SPINE Volume 47, Number 4, pp 303–308

Spine

SURGERY

OPEN

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

Spine 2022;47:303–308

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Acknowledgment date: April 18, 2021. First revision date: July 29, 2021. Acceptance date: August 17, 2021.

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The manuscript submitted does not contain information about medical device(s)/drug(s).

The Competitive State Financing of the Expert Responsibility Area of Tampere University Hospital funds were received in support of this work.

No relevant financial activities outside the submitted work.

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DOI: 10.1097/BRS.0000000000004242

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%

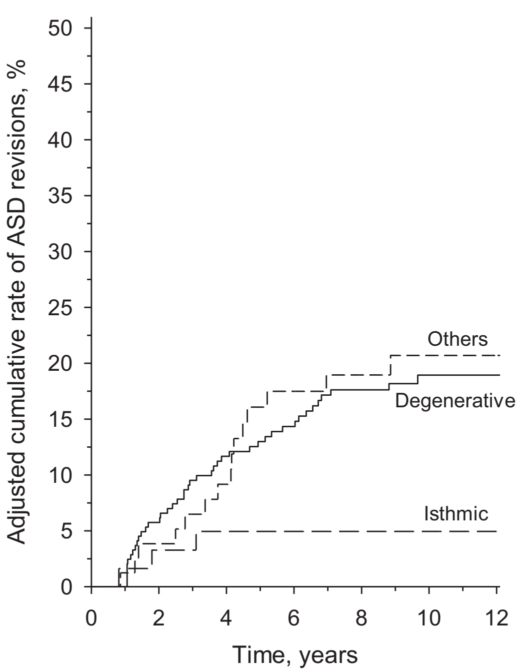

Figure 1. The cumulative rate of revisions for adjacent segment disease (ASD) between groups of surgical indications adjusted by age, sex, fusion length and caudal end of fusion ("Isthmic" = isthmic spondylolisthesis (IS); "Degenerative" (DLSD) includes spinal stenosis with or without degenerative spondylolisthesis;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

in patients with IS – less than a 4th of that (21%) in patients with DLSD or other indications.

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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