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Clinical Study

Long-term outcome after spinal fusion for isthmic spondylolisthesis in adults

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Abstract

BACKGROUND CONTEXT: Data on the long-term outcome after fusion for isthmic spondylolisthesis are scarce.

PURPOSE: To study patient-reported outcomes and adjacent segment degeneration (ASD) after fusion for isthmic spondylolisthesis and to compare patient-reported outcomes with a control group.

STUDY DESIGN/SETTING: A prospective study including a cross-sectional control group.

PATIENT SAMPLE: Patients with isthmic spondylolisthesis underwent posterior lumbar interbody fusion (PLIF) (n=86) or posterolateral fusion (PLF) (n=77). Patient-reported outcome data were available for 73 patients in the PLIF group and 71 in the PLF group at a mean of 11 (range 5–16) years after baseline. Seventy-seven patients in the PLIF group and 54 in the PLF group had radiographs at a mean of 14 (range 9–19) years after baseline. One hundred thirty-six randomly selected persons from the population served as controls for the patient-reported outcomes.

OUTCOME MEASURES: Patient-reported outcomes include the following: global outcome, Oswestry Disability Index, Disability Rating Index, and Short Form 36. The ASD was determined from radiographs using the University of California Los Angeles (UCLA) grading scale.

METHODS: : The chi-square test or analysis of covariance (ANCOVA) was used for group comparisons. The ANCOVA was adjusted for follow-up time, smoking, Meyerding slippage grade, teetotaler (yes/no) and, if available, the baseline level of the dependent variable.

RESULTS: There were no significant patient-reported outcome differences between the PLIF group and the PLF group. The prevalence of ASD was 42% (32/77) in the PLIF group and 26% (14/54) in the PLF group (p=.98). The patient-reported outcome data indicated lower physical function and more pain in individuals with surgically treated isthmic spondylolisthesis compared to the controls.

CONCLUSIONS: PLIF and PLF groups had similar long-term patient-reported and radiological outcomes. Individuals with isthmic spondylolisthesis have lower physical function and more pain several years after surgery when compared to the general population.

Keywords: Adjacent segment degeneration; Adult; Isthmic spondylolisthesis; Long-term follow-up; Outcome

FDA device/drug status: Not applicable.

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Introduction

Isthmic spondylolisthesis is most commonly asymptomatic. The majority of cases are diagnosed due to incidental findings [1, 2]. Approximately 25% develop symptoms in adulthood [2–4]. Resolution of pain occurs in approximately 70% after nonoperative therapies, leaving 30% to surgical intervention [5]. Surgical treatment has better outcomes than continued nonoperative treatment in such cases [6], even though the current long-term evidence is derived from only one randomized controlled trial [7]. Decompression and fusion is a common procedure for managing this disorder and several surgical techniques for spinal fusion in isthmic spondylolisthesis are available, but at present there is no gold standard technique [7–9].

Interbody fusion has biomechanical advantages compared to posterolateral fusion (PLF) due to the anterior column support, indirect foraminal decompression, restoration of lordosis, and reduction of the slip via ligamentotaxis [10]. Studies have failed to show superior outcomes after interbody fusion surgery when compared to less complex techniques [9, 11, 12]. Based on Swedish spine registry data, there was no difference in outcome between different surgical fusion techniques at a mean of 6.9 years, but the risk of additional surgery was 2 to 4 times higher for instrumented fusions compared to noninstrumented fusion [13].

Spinal fusion irreversibly alters the normal biomechanics of the spine and eliminates motion at the fused segment, causing an increased mechanical stress at the adjacent segments [14–17]. Adjacent segment degeneration (ASD), the degenerative changes that develop in the mobile segments adjacent to a spinal fusion, can be a potential long-term complication after lumbar fusion [18]. The reported incidence of ASD varies from 5% to 27% depending on the definition of ASD [19–24]. The radiographic incidence of ASD is higher than the symptomatic incidence [18], whereas the latter can be a cause of revision surgery [25, 26].

It is still unclear if there is any radiological difference regarding the incidence of ASD between different surgical fusion techniques for isthmic spondylolisthesis. Also, long-term data concerning health-related quality of life of surgically treated isthmic spondylolisthesis are scarce. We tried to improve the knowledge base by comparing patients surgically treated with two different techniques for isthmic spondylolisthesis as well as the general population. We hypothesized that long-term patient-reported and radiological outcomes would not be dependent on surgical technique and that surgical treatment normalizes patients' health-related quality of life.

Materials and methods

Study patients included the following: (i) those from follow-up of a prospective consecutive cohort enrolled between 1997 and 2003 who were treated with posterior lumbar interbody fusion (PLIF) [9], (ii) a historical cohort from a randomized controlled trial in which patients were enrolled between 1990 and 1995 and were treated with PLF with or without instrumentation [8, 24], and (iii) controls from the general population without known isthmic spondylolisthesis enrolled between 2014 and 2015.

For the patient cohorts, the inclusion criteria were identical. The criteria were as follows: 18 to 55 years of age with low back pain with or without sciatica, severely restricted functional ability for more than 1 year, and isthmic spondylolisthesis of any grade at any lumbar level. Patients with previous surgery and conditions deemed to affect the capacity to participate in the study (eg, psychiatric disorders and drug or alcohol abuse) were excluded.

For this study, the group of patients treated with PLIF were contacted and asked to participate in long-term follow-up consisting of patient reported outcome questionnaires and radiographs. These were not necessarily performed at the same time point. The flow chart for the inclusion of patients in the present study is shown in Fig. 1.

For all patients, the mean follow-up time of patient reported outcome was 11 (range 5–16) years, and for radiographs it was 14 (range 9–19) years. For the PLIF group, the mean follow-up time of patient reported outcome was 13 (range 11–16) years, and for radiographs it was 15 (range 9–19) years. Corresponding follow-up times for the PLF group were 9 (range 5–13) and 12 (range 10–16) years [7, 24]. Controls were surveyed only once and not followed up.

Surgery

Details of preoperative investigations and surgery have been presented earlier. Magnetic resonance imaging (MRI) or computer tomography myelography was used to assess nerve root compression and foraminal stenosis [8, 9].

The PLIF group was operated on with autograft and carbon fiber ramps at the level of the slip with pedicle fixation, and decompression was performed by removing the loose lamina and releasing the nerve roots [9].

In the PLF cohort, patients were operated on with PLF in situ with autologous bone transplantation harvested from the right iliac crest. In addition, 37 patients were randomized to receive instrumentation consisting of pedicle screw fixation. The patients that were randomized to PLF without instrumentation wore a daytime lumbar brace for 6 months. The Gill procedure and nerve root release were performed in all patients with sciatica (73%) [8]. No outcome differences have previously been found between the groups with or without instrumentation. Data for these are therefore reported as one single group [7].

Patient-reported outcome

Patient-reported outcome measures developed to assess quantitative data regarding general health, function, and pain were used and included global outcome,

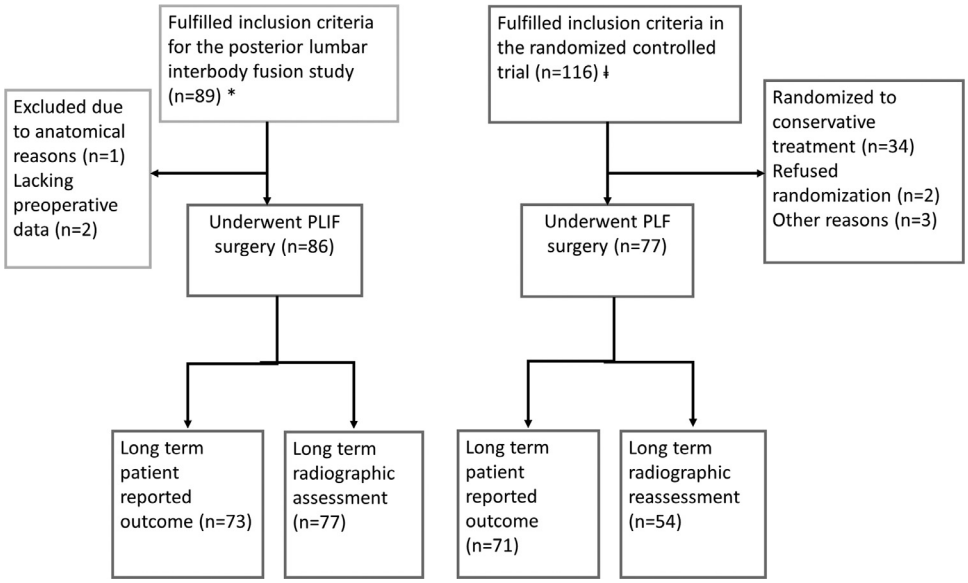

Fig. 1. Flowchart of patients in the posterior lumbar interbody fusion (PLIF) and the posterolateral fusion (PLF) groups [7–9]. * Patients originally enrolled between 1997 and 2003 [9]. Patients originally enrolled between 1990 and 1995 [8].

Oswestry Disability Index, Disability Rating Index (DRI), Short Form 36, and some general questions [27].

For global outcome, the patient classifies the outcome of the surgery. The question was formulated as follows: "How is your pain today when compared to before surgery?" and the four answer alternatives were dichotomized into "Much better" and "Better" versus "Unchanged" and "Worse." The back-specific Oswestry Disability Index [28] scored from 0 (best possible back function) to 100 (worst possible back function). The Short Form 36 was assessed according to the mental component summary score and the physical component score, where 0 is equivalent to maximum disability and a score of 100 is equivalent to no disability [29–31]. DRI is composed of 12 functional visual analog scales that assess dressing, outdoor walking, climbing stairs, sitting for a longer time, standing bent over a sink, carrying a bag, making a bed, running, light work, heavy work, lifting heavy objects, and participating in exercise/sports. The mean of the 12 functional visual analog scales divided by 12 provides the DRI, ranging between 0 and 100 [32].

Radiological analysis

Standard anterioposterior and lateral supine spine radiographs of the lumbar spine in the horizontal position were obtained at the time of surgery and at the follow-up. The University of California Los Angeles (UCLA) grading scale of disc degeneration, a semiquantitative morphologic disc degeneration scale based on disc height reduction, presence of osteophytes, and end plate sclerosis, was used [21]. The pretreatment and long-term radiographs were compared, and the degeneration of the first disc above the level of fusion at the long-term follow-up was subsequently graded. There were three independent observers: two orthopedic spine surgeons with 12 and 26 years of experience and one radiologist with 18 years of experience. If no consensus could be reached among the spine surgeons, the radiologist would determine the grading. The pretreatment radiographs from the PLF group and PLIF group and the posttreatment radiographs from the PLF group had been analyzed by one of the orthopedic spine surgeons before, 9 years earlier [24], but all the radiographs were in this study assessed without knowledge of the previous findings.

Radiographs were classified as normal (grade 1), disc space narrowing (grade 2), presence of osteophytes (grade 3), and end plate sclerosis (grade 4). After the first grading, the spine surgeons were unanimous in their grading decision in 110 of 131 patients (84%). After a second round, including the radiologist decision, all radiographs had been classified.

Additional surgery

Data on reoperations were obtained from the questionnaires, radiographs, and patient files.

Controls

By means of the Swedish population register, controls (without any known isthmic spondylolisthesis) matched for age, gender, and geographic area of residence with the patients treated with PLIF were identified. The same questionnaire with the exception of the global outcome question was sent to 265 individuals, of which 138 individuals answered (52%), 2 were recently deceased, 15 declined, and 110 did not respond. Two responders were excluded, because they were already patients in the PLIF group;

therefore, 136 controls remained for analysis. The controls were not examined.

Statistics

Descriptive data are presented as mean (range), mean (standard deviation), mean (95% confidence interval), or number (%). In case of missing data, cases were excluded analysis by analysis. The Chi-square test or analysis of covariance (ANCOVA) was used for group comparison. The ANCOVA was adjusted for follow-up time, smoking, Meyerding slippage grade, teetotaler (yes/no), and, if available, the baseline level of the dependent variable. The results from the UCLA grading scale of disc degeneration were dichotomized into two groups: normal (grade 1) versus adjacent segment degeneration (grades 2, 3, and 4) when comparing the surgical groups. In a secondary analysis, patients were divided into groups according to grade of disc degeneration (normal vs adjacent segment degeneration). A p-value of $<.05$ was considered significant. Statistical analyses were performed with IBM SPSS v22.

Sample size

Because the study mainly is based on already existing cohorts [8, 9, 24], a power analysis was not performed.

Study approval

Approval for this study has been obtained from the Ethical Review Board in Stockholm, with the registration number 2012/206-31/1.

Results

Baseline data for the patient cohorts are presented in Table 1.

Patient reported outcome

Both patient groups improved their DRI after surgery with no statistically significant difference between the groups (Fig. 2 and Table 2). When the surgical groups were compared to the controls, both surgical groups scored significantly worse on all parameters with the exception of the Short Form 36 mental component score, which did not differ significantly between the PLIF group and the controls (Table 2).

Radiological analysis

The prevalence of radiological adjacent segment degeneration was 32 of 77 (42%) patients in the PLIF group and 14 of 54 (26%) in the PLF group (p=.98), after adjustment. In the secondary analysis, which divided the patients according to grade of disc degeneration, adjacent segment degeneration was associated with higher age but not with patient-reported outcomes (Table 3)

Table 1
Descriptive data at the time of surgery for the two groups of patients that participated in the long-term follow-up. They were treated surgically for isthmic spondylolisthesis with posterolateral fusion (PLF) between 1990 and 1995 [6] or posterior lumbar interbody fusion (PLIF) between 1997 and 2003 [9]. Data are presented as crude means (95% confidence intervals) or number (%). Statistical analysis was performed with the Pearson chi-square test or analysis of variance. The p-value is shown for the comparison of the two groups

Baseline characteristics	PLIF (n=73)*	PLF (n=71)*	p Value
Age (y)	40 (37–42)	39 (37–42)	.85
Women	49 (67%)	37 (52%)	.07
Leg pain	51 (70%)	43 (61%)	.24
Level of lysis			.24
L5	56 (77%)	60 (84%)	
Other level	17 (23%)	11(16%)	
Meyerding slip			.001
Grade 1 slip	64 (88%)	43 (60%)	
Grade 2 slip	7 (9%)	26 (36%)	
Grade 3 slip	2 (2%)	2 (3%)	
BMI	26.8 (25.8–27.8)	26.1 (25.1–27.2)	.38
Married or cohabitant	47 (64%)	53 (76%)	.14
Smoking	15 (20%)	40 (56%)	<.001
Immigrants	16 (22%)	20 (28%)	.39
Teetotaler (drinks no alcohol)	11 (16%)	24 (34%)	.011
Sick leave or disability pension	46 (63%)	51 (73%)	.21
Exercise	37 (51%)	30 (44%)	.39
DRI baseline	46 (42–51)	49 (44–53)	.48

DRI, Disability Rating Index; BMI, Body Mass Index.
*Numbers do not always correspond to the group numbers due to missing data.

Additional surgery

Additional surgery was experienced by 6 patients in the PLIF group (2 reoperations due to pseudoarthrosis, 1 due to disc herniation, and 3 implant removals due to local irritation) and 11 patients in the PLF group (2 reoperations due to nerve root irritation, 1 pseudoarthrosis, 1 due to disc herniation, and 7 implant removals due to local irritation) (p=.13). Four of the controls had had surgery to the spine due to disc herniation before answering the questionnaire.

Nonresponse Analysis

There were no statistically significant differences in the baseline variables between the patients who did and those who did not respond to the long-term follow-up questionnaires (all $p \geq .15$; Supplementary Table 1).

Discussion

Our data indicate that the type of surgery for isthmic spondylolisthesis is unrelated to outcome. A superior long-term outcome for circumferential fusion compared to PLF has been reported from a randomized controlled trial including degenerative lumbar disorders, but also patients

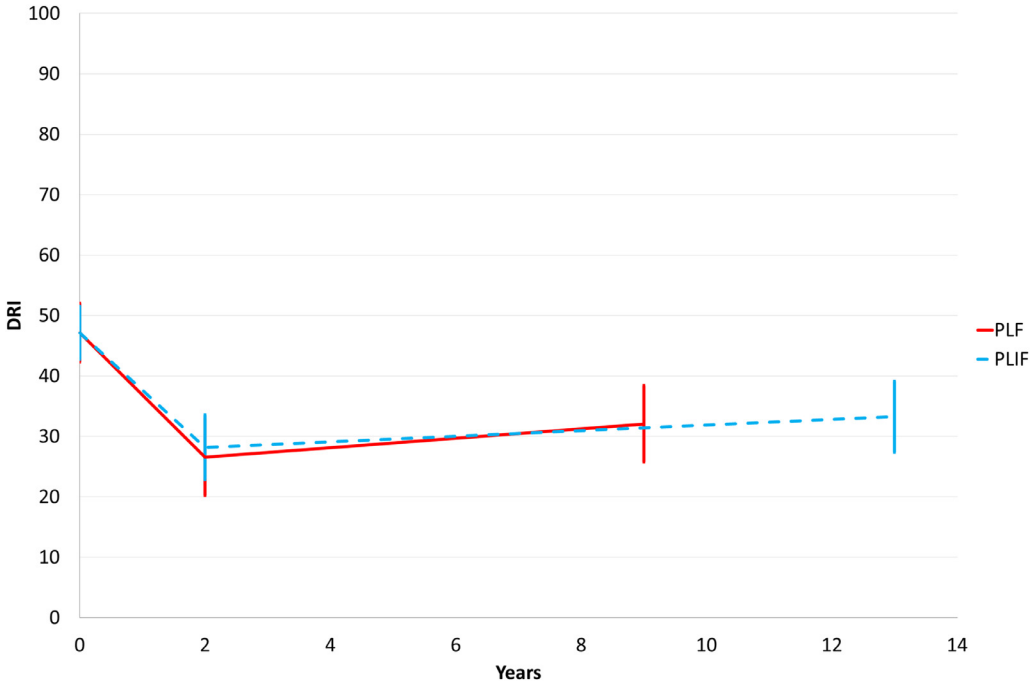

Fig. 2. Pairwise comparison of Disability Rating Index (DRI) longitudinal data confirmed that both groups improved their outcome measures from baseline to the 2-year follow-up (both p<.001). The p-value for the pairwise comparison of the 2-year to long-term follow-up was .024 for the posterolateral fusion (PLF) group and .067 for the posterior lumbar interbody fusion (PLIF) group. Data are presented as crude means (95% confidence intervals).

Table 2
Long-term follow-up data presented as adjusted mean (95% confidence intervals) or number (%) for the two groups of patients treated surgically for isthmic spondylolisthesis; posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF), and the population-based controls. The p-values for comparison between the surgical groups are adjusted for follow-up time, smoking status, teetotaler, Meyerding slip, and, if available, the baseline level of the dependent variable. The comparisons between the surgical groups and controls were adjusted for age at follow-up and smoking status

Long-term follow-up	PLIF (n=73)*	PLF (n=71)*	Controls (n=136)	p value (PLIF vs PLF)	p Value (PLIF vs control)	p Value (PLF vs control)
Age at follow-up (y)	54 (51–56)	48 (46–51)	55 (53–57)	.44	.26	<.001
Smoking	10 (14%)	36 (54%)	18 (13%)	<.001	.85	<.001
ODI	24 (17–31)	23(17–30)	8 (5–11)	.89	<.001	<.001
DRI	36 (28–44)	28 (19–36)	24 (22–27)	.24	<.001	.002
Global outcome				.16	NA	NA
“Much better” or “Better”	59 (83%)	40 (73%)	NA			
“Unchanged” or “Worse”	12 (17%)	15 (27%)	NA			
SF 36 mental component score	48 (43–52)	44 (40–49)	49 (47–51)	.37	.79	.12
SF 36 physical component score	39 (35–44)	40 (36–45)	49(47–51)	.77	<.001	<.001

NA, data not applicable; ODI, Oswestry Disability Index; DRI, Disability Rating Index; SF 36, Short Form 36.
*Numbers do not always correspond to the group numbers due to missing data.

with isthmic spondylolisthesis. However, the subgroup of 43 patients with isthmic spondylolisthesis failed to show any difference in outcome in relation to the surgical technique [33]. A previous meta-analysis of surgical data with follow-up times between 3 and 10 years concluded that PLIF resulted in higher fusion rates than PLF in the treatment of isthmic spondylolisthesis but not in differences in patient-reported outcome measures [34]. Another meta-analysis showed no significant differences in clinical outcomes between two interbody techniques [35].

In a long-term follow-up of a randomized controlled study of 95 patients with severe chronic low back pain operated on with interbody fusion with PLF and PLF alone, the patient-reported outcome was independent of the fusion technique [36]. Radiological adjacent segment degeneration correlated significantly with higher age and worse outcome [36].

Our data indicate that age and time affect the adjacent segment degeneration in surgically fused patients, but these do not affect the patient-reported outcome. However, isthmic spondylolisthesis patients have considerably worse health-related quality of life many years after surgery compared to age, gender, and geographically matched controls.

Table 3
Adjacent segment degeneration in relation to outcome. Data are presented as adjusted mean (95% confidence intervals) or number (%). The p-value has been obtained from analysis of variance after adjustment for follow-up time, smoking status, teetotaler, Meyerding slip, and, if available, the baseline level of the dependent variable for the comparison of the two groups

Long-term follow-up	Normal (n=85)*	ASD (n=46)*	p Value
Follow-up time X-ray	13.6(13.4–13.8)	13.7 (13.4–14.1)	.35
Age (y)	52 (49–55)	58 (54–61)	.01
Smoking status	29 (37%)	9 (21%)	.08
ODI	22 (18–27)	26 (20–32)	.38
DRI	33 (27–38)	33 (26–40)	.95
Global outcome			.39
Much better or Better	59 (82%)	33 (77%)	
Unchanged or Worse	13 (18%)	10 (23%)	
SF 36 mental component score	47 (44–50)	44 (40–48)	.34
SF 36 physical component score	41 (38–44)	38 (34–42)	.24

ODI, Oswestry Disability Index; DRI, Disability Rating Index; SF 36, Short Form 36.

*Numbers do not always correspond to the group numbers due to missing data.

Even though we have not performed a cost-benefit analysis, previous studies suggest that interbody fusion creates more bleeding, a longer surgery time, a higher risk for complications, and a higher risk for additional surgery compared to noninstrumented or instrumented PLF [9, 13, 37].

Lumbar fusion may accelerate degeneration at the adjacent segments, as compared to natural history [24]. However, age and genetics seem to have a larger impact than the actual fusion on development of adjacent segment degeneration [37]. The importance of age is supported by the present data. Radiographic degeneration at adjacent segments is very common but is not always related to clinical symptoms. A review article reported that the incidence of radiographic adjacent segment degeneration ranged from 8% to 100%, whereas the incidence of symptomatic adjacent segment degeneration was much lower, ranging from 5% to 18% [18]. The great variance in reported incidence is most probably due to different populations and differing diagnostic methodologies. However, only a small percentage of symptomatic adjacent segment degeneration requires a second surgery [18, 19, 21]

Str*engths and limitations*

The strengths of our study include identical inclusion and exclusion criteria in the two surgical groups, a long follow-up, a follow-up rate exceeding 80%, validated patient-reported outcome measurements, and standardized radiographs, with disc degeneration assessed by a validated method by experienced personnel. It also includes a homogeneous population with only isthmic spondylolisthesis patients, which makes the results easier to interpret.

Nevertheless, the design of this study brings on a number of limitations. Some of the most important are the nonrandomized design and the varying follow-up times. The patients were included at different time periods and differed at baseline concerning smoking and alcohol consumption. We have tried to take this into account by adjusting for these and other possible confounders, but this may weaken the strength of the results.

The higher proportion of smokers concurred with a timeline analysis and would possibly give a higher risk of disc degeneration for the PLF group [38, 39], but this negative effect could be counteracted by the slightly younger age in this group. All analyses were adjusted to compensate for these differences.

Degeneration can be measured with radiographs and magnetic resonance imaging. We chose the former due to previous experience and simplicity with this methodology. Our study size is fairly small but outnumbers many other studies when taking the follow-up time into account [40]. One of the observers had previously analyzed the pretreatment radiographs of both groups and the posttreatment radiographs in the PLF group but was unaware of his assessment 9 years earlier during the reanalysis. We cannot exclude the possibility of recollection bias, but we think it is unlikely due to the long time span between the analyses. The questionnaire data and the radiographs were not collected at the same time, and the association between these two can therefore be questioned. On the other hand, our results do not differ from previously published data and disc degeneration is likely to be a slow process, so we assume them to be reliable [36, 40]. The controls were matched to only the PLIF group. Age ranges do however overlap with the PLF group, giving good possibilities for adequate statistical adjustments, and analyses were without statistically significant differences between the groups. In addition, there were no differences between the surgical groups indicating that the findings compared to the controls are relevant.

Conclusions

Despite the theoretical advantages of interbody fusion compared to PLF, no improvement of patient-reported or radiological outcome could be demonstrated. Anterior support in the treatment of adult isthmic spondylolisthesis is not necessary.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.spinee.2018.08.008.

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