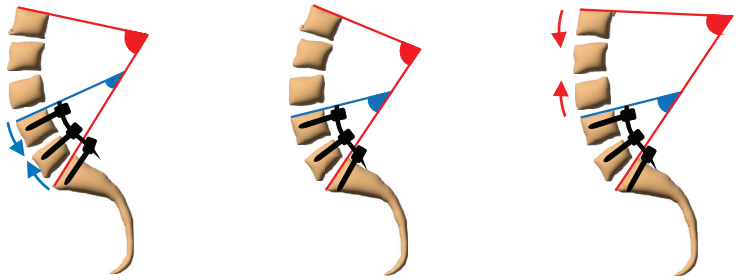
Although the impact of sagittal alignment has been verified on postoperative pain, function, and HRQoL, its significance for ASD pathogenesis is more obscure (Korovessis et al., 2010, Lazennec et al., 2000, Le Huec et al., 2015, Phan et al., 2018,

Anandjiwala et al., 2011, Alentado et al., 2016). Yet, it would be the single most important factor for the surgeon to target, if relevant here.

Studies evaluating the impact of sagittal alignment on ASD development by comparing patients with and without ASD in a minimum of 5-year follow-up are listed in **Table 8**. All studies were retrospective with contradictory findings. The strongest finding supporting the relevance of alignment was the case-control study of Rothenfluh el al. (2015) that observed higher PI, lower LL, and greater PI-LL difference in patients who underwent revision for ASD than in the controls. Moreover, OR for ASD was 10.6 with the PI-LL mismatch of ≥10°. A French case-control study found a small, but statistically significant difference in postoperative LL (44.2° vs. 49.5°, p = 0.040) and a difference in the prevalence of PI-LL mismatch (59.55 vs. 26.2%, p = 0.002) (Dallaudiere et al., 2020). Slightly greater loss of LL during the index L4–S1 fusion was discovered in patients who ended up in revision for ASD (-9.0° vs. -3.1°, p = 0.033) (Michael et al., 2019). That study featured an unconventional AxiaLIF technique (axial lumbar interbody fusion utilizing paracoccygeal transsacral trajectory to the lowest lumbar spine), that has been associated with a risk of major complications (Cragg et al., 2004, Aryan et al., 2008, Issack et al., 2014).

A cohort study with a marginally larger study population than the aforementioned observed no differences in pre- or postoperative LL or SL between ASD patients and controls (Wang et al., 2021). A study with the longest follow-up (average 11.6 years) found LL, PI, PT, and PI-LL insignificant to surgically relevant ASD (Nakashima et al., 2015). They also studied the progress of radiological adjacent segment degeneration, for which a high PI was found as a risk factor during the first five years.

A cohort study with the largest population found LL and SL indifferent between ASD and non-ASD patients (Zheng et al., 2020). Further, they studied the relevance of lordosis distribution index (LDI) (**Figure 12**), which means the proportion of lower lumbar lordosis (L4–S1 segment) to total LL (L1–S1). Because all surgeries in their data were L4–S1 fusions, LDI also represented the proportion of fusion segment lordosis to LL (**Figure 14**). LDI did not differ between the groups. However, patients distributed differently if stratified to low, normal, and high LDI cohorts ($p<0.001$). ASD patients were more often located in low LDI but especially in high LDI cohorts. This raises a question but offers no answer whether this indicated more upper lumbar hypolordosis (given the same SL)–potentially reflecting reduced mobility–in the ASD group.



	Low LDI (SL / LL) LDI <0.5 Potential explanations: • **Low SL** • Upper lumbar hyperlordosis	**Normal LDI** (SL / LL) 0.5 ≤ LDI ≤ 0.8 Potential explanations: • **Normal SL**	**High LDI** (SL / LL) LDI > 0.8 Potential explanations: • (High SL) • **Upper lumbar hypolordosis** • Roussouly 1 morphology
ASD patients	23.5%	35.3%	**41.2%**
Non-ASD patients	6.6%	**76.5%**	16.9%

Figure 14. Distribution of ASD and non-ASD patients according to lordosis distribution index (LDI) in the study of *Zheng et al., 2020.*

Summing up the findings, sagittal alignment probably has a role in ASD development, but the causality is more complex than occasionally proposed (Park et al., 2004, Hashimoto et al., 2019).

Table 8. Studies evaluating the effect of sagittal balance on ASD development with a minimum mean follow-up of 5 years.

			ASD	Controls		
Authors	**Study design**	**Surgical procedure**	n	n	**Mean follow-up**	**Findings**
Dallaudiere et al., 2020	Retrospective case-control study	Posterior fusion, 2–10 levels	42	42	77 vs. 115 mo	Postoperative LL 44.2° vs. 49.5°, P = 0.040; Prevalence of mismatch PI-LL>10° 59.5% vs. 26.2%, p = 0.002
Michael et al., 2019	Retrospective cohort study	AxialLIF, 2 levels	10	64	6 yrs	Greater loss of LL with ASD (-9.0° vs. -3.1°, p = 0.033)
Nakashima et al., 2015	Retrospective case-control study	PLIF, 1–2 levels	10	91	11.6 yrs	LL, PI, PI-LL, PT n.s.; However, high PI a risk factor for early-onset radiographic ASDegeneration
Rothenfluh et al., 2015	Retrospective case-control study	Posterior fusion, 1–3 levels between L2–S1	45	39	49 vs. 84 mo	Postoperatively PI 60.9° vs. 51.7°, p = 0.001; LL 48.1° vs. 53.8°, p = 0.012); PI-LL 12.5° vs. 3.4°, p = 0.001. When dividing patients into PI-LL<10° and ≥10°, OR 10.6 for ASD with mismatch of ≥10°
Wang el al., 2021	Retrospective cohort study	LLIF with/without PLF	20	129	7 yrs	Pre- or postoperative LL or SL n.s. between the groups
Zheng el al., 2020	Retrospective cohort study	PLIF L4–S1	17	183	63 vs. 85 mo	LL, SL, and LDI n.s .btw groups; However, when grouping patients by LDI, portion of patients with LDI in middle range 35.3% vs. 76.5%, p<0.001

AxiaLIF = axial lumbar interbody fusion, LLIF = lateral lumbar interbody fusion, PLF = (instrumented) posterior lumbar fusion, PLIF = posterior lumbar interbody fusion
LL = lumbar lordosis, SL = segmental lordosis (of the fusion segment), PI = pelvic incidence, PT = pelvic tilt, LDI = lordosis distribution index
n.s. = not significant, yrs = years, mo = months, OR = odds ratio

3 AIMS OF THE STUDY

The aim of this thesis was to evaluate the long-term outcome of lumbar spine fusion surgery. Detailed aims were:

1. To evaluate the effect of LSF on disability, health-related quality of life, and mortality in a 5-year follow-up, and to compare these results with the general population.

2. To elucidate whether depressive symptoms influence the 5-year outcome of LSF.

3. To determine the incidence of revisions for adjacent segment disease in a 10-year follow-up of LSF and compare it between isthmic spondylolisthesis and degenerative spinal disorders.

4. To evaluate the impact of sagittal alignment on the development of adjacent segment disease in a 10-year follow-up of LSF.

4 SUBJECTS AND METHODS

4.1 Subjects

4.1.1 Patients

In 2008–2012, all patients scheduled for elective LSF surgery in Tampere University Hospital and Central Finland Central Hospital were invited to participate in a prospective follow-up. Recruitment took place at the preoperative visit to the orthopedic surgeon. Surgery and the succeeding follow-up were arranged according to normal clinical practice. At the time of surgery, the surgeon filled in details about the surgical indication and procedure. Throughout the data collecting period, only 10 patients refused to participate.

Consecutive series of elective LSF surgeries performed in both hospitals formed the study populations in Studies **I** (n=523) and **II** (n=392). Exclusion criteria were tumor, acute fracture, neuromuscular, and idiopathic scoliosis being the indication for surgery.

Table 9. Subject demographics and clinical data.

	Patients				*Population*
	Study I	**Study II**	**Study III**	**Study IV**	**Study I**
	n = 523	n = 392	n = 365	n = 215	n = 682
Age, mean y (SD)	61 (12)	61 (12)	62 (12)	66 (10)	64 (12)
Women, n (%)	357 (68)	277 (71)	241 (66)	164 (76)	454 (67)
BMI, mean (SD)	28.6 (4.6)	28.6 (4.6)	28.3 (4.3)	28.6 (4.4)	26.9 (4.4)
Smoking*, n (%)	82 (16)	57 (15)	27 (7)	12 (6)	88 (13)
Education*, mean y (SD)	11.5 (2.7)	11.5 (2.7)	11.5 (3.8)	11.1 (3.9)	11.6 (4.0)
Co-morbidities*, n (%)					
Cardiological	263 (50)	189 (48)	184 (50)	118 (60)	278 (41)
Respiratory	49 (9)	36 (9)	21 (6)	11 (6)	66 (10)
Neurological	20 (4)	14 (4)	7 (2)	5 (3)	36 (5)
Rheumatoid	49 (9)	39 (10)	21 (6)	14 (7)	32 (5)
Diabetes	57 (11)	41 (10)	41 (11)	24 (12)	87 (13)
Psychiatric	9 (2)	6 (2)	7 (2)	5 (3)	25 (4)

* = self-reported, SD = standard deviation, BMI = body mass index, y = years

Demographic and clinical data of the participants are depicted in **Table 9**. Surgical indications are presented in **Table 10**.

Table 10. Indications for surgery.

	Study I n = 523 (%)	Study II n = 392 (%)	Study III n = 365 (%)	Study IV n = 215 (%)
Degenerative spondylolisthesis (DS)	251 (48)	202 (52)	178 (49)	172 (80)
Isthmic spondylolisthesis (IS)	78 (15)	55 (14)	64 (18)	-
Spinal stenosis (LSS)	68 (13)	45 (11)	44 (12)	43 (20)
Degenerative disc disease (DDD)	42 (8)	27 (7)	-	-
Deformity	31 (6)	24 (6)	26 (7)	-
Postoperative conditions	47 (9)	34 (9)	44 (12)	-
Others (e.g., posttraumatic conditions)	6 (1)	5 (1)	9 (2)	-

A consecutive series of primary elective surgeries performed in Tampere University Hospital (n=365) constituted the population of Study **III**. In addition to the exclusion criteria of studies **I** and **II**, patients with fusion reaching thoracic spine as well as former fusion prior to data collecting period were excluded. Surgical indications were categorized into

1) isthmic spondylolisthesis (IS),
2) DLSD = degenerative lumbar spine disorders (i.e., spinal stenosis with or without degenerative spondylolisthesis), and
3) others (i.e., deformities, postoperative conditions following decompression, posttraumatic conditions).

Patients with IS were significantly younger, more often men, more educated, and they underwent shorter fusions more often reaching sacrum than the other patients (**Table 11**). Demographically, DLSD group paralleled the third group.

Out of Study **III** patients, those with IS or a primary degenerative spinal disorder (n=286) were included in Study **IV**. Any antecedent spinal surgery was an exclusion criterion in addition to the aforementioned.

Table 11. Patient demographics and surgical details of Study **III** according to surgical indication.

	IS n = 64	DLSD n = 222	Others n = 79
Age, mean y (SD)	48 (12)	65 (10)	64 (12)
Women, n (%)	28 (44)	169 (76)	44 (56)
Education*, mean y (SD)	13.1 (3.9)	11.2 (3.9)	11.0 (3.8)
Fusion			
Lowest intstrumented vertebra, n (%)			
-L3	0 (0)	1 (0)	2 (3)
-L4	1 (2)	9 (4)	3 (4)
-L5/6	10 (16)	117 (53)	27 (34)
-S1	53 (83)	95 (43)	47 (59)
Length, levels, n (%)			
1	36 (56)	61 (27)	8 (10)
2	21 (33)	89 (40)	22 (28)
3	7 (11)	54 (24)	30 (38)
4	0 (0)	17 (8)	11 (14)
5	0 (0)	1 (0)	8 (10)
Interbody cage (TLIF/PLIF), n (%)	35 (55)	24 (11)	7 (9)

* = self-reported
TLIF = transforaminal lumbar interbody fusion, PLIF = posterior lumbar interbody fusion
IS = isthmic spondylolisthesis
DLSD = degenerative lumbar spine disorder, i.e., spinal stenosis with or without degenerative spondylolisthesis
Others encompass deformities, postoperative conditions following decompression, and posttraumatic conditions

4.1.2 General population sample

Age-, sex-, and residential area matched control cohort (n=1140) for all LSF patients was raised by Official Statistics of Finland (Statistics Finland, 2010), to represent the general population. Controls were requested to complete a series of questionnaires in 2010 and 2015 (**Figure 15**). A matched sample was retrieved in Studies **I** (n=682) and **II** (n=477). Demographic data of the population sample are presented in **Table 9**. 23% of the population reported to have experienced spinal problems.

4.2 Study design

Study setting in studies **I–III** was a prospective follow-up after LSF surgery. Study **IV** was a retrospective analysis of prospectively collected data.

4.2.1 5-year outcome (Studies I and II)

In Studies **I** and **II**, the 5-year outcome of LSF surgery was evaluated with a series of questionnaires the patients completed at explicit time-points (**Figure 15**). In analysis, all clinical data were retrieved from a spinal database set up for the prospective follow-up. Further, PROMs were compared between patients and the general population sample. Mortality data were extracted from Statistics of Finland (Statistics Finland, 2010), and they were compared between patients and controls.

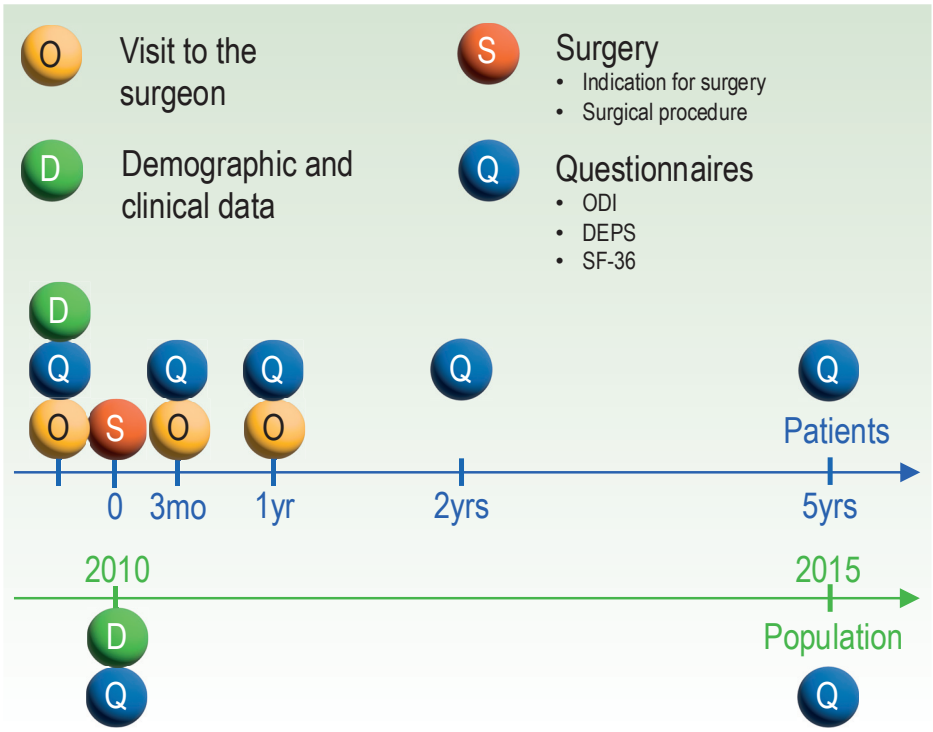


Figure 15. Timepoints for data acquisition and treatment-related visits.

4.2.2 Adjacent segment disease (ASD) (Studies **III** and **IV**)

A consecutive series of patients undergoing LSF in Tampere University Hospital constituted the population for Study **III**. All spinal reoperations until 2020 were collected from the hospital records. Indications for all reoperations were determined by exploring the patient records and radiological studies. Possible dates of death were collected for the survival analysis. Rates of ASD revision surgeries were calculated for different LSF indications in Study **III**. The risk of ASD revision was compared between different LSF indications.

Study **IV** evaluated the impact of sagittal alignment on ASD revision risk. The most heterogeneous diagnostic group (the third group) of Study **III** was not included to facilitate the interpretation of results. Sagittal alignment was determined from lumbar standing radiographs. Only degenerative patients were included in the risk analysis as Study **III** proved the isthmic spondylolisthesis (IS) cohort irrelevant here.

4.3 Methods

4.3.1 Surgery

All surgeries were instrumented posterolateral fusions performed through a midline incision and combined with necessary decompression (**Figure 16**). Interbody spacers (PLIF/TLIF) were used at the discretion of the surgeon.

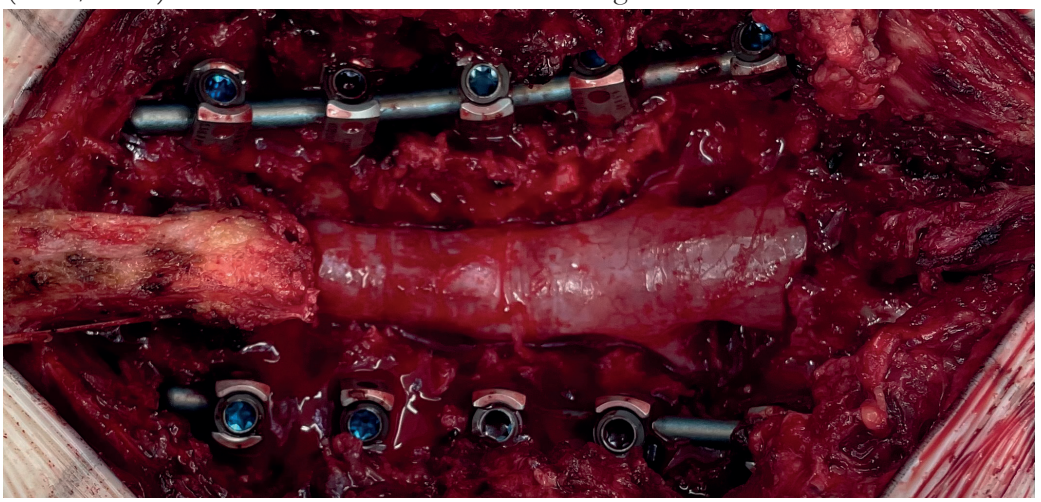


Figure 16. Open L2–S1 fusion combined with voluminous decompression in the treatment of severe multilevel stenosis.

4.3.2 Oswestry disability index (ODI) (**I–IV**)

ODI consists of 10 items (0–5 points each). The total score ranges from 0 to 100 and represents the mean of each answered subgroup. Scores are defined by the scales in the original publication as depicted in **Table 12** (Fairbank et al., 1980). In lumbar spine surgery setting, a minimum clinically important difference (MCID) of -12.8 points has been reported (Copay et al., 2008).

Table 12. Oswestry Disability Index (ODI). Interpretation of disability according to the ODI score as stated in *Fairbank et al., 1980*.

ODI score	Interpretation
0–20	Minimal disability
20–40	Moderate disability
40–60	Severe disability
60–80	Patient is crippled
80–100	Patient is bed-bound or exaggerating his/her symptoms

4.3.3 The 36-item short-form health survey (SF-36) (**I**)

SF-36 questionnaire was used to measure the health-related quality of life (HRQoL) in the subjects. Its eight dimensions were aggregated into two summary measures: the Physical Component Summary score (PCS) and the Mental Component Summary score (MCS), both ranging between 0–100 with higher scores reflecting better health (Ware et al., 1994). Copay et al. (2008) reported an MCID of 4.9 points for PCS in lumbar spine surgery settings. Similar has not been reported for MCS.

4.3.4 Depression scale (DEPS) (**II**)

Patients were screened for depressive symptoms using the Finnish version of Depression scale (DEPS) (Poutanen et al., 2008). The questionnaire has ten items (0–3 points each), with the total score ranging between 0–30 points. Patients were dichotomized as depressive or non-depressive with a cutoff value of 12 points. This has been reported to have 75% sensitivity and 70% specificity in detecting clinical depression (Poutanen et al., 2010).

4.3.5 Radiological measurements (**III–IV**)

Lumbar spine alignment was evaluated by determining lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), pelvic tilt (PT), and segmental lordosis (SL) (**Figure 10**). PI-LL mismatch >9° was used as a threshold for poor alignment, *i.e.*, hypolordosis. Measurements were made by a spine surgeon from preoperative and postoperative (at 3 months) standing lumbar radiographs. Full spine standing radiographs were not routinely used in the data collecting period.

4.4 Statistics

Data were presented as means with standard deviation (SD) or counts with percentages. Statistical comparisons were made using t test, analysis of variance (ANOVA), Pearson's $\chi 2$ test, or generalized linear models with appropriate distribution and link function. The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in the case of a violation of the assumptions (*e.g.*, non-normality). The normality of variables was evaluated graphically and using the Shapiro-Wilk W test. All analyses were performed using STATA software, version 15.1 or 16.1 (StataCorp LP, College Station, TX).

4.4.1 Study **I**

Repeated measures in the changes of scores between groups were analyzed using mixed-effects models, with an unstructured covariance structure (Kenward-Roger method to calculate the degrees of freedom). As the use of mixed models allows for analysis of unbalanced datasets without imputation, all available data were analyzed using the full analysis set. Cumulative mortality was estimated using Kaplan-Meier survival analysis and compared between groups with the log-rank test. Cox proportional hazards model was used to calculate the adjusted hazard ratio (HR) and 95% confidence intervals for death.

4.4.2 Study **II**

Repeated measures for continuous and binary outcomes were analyzed using generalizing estimating equation (GEE) models (exchangeable correlation structure)

with an appropriate distribution and link function. Models included sex, age, and education years as covariates. Penalized maximum likelihood logistic regression (Firthlogit) or exact logistic regression were used with situations in which the event of interest was rare.

4.4.3 Study III

Crude cumulative ASD revision rates were estimated using Kaplan-Meier method and compared between groups with the log-rank test. Adjusted (age, sex, fusion length, and the lowest instrumented vertebra) Kaplan-Meier cumulative rates were estimated using two propensity score-based techniques: stratification and weighting (MMWS, marginal mean weighting through stratification) (Linden, 2014). MMWS is an extension of propensity score matching that combines propensity score stratification and inverse probability of treatment weighting. Log-rank test with exact p-values was used to identify a statistical difference between the cumulative proportions.

4.4.4 Study IV

Cox proportional hazards regression models were used to estimate the adjusted hazard ratios (HR) and their 95% confidence intervals (CIs). Age, sex, fusion length, and the lowest instrumented vertebra were used as covariates in these models. The possible non-linear relationship between LL-SL and the ASD revision risk was modeled using restricted cubic splines with four knots at the 5th, 35th, 65th and 95th percentiles. Spline functions were estimated using multivariable Cox proportional hazard regression models, including age, sex, fusion length, and the lowest instrumented vertebra as covariates.

4.5 Ethical considerations

All participants gave a written informed consent for participation into the study. The study was observational by nature, with no interference to clinical decision-making. Ethical boards of Tampere University Hospital and Central Finland Central Hospital did approve the study.

5 RESULTS

5.1 5-year outcome

5.1.1 Disability (I)

From the preoperative level of 46 (SD 16), a significant improvement in ODI was observed throughout the follow-up period (**Figure 17 A**), ODI change remaining -26 (95% CI: -24 to -28, $p < 0.001$) at 5 years. However, ODI prevailed significantly higher in patients than in the population, $p < 0.001$. When analyzing short (1–2 levels) and long (over 2 levels) fusions separately, a comparable change was seen in both subgroups (**Figure 17 B**).

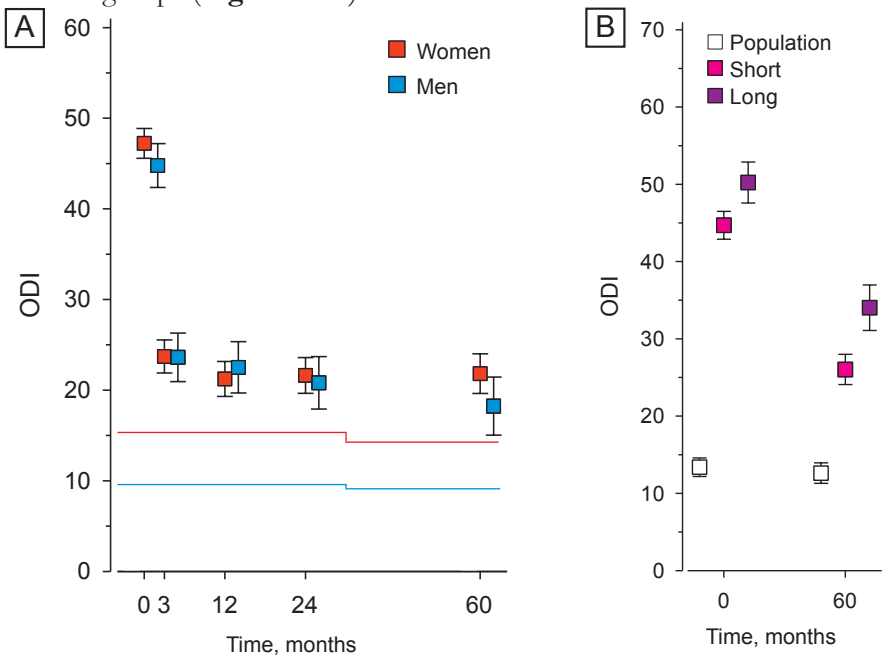


Figure 17. **A.** The mean (95% CI) Oswestry Disability Index (ODI) in patients (blocks) and the population (lines) according to sex. **B.** ODI in patients according to fusion length (short = 1–2 levels; long = over 2 levels). Groups adjusted by age, sex, and education years.

5.1.2 Health-related quality of life (HRQoL) (I)

With SF-36, the patients' baseline PCS and MCS were 27 (SD 7) and 47 (SD 13), respectively. At 5 years beyond LSF, the change in PCS was 8 (95% CI: 7 to 9), $p < 0.001$, and the change in MCS was 4 (95% CI: 3 to 7), $p < 0.001$ (**Figure 18**). In the population, PCS and MCS remained stable at 45 (SD 11) and 53 (SD 11). While patients scored significantly lower than the population in the preoperative MCS, both sexes reached the population at 3 months after LSF. Women sustained this benefit at 5 years, while men had slightly regressed at that point. PCS was lower with long fusions as compared to short fusions, but MCS did not differ according to fusion length (**Figure 19**).

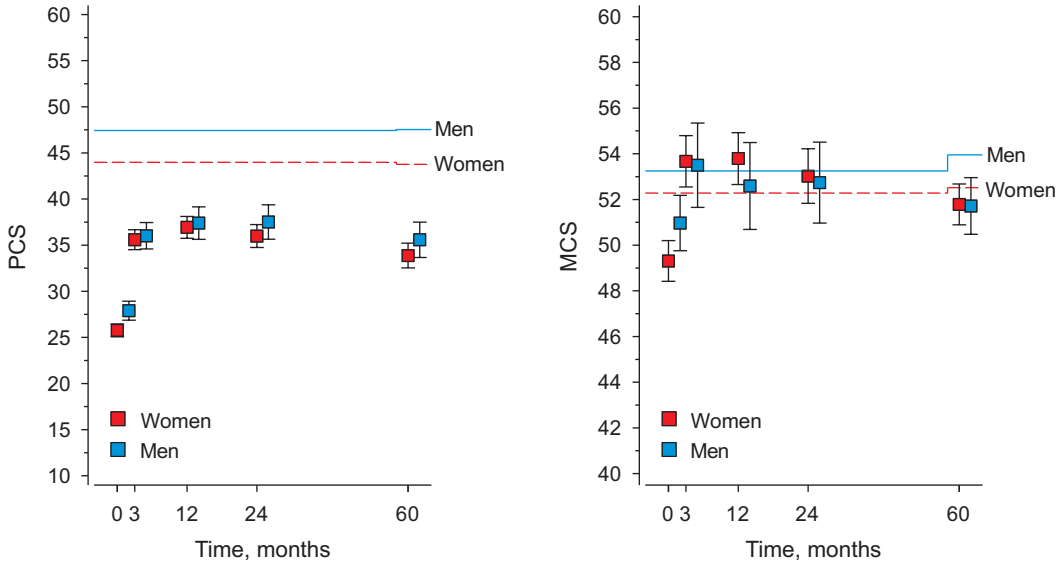


Figure 18. The mean (95% CI) physical (PCS) and mental (MCS) component summary scores in patients (blocks) and the population (lines) according to sex. Groups adjusted by age, sex, and education years.

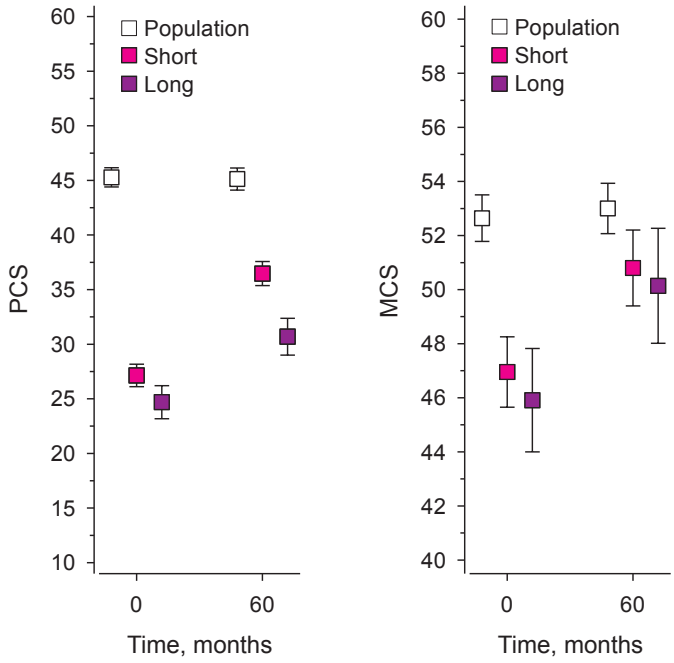


Figure 19. The mean (95% CI) physical (PCS) and mental (MCS) component summary scores in patients according to fusion length (short fusion = 1 to 2 levels; long fusion = over 2 levels), and in the population. Groups adjusted by age, sex, and education years.

5.1.3 Depressive symptoms (**II**)

The mean DEPS score in patients decreased close to the population level 3 months after surgery, and the decrease remained significant still at 5 years (**Figure 20 A**).

The preoperative prevalence of depressive symptoms (DEPS ≥ 12) [35% (95% CI 30% to 40%)] diminished to 13% (95% CI 10% to 17%) at 3 months, and it pivoted to 24% (95% CI 20% to 29%) at 5 years beyond surgery. Data are shown in **Figure 20 B**.

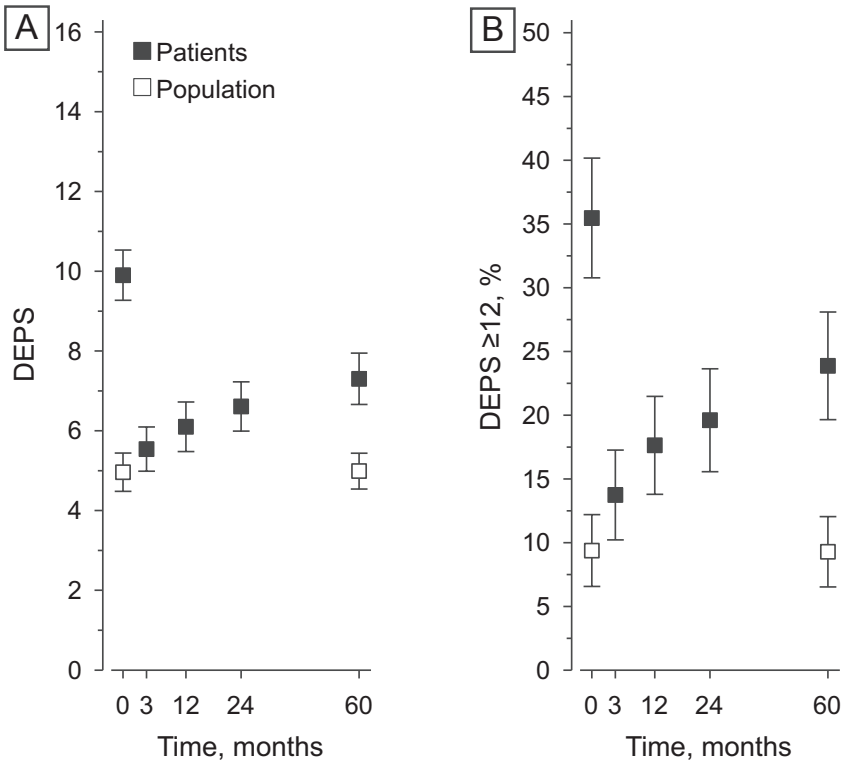


Figure 20. A. Changes in the Depression scale (DEPS) after surgery. **B.** The prevalence of depressive symptoms (DEPS ≥12) after surgery. Groups adjusted by age, sex, and education years. Reprinted with permission from Wolters Kluwer Health, Inc. (**II**)

ODI improvement was aligned between preoperatively depressive (DEPS ≥ 12) and non-depressive patients with the corresponding ODI changes of -20 (95 CI -24 to -17) and -18 (95% CI -20 to -16) (**Figure 21**).

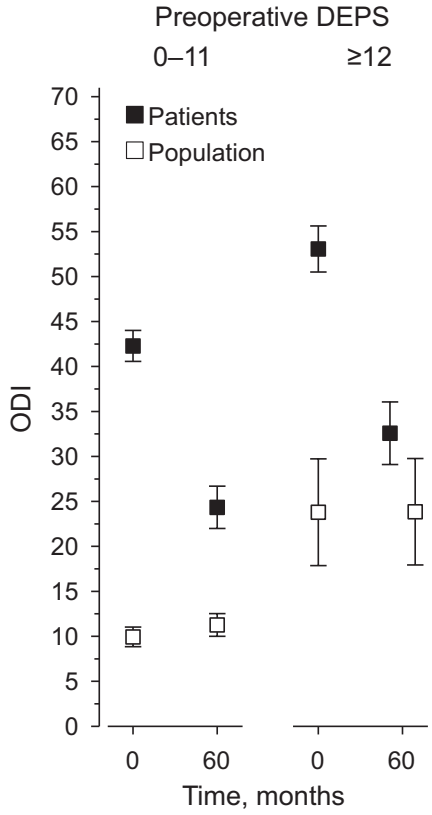


Figure 21.

ODI changes in the non-depressive (DEPS <12) and depressive (DEPS ≥ 12) patients at 5 years after surgery, and in the population. Groups adjusted by age, sex, and education years. Reprinted with permission from Wolters Kluwer Health, Inc. (**II**)

5.1.4 Mortality (**I**)

The 5-year mortality of patients [3.4% (95% CI: 2.2 to 5.4)] did not differ from the mortality of 4.8% (95% CI: 3.5 to 6.7) amid the population. Age-, sex-, and comorbidity adjusted HR of 0.86 (95% CI: 0.48 to 1.53) was calculated for death after LSF. Three most frequent causes of death in patients were cardiac (63%), cancer (21%), and external causes (11%), and in the population, they were cardiac (45%), cancer (24%), and respiratory causes (12%).

5.2 Revisions for adjacent segment disease (ASD)

5.2.1 Surgical indication as a risk factor (**III**)

In the whole study population, a total of 3112 person-years were followed-up, of which 608 (median 9.7) years in the IS group, 1852 (median 9.4) years in the DLSD group, and 653 (median 9.4) in the third group. The revision rate was remarkably lower with IS than in the other groups (**Table 13**). Within DLSD group, patients with or without spondylolisthesis did not statistically differ from each other [rates of 17.9 (95% CI: 12.8 to 24.6) and 30.4 (95% CI: 18.8 to 46.8), p = 0.058].

Table 13. Crude ASD revision rates throughout the whole follow-up period in all patients and according to surgical indication.

Indication for surgery	Revision rates for ASD (%)	95% CI (%)
All patients	17.8	14.0 to 22.1
1) IS	4.8	1.6 to 22.1
2) DLSD	20.5	15.6 to 26.7
3) other reasons	20.6	12.9 to 31.9

p=0.023 (Log-rank test)
IS = isthmic spondylolisthesis
DLSD = degenerative lumbar spine disorders, *i.e.*, spinal stenosis with or without degenerative spondylolisthesis
Others encompass deformities, postoperative conditions following decompression, and posttraumatic conditions

During the follow-up, 11% of the patients underwent some other spinal reoperation although they were not reoperated for ASD. Indications for those reoperations are depicted in **Table 14**. Hence, a total of 28.8% of all patients underwent a spinal reoperation during the follow-up.

Table 14. Rates of spinal reoperations amid the non-ASD patients.

Indication for reoperation	N	%
Pseudoarthrosis	13	4.3
Early (<1 year) implant failure	8	2.7
Hematoma	8	2.7
Infection	2	0.7
Residual stenosis	2	0.7
Screw malposition	2	0.7
Distant (>2 levels) stenosis	2	0.7
Others *(include back pain attributed to instrumentation, and sacral neoarthrosis)*	3	1.0

To eliminate potential bias from differences in patient demographics and surgical procedures, groups were adjusted by age, sex, fusion length, and the level of the lowest instrumented vertebra. Thereafter, adjusted cumulative ASD revision rates were calculated and are depicted in **Figure 22**. Following the same adjustments, the hazard ratio (HR) for ASD revisions was 3.92 (95% CI: 1.10 to 13.96), p = 0.035, when comparing DLSD group to IS group, and it was 4.27 (95% CI: 1.11 to 15.54), p = 0.036, when comparing the third group to IS group. Further, these findings were not changed if the use of interbody cage was added to the multivariate model.

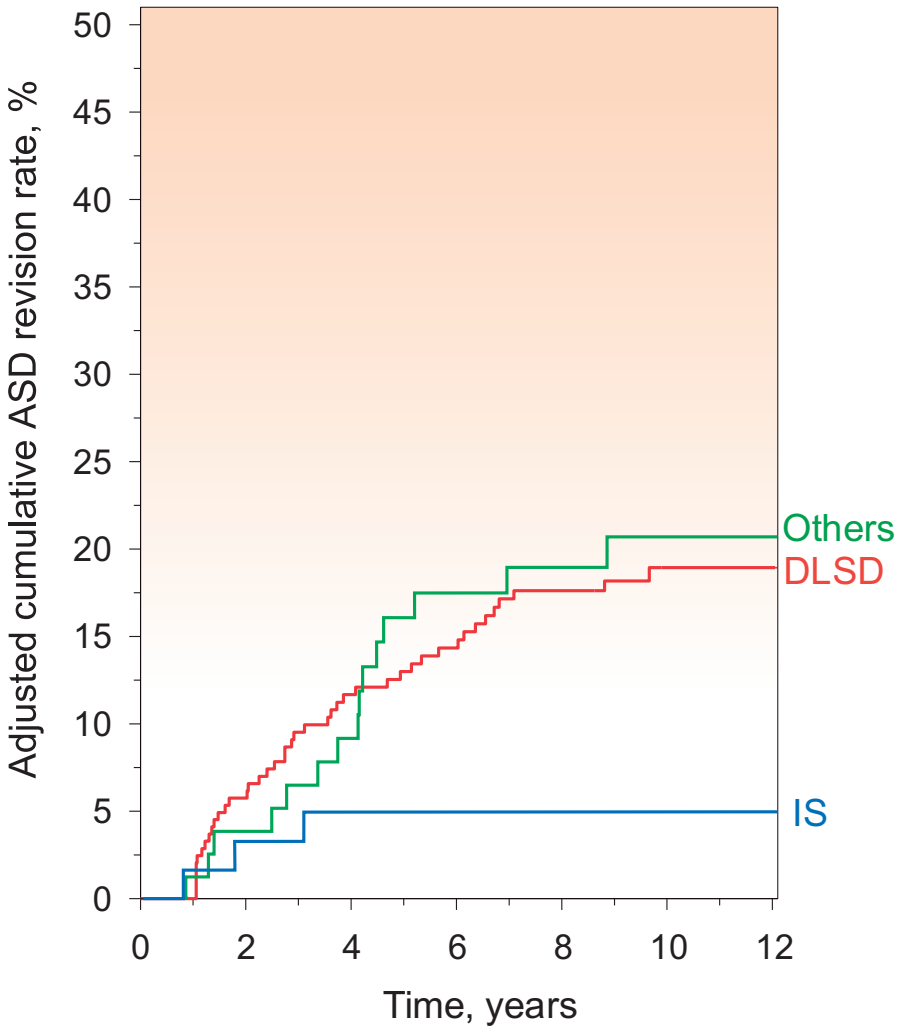


Figure 22. Adjusted cumulative ASD revision rates according to surgical indication. The groups were adjusted by age, sex, fusion length, and the lowest intstrumented vertebra.
IS = isthmic spondylolisthesis
DLSD = degenerative lumbar spine disorders, i.e., spinal stenosis with or without degenerative spondylolisthesis
Others encompass deformities, postoperative conditions following decompression, and posttraumatic conditions

5.2.2 Alignment as a risk factor (**IV**)

Throughout the follow-up (median 9.2 years), 43 (20%) patients with DLSD underwent a revision for ASD.

Lumbopelvic parameters by mean remained unchanged after LSF (**Table 15**). By mean, PI-LL difference remained in the range of normal lordosis. However, 83 (39%) patients could be judged hypolordotic after surgery based on the PI-LL mismatch of >9º.

Postoperative imbalance (PI-LL >9º) did not result in significantly increased revisions for ASD in the Cox multivariate model. The crude (unadjusted) hazard ratio (HR) of 1.46 (95% CI 0.80 to 2.66), and adjusted (by age, sex, PI, fusion length, and the lowest instrumented vertebra) HR of 1.69 (95% CI 0.87 to 3.29) prevailed statistically insignificant.

Table 15. Lumbopelvic parameters (º) before and after LSF surgery in patients with degenerative spinal disorders.

	Preoperative Mean (SD)	Postoperative Mean (SD)
LL	50 (13)	49 (12)
PI	56 (10)	..
PI-LL	6.7 (11.1)	6.7 (11.1)
PT	20 (8)	21 (7)
SS	37 (9)	36 (8)
SL	29 (14)	27 (12)
LL-SL	21 (14)	22 (13)

LL = lumbar lordosis, PI = pelvic incidence, SS = sacral slope, PT = pelvic tilt, SL = segmental lordosis, SD = standard deviation

We hypothesized that postoperative segmental hypolordosis might lead to hyperlordosis outside the fusion segment (LL-SL) as a compensatory mechanism. Accordingly, this hyperlordosis might have predisposed to ASD through increased stress at the adjacent level. Notwithstanding, we found that higher LL-SL was associated with reduced revisions for ASD with HR of 0.94 (95% CI: 0.91 to 0.97). Evaluating the effect of continuous LL-SL difference on the revision risk reinforced this finding (**Figure 23**).

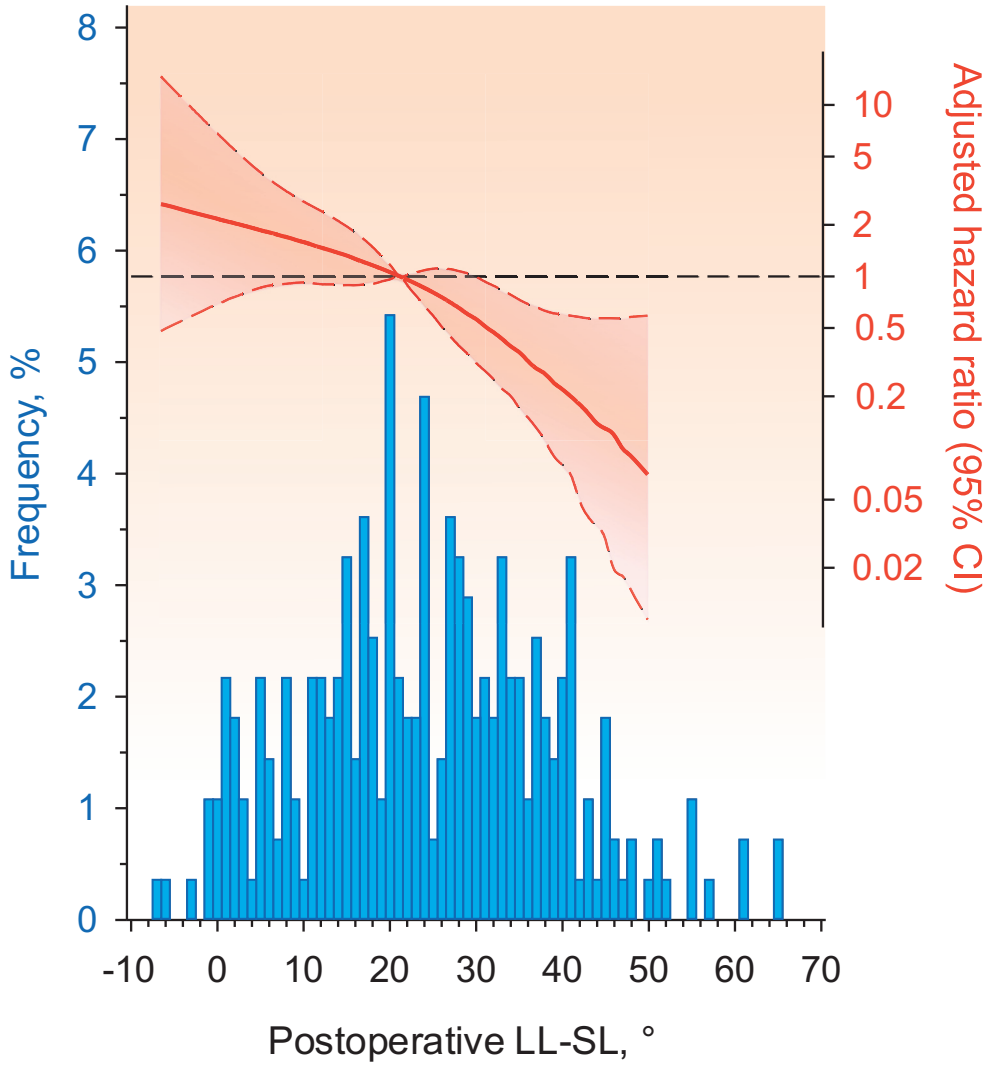


Figure 23. Higher lordosis in the mobile segment of lumbar spine (LL-SL) after LSF was associated with less revisions for ASD.
Blue bars illustrate the distribution of the mobile segment lordosis (LL-SL). Red line illustrates the adjusted (by age, sex, pelvic incidence, fusion length, and the lowest intsrumented vertebra) hazard ratio for ASD revisions. The reference (HR 1) was set to the median of LL-SL (21°).

6 DISCUSSION

Pain and disability are the main incentives for LSF surgery. In this thesis, we focused to evaluate how the previously reported short-term benefits of LSF surgery are preserved in a longer follow-up (Pekkanen et al., 2014, Weinstein et al., 2007, Strömqvist et al., 2013, Möller and Hedlund, 2000b). The 5-year outcome was investigated using established instruments for disability and health-related quality of life (ODI and SF-36) (**Figure 24**), and mortality data. Potential confounding effect of depressive symptoms was elucidated using DEPS and ODI.

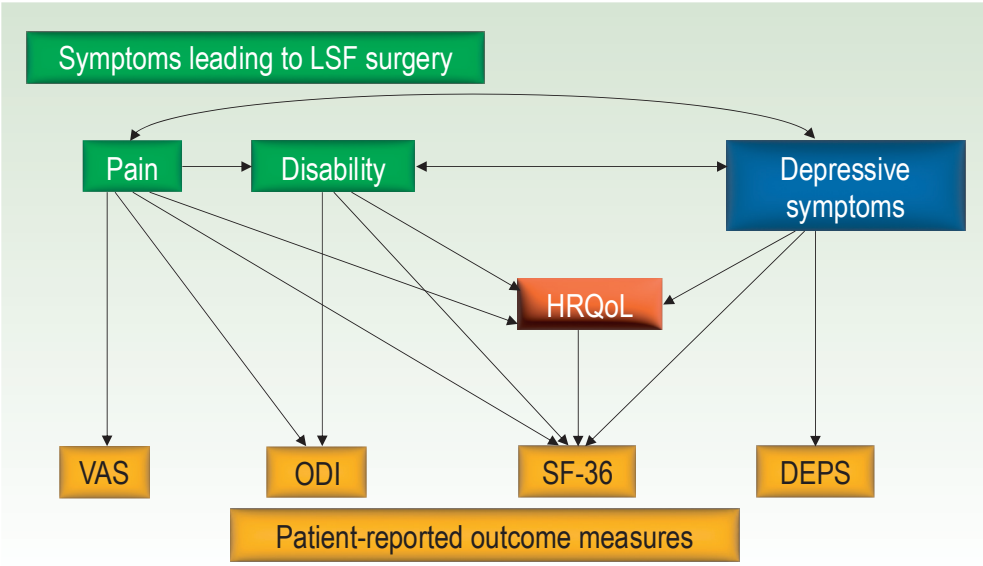


Figure 24. An illustration depicting how the symptoms that lead to LSF surgery are reflected in common outcome instruments.

High occurrence of ASD may compromise the long-term benefits of LSF surgery (Maruenda et al., 2016). Moreover, results of revision surgeries for ASD are reported among the poorest across specific LSF indications (Glassman et al., 2009). Therefore, it is paramount to be aware of all possible means to minimize the risk of ASD. In this study, 10-year revision rates for ASD were determined for different

surgical indications. Finally, the potential effect of sagittal alignment on the revision risk was evaluated in patients with degenerative spinal disorders.

6.1 Patient characteristics

Our study population consisted of a district-based cohort of non-selected patients undergoing LSF surgery. This features a population-based sample of elective LSF patients and surgeries in Finland. The female over-prevalence in this study (68%) was aligned with a report from the United States (58% women amid a total of 2.8 million spinal fusions for degenerative spinal indications) (Martin et al., 2019). In Study **III**, the sex distribution was even more uneven in the DLSD cohort (spinal stenosis with or without spondylolisthesis) (76% women). Men were overrepresented with IS (56%). Mean age (61 years in all patients) was slightly higher than what was reported from the US (57 years) (Martin et al., 2019).

Our patient cohort was largely comparable with the general population sample (matched with age, sex, and residential area) in terms of comorbidities (**Table 9**). The lower prevalence of cancer (1% vs. 2%, p=0.031) and psychiatric comorbidities (2% vs. 4%, p=0.043) were apparently consequential to surgical patient selection. Rheumatoid comorbidities were more frequent in patients than in the population (9% vs 5%, p<0.001), potentially reflecting an increased need for spine surgeries with rheumatoid conditions (Kang et al., 2016). The self-reported prevalence of spinal problems in the population sample (23%) was accordant with prior reports (Manchikanti et al., 2014).

6.2 5-year outcome

Our results demonstrated sustainment of the benefits of LSF throughout the 5-year follow-up. Patients, nevertheless, did not reach the functional level of the population at any stage.

This study encompassed heterogeneous indications for LSF, reflecting the spectrum of elective LSF patients. The severe baseline disability (ODI 46) and the change at the 5-year follow-up (-26) were consistent with prior reports including diverse LSF indications (baseline mean ODI ranging from 41 to 72, and mean change from -10 to -28, correspondingly) (**Table 5**) (Maruenda et al., 2016, Høy et al., 2017, Owens et al., 2016, Glassman et al., 2012).

Most long-term reports consist of selected patient series. Studies that exhibited LSF outcomes for DDD or CLBP demonstrated only modest functional improvement (mean ODI changes between -10 and -19) (Luckenbill et al., 2015, Hedlund et al., 2016, Froholdt et al., 2012, Sköld et al., 2013, Mannion et al., 2013). Generally, superior benefits (mean ODI changes ranging from -18 to -45) were depicted after LSF for degenerative indications, such as LSS or DS (Pourtaheri et al., 2015, Gaffney et al., 2019, Hu et al., 2019, Liao et al., 2011, Bredin et al., 2017, Korovessis et al., 2010, Lim et al., 2020). Glassman et al. (2009) represented momentous variation in LSF outcome according to surgical indication. Contrary to that, Pekkanen et al. (2014) found all diagnostic cohorts to gain analogous functional benefits from LSF. The discrepancy possibly can be explained by inaccuracy in the definitions of certain indications and the differences in practices, especially in patient selection. Understandably, this also confounds comparisons between the studies.

Predominantly, the effect of surgery is less overt in HRQoL than in pain or disability measures, reflecting the fact that patients can adapt to their restrictions (DeVine et al., 2011). Nevertheless, clinically meaningful improvement in PCS was seen in this study (8 points still at 5 years) as well as in the previous reports (ranging between 10–16) (**Table 5**) (Lim et al., 2020, Glassman et al., 2012). In a study analyzing the impact of BMI on LSF outcome (Owens et al., 2016), the change in PCS undercut the reported MCID of 5 points (Copay et al., 2008). On the other hand, Korovessis et al. (2009) reported a surprisingly high change of 32 points in PCS after LSF. In general, changes in ODI and PCS seem to parallel each other to some extent.

MCS was infrequently disclosed in long-term reports of LSF. General spine surgery related MCID value for MCS has not been published. Lim et al. (2020) reported the long-term change of 6 points in men, and 7 points in women. Those exceeded the change of 4 points in our study. However, built-in with the SF-36 instrument, a low PCS score tends to raise the MCS score, which may lead to underestimation of MCS change in conditions with severe disability (Laucis et al., 2015). Hence, PCS changes generally surpass MCS changes, especially with orthopedic patients. Defining condition-specific MCID values for MCS, in the future, may help assess the LSF-induced improvement on mental well-being.

Fusion length did not affect the outcome in this study. Physical improvements were comparable after short and long fusions, although patients with long fusion stayed slightly below those with short fusion. MCS, nevertheless, did not diverge between the subgroups. Previously, slightly better clinical course has been recorded with short fusions for degenerative lumbar disease when compared to long fusions

(Lee et al., 2015). However, with degenerative scoliosis the fusion length was insignificant regarding the clinical outcome (Phan et al., 2017).

Prior studies concur with our finding of the sustainment of functional benefits (Høy et al., 2017, Kroeze et al., 2020). One study with a high incidence of ASD reported a loss of functional benefits at 10 years (Maruenda et al., 2016). However, after revision surgery the functional level again paralleled the earlier satisfactory results.

Studies comparing LSF outcome with a matched population are limited. Mokhtar et al. (2010) found HRQoL of patients with DS to approach that of a matched population at 2 years following single-level LSF. The long-term (mean 9 years) results of an RCT on adults with IS demonstrated that both surgically and conservatively treated patients remained under the general population in disability and HRQoL (Ekman et al., 2005). In contrast, Poussa et al. (2006) demonstrated in an average of 14.8-year follow-up that adolescents with high-grade IS achieved the general population after surgical treatment. In the present study, patients remained physically below the population. However, MCS in our patients reached the population level postsurgery, but males slightly subsided beneath the population by 5 years. Our data provide no explanation for this dissociation.

In addition to the benefits on functioning and HRQoL, surgical outcome can be assessed through the complication rate and mortality. Previous studies have not demonstrated increased mortality beyond LSF surgery (Yavin et al., 2017, Lurie et al., 2015, Cummins et al., 2021, Salmenkivi et al., 2017). Our finding was on par with those–notwithstanding the higher prevalence of cardiac comorbidities in patients than in the population (50% vs. 41%, $p<0.001$). Of course, patients ending up in LSF surgery are always selected so that those with the stoutest co-morbidities and the highest risk of death are not operated on at all.

6.3 Depressive symptoms

Preceding studies have exhibited conflicting findings about whether depression compromises LSF outcome (Derby et al., 2005, Trief et al., 2006, Wagner et al., 2020, Anderson et al., 2015). In the present study, the preoperatively depressive patients were functionally inferior to their non-depressive counterparts, but both groups gained a similar step upward. In the study of Wagner et al (2020), the preoperatively inferior depressive patients even approached the rest in pain, disability and HRQoL postsurgery. These contradicted the finding of Derby et al. (2005) about poor

preoperative MCS correlating with lower improvement to PCS. In Trief et al. (2006), patients' better preoperative mental status correlated with better pain relief and functional status at 2 years.

In this study, the preoperative prevalence of depressive symptoms in patients was triple to that in the population. The difference vanished soon after surgery, but the depressive symptoms had partially recurred by 5 years. Presumably, a considerable proportion of our patients' depressive symptoms was consequential to their long-lasted pain and disability. Partial return of depressive symptoms may reflect the higher level of disability among the preoperatively depressive patients or those patients' higher susceptibility to depressive symptoms.

All our patients had passed the preoperative judgement between surgical and conservative management. Hence, it is possible that our patients' depressive symptoms were not completely similar with those reported to occur in a strong connection with CLBP (Currie and Wang, 2004). We can figure out that with a clear surgical indication, depression does not need to exclude patients from LSF surgery.

6.4 Adjacent segment disease (ASD)

6.4.1 Surgical indication and ASD

Pre-existing literature provides no good comparisons of ASD incidences across different LSF indications. That makes the present finding of the 4-fold difference in ASD revision rates between IS and degenerative spinal disorders novel. In this study, the 10-year incidence of ASD revisions with IS (4.8%) was consistent with the corresponding 10-year incidence following ALIF for grade I IS (4.1%) (Choi et al., 2014). Moreover, revisions were sporadic with IS, while they accumulated linearly over time with degenerative disorders (**Figure 22**). With degenerative disorders, our ASD revision rate (21%) concurred with the reported rates of 17.4% in a 5-year follow-up (Lad et al., 2014) and 20% in a 10-year follow-up (Gillet, 2003).

When inspecting more in-depth those patients with IS who ended up in a revision for ASD (n = 3), all those underwent revision in the first 3 years. First of them had a disc herniation extirpated from the adjacent level during the initial surgery. The second one had degeneration in the adjacent segment facets already at the index surgery, and that turned into radiological and symptomatic instability afterward. The third one underwent two-level fusion and later acquired symptomatic stenosis to the

rostral junction which primarily had only mild disc degeneration. In retrospect, possibly at least the first of those three revisions could have been avoided with a different surgical strategy.

In study **III**, the DLSD group (encompassing LSS with or without DS) and the third group (encompassing deformities, postoperative conditions, and posttraumatic conditions) had an equal risk for ASD revision. Moreover, those groups were demographically similar. In fact, in 90% of cases, the primary etiology amid the third group was degenerative. Our findings expressly support the role of degenerative spinal disease in ASD pathogenesis resulting in linearly accumulating revisions for ASD. That also explains the sparsity of ASD with IS.

6.4.2 Alignment and ASD

Prior literature is ambivalent regarding the role of sagittal alignment as a risk factor for ASD (Rothenfluh et al., 2015, Dallaudiere et al., 2020, Nakashima et al., 2015, Anandjiwala et al., 2011, Alentado et al., 2016). This is a complex issue to investigate. Revision surgery as an outcome potentially incurs significant bias because no definitive criteria for revision surgery exist. Accordingly, one could consider radiological adjacent segment degeneration as more appropriate outcome. However, studies report wide discrepancies between prevalences of radiological and clinically relevant ASD (Ekman et al., 2005, Seitsalo et al., 1997, Okuda et al., 2018). Moreover, ASD as a progressive phenomenon sets demands to the statistical methods used.

In this study, lumbar alignment by the parameter means remained unchanged during LSF (**Table 15**). With an artificial threshold of 9º in PI-LL, 39% of the patients could be considered hypolordotic after surgery. Hence, all surgeries did not meet the present conception of appropriate alignment. This balance disturbance, however, did not result in statistically significant increase in the risk of revision for ASD. That contradicts the finding of Rothenfluh et al. (2015), which demonstrated the PI-LL mismatch of >10º as a significant risk factor for ASD. In another 11.6-year follow-up after PLIF, the PI-LL mismatch was not found to increase revisions for ASD (Nakashima et al., 2015). It is possible that type II error existed with our results, and statistical significance could have been established with larger study population. Yet, in that case, we deem the connection between segmental hypolordosis and ASD development limited, and not quite straightforward–recalling the findings of study **III**.

Moreover, use of the PI-LL mismatch as an indicator of malalignment may not suffice to all cases. Despite of appropriate total lordosis, the lordosis distribution may be suboptimal. This applies especially to Roussouly type 1, with which all lumbar lordosis concentrates to low lumbar spine (Roussouly et al., 2003, Roussouly and Pinheiro-Franco, 2011, Yilgor et al., 2017). With such the lordosis maldistribution may potentially strain the adjacent segment in the way that prompts ASD (Bari et al., 2021).

An interesting secondary finding here was that, following LSF, lordosis in the mobile lumbar segment (LL-SL) seemed to protect against revisions for ASD. HR of 0.9 (95% CI: 0.9 to 1.0) of course indicated only modest albeit statistically significant effect, but analysis of continuous LL-SL (**Figure 23**) reflected a strong effect on the risk. Our data provided no answer whether this in fact reflected more the alignment or the mobility of the mobile segment. It is also possible that some of the patients had unmet need for compensation both before and after surgery given their stiff spine. Earlier, diffuse idiopathic skeletal hyperostosis (DISH), a condition resulting in severely restricted spinal mobility, was reported as a significant risk factor for ASD following short segment LSF (Otsuki et al., 2015). We presume that pursuit of adequate segmental lordosis in ASD prevention might be most beneficial with degenerative conditions accompanied with reduced mobility.

The case for how much balance contributes to ASD pathogenesis continues to be open. Our findings emphasize the role of disc degeneration in ASD pathogenesis. As spinal degeneration is particularly associated with the individual's biological characteristics–instead of merely age and biomechanical factors–the risk of developing ASD significantly varies across individuals (Cheung et al., 2010). At the presentation of a manifest short-segment spinal issue, disc degeneration may, in fact, lie behind widely (Teraguchi et al., 2014, Lai et al., 2022). Degeneration in the adjacent disc may be latent or mild at the time of LSF surgery, but progress and potentially end up in instability as ASD emerges. There are several classification systems for disc degeneration, the MRI-based Pfirrmann classification being the most used (Pfirrmann et al., 2001). Its modification has been introduced to increase sensitivity to discriminate higher stages of degeneration in older age cohorts (Griffith et al., 2007). Yet, conventional MRI sequences being relatively insensitive with mild degeneration, Benneker and colleagues developed an axial T2 mapping based method to distinguish even mild disc degeneration (Benneker et al., 2005, Watanabe et al., 2007, Hoppe et al., 2012). Notwithstanding, in this study, we did not analyze the grade of degeneration at the locus of future ASD at the time of index surgery.

Even if balance contributed limited to ASD progression, there is evidence that balance impacts the clinical outcome of LSF (Videbaek et al., 2011, Korovessis et al., 2010, Lazennec et al., 2000). Moreover, kyphotic fusion segment significantly hampers future revision surgeries, where restoration of reasonable alignment is even more troublesome (Berjano et al., 2013). Therefore, restoration or preservation of segmental lordosis is essential in every LSF operation.

6.5 Strengths and limitations

Prospective data collection in real clinical environment was a strength of the present study. Since practically all LSF surgeries in Finland, especially in the data collecting period, were performed in public central hospitals, our data featured population-based samples of LSF patients and surgeries. Surgeries were performed by experienced spine surgeons in a standardized manner thus reducing the risk of false negative nullification of the surgical potential. That yielded an optimal basis for the evaluation of the overall long-term benefit. Our results demonstrated efficacy of surgery despite a relatively high 10-year reoperation rate (28.8%), which nevertheless has been declared an inherent disadvantage of LSF surgery (Martin et al., 2007). More, this proof of the real-life efficacy of treatment was neither voided by the fact that not all surgeries met the alignment goals nowadays proposed appropriate.

Other strengths were use of common and validated outcome measures (ODI, SF-36), a relatively large study population, and robust statistical methodology. Mortality data were retrieved from a reliable national registry (Statistics Finland, 2010).

Lack of control cohort treated without surgery can be counted as a limitation of this study. Helenius and colleagues demonstrated surgical treatment for adolescent idiopathic scoliosis result in significant improvement in back pain and HRQoL as compared with patients not treated surgically (Helenius et al., 2019). Moreover, after surgery, the patients paralleled the general population in HRQoL except for function. Natural course of distinguished spinal stenosis is not favorable in the majority of patients (Johnsson et al., 1992, Matsudaira et al., 2016). Thus, long-term surgical benefits demonstrated in this study apparently cannot be explained by spontaneous healing tendency of the spinal conditions.

One disadvantage harassing long-term follow-ups is that practices may change over time along with scientific progress. Therefore, the long-term results potentially do not respond to the most recent questions. A recognized change after the data

collecting period has been the increased management of DS with decompression without fusion, largely due to the Swedish RCT (Försth et al., 2016, Ponkilainen et al., 2021). Whether this will change the now reported 5-year outcome of LSF surgery will become evident later. Moreover, implementation of LSF has changed with time. In study **III**, interbody spacers were used in 55% of patients with IS and in 10% of other patients. At that time (2008–2012), interbody spacers were exploited mainly to foraminal decompression and prevention of early instrumentation failures. Use of interbody spacers in the management of sagittal alignment has expanded thereafter. More, desired goal has been toward shorter yet more stable fusions. Whether this has been achieved, remains unknown. Potentially these changes influence the occurrence of ASD. However, literature have not certified an impact of the use of interbody spacer on ASD progression (Videbaek et al., 2011, Høy et al., 2017). Findings are controversial about the contributory role of fusion length (Wang et al., 2021, Burch et al., 2020). Even preserved mobility after TDR does not seem to protect against ASD (Kitzen et al., 2021). Hence, we do not expect potential changes in the details of LSF execution to much alter the present findings regarding ASD.

A clear limitation in this study was the use of revision surgery as an endpoint. Ending up in revision surgery is always based on an individual decision between the surgeon and patient. Older patients sustaining more comorbidities are more likely to be refused the considered revision surgery on the basis of surgical risks or lower functional demands. However, the lowest revision rate was here reported among patients with IS who were the youngest and healthiest. Hence, without this potential bias, our finding could have been even stronger.

Paucity of determining the baseline status of the future ASD level at the time of index surgery may have confounded our results. According to the definition of ASD, the possible physiological (non-symptomatic) degeneration at the adjacent disc becomes symptomatic only after the index surgery. Nevertheless, we can presume that not many symptomatic levels have been left outside the fusion segment at a time when the preference of shorter fusions obviously was vaguer than today at our institution. More, we were not able to scrutinize the role of the stage of disc degeneration to the risk of ASD.

Use of PI-LL mismatch as an indicator of malalignment and not considering the lordosis distribution and Roussouly morphotypes may have caused inaccuracy in the detection of malalignment. This may have biased our results. However, Roussouly type 1 morphology is the most infrequent of the morphotypes thus reducing this potential bias (Laouissat et al., 2018). Moreover, as full spine radiographs were not

routinely obtained in the data collecting period, we were not able to evaluate the sagittal balance and compensatory mechanisms in totality.

Evaluating benefits on pain, disability, and HRQoL is an established means to measure the success of elective surgery (DeVine et al., 2011). In this study, evaluation of pain relief was built-in the ODI and SF-36 instruments. Here, we did not report back and leg VAS scores. Therefore, we could not evaluate specifically the relief to back or radicular pain.

6.6 Future prospects

In some countries, national spine registries have been in use for years (Strömqvist et al., 2013, Simony et al., 2014, Grovle et al., 2019). Finnish national spine registry is still in its infancy (Mäntymäki et al., 2021). In the future, the registry is to allow for quality control and to produce especially epidemiological data. Yet, detailed questions regarding specific diagnostic subgroups or comparisons of treatment modalities may still warrant tailored study settings with strictly defined criteria.

We investigated LSF benefits. In the future, studies on the efficiency (cost-effectiveness) of treatment are increasingly required alongside this (Glassman et al., 2012, Weinstein et al., 2014, D'Souza et al., 2019). Clinicians are best to be involved in that research.

Ever-accumulating clinical data open the doors to the entry of artificial intelligence (AI) into spine surgery (Martin and Bono, 2021). Spinal deformities are among the most complex conditions requiring extensive surgeries encumbered with high risks (Sciubba et al., 2015, Lenke et al., 2016). With their multifactorial pathogenesis, the relevance of individual risk factors for individual patients may be difficult to determine despite of statistically significant findings on the population means. With modern surgical technologies, radiological and clinical data are continuously stored in the digital form. In the future, potentially AI with machine learning will provide superior tailored treatment solutions by processing this colossal amount of information (Joshi et al., 2019, Campagner et al., 2020, Lopez et al., 2022, Pellisé et al., 2022). Along that, our understanding of the mechanisms underlying complex spinal pathologies will improve.

7 CONCLUSIONS

1. The benefits of LSF surgery on function and well-being of a heterogeneous group of patients were mostly preserved at 5 years. However, patients did not reach the physical level of the general population. LSF surgeries did not increase mortality.

2. Patients with depressive symptoms gained equal functional benefit from LSF surgery with their non-depressive counterparts. Moreover, depressive symptoms were resolved to the level of population soon after surgery, although they had partially recurred by 5 years.

3. Revisions for ASD infrequently followed LSF for isthmic spondylolisthesis, whereas they accumulated almost linearly over time following LSF for degenerative spinal disorders. A fifth of patients with degenerative spinal disease underwent revision for ASD within 10 years of LSF.

4. Sagittal alignment in LSF appeared to have at most only a limited role in the development of ASD. We could not establish the effect of poor balance on the risk of revision for ASD. Nonetheless, sagittal alignment in ASD prevention might be most influential with degenerative spinal conditions accompanied with restricted mobility.

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ORIGINAL PUBLICATIONS

PUBLICATION I

Disability, Health-Related Quality of Life and Mortality in Lumbar Spine Fusion Patients-A 5-Year Follow-Up and Comparison With a Population Sample

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Disability, Health-Related Quality of Life and Mortality in Lumbar Spine Fusion Patients—A 5-Year Follow-Up and Comparison With a Population Sample

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Abstract

Study Design: Prospective follow-up study.

Objectives: We aimed to assess the effect of lumbar spine fusion (LSF) on disability, health-related quality of life and mortality in a 5-year follow-up, and to compare these results with the general population.

Methods: 523 consecutive LSF operations were included in a prospective follow-up. Disability was assessed by the Oswestry Disability Index (ODI), and HRQoL by the 36-item Short Form (SF-36) questionnaire using the physical and mental summary scores (PCS and MCS). The patients were compared with an age-, sex-, and residential area matched general population cohort.

Results: The preoperative ODI in the patients was 46 (SD 16), and the change at 5 years was −26 (95% CI: −24 to −28), $p < 0.001$. In the population, ODI (baseline 13, SD 16) remained unchanged. The preoperative PCS in the patients was 27 (SD 7), in the population 45 (SD 11), and the increase in the patients at 5 years was 8 (95% CI: 7 to 9), $p < 0.001$. The patients did not reach the population in ODI or PCS. The baseline MCS in the patients was 47 (SD 13), and the change at 5 years 4 (95% CI: 3 to 7), $p < 0.001$. MCS of the females reached the population at 5-year follow-up. When analyzing short and long fusions separately, comparable changes were seen in both subgroups. There was no difference in mortality between the patients (3.4%) and the population (4.8%), hazard ratio (HR) 0.86.

Conclusions: Although the patients who had undergone LSF benefited from surgery still at 5 years, they never reached the physical level of the population.

Keywords
lumbar spinal fusion (LSF), outcome, longer follow-up, population sample, mortality

Introduction

The incidence of lumbar spine fusion (LSF) surgery has increased markedly in the western countries during the past decades.[1] Spinal pathologies leading to LSF are heterogeneous.[2] Common indications for fusion are degenerative and isthmic spondylolisthesis and deformity corrections. The efficacy of the fusion surgery is established in several indications.[3,4] Some indications are more controversial: some recent studies question the need of combining fusion to decompression in degenerative spondylolisthesis,[5,6] and LSF in degenerative disc disease (DDD) is probably not reasonable in most cases.[7]

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The knowledge of the long-term consequences of LSF is important. On one hand, fusion surgery requires heavy hospital costs and long recovery periods from the patient. On the other hand, spinal disorders behind the surgery are often severely disabling. The health burden of lumbar spinal stenosis on health-related quality of life (HRQoL) is reported to equal to diabetes, heart disease, arthritis or stroke.[8]

We have previously shown disability and HRQoL in patients undergoing LSF to improve in several spinal disorders in a 2-year follow-up.[9] Many LSF reports with longer follow-up focus on specific diagnoses or selected patient material or compare interventions, such as operative and conservative treatment.[3,7] To our knowledge, no one has previously published a health-care district based study evaluating the disability, HRQoL and mortality among LSF patients in a 5-year follow-up. The aim of the present study is to assess the changes from LSF to disability, HRQoL and mortality in a prospective, 5-year follow-up of non-selected patients. We also compare the results with a general population sample.

Material and Methods

Finland has a national health insurance system, and therefore a particular hospital mainly covers the population of a particular area. Tampere University Hospital and Central Finland Health Care District are 2 public units that exclusively perform spinal fusion surgery in Pirkanmaa and Central Finland districts covering together around 775 000 inhabitants. Since 2008 all patients undergoing non-urgent LSF surgery have been invited to a prospective follow-up study. Surgeons filled up the data in their daily practice and patients answered the questionnaires at strict time-points pre- and post-operatively. All patients signed a written consent, and ethical committees of both hospitals approved the study.

The data of 523 consecutive patients was available for the present study. The fusion indications were as follows: degenerative spondylolisthesis (48%), isthmic spondylolisthesis (15%), spinal stenosis (13%), postoperative conditions (9%), degenerative disc disease (8%), degenerative scoliosis (6%), others, like posttraumatic conditions and posttraumatic instability (1%). All patients underwent posterolateral instrumented fusion with or without posterior interbody fusion (PLIF/TLIF) combined with necessary decompression. Out of all LSF operations, 357 (68%) were short fusions (1 or 2 levels), while 166 (32%) of all fusions were long (over 2 levels).

The LSF patient cohort was compared with a general population sample (n = 682) matched by age, sex and residential area. Statistics Finland performed the sampling and collected the data from the same cohort in 2010 and 2015.[10] Data was collected twice to eliminate the possible effect of aging. The mortality data was extracted from Official Statistics of Finland.[10]

The main outcome measures were the Oswestry Disability Index (ODI) for disability and the Short-Form-36 Questionnaire (SF-36) for Health-Related Quality of Life (HRQoL). The ODI is one of most widely used back-specific disability measurement tools in both clinical work and research.[11] The ODI score represents the percentage the patient achieved of the maximum number of points. According to the original publication, the scores are grouped into 5 categories: 0–20 minimal, 20–40 moderate, 40–60 severe disability; 60–80 crippled and 80–100 indicates that the patient is either bed-bound or exaggerating his or her symptoms.[12] The Finnish validated version 2.0 of the ODI was used in this study.[13] The SF-36 is a generic patient-assessed health outcome measure for the health-related quality of life reflecting patients' health state and wellbeing.[9] In the analysis the 8 dimensions of the SF-36 score were aggregated into 2 summary measures. The Physical Component Summary Score (PCS) consists of Physical Functioning, Role Physical, Bodily Pain and General Health dimensions, and the Mental Component Summary Score (MCS) consists of Mental Health, Vitality, Social Functioning and Role-Emotional dimensions.

Statistics

Data is presented as means with standard deviation (SD) and as counts with percentages. Statistical comparisons between the population and the patients were made using t test for continuous variables and Pearson's Chi-Square (χ^2) for categorical variables. Repeated measures in changes in the physical and mental (MCS) component summary scores between groups were analyzed using mixed-effects models, with an unstructured covariance structure (Kenward-Roger method to calculate the degrees of freedom). As the use of mixed models allows for analysis of unbalanced datasets without imputation, we analyzed all available data, using the full analysis set. Cumulative mortality was estimated using Kaplan–Meier survival analysis and compared between groups with the log-rank test. We used Cox proportional hazards model to calculate the adjusted hazard ratios (HR) and 95% confidence intervals for death. The normality of variables was evaluated graphically and using the Shapiro–Wilk W test. Stata 15.1, StataCorp LP (College Station, TX, USA) statistical package was used for the analyses.

Results

The patient demographic and clinical characteristics are shown in Table 1. In a total of 523 patients (68% females), the mean age at surgery was 61 years (SD 12). In the general population (n = 682) (67% females) the mean age was 64 years (SD 12). The Body Mass Index (BMI) was statistically higher among the patients than in the general population, although both groups were by mean classified over-weighted according to the WHO classification (World Health Organization).[14] Cardiac and rheumatoid co-morbidities were overrepresented among the patients, whereas psychiatric disorders, other musculoskeletal disorders and cancer were more frequent in the population. 23% of the control population reported to have spinal problems.

Table 1. Baseline Demographic and Clinical Characteristics of the Patients and the Population.

	Population, n = 682	Patients, n = 523	*P* value
Women, n (%)	454 (67)	357 (68)	0.53
Age, mean y (SD)	64 (12)	61 (12)	<0.001
BMI, mean (SD)	26.9 (4.4)	28.6 (4.6)	<0.001
Co-morbidities, n (%)			
Cardiological	278 (41)	263 (50)	<0.001
Respiratory	66 (10)	49 (9)	0.86
Neurological	36 (5)	20 (4)	0.23
Rheumatoid	32 (5)	49 (9)	<0.001
Diabetes	87 (13)	57 (11)	0.32
Psychiatric	25 (4)	9 (2)	0.043
Musculosceletal	55 (8)	20 (4)	0.003
Cancer	14 (2)	3 (1)	0.031
Smoking, n (%)	88 (13)	82 (16)	0.20
Education, mean y (SD)	11.6 (4.0)	11.5 (2.7)	0.56

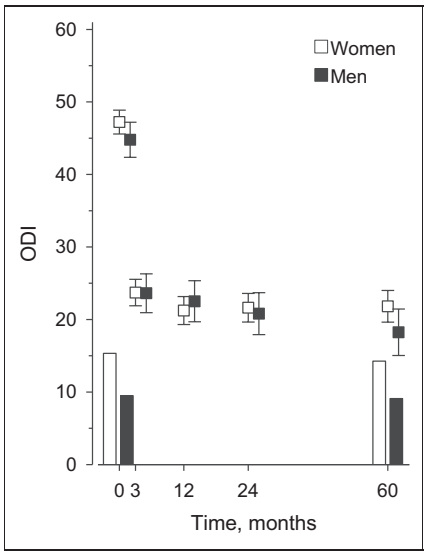

Figure 1. The mean (95% CI) Oswestry Disability Index (ODI) in the patients and the population (blocks and bars), divided to females and males (white and black). Groups adjusted by age, sex and education years.

The preoperative ODI in the patients was 46 (SD 16). A significant improvement was seen at 3 months, and the ODI change remained −26 (95% CI: −24 to −28), $p < 0.001$ at 5 years. In the population, the baseline ODI was 13 (SD 16) remaining stable at 5 years, [−1 (95% CI: 0 to −2)]. Throughout the 5-year follow-up period, the ODI was significantly poorer in the patients than in the population, $p < 0.001$. Figure 1 shows the ODI in the patients and the population divided by sex.

In HRQoL, the preoperative PCS in the patients was 27 (SD 7). The change was 8 (95% CI: 7 to 9), $p < 0.001$ at 5 years. The baseline PCS in the population was 45 (SD 11) and remained unchanged [0 (95% CI: −1 to 1)]. The patients did not reach the population in the 5-year follow-up. Figure 2A shows PCS in the patients and the population divided by sex.

The preoperative MCS in the patients was 47 (SD 13), and the change was 4 (95% CI: 3 to 7), $p < 0.001$ at 5 years. In the population, the baseline MCS was 53 (SD 11), and it remained unchanged [0, (95% CI: −1 to 1)]. While the baseline MCS was significantly lower in the patients than in the population, the statistical difference disappeared at 3 months. Females preserved this benefit at 5 years, while MCS in males deteriorated slightly. Figure 2B shows MCS in the patients and the population divided by sex.

When analyzing the short and the long fusion subgroups separately, ODI was higher and PCS lower before and 5 years after surgery, but the changes were comparable (Figure 3). MCS did not differ at any timepoint between the short and the long fusion subgroups. Neither of the subgroups reached the population at any timepoint.

The 5-year mortality of the patients was 3.4% (95% CI: 2.2 to 5.4). It did not statistically differ from the mortality of 4.8% (95% CI: 3.5 to 6.7) in the population. The age, sex and co-morbidity adjusted HR was 0.86 (95% CI: 0.48 to 1.53). Three most common causes of death in the patients were cardiogenic (63%), cancer (21%) and external causes (11%), and in the population, they were cardiogenic (45%), cancer (24%) and respiratory causes (12%).

Discussion

The present study shows the 5-year outcome of LSF in function, HRQoL and mortality in a consecutive patient series. The overall trend was that the considerable benefits of surgery were mostly preserved still at 5 years. According to the ODI or the physical component of HRQoL, the patients, however, did not reach their general population controls matched by age, sex and residential area.

The preoperative ODI of 46 points indicates severe disability.[12] The clinically significant improvement of 26 points in the ODI was seen at 5-year follow-up. The minimum clinically important difference (MCID) in the ODI is reported to be 12.8 points.[15] The literature presents preoperative ODI variation from 40 to 63, and postoperative changes from −12 to −44.[3,16-18] Endler et al. found the postoperative ODI to remain stable in a long follow-up (mean 6.9 years) of fused isthmic spondylolisthesis patients.[3] Also in the RCT of Ekman et al. concerning isthmic spondylolisthesis patients, the ODI did not significantly change between 2 and 5 years after surgery.[19] Zigler et al. observed 64.8% of fused DDD patients to have at least 15% improvement in the ODI at 2 years.[16] 83.3% of those patients retained the benefit still at 5 years. Hoy et al. found no deterioration in ODI from 2 to 5-10 years postoperatively in patients fused due to heterogeneous indications.[18] Therefore, our results are comparable with the earlier studies, that indicate the improvement in functioning to persist even in a longer follow-up.

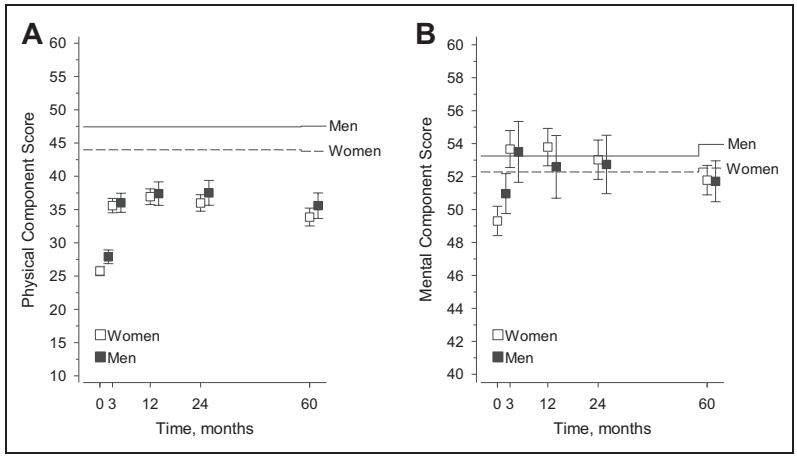

Figure 2. A and B, The mean (95% CI) physical and mental component summary scores of SF-36 (HRQoL) in the patients (blocks and bars) and the population (lines), divided to females and males (white/dashed and black). Groups adjusted by age, sex and education years.

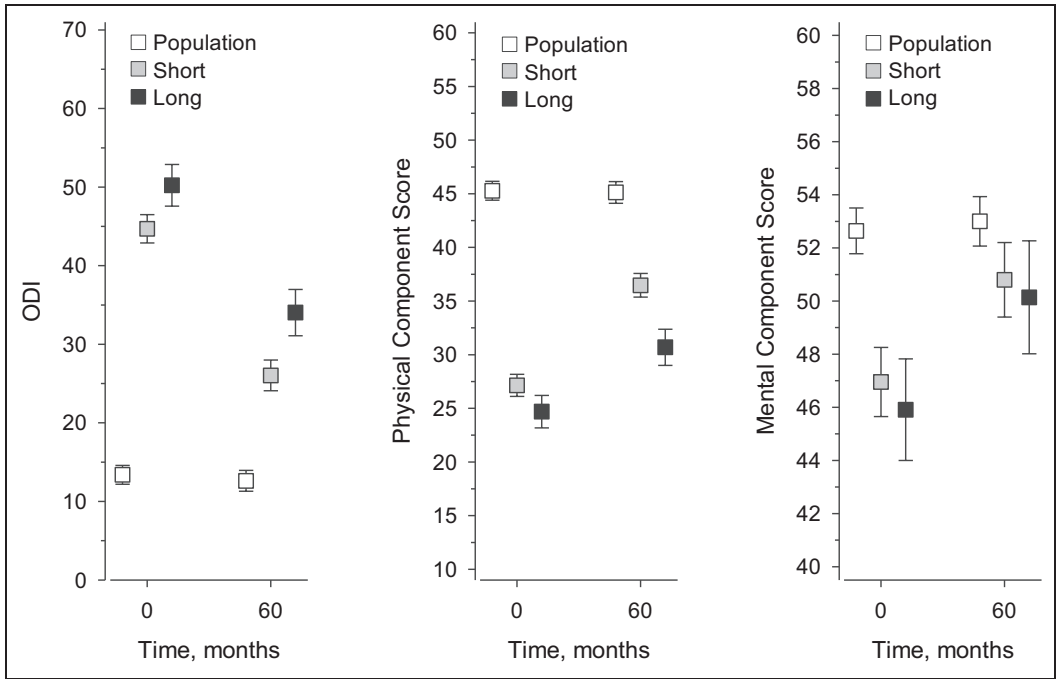

Figure 3. The mean (95% CI) Oswestry Disability Index (ODI), the physical and mental component summary scores of SF-36 (HRQoL) in the patients divided by fusion length (gray = short fusion = 1 to 2 levels, black = long fusion = more than 2 levels; white = population). Groups adjusted by age, sex and education years.

The improvement in the physical aspect of HRQoL was clear from the early recovery phase and remained quite stable. The PCS change of 8 (95% CI: 7 to 9) points at 5 years exceeds 4.9, which is reported to be the minimum clinically important difference (MCID) for PCS.[15] Rampersaud et al. show PCS change of 10.4 points at 2 years after LSF in degenerative spondylolisthesis patients.[20] In the register-based LSF study of Endler et al., there was no deterioration in PCS between 2

and 5 years after surgery.[3] The PCS changes compares with the ODI changes, which supports the assumption that they partly describe the same aspects of functioning.

The MCS change also was statistically significant during the whole follow-up period. The change was 4 (98% CI: 3-5) points at 5 years. Clinical relevance of this is, nevertheless, difficult to determine, since the MCID for MCS in a lumbar spine surgery specific context has not been published. In the SF-36 instrument, a low PCS score tend to raise the MCS score, which may lead to underestimation of the mental component change in conditions with remarkable physical disability.[21] There was a difference between the sexes: only females reached their general population controls at 5 years in MCS.

When dividing the patients to short and long fusion subgroups, a comparable improvement was seen in all variables between the subgroups. Disability was higher in the long fusion subgroup before and after surgery. Even the short fusion subgroup did not reach the population in functioning.

To our best knowledge, there are not many studies comparing the LSF outcome with a matched population. This makes the present study novel. In the field of orthopaedics, the efficacy of big joint arthroplasties is well documented due to comprehensive arthroplasty registries and rich literature.[22] The outcome of arthroplasty surgery can be used as a benchmark in the assessment of LSF benefits.

Mokhtar et al. compared LSF patients and total hip and total knee arthroplasty (THA and TKA) patients with an age matched general population.[23] The spinal patients had a single level degenerative spondylolisthesis, and they were treated with decompression and a single level fusion. They found the HRQoL of LSF patients to approach the population in a 2-year follow-up. Improvement in PCS (of SF-12) was 11 points in the LSF and THA cohorts, while it was 8 points in the TKA cohort. The MCS improvement in the LSF cohort was 4 points, and the postoperative MCS scores were congruent between the cohorts and the population. Our patients, however, did not reach the population in PCS at any time-point. The key explanation for this discrepancy is probably the difference in indications for surgery. We included all elective surgeries, also multilevel pathologies and postoperative conditions in contrast to a single diagnostic entity. Revisions were not analyzed separately here. Rampersaud et al. have also compared spinal stenosis surgery (decompression with or without fusion) with THA and TKA surgery between matched patient cohorts.[24] They found similar cost-utility ratios in a combined spine surgery cohort (decompression only and fusion) as THA and TKA cohorts. The 5-year health utility was nevertheless lower after spinal stenosis surgery than after arthroplasties. Mannion et al. compared different types of degenerative lumbar spine surgeries with THA and TKA.[25] They found joint replacements more successful at 12 months than spine surgery, even though the baseline level was better among THA patients. Considering these, LSF surgery in general does not seem to produce the same level of functional benefit as arthroplasties.

Our patient cohort was quite comparable with the population cohort in most of the comorbidities (Table 1). The differences in psychiatric or musculo-skeletal comorbidities or cancer prevalence are most probably caused by patient selection in the surgical decision making. The self-reported prevalence of spinal problems (23%) in the control population is congruent with previous epidemiological studies.[26] Rheumatoid diseases were overrepresented in the patient group (9% to 4%). It is possible that rheumatoid diseases are related to an increased need for spinal surgery.[27] Cardiac conditions were also more prevalent among the patients than in the general population (50% to 41%). However, this study shows the mortality of the patients to be at the same level with the mortality of the population. Despite the chronic nature of the spinal disease, it did not increase mortality—even despite of higher cardiac co-morbidity prevalence. Of course, bias probably exists here: the patients with better condition more often end up in LSF. To our knowledge, no study with this long follow-up has compared the mortality of LSF patients with a matched population. Lurie et al. reported the 8-year mortality in an RCT comparing operative and conservative treatment in lumbar spinal stenosis.[28] The mortality of the operative group (8%) was lower than would have been expected on the basis of the age- and sex-specific mortality rate (13%). Perhaps here also existed positive selection bias with the patients ending up in RCT as surgical candidates. In the review article of Yavin et al., mortality was not associated with any treatment modality in 20 studies concerning degenerative lumbar spine.[2]

Studies with long-term follow-ups are necessary to assess the possible benefits of LSF. Need for these operations is increasing with the aging population. It is estimated that one fifth of people over 65 years suffers from lumbar spinal claudication, and half of those have serious daily limitations and disability.[2,29]

Conclusion

LSF surgery benefits a heterogeneous group of patients in disability and HRQoL. The positive change is mostly sustained in a 5-year follow-up. Despite the improvement, the patients did not reach the physical level of the population. The mortality of the patients is at the same level as in the population.

Authors' Note

Leevi Toivonen and Liisa Pekkanen contributed equally to the writing of the manuscript. This study was approved by ethics committees of Tampere University Hospital and Central Finland Health Care District. Informed consent was obtained from all individual participants included in the study.

Declaration of Conflicting Interests

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PUBLICATION II

Influence of Depressive Symptoms on the Outcome of Lumbar Spine Fusion-A 5-year Follow-up Study

Toivonen L, Häkkinen A, Pekkanen L, Salonen A, Kautiainen H, Neva MH.

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PUBLICATION III

Isthmic Spondylolisthesis is Associated with Less Revisions for Adjacent Segment Disease After Lumbar Spine Fusion Than Degenerative Spinal Conditions: A 10-Year Follow-Up Study

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Isthmic Spondylolisthesis is Associated with Less Revisions for Adjacent Segment Disease After Lumbar Spine Fusion Than Degenerative Spinal Conditions

A 10-Year Follow-Up Study

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Study Design. Prospective, follow-up study.

Objective. We aim to compare the rate of revisions for ASD after LSF surgery between patients with IS and DLSD.

Summary of Background Data. ASD is a major reason for late reoperations after LSF surgery. Several risk factors are linked to the progression of ASD, but the understanding of the underlying mechanisms is imperfect. If IS infrequently becomes complicated with ASD, it would emphasize the role of the ongoing degenerative process in spine in the development of ASD.

Methods. 365 consecutive patients that underwent elective LSF surgery were followed up for an average of 9.7 years. Surgical indications were classified into 1) IS (n = 64), 2) DLSD (spinal stenosis with or without spondylolisthesis) (n = 222), and 3) other reasons (deformities, postoperative conditions after decompression surgery, posttraumatic conditions) (n = 79). All spinal reoperations were collected from hospital records. Rates of revisions for ASD were determined using Kaplan–Meier methods.

Results. Altogether, 65 (17.8%) patients were reoperated for ASD. The incidences of revisions for ASD in subgroups were 1) 4.8% (95% CI: 1.6%–22.1%); 2) 20.5% (95% CI: 15.6%–26.7%); 3) 20.6% (95% CI: 12.9%–31.9%). After adjusting the groups by age, sex, fusion length, and the level of the caudal end of fusion, when comparing with IS group, the other groups had significantly higher hazard ratios (HR) for the revision for ASD [2) HR (95% CI) 3.92 (1.10–13.96), $P = 0.035$], [3) HR (95% CI) of 4.27 (1.11–15.54), $P = 0.036$].

Conclusion. Among patients with IS, the incidence of revisions for ASD was less than a 4th of that with DLSD. Efforts to prevent the acceleration of the degenerative process at the adjacent level of fusion are most important with DLSD.

Key words: adjacent segment disease, adjacent segment pathology, degenerative lumbar spine disorders, degenerative spinal disorders, degenerative spondylolisthesis, isthmic spondylolisthesis, lumbar spine fusion, revisions, spinal stenosis.
Level of Evidence: 3
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Lumbar spine fusion (LSF) surgery has been shown to decrease disability and improve health-related quality of life in several spinal disorders.[1–3] Degenerative lumbar spine disorders (DLSD) are by far the most common reason for LSF surgery.[4,5] Isthmic spondylolisthesis (IS), which is caused by congenital defect or a stress fracture in pars interarticularis, is the most frequent nondegenerative indication covering up to 20% of LSF surgery.[5,6] The reports of promising results of LSF surgery have led to remarkable increase in it during the last decades.[7] However, LSF surgery is associated with a significant risk for repeat surgeries, which are undesirable consequences of surgery causing distress to patients and economic burden to patients, employers, and societies.[8]

Adjacent segment pathology is a degenerative condition that develops to the disc level adjacent of fusion.[9]

Approximately 25% to 30% of radiological adjacent segment degenerations are assumed to proceed to a symptomatic adjacent segment disease (ASD), where symptoms are generated by neural compression or instability.[10] Terminology concerning the condition, however, is not consistent in the literature. In the present study, we use the term 'ASD' to refer to a symptomatic deterioration of adjacent segment.

ASD is a major cause of late reoperations after LSF.[11] Meta-analysis by Xia et al[12] calculated a pooled prevalence of 26.6% for radiological adjacent segment degeneration after LSF. Already at a 4-year follow-up, the cumulative risk for reoperation for ASD has been reported to be as high as 8.7%.[13]

Several potential risk factors are linked to the progression of ASD: age, genetic factors, pre-existing adjacent segment degeneration or stenosis, laminectomy at adjacent level of fusion, osteoporosis, poor sagittal balance.[10,11] The role of different surgical indications behind the development of ASD, nevertheless, has not been thoroughly investigated. IS, in a fundamental way, differs from DLSD. There is little evidence that it might infrequently become complicated with ASD.[14,15] However, this is a question of utmost importance, since if ASD develops as a consequence of the ongoing degenerative process in spine, the impact of different surgical methods in the prevention of ASD, including minimally invasive techniques, remains unanswered. The role of different surgical techniques here, naturally, warrants a proper randomized setting to be resolved.

The aim of the present study was to determine the incidence of reoperations for ASD in a prospective, 10-year follow-up and compare them between IS and DLSD. We hypothesized revisions for ASD to be significantly less frequent among patients with IS. As degenerative spinal disorders are a heterogeneous entity, we formed 2 groups: clear DLSD (spinal stenosis with or without spondylolisthesis) and ''other indications'' to help draw conclusions.

MATERIALS AND METHODS

Patients

Between 2008 and 2012, all elective LSF patients (N = 433) in Tampere University Hospital were invited to participate in a prospective follow-up study. As Finland has a national health insurance system, all LSF surgeries and reoperations within a certain population are performed at a certain hospital. At the baseline, demographic data were recorded by the study personnel and the patient. Surgeons filled in diagnoses and surgical details. The patients filled in Oswestry Disability Index, Depression scale, and a visual analogue scale for back and leg pain at the baseline.

In the present analysis, exclusion criteria were 1) a fusion reaching thoracic spine, 2) former fusion performed prior to data collection period, 3) tumor or 4) an acute fracture. Late conditions after a fracture or previous decompression surgery were included. All primary surgeries were open, instrumented posterolateral fusions performed form midline incision combined with necessary decompression. Interbody fusion (transforaminal lumbar interbody fusion [TLIF]/posterior lumbar interbody fusion [PLIF]) was used by surgeon's consideration. Surgical indications were grouped into 1) IS, 2) DLSD (spinal stenosis with or without degenerative spondylolisthesis) and 3) other reasons (deformities, postoperative conditions after decompression, posttraumatic conditions).

The follow-up continued to June of 2020. All spinal reoperations during the follow-up were collected from the patient records. Indications for index surgeries and reoperations were confirmed from the patient records, radiographs and magnetic resonance images. The residential status of the patients was checked after the follow-up to clarify the number of possible dropouts.

Statistics

The descriptive statistics are presented as means with standard deviation, as medians with interquartile range or counts with percentages. Statistical comparisons between groups were done using analysis of variance, and chi-square test. In the case of violation of the assumptions (*eg*, non-normality) for continuous variables, a bootstrap-type method or Monte Carlo *P*-values (small number of observations) for categorical variables were used. Crude cumulative rate of revisions for ASD were estimated using Kaplan–Meier method and compared between groups with the log-rank test. Adjusted (age, sex, fusion length, and the level of caudal end of fusion) Kaplan–Meier cumulative rate were estimated using 2 propensity score-based techniques, stratification and weighting (marginal mean weighting through stratification).[16] Marginal mean weighting through stratification is an extension of propensity score matching that combines propensity score stratification and inverse probability of treatment weighting. Log-rank test with exact *P*-values will be identified cumulative proportion statistical difference. Cox regression model could not be used because proportional-hazards assumption was violated. The normality of variables was evaluated graphically and using the Shapiro–Wilk test. All analyses were performed using STATA software, version 16.1 (StataCorp LP, College Station, TX).

RESULTS

A total of 365 (84%) patients met the inclusion criteria. Diagnostic groups included 1) IS (n = 64), 2) DLSD [n = 222; spinal stenosis with (80%) or without (20%) degenerative spondylolisthesis] and 3) other reasons [n = 79; including deformities (33%), postoperative conditions after decompression (56%), posttraumatic conditions (10%)]. Patients with IS were significantly younger, more were men, more educated, and they undergone shorter fusions which more often reached sacrum when comparing with other patients, as seen in Table 1. Demographically, the DLSD group resembled the 3rd group.

TABLE 1. Demographic Data, Self-reported (*) Prevalence of Symptoms and Comorbidities and Questionnaires at the Baseline, and Type of Primary Surgery Divided by Surgical Indication (DLSD Includes Spinal Stenosis With or Without Degenerative Spondylolisthesis; "Other Reasons" Include Deformities, Postoperative Conditions After Decompression and Posttraumatic Conditions)

	IS, N = 64	DLSD, N = 222	Others, N = 79	*P*-value
Women, n (%)	28 (44)	169 (76)	44 (56)	<0.001
Age, mean (SD)	48 (12)	65 (10)	64 (12)	<0.001
BMI, mean (SD)	27.8 (4.3)	28.4 (4.5)	28.3 (4.1)	0.49
Smoking*, n (%)	7 (11)	12 (6)	8 (10)	0.21
Education years*, mean (SD)	13.1 (3.9)	11.2 (3.9)	11.0 (3.8)	0.002
Physical activity*, h/wk, median (IQR)	6.0 (3.0, 10.0)	4.5 (2.0, 9.0)	4.6 (2.0, 10.0)	0.099
Duration of spinal problem*, yr, median (IQR)	10.0 (5.0, 25.0)	9.5 (4.0, 20.0)	15.0 (5.0, 25.0)	0.097
Back pain*, VAS, mean (SD)	60 (25)	62 (26)	72 (22)	0.005
Leg pain*, VAS, mean (SD)	56 (26)	67 (23)	70 (24)	0.001
ODI*, mean (SD)	42 (15)	46 (15)	51 (18)	<0.001
DEPS*, mean (SD)	9.2 (6.7)	10.5 (6.0)	10.9 (6.9)	0.12
Co-morbidities*, n (%)				
Cardiovascular diseases	22 (36)	119 (58)	43 (63)	0.003
Diabetes	5 (8)	24 (12)	12 (18)	0.25
Mental disorders	2 (3)	5 (2)	0 (0)	0.36
Lung diseases	6 (10)	12 (6)	3 (4)	0.41
Neurological disorders	2 (3)	5 (2)	0 (0)	0.36
Rheumatic diseases	0 (0)	1 4 (7)	7 (10)	0.029
Fusion, n (%)				
Lower end vertebra				<0.001
-L3	0 (0)	1 (0)	2 (3)	
-L4	1 (2)	9 (4)	3 (4)	
-L5/6	10 (16)	117 (53)	27 (34)	
-S1	53 (83)	95 (43)	47 (59)	
Length, levels, n (%)				<0.001
1	36 (56)	61 (27)	8 (10)	
2	21 (33)	89 (40)	22 (28)	
3	7 (11)	54 (24)	30 (38)	
4	0 (0)	17 (8)	11 (14)	
5	0 (0)	1 (0)	8 (10)	
Interbody cage (TLIF/PLIF), n (%)	35 (55)	24 (11)	7 (9)	<0.001

DEPS indicates Depression scale; DLSD, degenerative lumbar spine disease; IQR, interquartile range; IS, isthmic spondylolisthesis; ODI, Oswestry Disability Index; PLIF, posterior lumbar interbody fusion; SD, standard deviation; TLIF, transforaminal lumbar interbody fusion; VAS, visual analogue scale.

**Self-reported.*

In the whole study population, a total of 3112 person–years were followed up, of which 608 (median 9.7) years in the IS group, 1852 (median 9.4) years in the DLSD group, and 653 (median 9.4) years in the 3rd group. The rate of revisions for ASD in the follow-up is presented in Table 2. Altogether, 95% of the patients that were reoperated for ASD underwent elongation of the fusion, while 5% of them underwent only decompression. None of the merely decompressed patients ended up to additional surgery during the follow-up.

As the DLSD group consists of patients with spinal stenosis with or without degenerative spondylolisthesis, we calculated the revision rates between these subgroups, but they did not significantly differ [17.9 (95% CI: 12.8–24.6) without spondylolisthesis, 30.4 (95% CI: 18.8–46.8) with spondylolisthesis, $P = 0.058$].

In the follow-up, 11% of the patients underwent some other spinal reoperation even though they were not reoperated for ASD. Most common reasons for these other reoperations were instrumentation failure or pseudoarthrosis (53%), and hematoma or infection (25%).

Out of the patients that did not undergo revision for ASD, 4 (6.3%) of patients with IS, 16 (7.2%) of patients with DLSD, and 5 (6.3%) of the other patients had moved away during the follow-up. All of them, nevertheless, underwent at least a 1-year follow-up visit at our unit.

To eliminate the bias from differences in demographic or surgical details, the groups were adjusted by age, sex, fusion

TABLE 2. The Crude Rate of Revisions for ASD During the Whole Follow-up Period in all Patients and Subgroups by Surgical Indication (DLSD Includes Spinal Stenosis With or Without Degenerative Spondylolisthesis; "Other Reasons" Include Deformities, Postoperative Conditions After Decompression and Posttraumatic Conditions)

Indication for surgery	Rate of revision for ASD (%)	95% CI (%)
All patients	17.8	14.0 to 22.1
• IS	4.8	1.6 to 22.1
• DLSD	20.5	15.6 to 26.7
• others	20.6	12.9 to 31.9
$P = 0.023$ (Log-rank test)		

ASD indicates adjacent segment disease; CI, confidence interval; DLSD, degenerative lumbar spine disease; IS, isthmic spondylolisthesis.

length, and caudal end of fusion. After that, the cumulative rate of revisions for ASD is presented in Figure 1. After the same adjustments, when comparing with IS group, the DLSD had a hazard ratio (95% CI) of 3.92 (1.10–13.96), $P = 0.035$ for ASD revision, and the 3rd group had that of 4.27 (1.11–15.54), $P = 0.036$, correspondingly. Further, these results were not changed by increasing the use of interbody cage to the multivariate model.

DISCUSSION

In a 10-year follow-up, the incidence of revisions for ASD was 18% among all LSF patients. The incidence was 4.8% in patients with IS – less than a 4th of that (21%) in patients with DLSD or other indications.

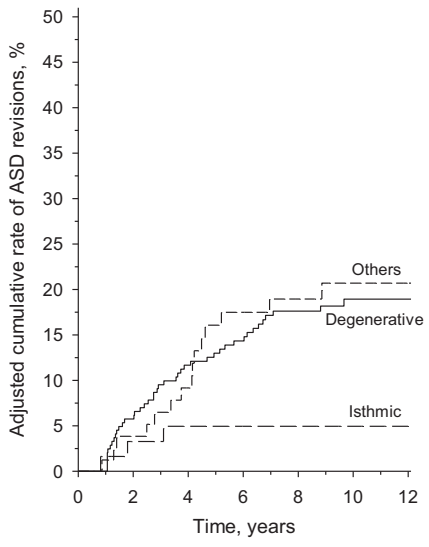

Figure 1. The cumulative rate of revisions for adjacent segment disease (ASD) between groups of surgical indications adjusted by age, sex, fusion length and caudal end of fusion ("Isthmic" = isthmic spondylolisthesis (IS); "Degenerative" (DLSD) includes spinal stenosis with or without degenerative spondylolisthesis; "Others" include deformities, postoperative conditions after decompression and posttraumatic conditions).

As expected, patients with IS remarkably differed from all other patients. They were younger, more educated, had lesser cardio-vascular comorbidities and their disability and intensity of pain prior to index surgery was lower. The DLSD group, on the other hand, demographically resembled the 3rd group which included patients with deformity, and postoperative and posttraumatic conditions. In addition, the incidences of revisions for ASD were similar between these 2 groups. In fact, the 3rd group mainly can be considered degenerative, as well, since the primary disorder in almost 90% of them was also degenerative. However, the diagnoses in the 3rd group (deformities, postoperative and posttraumatic conditions) represent special cases requiring more individual consideration. Therefore, we excluded them from the main comparison between IS and DLSD. The duration of the spinal problem prior to the index surgery was considerably long, with median of 10 to 15 years, in all 3 groups.

IS is caused by a defect in pars interarticularis acquired during the first 2 decades of life.[6] It can usually be considered a problem of only 1 spinal segment. Contrary to that, DLSD generally develops later, and the degeneration usually exists in multiple levels even in cases, where the target of surgery is at 1 or 2 levels. In the present study, as well, patients DLSD underwent longer fusions than patients with IS (Table 1).

Knowledge of the incidence of ASD is weak due to variation between the definitions of ASD and duration of follow-ups. Meta-analysis by Xia et al[12] reported an occurrence of 5% to 77% for radiological adjacent segment degeneration and 0% to 27% for ASD after LSF. Lad et al[17] reported an overall 5-year reoperation rate of 17.4% after LSF performed for spinal stenosis. In a 10-year follow-up, Gillet[18] reported an incidence of 20% for revisions for ASD after LSF with degenerative conditions. The corresponding incidence of 21% in the present study confirms the overall incidence of 20% for revisions for ASD after LSF with DLSD.

The previous reports suggest low incidence of ASD specifically with IS. In a retrospective, 15-year follow-up of

young IS patients by Seitsalo et al,[19] 17% to 31% of patients developed radiological adjacent segment degeneration after LSF. The condition of the disc above the olisthetic segment, nevertheless, did not differ between patients treated operatively or conservatively for the same condition. However, Ekman et al[20] demonstrated at least mild degenerative adjacent segment changes in 48% of patients with IS after laminectomy and fusion in a 12.6-year follow-up. The clinical importance of these, nevertheless, was marginal. In a 5.9-year follow-up of patients with low-grade IS, Bae et al[14] found that only 1.9% of patients developed symptomatic ASD after mini-anterior lumbar interbody fusion or mini-TLIF surgery. In an average of 11-year follow-up after combined anterior lumbar interbody fusion and percutaneous transpedicular fixation for low-grade IS by Choi et al,[15] 38.8% of the patients developed radiological adjacent segment degeneration, and 12.2% of the patients developed symptomatic ASD, but only 4.1% of the patients underwent revision surgery. Sakaura et al[21] reported a rate of 10% for symptomatic ASD after single level PLIF surgery for low-grade IS in a 5.6-year follow-up. Like Sakaura et al, we also performed surgeries through open, midline incision. Nevertheless, our revision rate of 4.8% in a 9.7-year follow-up with IS was congruent with that of Choi et al[15] who combined anterior and mini-posterior approach. This finding does not support the idea that surgical approach plays a crucial role in the progression of ASD. In general, ASD seems infrequent with IS.

There exist no general criteria when to perform a revision for ASD. The surgeon always makes a subjective decision with the patient concerning the revision surgery. Occasionally, even symptomatic patients are ruled to conservative treatment, when surgical risks are considered too high. This makes comparison of revision rates between studies challenging. This study showed that patients with IS are younger and have less cardio-vascular comorbidities than patients with DLSD. Taking this into account, patients with IS are probably more likely to end up in revision for ASD.

In this study, only 3 (4.7%) patients with IS ended up in a revision for ASD – and all of them in the first 3 years. We retrospectively analyzed these cases. First of these patients underwent extirpation of a disc prolapse from the adjacent level at the index LSF operation and later developed instability requiring additional stabilization. The second one had degeneration in the adjacent level facets already at the index surgery, and that turned into radiological and symptomatic instability afterwards. The third one underwent a 2-level fusion and later acquired symptomatic stenosis to the adjacent level that primarily had only mild disc degeneration.

In a 10-year follow-up by Okuda et al,[22] most revisions for ASD were performed over 5 years after LSF. They associated high pelvic incidence with early revisions for ASD. We assume that a considerable portion of early revisions might be linked to technical issues and might be avoided by better implementation of surgery. In the present study, in retrospect, we think that at least the first of the 3 revisions for ASD among patients with IS potentially could have been avoided. However, the revisions for ASD in patients with DLSD quite linearly cumulated by time. This emphasizes the role of the ongoing degenerative process in spine in the progression of ASD. Of course, this process is multifactorial. The present study cannot answer to what extent other surgery-related factors, such as postoperative balance, contribute to this process.

The main strength of this study is the planned, prospective setting with a heterogeneous study population representing the spectrum of elective patients ending up in LSF surgery. All groups underwent the same, posterior surgical procedure by the same surgeons. As our clinic is the only unit performing LSF surgery in a certain geographical catchment area, our study setting to some extent resembles a population-based setting making our findings widely generalizable.

The patients that had left our region during the follow-up, potentially bias our findings. However, the number of dropouts was low, and the rate was similar between the groups, (IS: 6.3%, DLSD: 7.2%, and others: 6.3%), so we consider this bias nonsignificant.

The demographic and surgical differences between the groups can be seen as another limitation in this setting, although they are consequences of the underlying pathology leading to LSF. Nevertheless, we used adjustments by age, sex, fusion length, and caudal end of fusion to eliminate this bias. The use of interbody cage was considerably different between the groups. Here, the surgical approach was the same, and at the time of data collection, the main indication for the use of interbody cage (TLIF or PLIF) was foraminal decompression and strengthening the fusion to prevent early instrumentation failures. The use of TLIF cage to correct the sagittal alignment has increased afterwards. However, including the use of interbody cage to the analysis did not change the results.

CONCLUSION

A 10-year incidence of revisions for ASD after LSF was 18%. With IS the revisions for ASD were infrequent – the incidence was less than a 4th of that with DLSD. Efforts to prevent an acceleration of the degenerative process at the adjacent level of fusion are most important with DLSD.

➢ Key Points

- ❑ This prospective study assessed the 10-year incidence of revisions for ASD after LSF.
- ❑ ASD was infrequent among patients with IS.
- ❑ The rate of revisions for ASD among patients with degenerative spinal disorders was over 4-fold to that of patients with IS.

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PUBLICATION IV

Postoperative sagittal balance has only a limited role in the development of adjacent segment disease after lumbar spine fusion for degenerative lumbar spine disorders: A sub-analysis of the 10-year follow-up study

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Postoperative Sagittal Balance Has Only a Limited Role in the Development of Adjacent Segment Disease After Lumbar Spine Fusion for Degenerative Lumbar Spine Disorders: A Subanalysis of the 10-year Follow-up Study

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Study Design. Retrospective additional analysis of a prospective follow-up study.

Objectives. We aimed to find out whether poor postoperative sagittal alignment increases revisions for adjacent segment disease (ASD) after lumbar spine fusion (LSF) performed for degenerative lumbar spine disease.

Summary of Background Data. Revisions for ASD accumulate over time after LSF for degenerative lumbar spine disease. The etiology of ASD is considered multifactorial. Yet, the role of postoperative sagittal balance in this process remains controversial.

Materials and Methods. A total of 215 consecutive patients who had undergone an elective LSF surgery for spinal stenosis with (80%) or without (20%) spondylolisthesis were analyzed. Spinal reoperations were collected from the hospital records. Preoperative and postoperative sagittal alignment were evaluated from standing radiographs. The risk of revisions for ASD was evaluated by Cox proportional hazards regression models.

Results. We did not find the poor postoperative balance [pelvic incidence−lumbar lordosis (LL) > 9°] to significantly increase the risk of revisions for ASD. crude hazard ratio (HR) = 1.5 [95% confidence interval (CI): 0.8–2.7], adjusted (by age, sex, pelvic incidence, fusion length, and the level of the caudal end of fusion): HR = 1.7 (95% CI: 0.9–3.3). We found higher LL outside the fusion segment (LL−segmental lordosis) to decrease the risk of revisions for ASD: HR = 0.9 (95% CI: 0.9–1.0).

Conclusion. Poor sagittal balance has only a limited role as a risk factor for the revisions for ASD among patients with degenerative spinal disease. However, the risk for ASD might be the greatest among patients with reduced spinal mobility.

Key words: lumbar spine fusion, degenerative spinal disease, sagittal balance, revisions, adjacent segment disease, adjacent segment pathology

Level of Evidence: 3

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Lumbar spine fusion (LSF) surgery is a common procedure in the treatment of several spinal pathologies. Degenerative lumbar spine disorders (DLSDs) are the most common reason for LSF, while isthmic spondylolisthesis (IS) covers up to 20% of the cases.[1,2] LSF surgeries occasionally become complicated by the need for repeat surgeries.[3,4] Adjacent segment disease (ASD) is a major reason for late reoperations after LSF.[5] By definition, ASD is a degenerative condition that postoperatively develops to the disk level next to the fusion segment and causes symptoms via instability or neural compression.[6] ASD is the most frequent among the patients with DLSD where reoperations accumulate by time, on contrast to the patients with IS, who infrequently acquire this complication.[4,7,8]

Etiology of ASD is thought to be multifactorial. Yet, the detailed pathogenesis remains not thoroughly clarified. On the one hand, LSF surgery may contribute to the pathogenesis by altering the adjacent level biomechanics. On the other hand, the ongoing degenerative process outside the fusion itself seems to have a significant role, as well.[9] Several potential risk factors are linked to the progression of ASD, but their significance varies in the literature.[5,10] Sagittal alignment after LSF is generally considered relevant here, so that failure to restore normal lordosis or loss of lordosis in LSF increases the risk of ASD.[5,11] If the postoperative balance can be linked to the occurrence of ASD, this would also support the role of surgery in the pathogenesis of ASD.

In a 10-year prospective follow-up study of elective LSF surgeries performed in a single university center, we found revisions for ASD to accumulate over time among patients with DLSD while they were sporadic with IS. Here, we performed additional analysis among the DLSD patients to find out whether poor postoperative sagittal alignment increases the revisions for ASD in a 10-year follow-up after LSF.

MATERIALS AND METHODS

Patients

Between 2008 and 2012, all elective LSF patients in Tampere University Hospital were recruited into a prospective follow-up study. In Finland, a single public unit performs LSF surgeries and reoperations for a certain population. Hence, the study population represents a certain geographical catchment area. At the baseline, surgeons and study personnel filled in the demographic and surgical data, and the patients answered the following questionnaires: Oswestry Disability Index, Depression Scale, and a Visual Analog Scale for back and leg pain. All patients signed written consent, and the Tampere University Hospital Ethics Committee approved the study (R07108).

As ASD is mainly related to degenerative spinal disorders, we excluded patients with IS here. Our previous follow-up showed deformity patients to resemble DSLS patients demographically and in terms of revisions for ASD.[4] However, given their condition which potentially requires more extensive surgery and individual judgement, we excluded patients with deformity here to facilitate answering to the present question. Hence, our exclusion criteria were: (1) fusion reaching the thoracic spine, (2) former spine surgery, (3) IS, (4) deformity, (5) fracture, or (6) tumor. Our whole study population suffered from degenerative lumbar spine pathology with related neural compression, that is, spinal stenosis with (80%) or without (20%) spondylolisthesis. Fusion was implemented to address the spondylolisthesis or to facilitate foraminal decompression. All surgeries were instrumented posterolateral fusions from midline incision with or without interbody fusion (transforaminal lumbar interbody fusion/posterior lumbar interbody fusion) combined with necessary decompression.

We investigated all spinal reoperations from the patient records. Death or reoperation for ASD ended the follow-up of a single patient—otherwise, the follow-up continued to June of 2020.

Spinopelvic Parameters

Lumbar lordosis (LL), pelvic incidence (PI), sacral slope, pelvic tilt, and segmental lordosis (SL) of the fusion segment were determined from sagittal standing lumbar spine radiographs before and 3 months after surgery. The preoperative standing radiograph was missing from 7 patients —they were excluded from the analysis. Figure 1 shows the definitions of these parameters. PI is regarded a constant value determined by individual pelvic anatomy. We determined LL as an angle between the upper endplates of L1 and S1 vertebrae. Schwab *et al*[12] postulated a formula $LL = PI \pm 9°$ in the normal population. According to that, the patient can be considered hypolordotic in spine surgery settings with $PI–LL > 9°$. The optimal target lordosis in LSF, however, decreases with the patient's age.[13,14] A single threshold was chosen for statistical analysis. Further, analyses were performed separately to the patients under and over 65 years to avoid the potential effect of the difference between the age-appropriate threshold and the fixed cutoff of 9°. Sacral slope describes the pelvic alignment, and pelvic tilt indicates the amount of pelvic retroversion which is needed to maintain a standing posture. After LSF, LL–SL represents the mobile segment of the lumbar spine.

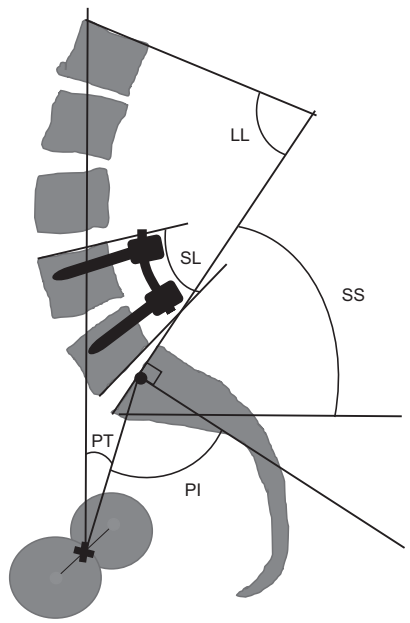

Figure 1. Lumbar spinopelvic parameters: lumbar lordosis (LL), pelvic incidence (PI), sacral slope (SS), pelvic tilt (PT), and segmental lordosis (SL) of the fusion segment. Values are presented in degrees. full color online

Statistics

The descriptive statistics are presented as means with SD, as medians with interquartile range or as counts with percentages. Cox proportional hazards regression models were used to estimate the adjusted hazard ratios (HRs) and their 95% confidence intervals (CIs). Age, sex, fusion length, and the level of the caudal end of fusion were used as covariates in these models. The possible nonlinear relationship between LL and SL and the risk of revision for ASD was modeled using restricted cubic splines with 4 knots at the fifth, 35th, 65th, and 95th percentiles. Spline functions were estimated using multivariable Cox proportional hazard regression models, including age, sex, fusion length, and the level of the caudal end of fusion as a covariate. All analyses were performed using STATA software, version 16.1 (StataCorp LP, College Station, TX).

RESULTS

A total of 215 patients (mean age: 66 yr, SD: 10 yr) met the inclusion criteria. Most of them were women (76%) who most commonly underwent two-segment fusion in the lower lumbar spine (Table 1).

During the follow-up with a median of 9.2 years, 43 (20%) patients underwent a revision for ASD.

The spinopelvic parameters of the patients were equal preoperatively and postoperatively (Table 2). By mean, the difference PI–LL ranged in normal lordosis before and after surgery. However, 83 (39%) patients were hypolordotic after surgery according to the mismatch of PI–LL $>9°$.

The postoperative imbalance (PI–LL $>9°$) did not result in a significantly increased risk of revision for ASD according to the Cox multivariate model. The crude HR of 1.5 (95% CI: 0.8–2.7) and adjusted (by age, sex, PI, fusion length, and the level of the caudal end of fusion) HR of 1.7 (95% CI: 0.9–3.3) remained statistically insignificant. HR was the same, insignificant, if patients under and over 65 years were analyzed separately.

Postoperative segmental hypolordosis might lead to hyperlordosis outside the fusion segment (LL–SL) as a compensatory mechanism. Nevertheless, we found higher LL –SL to result in less revisions for ASD: HR = 0.9 (95% CI: 0.9–1.0). The effect of continuous difference LL–SL on revisions for ASD is shown in Figure 2 reinforced this finding.

DISCUSSION

Among patients who underwent LSF surgery for DLSD, we did not find postoperative hypolordosis (by PI–LL $>9°$) to result in a significant increase of the risk for revision for ASD during a 10-year follow-up. However, mismatch of 9° does not always represent a clinical threshold for satisfactory and poor alignment. Older age groups reportedly tolerate lower lordosis and greater mismatch than younger patients.[13,14] Nevertheless, one fixed cutoff was used to differentiate good and poor alignment in statistical analysis.

As previously indicated, revisions for ASD are infrequent after LSF for IS.[4] Contrary to that, they accumulate almost linearly over time among patients that have undergone LSF for

TABLE 1. The Baseline Demographic Data, Self-reported (*) Symptoms and Comorbidities, and the Type of Primary Surgery

	N = 215
Women [n (%)]	164 (76)
Age [mean (SD)]	66 (10)
BMI [mean (SD)]	28.6 (4.4)
Smoking* [n (%)]	12 (6)
Education years [mean (SD)]	11.1 (3.9)
Physical activity* [mean (SD)] (h/wk)	4 (2, 9)
Duration of the spinal problem* [median (IQR)] (y)	9 (4, 20)
Back pain* VAS [mean (SD)]	61 (26)
Leg pain* VAS [mean (SD)]	68 (23)
ODI* [mean (SD)]	45 (15)
DEPS* [mean (SD)]	10.5 (6.1)
Comorbiditie* [n (%)]	
Cardiovascular	118 (60)
Diabetes	24 (12)
Psychiatric disorder	5 (3)
Pulmonary	11 (6)
Neurological	5 (3)
Rheumatoid	14 (7)
Indication for surgery	
Spinal stenosis with spondylolisthesis [n (%)]	172 (80)
Spinal stenosis without spondylolisthesis [n (%)]	43 (20)
Fusion	
Level of the lower end [n (%)]	
L3 or L4	9 (4)
L5 or L6	114 (53)
S1	92 (43)
Length, levels [n (%)]	
1	59 (27)
2	84 (39)
3	54 (25)
4	17 (8)
5	1 (0)
Interbody cage (TLIF/PLIF) [n (%)]	23 (11)

BMI indicates body mass index; DEPS, Depression Scale; IQR, interquartile range; ODI, Oswestry Disability Index; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; VAS, Visual Analog Scale.

TABLE 2. The Spinopelvic Parameters (°) Before and After Lumbar Spine Fusion Surgery

	Mean (SD)	
	Preoperative	**Postoperative**
LL	50 (13)	49 (12)
PI	56 (10)	—
PI–LL	6.7 (11.1)	6.7 (11.1)
PT	20 (8)	21 (7)
SS	37 (9)	36 (8)
SL	29 (14)	27 (12)
LL–SL	21 (14)	22 (13)

LL indicates lumbar lordosis; PI, pelvic incidence; PT, pelvic tilt; SL, segmental lordosis; SS, sacral slope.

DLSD. This phenomenon highlights the role of the ongoing degenerative process in the spine in the development of ASD.

Generally, the effect of postoperative sagittal alignment on clinical outcome is established, but its role in the prevention of ASD is more unclear.[15,16] In the literature, the case-control study of Djurasovic and colleagues is often referred to as a proof of an association between postoperative hypolordosis and the increased revisions for ASD.[5,11,17] In that study, the mean interval between the initial surgery and the revision was 58 months, while the mean follow-up period for controls was only 55 months, which we consider relatively short. As revisions accumulate over time, and secondly, patients may die during the follow-up, we consider the Kaplan-Meier method an appropriate way to assess this phenomenon.

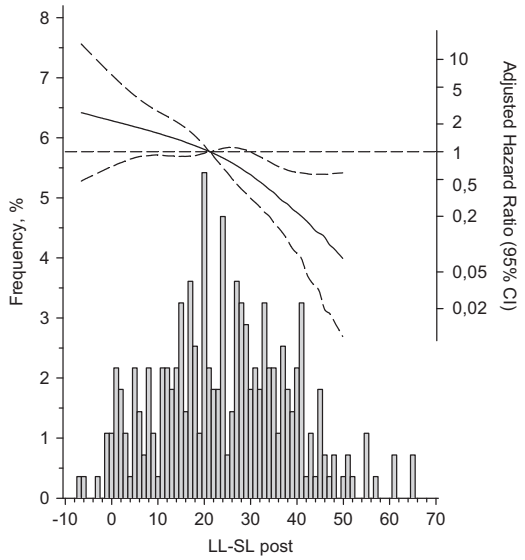

Figure 2. Higher lordosis in the mobile segment of the lumbar spine (LL−SL) after lumbar spine fusion was linked to decreased revisions for adjacent segment disease. Reference level (hazard ratio = 1) of LL−SL was here set to 21°. CI indicates confidence interval; LL, lumbar lordosis; SL, segmental lordosis.

Kim *et al*[18] retrospectively analyzed 69 patients who underwent L4–L5 fusion for IS or degenerative spondylolisthesis. They concluded that maintaining a segmental lordosis of 20° or more was important in the prevention of ASD. Bae *et al*,[19] in their retrospective analysis, suggested that restoration of segmental lordosis is important in the prevention of ASD. Nevertheless, they found only a statistically insignificant difference of 3° between ASD and non-ASD groups. In a prospective 5-year follow-up after LSF, Anandjiwala *et al*[20] found preexisting adjacent segment degeneration, not postoperative balance, to be a risk factor for radiological ASD. Furthermore, they found no correlation between the clinical outcome and radiological ASD. In a retrospective 10-year follow-up of posterior lumbar interbody fusion surgeries, Nakashima *et al*[21] found high PI, not LL, a significant risk factor for early-onset ASD. In a retrospective analysis of Alentado *et al*,[10] SL and LL were not significant risk factors for ASD.

Despite a relatively large study population and a long follow-up, we did not find a statistically significant effect of poor postoperative balance on the rate of revisions for ASD. Hence, we postulate that alignment plays a less significant role in the multifactorial pathogenesis of ASD than commonly proposed. We consider the ongoing degenerative spinal disease the most important single factor in this entity.

Poor segmental alignment requires compensatory mechanisms from the patient to maintain global balance. Hyperlordosis in the mobile segment of the lumbar spine, usually above the fused segment, is one of the compensatory mechanisms after LSF.[22] Thus, we expected higher LL–SL to relate to increased revisions for ASD caused by the increased stress at the adjacent segments. However, the connection was the opposite. This may indicate that the patients with mobile spine present more capacity to compensate and thus less stress to the adjacent segments. Moreover, Figure 2 indicated a strong effect from the change in LL–SL on the revisions for ASD. Our data provide no definitive answer whether this, in fact, more reflects the individual alignment or mobility in the mobile segment. It is also possible that some of the patients had an unfulfilled need for compensation before and after surgery due to a stiff spine. Earlier, diffuse idiopathic skeletal hyperostosis, a condition resulting in severely restricted spinal mobility, is reported as a significant risk factor for ASD after short segment LSF.[23] We assume that the benefit of reasonable segmental lordosis in the prevention of ASD might be the most important with reduced spinal mobility.

During the data collecting period, use of interbody cage was less common than nowadays. The main indication for interbody cage then was foraminal decompression or strengthening the fusion to prevent instrumentation failures.

The use of transforaminal lumbar interbody fusion in the correction of sagittal alignment has increased thereafter. Therefore, we did not assess the role of the interbody cage in the prevention of ASD here.

Although the connection between postoperative sagittal alignment and the occurrence of ASD seems less straightforward as occasionally proposed, the pursuit of normal alignment is important, especially for the clinical outcome. In this study, we have not investigated how postoperative sagittal balance affects the functionality or the health-related quality of life. Moreover, ending up in kyphosis during LSF surgery usually hampers future revision surgeries, where restoring normal balance may require considerably heavier surgery. All this might have the greatest impact with limited spinal mobility.

This study does not prove that sagittal alignment has no effect on the development of ASD. However, our results reinforce the perception from the literature that sagittal alignment has only a limited effect on the progression of ASD.

CONCLUSION

Poor sagittal alignment (mismatch PI–LL $>9°$) did not significantly increase revisions for ASD in a 10-year follow-up of the patients who underwent LSF for DLSD. Achieving appropriate segmental lordosis in LSF might be the most important in patients with reduced spinal mobility.

➢ Key Points

- ❑ We performed a retrospective additional analysis to evaluate the effect of sagittal alignment on the risk of revisions for adjacent segment disease after LSFs.
- ❑ The study population had been prospectively followed up for 10 years after having undergone LSF for a degenerative spinal disorder (stenosis with or without spondylolisthesis).
- ❑ We did not find poor postoperative balance to significantly increase the risk of revisions for ASD.

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