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REVIEW

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Fusion for low-grade adult isthmic spondylolisthesis: a systematic review of the literature

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Abstract The objective of this study was to evaluate which fusion technique provides the best clinical and radiological outcome for adult low-grade lumbar isthmic spondylolisthesis, and to assess the overall clinical and radiological outcome of each fusion technique. A systematic review was performed. Medline, Embase, Current Contents, and Cochrane databases as well as reference lists of selected articles were searched. Randomised controlled trials (RCTs) were used to evaluate the best treatment; controlled studies and non-controlled studies were used to determine the outcomes after surgery. Two independent reviewers evaluated the studies with the methodological checklists of van Tulder and Jadad for the randomised studies and of Cowley for the non-randomised studies. The search resulted in 684 references and eventually 29 studies met the inclusion criteria, of which eight were RCTs, four were prospective, and 17 were retrospective case series. Ten of the case series did not clearly identify consecutive patient selection. All the eight RCTs evaluated the effect of different techniques of posterolateral fusion (PLF). Evidence was found that the PLF was superior to non-operative treatment (exercise). Circumferential fusion was compared to PLF, but no difference could be found. PLF with or without instrumentation was evaluated in three studies, but no benefits from additional instrumentation were found. Other comparisons within PLF showed no effect of decompression, alternative instrumentation, or bone graft substitute. The 21 case series included 24 patient groups. PLF was used in 15 groups, good or excellent clinical outcome varied from 60 to 98% and fusion rate varied from 81 to 100%. Anterior interbody fusion was used in five groups, good or excellent clinical outcome varied from 85 to 94% and fusion rate varied from 47 to 90%. Posterior interbody fusion was used in two groups, good or excellent clinical outcome was 45% and fusion rate was 80 and 95%, respectively. Reduction, loss of reduction, and lordotic angles before and after the treatment was reported in only four studies. Average reduction achieved was 12.3%, average loss of reduction at follow-up was 5.9%. Preoperative lordotic angles were too heterogeneous to pool the results. Adjacent segment degeneration was not reported in any of the publications. A wide variety of complications were reported in 18 studies and included neurological complications, instrument failure, and infections. Fusion for low-grade isthmic spondylolisthesis has better outcomes than non-operative treatment. The current study could not identify the best surgical technique (PLF, PLIF, ALIF, instrumentation) to perform

the fusion. However, instrumentation and/or decompression may play a beneficial role in the modern practice of reduction and fusion for low-grade isthmic spondylolisthesis, but there are no studies yet available to confirm this. The outcomes of fusion are generally good, but reports vary widely.

Keywords Lumbar vertebrae · Spondylolisthesis · Spinal fusion · Evidence based medicine · Review literature

Introduction

Lumbar low-grade isthmic spondylolisthesis in adults (> 18 years old) is defined as an osseous discontinuity of the vertebral arch at the isthmus—the pars interarticularis—predominantly occurring in the fifth lumbar vertebra. Histologically, the defect is characterised by ordered fibrous and fibrocartilaginous tissue without evidence of heightened tissue remodelling or bone turnover [38, 46]. The degree of anterior slippage in isthmic spondylolisthesis can be rated using four grades, according to Meyerding [26], where grades II or lower have slippages of 50% or less. Progression of the disease can occur through hyper-mobility of the affected motion segment causing a more rapid disc degeneration and subsequently listhesis and radiculopathy. In this way, an asymptomatic disc can become symptomatic after decades [10]. Adjacent segments can also become affected through biomechanical alterations [32].

Several epidemiological studies have revealed that the incidence of symptomatic listhesis in Caucasian populations varies from 4 to 6% [25, 38], but rises as high as 26% in secluded Eskimo populations [36] and varies from 19 to 69% among first-degree relatives of the affected patients [22].

Some patients can benefit from conservative treatment including physical therapy, braces, or pain medication. With regard to surgical treatment, there are several different options, among which posterolateral fusion (PLF) is one. The aim of fusion is to reduce the pain by reducing the motion of the segment. Other treatment options include decompression (Gill laminectomy) [12], supplemental instrumentation, and supplemental anterior column support. Controversies exist about the effectiveness of these treatment options that can be used separately or in any combination [27].

The theoretical advantages of supplementary pedicle screw fixation are the ability to correct the deformity and to reduce the listhesis. The rigid fixation is expected to give better fusion rates [9]. The disadvantages include the extra costs, a more extensive surgical trauma, and the risk of neurological complications because of misplaced pedicle screws. Besides, it has been speculated that rigid fixation may increase the pseudoarthrosis rate because of stress-shielding or may increase adjacent segment degeneration.

The goal of this study was to determine which fusion technique gives the best clinical and radiological outcome in patients with low-grade lumbar spondylolisthesis. Further, we wanted to answer the following questions:

- What are the fusion rates acquired with the fusion techniques described?
- How much correction is obtained with each procedure?
- How much correction is lost after reduction of the listhesis?
- What are the lordotic angles before and after the treatments?
- Does adjacent segment degeneration occur?
- What are the complication rates of the techniques described in the studies?

Methods

Search strategy for identification of studies

In order to obtain all the relevant literature, we used a sensitive search in the most common databases of published literature:

- The Cochrane database of randomised controlled trials (RCTs) (2004 issue 1)
- Current contents (1996–March 2004)
- Medline (through Pubmed; 1966–March 2004)
- Embase (through March 2004)

The search strings are given in Table 1, the strings in the second column were used and connected with 'OR' within the cells and with 'AND' between the cells. The search strategy was adopted for the different databases. We made no restrictions on the basis of language or date. From the articles that were selected, the references were screened.

Selection of studies

Two independent reviewers selected the articles. A consensus was strived for, but when it could not be reached, a third reviewer was consulted. The selection was not done blindly, although, when selecting titles and abstracts, the rest of the information was concealed. The articles were selected on the basis of the title and the abstract with the following criteria:

- The intervention(s) used had to include at least one surgical treatment. The description of the intervention must have been sufficiently detailed to reproduce the intervention. Items are: description of use of

Table 1 Search strings

Dimension	Search strings
Indication	Spondylolisthesis (MH)
	Isthmic (TW)
	Lytic (TW)
	Lumbar vertebrae (MH)
	Low-grade (TW)
Treatment	Spinal fusion (MH)
	Fusion (TW)
	Arthrodesis (MH)
	Spondylodesis (TW)
	Internal fixators (MH)
Study type	Randomised controlled trial (PT)
	Controlled clinical trial (PT)
	Clinical trial (PT)
	Multicentre studies (PT)
	Multicase review (PT)
	Trial (TW)
	Random* (TW)
	Controlled (TW)
	Prospective* (TW)

PT publication type, *TW* free textword, *MH* mesh heading, wildcard used

instrumentation, application of decompression, and intention to reduce the listhesis
- The indication on which patients received this treatment had to be adult low-grade (grades I and II, or less than 50% slip) isthmic spondylolisthesis at one lumbar level that failed to respond to conservative treatment.
- The outcome parameter had to be a radiological, clinical, or functional measure. Examples of these outcome measures are SF-36, Womac, Oswestry Disability Index, pain scores, complication rates, fusion rates, and reoperation rate.
- At least ten patients with the treatments and indications mentioned above were included.
- When the spondylolisthesis group was a subgroup (<95%), there had to be subgroup results given for this group.
- The article had to be published in a peer-reviewed journal.

If the relevance could not be ascertained on the basis of the abstract, the complete article was retrieved and compared against the same criteria. References were managed with the aid of Reference manager (ISI ResearchSoft, USA), where relevant information regarding source of the reference, reason, and stage of exclusion were noted.

Methodological quality assessment

Two independent reviewers assessed the methodological quality of the selected articles and again a consensus was strived for, and if necessary, a third reviewer was consulted. The methodological quality was assessed with the aid of a checklist used in systematic literature reviews of spine surgery by van Tulder [42, 43]. As the van Tulder checklist is intended for RCTs, we chose to use the checklist used by Cowley [7] that has three scores for studies classified as RCT, non-RCTs (concurrent and other), and non-controlled studies (cohort, prospective, cross sectional, historical). Items of the van Tulder checklist are given in Table 2, and the items of the Cowley non-controlled studies checklist are given in Table 3. The items were scored with a 'yes', 'no', or 'unsure'.

Analysis

The data was extracted by one reviewer and confirmed by a second reviewer. Standard deviation was used when available, or else it was imputed from ranges if available. Evidence on the best treatment available was based on the RCTs found in the search. The anticipated contrasts were: with or without decompression, with or without reduction, anterior versus posterior fusion, non-instrumented fusion versus instrumented fusion. For dichotomous outcomes, the relative risks were calculated. For continuous outcomes, a weighted mean difference (WMD) was calculated. With sufficient data, subgroup analyses were conducted to assess the effects of age, gender, disease severity, and follow-up time on the outcomes. Best evidence synthesis was performed stratified for studies meeting 50% or more as opposed to those meeting less than 50% of the quality criteria on the van Tulder list.

Evidence on the effect of the treatments found was based on the non-randomised studies. Best evidence synthesis was performed for studies providing consecutive patient selection and completeness of treatment description.

Results

Search results

The consecutive searches resulted in 481 references in Medline, 71 in Embase, 46 in Current Contents, and 3 in Cochrane; duplicate references were not included. Another 83 were found after screening the reference lists of the selected articles. Thus, a total of 684 titles and abstracts were available for selection.

From title 366, and from abstract 158 references could be excluded as the topic of the article was clearly not relevant for the objective of the review. Two articles could not be traced [3, 13]. One hundred and twenty-nine references were excluded after reading the complete article because of the following reasons: the type of listhesis was not appropriate or unknown (46), there were no subgroup results given (35), the report did not contain (original) data (18), or there were less than ten patients included (16). As a result, only 29 articles were included in the review.

Table 2 Methodological quality of included randomised controlled trials

Study Total	Moller [28] 8	Thomsen [40] 6	McGuire [24] 4	France [11] 1	Carragee [2] 7	Johnsson [16] 7	Moller [29] 5	Christensen [5] 4
Is a valid randomisation technique applied?	Yes	Yes	Unsure	Yes	Yes	Yes	Unsure	Yes
Was the treatment allocation concealed?	Yes	Yes	Unsure	Unsure	Yes	No	Yes	Yes
Are the patient groups comparable on prognostic factors?	Yes	Yes	Unsure	Unsure	Yes	Yes	Yes	Unsure
Is the patient blinded for the treatment allocation?	No	No	No	Unsure	No	No	No	No
Is the surgeon blinded for the treatment allocation?	No	No	No	No	No	No	No	No
Is the outcome assessor blinded for the treatment allocation?	No	No	No	Unsure	No	No	Unsure	No
Are the co-interventions described in sufficient detail?	Yes	Unsure	Yes	No	Yes	Yes	No	Unsure
Is the compliance acceptable?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Is the dropout rate given and acceptable? ($< 10\%$)	Yes	Yes	Yes	No	Yes	Yes	Yes	Unsure
Is the timing of the outcome assessments comparable between groups and consistent within groups?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Is an intention to treat analysis given?	Yes	No	No	No	No	Yes	No	No

There were eight prospective RCTs available for the best surgical treatment analysis. Twenty-one observational studies with 24 patient groups were available to give the results for the outcome after surgical treatment. The observational studies included four prospective consecutive studies and 17 retrospective studies, of which 11 used consecutive and 6 non-consecutive patient selection. In fact, three of the observational studies included a control group, but no effort was made to match the study groups at any variable, so these study groups are analysed as separate patient groups. Five studies with seven patient groups fulfilled the criteria of adequate treatment information and consecutive patient selection.

Methodological quality of included studies

The methodological quality of the studies is given in Table 2 (van Tulder score for RCTs) and Table 3 (Cowley score for non-controlled studies). The van Tulder score for the randomised trials varied between 1 and 8 out of 11 possible points, of which four scored six or more points, thus being a 'high quality' study. In the selected articles blinding (surgeon, observer, or patient) was never used with certainty. Three studies had uncertainties regarding the randomisation procedure.

The Cowley score for the five non-controlled studies varied between 5 and 12 out of 17 possible points, of which 2 scored 9 or more points, thus being a 'high quality' study.

The best surgical treatment

All the eight RCTs evaluated the effect of the different techniques of PLF. PLF with or without instrumentation was evaluated in four studies [11, 24, 28, 40] (Table 4), no benefits from additional instrumentation was found in any of these studies. Meta-analysis was not performed on these four trials as the treatments applied were too heterogeneous: decompression was used in McGuire [24], it was unclear in France [11], and mixed in Moller [28] and Thomsen [40]. Also, reduction was not used by McGuire [24] and France [11] and was unclear in Moller [28] and Thomsen [40]. Two studies, those of Moller [28] and Thomsen [40], were available for the best evidence synthesis. In performing this best evidence synthesis, only fusion rates could be compared, as Thomsen [40] had not reported on the clinical outcomes and complications for the isthmic spondylolisthesis subgroup. Fusion was higher in both the Moller [28] (78 vs 65%) and Thomsen studies (84 vs 73%) for the non-instrumented group when compared to the instrumented group, but the difference was not significant.

Other modifications of PLF were compared in four studies (Table 5). These studies showed no effect of

Table 3 Methodological quality of included uncontrolled case series

Study Total	Knight [20] 12	Verlooy [44] 11	Suk [37] 7	Markwalder [23] 5	Kim [19] 5
Method of selection of patients identified and appropriateness	Yes	No	No	No	No
Number of patients deceased or lost to follow-up reported or included in appropriate statistical analysis	Yes	Yes	No	Unsure	No
Follow-up period range and mean given	Yes	Yes	Yes	Yes	Yes
Prosthesis models specified	Yes	Yes	No	Yes	No
Clearly defined criteria for measuring outcomes	Yes	No	No	No	No
Valid statistical analysis undertaken	Yes	No	Unsure	No	Yes
Data given for deceased patients	Yes	Yes	Yes	Unsure	No
Age range and mean age reported	Yes	Yes	Yes	Yes	Yes
Numbers of men and women given	No	Yes	Yes	Yes	Yes
Weight range and mean weight given	No	No	No	No	No
Preoperative diagnoses with percentages of patients given	Yes	Yes	No	Yes	Yes
Clinical evaluation independent of operating surgeon	No	Yes	No	Unsure	No
Radiological evaluation independent and blinded to clinical results	No	Yes	No	Unsure	No
Results given for specific models	No	Yes	Yes	No	No
Quantification of outcomes	Yes	No	Yes	No	No
Follow-up data compared with preoperative data (mean and range)	Yes	Yes	Yes	No	No
Independence of investigators (no vested interest) stated	Yes	No	No	No	No

addition of ALIF [5], decompression [2], or bone graft substitute [16]. Further evidence was found that the PLF was superior to exercise alone [29], but this is a low-quality study.

Outcome after surgical techniques

The 21 non-controlled case series included 24 patient groups. Details of included studies are given in Table 6 (adequately reported studies) and in Table 7 (other studies). PLF was used in 15 groups, good or excellent clinical outcome varied from 60 to 98% and fusion rate varied from 81 to 100%. Anterior interbody fusion was used in five groups, good or excellent clinical outcome varied from 85 to 94% and fusion rate varied from 47 to 90%. Posterior interbody fusion was used in two groups, good or excellent clinical outcome was 45% (only one group reported), and fusion rate was 80 and 95%,respectively. Knight [20] reported 79% good or excellent clinical outcome after posterolateral endoscopic foraminal decompression. Johnson [15] did not specify the treatments used.

Reduction, loss of reduction and lordotic angles before and after the treatment was reported in only four studies. There were three studies that reported adequately the preoperative, postoperative, and follow-up percentage of slip and lordotic angles [18, 23, 37]. All the three studies used PLF. The results of these studies are summarised in Table 8. The average reduction achieved was 12.3%, and the average loss of reduction at follow-up was 5.9%. One study reported that the reduction was maintained at follow-up [35]. It is not sure whether all the procedures intended to reduce the listhesis. Preoperative lordotic angles were too heterogeneous to pool the results.

A wide variety of complications were reported in 18 studies (including the RCTs) and included neurological complications, instrument failure, and infections. For PLF, we counted 64 complications in 545 patients (12%), of which eight were instrumentation failures in 388 patients with instrumented PLF. Davne [8] reported 4.3% screw breakage in a mixed population. For anterior interbody fusion, we counted 19 complications in 120 patients (16%). Thirty-seven patients of the 154 patients (24%) treated with posterior interbody fusion had serious complications. Adjacent segment degeneration was not reported in any of the publications. We did not include the patient numbers where the complications were not split for the subgroups required.

Discussion

Despite a relatively large number of studies available (eight RCTs and five adequate cohorts), we could not determine the best treatment for adult low-grade isthmic spondylolisthesis. PLF was the procedure most studied, but it could not be proven to be superior or inferior to a circumferential fusion. Supplemental decompression, osteogenic protein, or instrumentation could not be shown to be superior, and some results suggest that all the three are in fact inferior to PLF. The intention of the review was to perform a meta-analysis. This was not possible because of the limitations in the reports of the studies and the heterogeneity of the patients and treatments used. The results do

Table 4 Study characteristics—randomised studies comparing instrumented with non-instrumented posterolateral fusion

Study	Treatments (fusion technique)	Sample size	Age included	Grades included	Levels	Follow-up	Decompression	Reduction	Clinical outcome	Fusion	Complications	Van Tulder score
Moller [28]	PLF (IC)	41	39	I–III	L4–S1	2 Years	Mixed	?	66%	78%	1 Blind in one eye	8
	PLF (IC + CDI)	39	39						83%	65%	2 Revisions (persistent LBP); 2 revisions (L5 root damage with permanent sequelae)	
Thomsen [40]	PLF (IC)	19	NR	I–II	NR (subgr)	2 Years	Mixed	?	NR (subgr)	84%	NR (subgr)	6
	PLF (IC + CDI)	16	NR						NR (subgr)	73%	NR (subgr)	
McGuire [24]	PLF (IC)	14	32.8 (24–42)	I–II	L4–S1	> 2 Years	Yes	No	NR	72%	4 Revisions	4
	PLF (IC + VSP plate)	13	34.6 (24–42)						NR	78%	2 Revisions	
France [11]	PLF (IC)	11	NR	< 33%	?	40 Months	?	No	63%	NR (subgr)	NR (subgr)	1
	PLF (IC + VSP plate)	16	NR						62%	NR (subgr)	NR (subgr)	

PLF posterolateral fusion, *NR* not reported, *IC* iliac crest autograft, *VSP* variable screw placement, *CDI* Cottrel–Dubousset instrumentation, *subgr* results were not reported for the required patient group

show us the likely results that are to be obtained by the techniques described.

Despite the limitations of the selected studies, we have attempted to answer the questions raised in the introduction.

Clinical outcomes

- *What is the clinical outcome after the surgical treatment of spondylolisthesis?* PLF and anterior interbody fusion yield comparable results with good or excellent clinical outcome in generally above 80% of the cases. These techniques should be weighed against each other with the radiological results and complication rate involved. Posterior interbody fusion was used and reported in only one study with good or excellent results in only 45% of the cases. Although this is a good-quality study, it is doubtful if the result is a reliable estimate for general results of posterior interbody fusion, but the technique should be used with caution and should be thoroughly monitored. Posterolateral foraminal decompression showed good or excellent clinical outcome for leg pain of 79% in one good-quality study and is thus promising, but this should also be closely monitored.
- *What are the complication rates of the techniques described in the studies?* The complication rate is highly variable among the studies. From the distribution of the complications, it appears that the threshold for an event to be called a complication differs among the studies. On the whole, the complication rate is lower for the less-invasive procedure PLF than for AIF and PIF.

Radiological outcomes

- *What are the fusion rates acquired with the fusion techniques described?* Fusion rates are generally above 80% for PLF and posterior interbody fusion. Three of the five studies using anterior interbody fusion observed fusion rates of 60% or less, although in a controlled study [19] the results were not found to be different from that of PLF.
- *How much correction is acquired with the procedure?* From the three studies [18, 23, 37] that reported the preoperative and postoperative degree of the listhesis, it appears that low-grade ($< 50\%$) listhesis can be reduced to some extent (12%), but complete reduction is rarely achieved. The cohorts included patients operated until 1993. It is likely that with current instrumentation techniques greater reduction is obtained, but the data to show this is not yet available.
- *How much correction is lost after reduction of the listhesis?* Average loss of reduction at follow-up was

Table 5 Study characteristics—randomised studies posterolateral fusion with alternatives

Study	Treatments (fusion technique)	Sample size	Age included Average (range)	Grades included	Levels included	Follow-up	Decom-pression	Reduction	Posterior Instrument	Clinical outcome	Fusion	Reoperations	Van Tulder score
Carragee [2]	PLF (IC/Allo + screw/rod)	8	32.6 (21–49)	I–II	L5–S1	4.5 Years	Yes	No	Yes	75%	88%	NR (subgr)	7
	PLF (IC/Allo + screw/rod)	12	34.0 (19–51)				No			100%	100%	NR (subgr)	
	PLF (IC/Allo)	10	30.0 (22–39)	I–II	L5–S1	4.5 Years	Yes	No	No	60%	70%	NR (subgr)	
	PLF (IC/Allo)	12	31.7 (24–46)				No			91%	100%	NR (subgr)	
Johnsson [16]	PLF (OP-1)	10	42.9 (27–57)	< 50%	L4–L5	1 Year	No	No	No	NR	60%	2 Revisions (remaining L5 movement)	7
	PLF (IC)	10	40.4 (23–53)							NR	80%	1 Revision	
Moller [29]	PLF (IC ± CDI)	77	39	I–III	L4–S1	2 Years	Mixed	?	Mixed	74%	NR	2 Revisions (persistent LBP); 2 revisions (L5 root damage with permanent sequelae)	5
	Exercise	34	37				No	No	No	43%	NA	0	
Christensen [5]	PLF (IC + CDI) + AIF	24	? (subgr)	I–II (subgr)	? (subgr)	2 Years	Mixed	?	Yes	NR (subgr)	NR (subgr)	NR (subgr)	4
	PLF (IC + CDI)	19	? (subgr)							NR (subgr)	NR (subgr)	NR (subgr)	

CDI Cottrell–Dubousset instrumentation, *PLF* posterolateral fusion, *IC* iliac crest, *Allo* allograft, *AIF* anterior interbody fusion with Brantigan cage, *subgr* results were not reported for the required patient group, *NR* not reported, *NA* not applicable

Table 6 Study characteristics—studies with consecutive inclusion in non-randomised studies with information about posterior instrumentation, decompression, and reduction

Study	Study type	*N*	Average age (range)	Grades included	Levels included	Type of treatment	Follow-up	Posterior instr.	Decom-pression	Reduction	Clinical outcome	Fusion	Comp-lications	Cowley score
Knight [20]	Prospective treatment series	24	42.2 (22–72)	I–III	L4–S1	Posterolateral endoscopic foraminal decompression	34 Months	No	Yes	No	79%	NR	2 Revisions	12
Verlooy [44]	Prospective treatment series	20	42 (21–70)	I	L4–S1	PIF (IC) + laminectomy, DE	42 Months	No	Yes	No	45%	80%	1 L5 paresis, 13 minor sensory disturbances	11
Suk [37]	Retrospective controlled treatment series	40	44 (30–60)	I–III	L3–S1	PLF (steffee/CDI/ diapason)	5.4 Years	Yes	Yes	Yes	95%	92.5%	6:3 Non-union, 2 instrument failure, 1 infection	7
	Retrospective controlled treatment series	36	44 (30–60)	I–III	L3–S1	PLF (VSP/ diapason) + PIF (IC)	3.3 years	Yes	Yes	Yes	98%	100%	2:1 Infection, 1 neurology	
Markwalder [23]	Prospective patient cohort	72	40 (15–65)	I–III	L4–S1	PLF (Lois plates/CDI)	26 Months	Yes	No	Yes	96%	100%	12 Removal of material	5
Kim [19]	Retrospective controlled patient cohort	20	44.1 (21–62)	I–II	L3–S1	AIF	3.6 Years	No	Yes	No	85%	90%	7:2 Warm leg, 2 paralytic ileus, 1 urinary retention, 2 delayed union	5
	Retrospective controlled patient cohort	20	41.3 (21–57)	I–II	L3–S1	PLF (PS + blockbone)	2.3 Years	Yes	No	No	90%	95%	1:Screw loosening	

CDI Cottrell–Dubousset instrumentation; *IC* iliac crest autograft, *PIF* posterior interbody fusion, *AIF* anterior interbody fusion, *NR* not reported, *PLF* posterolateral fusion, *DE* discectomy

Table 7 Results from studies that do not provide adequate information on the treatments undergone and studies without consecutive patient inclusion

Study	Patient selection	Consecutive?	#	Age	Grades	Levels	Treatments	Follow-up	Posterior instr.	Decompression	Reduction	Clincal	Fusion	Complications	Cowley total
Moon [30]	Retrospective	No	10	?	I–II	L4–S1	AIF (Anterior Bayley–Badgley cages + IC)	6 Years	No	?	?	NR	60%	4 Non-fusion, 6 graft collapse	6
Christensen [6]	Retrospective	Yes	57	?	I–II	L4–S1	AIF (IC (Thomasen))	5–13 Years	No	No	?	NR	47%	NR	4
Tsuji [41]	Retrospective	Yes	17	29.8 ± 11.8	20.2% ± 10.8	L4–S1	AIF (ilium graft)	7 Years	No	?	?	94%	53%	1 Nerve root irritation	7
Tsuji [41]	Retrospective	Yes	16	39.2 ± 9.7	19.7 ± 10.9	L4–S1	AIF (ilium graft) + interspinous block	7 Years	No	?	?	94%	88%	1 Nerve root irritation	7
Johnson [15]	Retrospective	Yes	34	?	I–II subgroup	?	Mixed	36 Months	Mixed	Yes	?	50%	No subgr	NR	0
Chen [4]	Retrospective	No	118	45.5 (27–62)	I–III	L4–S1	PIF (BAK cage ± PS + local morselised graft) + laminectomy	33 Months	Yes	?	?	NR	95%	31:4 Dural tear; 3 nerve root; 9 suboptimal position cage; 3 cage retropulsion; 4 cage subsidence; 2 arachnoiditis; 6 pseudoarthrosis	4
Boos [1]	Prospective	Yes	32	52 (20–76)	I–II	L3–S1	PLF (AO internal fixator)	45 Months	Yes	Mixed	Mixed	NR	NR	NR	6
Nooraie [31]	Retrospective	No	45	43.5 (23–56)	I–II	L4–S1	PLF (CDI + graft)	12 Months	Yes	Mixed	?	98%	95%	2 Screw breakage	4
Thalgott [39]	Retrospective	No	21	45 (25–59)	I–III	L4–S1	PLF (DC plates + screws + IC)	36 Months	Yes	Yes	No	81%	81%	8:3 Infections, seroma, screw breakage (ALIF), malpositioned screw (asymptomatic), 2 mild nerve root irritation	8
Kaneda [18]	Retrospective	No	53	43.5 (16–59)	I–III, 26 ± 11	L3–S1	PLF (distraction rod + IC)	3.5 Years	Yes	Mixed	?	92%	91%	5 Pseudoarthrosis	9
Hanley [14]	Retrospective	Yes	50	36.5 (10–67)	I–III	L4–S1	PLF (IC) ± Gill	40 Months	No	Mixed	?	60%	88%	6 Pseudoarthrosis	7
Ricciardi [33]	Retrospective	Yes	18	33 (17–51)	I–III	L5–S1	PLF (PS + plate + IC) + Gill laminectomy	30 Months	Yes	Yes	?	88%	94%	4:1 Screw backed out, 1 suture abscess, 1 paresthesias, 1 deep wound infection	12
Wang [45]	Retrospective	No	21	34 (24–42)	0–I	L3–S1	PLF (PS) + AIF (IC/Allo)	30 Months	Yes	Yes	?	95%	95%	1 Collapse resulted in fusion, 1 L5 nerve root damage	8
Schnee [34]	Retrospective	No	14	53.4 (24–77)	I–II	?	PLF (PS) + laminectomy	18 Months	Yes	Yes	No	NR	100%	7 Wound infections, 1 foot drop, 1 gastro-intestinal bleeding	5
Kamioka [17]	Retrospective	No	13	49 (12–67)	24%	L3–S1	PLF (Zimmer plate + PS + IC)	29 Months	Yes	Yes	Yes	NR	92%	2 Screw fracture	7
L'Heureux [21]	Retrospective	No	33	38 (21–60)	2–41%	L4–S1	PLF ± AIF ± instr.	24 Months	Mixed	Mixed	No	NR	NR	15 Complications + 11 revisions	9
Spruit [35]	Retrospective	No	12	? (23–54)	< 50%	L3–L5	PLF (PS) + AIF (syncage + lamina graft) + laminectomy	2.1 years	Yes	Yes	Yes	NR	100%	2:1 Urinary tract infection, 1 warm leg	13

NR not reported, *subgr* results were not reported for the required patient group, *CDI* Cottrell–Dubousset instrumentation, *IC* iliac crest, *PLF* posterolateral fusion, *PIF* posterior lumbar interbody fusion, *AIF* anterior lumbar interbody fusion

5.9% [18, 23, 37], which means that about half of the acquired reduction is again lost at follow-up.

– *What are the lordotic angles before and after the treatments?* The interpretation of the acquired lordotic angles is somewhat more problematic because firstly, we have to identify the desired angles after the procedure. And secondly, only two papers [23, 37] address this aspect, and the methods used are not described. There appears to be some change possible, but also recurrent hyper- or hypolordosis can occur.
– *Is there adjacent segment degeneration?* Although a recent literature review [32] especially identified the use of pedicle screws in lumbar fusion to be associated with adjacent segment disease, this question could not be addressed in this review as there was no mention of adjacent segment degeneration in any of the publications. It may be that the rate of adjacent segment degeneration is lower than in patient cohorts treated for discogenic low-back pain, as the disc degeneration in the spondylolisthesis patients is not the primary pathology.

Methodological remarks and limitations of the study

The present study was aimed solely at identifying published peer-reviewed literature, so that publication bias cannot be entirely ruled out. Our search was intended to be sensitive by defining broad search criteria and not permitting limitations. Also, we screened the reference lists of the selected articles to minimise publication bias. The criteria for the diagnoses allowed are relatively narrow with the intention to produce a homogeneous patient group. As a result, we have excluded studies that did not provide adequate description of the patient population. This might have introduced selection bias as studies with the required patient sample may have been excluded because of insufficient description of the diagnoses in the article.

For the best treatment available, only RCTs were used. Some studies with control groups were identified, but these could not be used as controlled trials as there was no mention of any attempt to match the patient groups. Consecutive patient selection or sufficient information about the treatments undergone was no selection criteria as the randomisation process maintains an equal distribution among the groups whatever the criteria have been.

For the outcome after the surgical treatment, we only used non-randomised studies. We did not include the results from the RCTs in this analysis as the rigorous selection criteria usually applied in the RCTs produce selection bias in the results. Therefore, RCTs do not allow for a valid assessment of treatment outcomes in general, but are only useful to identify the best treatment. A weak point about the non-controlled studies is

Table 8 Results from studies providing data on the percentage of the spondylolytic slippage and lordotic angles

Study	Treatments	Sample size	Decompression	Reduction	Discectomy	Posterior Instrumentation	Graft	Correction			Lordotic angles		
								Pre-operative	Post-operative	Follow-up	Preoperative	Postoperative	Follow-up
Markwalder [23]	PLF (Lois plates/CDI)	72	No	Yes	Yes	Yes	?	21%	7.8%	17%	41.1	32.8	35.8
Kaneda [18]	PLF (distraction rod + IC)	53	Mixed	?	No	Yes	IC	26% (±11)	17% (±9)	21% (±10)	L3S1:25 L2L5:21	18 16	–
Suk [37]	PLF (VSP/diapason) + PLIF (IC)	36	Yes	Yes	Yes	Yes	IC	27.9% (±9.7)	13.5% (±7.3)	16.3% (±8.8)	12.2	15.4	12.4
Suk [37]	PLF (steffee/CDI/diapason)	40	Yes	Yes	Yes	Yes	IC	28.3% (±13.2)	15.1% (±7.7)	20.3% (±8.5)	19.9	18.9	16.5

CDI Cottrell–Dubousset instrumentation, *IC* iliac crest, *PLF* posterolateral fusion, *PLIF* posteriorlumbar interbody fusion

that, although they can mention consecutive patient selection, they usually include patients indicated for a certain treatment ('consecutive treatment selection'). When there are multiple treatment options available, there has been a preceding selection process allocating patients to treatments according to their diagnosis. Ideally, all patients with a certain diagnosis should be included. A critical note, therefore, can be made by this present study that these consecutive treatment series were allowed, allowing the possibility for selection bias in assessing the outcome after surgical treatments.

Conclusions

Implications for practice

Posterolateral fusion appears to be the general gold standard for the treatment of adult isthmic low-grade lumbar spondylolisthesis, although there is no scientific evidence to support this choice. Further, only one randomised trial has shown superior results for PLF as compared to conservative treatment (exercises). The use of PLF or surgery for that matter as a gold standard is thus not supported by rigorous scientific evidence. Supplemental to PLF, there is still no evidence to support the use of posterior instrumentation as clinical and radiological outcomes are not better and complication rates are higher. Decompression has not proven to be necessary (and may be detrimental [2]), but may be used in the clinical setting in case of nerve root pain. However, nerve root pain may also be caused by a dynamic stenosis due to instability. This is addressed by fusing the motion segment , and this may already be sufficient to treat the nerve root pain without decompression.

The role of sagittal alignment and the related possible benefits of reduction (and therefore also instrumentation) of the listhesis have not been adequately studied. This is immensely important, as these factors may be confounding variables that have made it impossible for us to determine the optimum surgical treatment strategy, and they may well influence the long-term outcome.

Despite the unproven effect of instrumentation, reduction, or anterior column support, many surgeons now use these modalities. This may be unscientific, but it may well be based on the surgeons' empirical experience. This implies that due to improved surgical possibilities, we may in the future be able to show beneficial effects. The challenge for us, as the spine surgical community, is to prove this.

Implications for research

Based on this study, we recommend that the following RCT be conducted comparing the following three surgical interventions:

1. Un-instrumented PLF without reduction (control group)
2. Reduction with modern instrumented PLF
3. Reduction with modern instrumented PLF with anterior column support.

The report of the trial should adequately describe patient characteristics, treatments applied, and outcome parameters used.

As new studies arise and new techniques are reported upon, the evidence changes and should be evaluated. We have set the goal to update this review every 2 years.

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