#### **REVIEW ARTICLE**



# Clinical effectiveness of reduction and fusion versus in situ fusion in the management of degenerative lumbar spondylolisthesis: a systematic review and meta-analysis

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#### Abstract

**Purpose** To compare the clinical effectiveness of reduction and fusion with in situ fusion in the management of patients with degenerative lumbar spondylolisthesis (DLS).

**Methods** The systematic review was conducted following the PRISMA guidelines. Relevant studies were identified from PubMed, Embase, Scopus, Cochrane Library, ClinicalTrials.gov, and Google Scholar. The inclusion criteria were: (1) comparative studies of reduction and fusion versus in situ fusion for DLS patients, (2) outcomes reported as VAS/NRS, ODI, JOA score, operating time, blood loss, complication rate, fusion rate, or reoperation rate, (3) randomized controlled trials and observational studies published in English from the inception of the databases to January 2023. The exclusion criteria included: (1) reviews, case series, case reports, letters, and conference reports, (2) in vitro biomechanical studies and computational modeling studies, (3) no report on study outcomes. The risk of bias 2 (RoB2) tool and the Newcastle–Ottawa scale was conducted to assess the risk of bias of RCTs and observational studies, respectively.

**Results** Five studies with a total of 704 patients were included (375 reduction and fusion, 329 in situ fusion). Operating time was significantly longer in the reduction and fusion group compared to in situ fusion group (weighted mean difference 7.20; 95% confidence interval 0.19, 14.21; P = 0.04). No additional significant intergroup differences were noted in terms of other outcomes analyzed.

**Conclusion** While the reduction and fusion group demonstrated a statistically longer operating time compared to the in situ fusion group, the clinical significance of this difference was minimal. The findings suggest no substantial superiority of lumbar fusion with reduction over without reduction for the management of DLS.

Keywords Degenerative spondylolisthesis · Lumbar spine · Reduction and fusion · In situ fusion · Meta-analysis · Review

# Introduction

Degenerative lumbar spondylolisthesis (DLS) is a pathological condition of the lumbar spine characterized by the anterior displacement of a superior vertebra over the adjacent caudal vertebra, while the neural arch remains intact [1, 2]. This condition is prevalent in our aging society and poses a significant financial burden on the healthcare system [3, 4]. Conservative management, including physical therapy, motion restriction, and analgesics, is usually effective in alleviating symptoms. However, surgical intervention becomes necessary when clinical symptoms worsen or conservative treatments fail [5–7]. Decompression and fusion surgery have been shown to provide long-term pain relief and functional improvement for patients with DLS [8–10].

The primary goals of surgical management for DLS are decompression of the affected neural structures and stabilization of the spinal segment [11]. Furthermore, intraoperative reduction of slippage has gradually attracted the attention of researchers and generated lively discussion in recent years. The reduction procedure may contribute to reducing slip distance, increasing segmental lumbar lordosis and intervertebral disc height, and potentially lead

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to better clinical outcomes or a higher fusion rate [12-15]. Nonetheless, this additional step may also introduce potential complications, such as neurologic deficits, hardware failure (screw loosening or pull out), prolonged operating time, or loss of reduction [12, 16-19]. Therefore, it remains uncertain whether the benefits of the reduction procedure outweigh the associated risks and improve the clinical prognosis of patients with DLS.

Previous studies have yielded conflicting results regarding the necessity and effectiveness of reduction procedures in the surgical management of DLS. Wegmann et al. [20] reported that reduction of the slipped vertebra was associated with improved postoperative disability and quality of life in patients with DLS. Conversely, other researchers proposed that intraoperative reduction did not result in better improvement in clinical and radiological outcomes [21–23]. Consequently, the debate on the role of reduction in DLS surgery persists. Considering that patients with DLS are often older and more prone to poorer prognoses, a comprehensive evaluation of the clinical effectiveness of reduction and fusion compared to in situ fusion in managing DLS is warranted [24, 25]. Therefore, the purpose of this study is to compare the clinical outcomes of reduction and fusion versus in situ fusion in patients with DLS and provide insights into the most effective surgical approach for this condition.

## Methods

The systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) reporting guidelines [26]. The study protocol was registered in PROSPERO to strengthen transparency and reliability (CRD42023391484) [27].

#### Search strategy

A comprehensive independent and duplicate search was performed in PubMed, Embase, Scopus, Cochrane Library, ClinicalTrials.gov, and Google Scholar databases to identify studies comparing reduction and fusion with in situ fusion in the management of DLS. Studies published in English from the inception of the databases to January 2023 were considered for inclusion. Reference lists of the obtained literature were also searched for additional articles. The search strategies for each database are detailed in the Supplementary Materials (p. 4).

#### Study selection

The criteria of study selection were based on the PICOS principle [28] as follows:

- P (Population): Adult patients with DLS who underwent lumbar fusion surgery
- I (Intervention): Reduction and fusion surgery
- C (Comparison): In situ fusion surgery
- O (Outcomes): Visual analogue scale (VAS) or numerical rating scale (NRS) for back/leg pain, Oswestry disability index (ODI), Japanese Orthopedic Association (JOA) score, operating time, estimated blood loss (EBL), surgical complications (e.g., screws loosening or pulled out, surgical site infection, cerebral fluid leakage, etc.) and medical complications (e.g., pulmonary embolism, deep vein thrombosis, urinary tract infection, etc.), fusion rate, reoperation rate
- S (Study design): Randomized controlled trials (RCTs) and observational studies published in English from the inception of the databases to January 2023

The exclusion criteria included:

- (1) Reviews, case series, case reports, letters, and conference reports.
- In vitro biomechanical studies and computational modeling studies.
- (3) No report on study outcomes.
- (4) Studies with < 10 patients per group.

Two independent reviewers (D.F.W. and W.W.) assessed the potential studies. A third reviewer (X.L.C.) was consulted to resolve the discrepancies between the two reviewers.

#### Data extraction

Data extraction was conducted independently by two reviewers (D.H. and C.K.) from the included studies regarding the first author, publication date, study design, number of patients, age, sex, follow-up duration, and outcome data. When the mean and standard deviation values were not reported, an estimation was made according to sample size, median, range, or interquartile range [29]. A standardized data extraction table was used to record relevant data. Discrepancies in extraction were resolved by consensus.

#### **Risk of bias**

The assessment of the methodological quality of the included studies was conducted using two different tools. For RCTs, the risk of bias 2 (RoB2) tool was used to

determine the potential bias caused by the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, or selection of the reported result [30]. The overall bias was rated as "low risk," "high risk," or "some concerns." For cohort studies, the Newcastle–Ottawa scale (NOS) containing the selection of subjects, comparability of the groups, and assessment of outcomes was used for the quality assessment [31]. The quality of each study was graded as low (0–3), moderate (4–6), or high (7–9). Two reviewers (D.F.W. and W.W.) used criteria to score the quality of the studies independently and to judge whether the studies fulfilled the appropriate criteria for quantitative meta-analysis. Any discrepancy was resolved by consensus.

#### **Statistical analysis**

Continuous variables were analyzed by calculating the pooled weighted mean difference (WMD) with a 95% confidence interval (CI). Dichotomous variables were calculated by the pooled relative risk (RR) with 95% CI. A heterogeneity test was performed using  $I^2$  statistics.  $I^2 > 50\%$  was considered to indicate substantial heterogeneity, and the random-effect model was employed for the analysis. Inversely, a fixed-effect model was used for  $I^2 < 50\%$ . Subgroup analysis of RCTs versus observational studies was conducted to explore potential heterogeneity. The statistical tests were 2-sided, and significance was defined as an alpha of 0.05 unless otherwise specified.

Sensitivity analysis for all outcomes was performed using the leave-one-out approach to assess the robustness of the results [32]. Publication bias for all outcomes was statically tested using Egger's linear regression test [33]. A p value of more than 0.05 indicated no publication bias.

Review Manager version 5.4 (The Nordic Cochrane Center, The Cochrane Collaboration, Denmark) was used for the pooled analysis. STATA version 17.0 (StataCorp LLC, USA) was used for the sensitivity analysis and the assessment of publication bias.

#### **Quality of evidence**

The overall quality of the evidence for each outcome was evaluated using the approach recommended by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group [34]. The quality of evidence was downgraded by one or two levels according to the limitation of the study design, inconsistency, indirectness, imprecision of results, or apparent publication bias.

#### Results

## **Study selection**

In total, 823 articles were initially identified through the search strategy (Fig. 1). After the removal of 346 duplicate records, 477 studies remained for further screening. Eighteen articles were identified for full-text reading after screening for eligibility. Thereinto, 13 studies were excluded for various reasons, including two studies that enrolled both degenerative and isthmic spondylolisthesis, three systematic reviews, two studies with no available data, one study with patients < 10 per group, and five non-comparative studies. Accordingly, five studies, consisting of one RCT and four cohort studies, were finally included in the current meta-analysis.

#### **Characteristics of the included studies**

The five included studies described a total of 704 patients with DLS, with 375 (53.3%) patients undergoing reduction and fusion and 329 (46.7%) in situ fusion [12, 14, 16, 35, 36]. For the reduction and fusion group, the average age was  $61.35 \pm 9.87$  years, compared to  $62.34 \pm 11.54$  years for the in situ fusion group. In the reduction and fusion group, 248 (66.1%) patients were female, and the number of females in the in situ fusion cohort was 218 (66.3%). Forest plots of age and sex were exhibited in the Supplementary Materials (p. 5). The included studies reported an average follow-up of 30.08 months. Outcomes analyzed in this meta-analysis included back pain intensity, leg pain intensity, ODI, JOA score, EBL, operating time, complication rate, fusion rate, and reoperation rate. The detailed characteristics of each study are summarized in Table 1.

#### **Risk of bias**

The quality assessment of the included RCT [12] was performed using the RoB2 tool [30]. The study had a low risk of bias for the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result (Supplementary Materials, p. 6). The remaining five cohort studies were evaluated using the NOS and selected as high quality [31] (Table 2).





## **Clinical outcomes**

#### **Back pain**

Back pain intensity was reported in four studies, including one RCT and three cohort studies (Fig. 2) [12, 14, 35, 36]. VAS score was implemented to evaluate the pain intensity in three of the studies [12, 14, 35], while NRS score was used by Chan et al. [36]. In total, 422 patients were included in the meta-analysis. There was no significant difference between two groups based on the pooled results (WMD = 0.04; 95% CI [-0.17, 0.26];  $I^2 = 0\%$ , P = 0.70).

## Leg pain

Leg pain intensity was reported in two cohort studies with a total of 271 patients (Fig. 3) [14, 36]. No statistical difference in leg pain assessment was found between the reduction and fusion and the in situ fusion cohorts according to the pooled results (WMD = -0.41; 95% CI [-0.87, 0.06];  $I^2 = 28\%$ , P = 0.09).

## ODI

Data for the ODI were extracted from one RCT and three cohort studies containing 422 patients (Fig. 4) [12, 14, 35, 36]. Pooled analysis exhibited no significant difference in ODI between the reduction and fusion and in situ fusion cohorts (WMD – 3.64; 95% CI [-8.10, 0.82];  $I^2 = 69\%$ , P = 0.11). Nonetheless, patients who underwent reduction procedure exhibited a much lower ODI than those with in situ fusion in Heo et al.'s [14] study, which might account for the substantial heterogeneity of the pooled results.

## JOA score

JOA score was assessed in one RCT and one cohort study (Fig. 5) [12, 35]. A total of 151 patients were included in the meta-analysis. The JOA score showed no statistical

References	Country	Study design	No of patient:	s	Mean age (SD)		Gender (fem:	ile/male)	Outcomes	Follow-up (Months)
			Reduction	In situ	Reduction	In situ	Reduction	In situ		
Lian et al. [12]	China	RCT	36	37	74.3	73.8	22/14	23/14	1345678	Mean 33.2, range 24–54
Scheer et al. [16]	USA	PCS	162	120	61.68 (10.43)	61.88 (11.76)	114/48	84/36	66789	Minimum 12
Fan et al. [ <b>35</b> ]	China	RCS	41	37	60.95 (9.06)	59.81 (9.34)	31/10	24/13	0345678	Reduction 30.78/In situ 28.95
Heo et al. [14]	Korea	PCS	32	33	59.1 (9.9)	61.3 (10.1)	21/11	24/9	00300	Reduction 31.7/In situ 36.8
Chan et al. [36]	USA	PCS	104	102	61.3 (9.5)	63.7 (12.6)	60/44	63/39	02356789	Minimum 24
SD standard deviation	on, RCT rand	omized controlled	trial, PCS prosp	sective cohc	ort study, RCS retro	spective cohort stu	dy			

 Table 1
 Characteristics of the enrolled studies

Back pain intensity; @ Leg pain intensity; @ Oswestry Disability Index; @ Japanese Orthopedic Association score; @ Estimated blood loss; @ Operating time; @ Complication rate; @ Fusion rate; @ Reoperation rate Θ

difference between cohorts according to the combined results (WMD = -0.01; 95% CI [-0.64, 0.62];  $I^2 = 36\%$ , P = 0.97).

# EBL

One RCT and three cohort studies reported the differences in EBL between the reduction and fusion versus in situ fusion cohorts (Fig. 6) [12, 16, 35, 36]. Pooled data with substantial heterogeneity indicated that intraoperative EBL was not statistically different between cohorts (WMD 14.42; 95% CI [-43.81, 72.65];  $I^2 = 85\%$ , P = 0.63). Varied surgical techniques in the enrolled studies might induce the significant heterogeneity of the pooled results.

## **Operating time**

Operating time was reported in one RCT and three cohort studies (Fig. 7) [12, 16, 35, 36]. Data from 639 patients were included in the meta-analysis. Results showed that patients who underwent reduction and fusion took longer operating time than those who received in situ fusion (WMD 7.20; 95% CI [0.19, 14.21];  $I^2 = 0\%$ , P = 0.04).

#### **Complication rate**

The reported complication included adjacent-segment degeneration [12], surgical site infection [12, 14, 16, 35, 36], cerebral fluid leakage [12, 16, 35], delirium [12], pedicle screws pulled out [12], neuropathic pain [12], low back pain [12], numbness [12], wound hematoma [16], pulmonary embolism [16], deep vein thrombosis [16], urinary tract infection [16], cage retropulsion or expulsion [16], adjacent-segment disease [36], suture granuloma [36], and delayed wound healing [35].

The complication rate was mentioned in one RCT and four cohort studies, enrolling 704 patients (Fig. 8) [12, 14, 16, 35, 36]. The complication rate was 15.2% (57/375) and 11.6% (38/329) in the reduction and fusion and the in situ fusion cohorts, respectively. No significant difference was found between cohorts based on the pooled results (RR 1.26; 95% CI [0.86, 1.84];  $I^2 = 0\%$ , P = 0.23).

#### **Fusion rate**

Fusion state was assessed with flexion–extension radiographs at 1 year for all of the patients in the study by Scheer et al. [16], and the angle difference of < 5 between flexion and extension indicated solid fusion. The radiographic signs of solid fusion were defined as Birdwell grade I or II in the study by Fan et al. [35]. The definition of solid fusion was not specified in the rest studies [12, 36].

Items	Scheer et al. [16]	Fan et al. [35]	Heo et al. [14]	Chan et al. [36]
Selection				
Representativeness of the exposed cohort	1	1	1	1
Selection of the non-exposed cohort	0	0	0	0
Ascertainment of exposure	1	1	1	1
Demonstration that outcome of interest was not present at start of study	1	1	1	1
Comparability				
Comparability of cohorts on the basis of the design or analysis	2	2	2	2
Outcome				
Assessment of outcome	1	1	0	1
Was follow-up long enough for outcomes to occur	1	1	1	1
Adequacy of follow up of cohorts	0	1	1	1
Total	7	8	7	8
Grade of quality	High	High	High	High

 Table 2
 Risk of bias assessment for cohort studies (the Newcastle–Ottawa scale)



Fig. 2	Forest	plot illustratin	g back pair	n intensity	of reduction	and fusion	group and i	n situ fusion	group
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	Reductio	n and Fu	ision	In-sit	u Fus	ion		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Chan 2021	2.2	3.1	104	2.2	2.9	102	32.2%	0.00 [-0.82, 0.82]	
Heo 2019	1.6	1.3	32	2.2	1	33	67.8%	-0.60 [-1.17, -0.03]	
Total (95% CI)			136			135	100.0%	-0.41 [-0.87, 0.06]	
Heterogeneity: Chi <sup>2</sup> = Test for overall effect:	1.40, df = : Z = 1.71 (F	1 (P = 0.09)	.24); I <sup>2</sup> = )	= 28%					-2 -1 0 1 2 Reduction and Fusion In-situ Fusion

Fig. 3 Forest plot illustrating leg pain intensity of reduction and fusion group and in situ fusion group

Radiographic fusion status was assessed in one RCT and three cohort studies (Fig. 9) [12, 16, 35, 36]. A total of 639 cases were available for analysis. The reported fusion rate ranged from 84.6% to 100% and 70.8% to 100% in the reduction and fusion and the in situ fusion cohorts, respectively. Pooled analysis suggested fusion rate was not statistically different between cohorts (RR 1.07; 95% CI

[0.96, 1.20];  $I^2 = 85\%$ , P = 0.19). However, the reported surgical techniques were varied, containing posterior lumbar interbody fusion (PLIF) [12, 14, 36], transforaminal lumbar interbody fusion (TLIF) [16, 35], anterior lumbar interbody fusion (ALIF) [36], and lateral lumbar interbody fusion (LLIF) [36], which may induce the substantial heterogeneity.





	Reductio	n and Fi	ision	In-si	tu Fusi	ion		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Fan 2016	23.49	1.58	41	23.35	1.46	37	87.9%	0.14 [-0.53, 0.81]	— <b>———</b> —
Lian 2013	22.1	3.6	36	23.2	4.3	37	12.1%	-1.10 [-2.92, 0.72]	
Total (95% CI)			77			74	100.0%	-0.01 [-0.64, 0.62]	$\bullet$
Heterogeneity: Chi <sup>2</sup> =	1.57, df =	1 (P = 0.	21); I <sup>2</sup> =	36%					
Test for overall effect:	Z = 0.03 (	P = 0.97	)						Reduction and Fusion In-situ Fusion





Fig. 6 Forest plot illustrating EBL of reduction and fusion group and in situ fusion group

#### **Reoperation rate**

Data on the reoperation rate were extracted from three cohort studies (Fig. 10) [14, 16, 36]. The reoperation rate was 2.68% (8/298) and 3.52% (9/255) in the reduction and fusion and the in situ fusion cohorts, respectively. There was no significant difference between groups (RR 0.79; 95% CI 0.32, 1.98;  $I^2 = 0\%$ , P = 0.61).

#### **Subgroup analysis**

The prespecified subgroup analyses were performed for all outcomes according to the type of study. The results in all subgroup analyses were generally consistent with the main analysis (Figs. 2, 4, 6, 7, 8, 9).

	Reductio	on and Fu	sion	In-si	tu Fusio	on		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.6.1 RCT									
Lian 2013	126.5	23.3	36	118.6	17.5	37	54.8%	7.90 [-1.57, 17.37]	<b>↓</b> _ <b>∎</b>
Subtotal (95% CI)			36			37	54.8%	7.90 [-1.57, 17.37]	
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 1.63	(P = 0.10)							
1.6.2 Observational s	studies								
Chan 2021	203.3	76.2	104	193	67.5	102	12.7%	10.30 [-9.35, 29.95]	
Fan 2016	186.34	46.14	41	183.24	43.72	37	12.4%	3.10 [-16.85, 23.05]	
Scheer 2015	228.28	73.63	162	222.44	60.25	120	20.1%	5.84 [-9.80, 21.48]	
Subtotal (95% CI)			307			259	45.2%	6.35 [-4.08, 16.78]	
Heterogeneity: Chi <sup>2</sup> =	0.26, df =	2 (P = 0.1)	88); I <sup>2</sup> =	0%					
Test for overall effect:	Z = 1.19	(P = 0.23)							
Total (95% CI)			343			296	100.0%	7.20 [0.19, 14.21]	
Heterogeneity: Chi <sup>2</sup> =	0.31, df =	3 (P = 0.5)	96); I <sup>2</sup> =	0%				-	
Test for overall effect:	Z = 2.01	(P = 0.04)	.,						-20 -10 0 10 20
Test for subgroup diff	erences: C	$hi^2 = 0.05$	df = 1	(P = 0.8)	(3), $I^2 =$	0%			Reduction and Fusion In-situ Fusion



	Reduction and	Fusion	In-situ F	usion		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M–H, Fixed, 95% Cl
1.7.1 RCT							
Lian 2013	8	36	8	37	19.1%	1.03 [0.43, 2.44]	<b>_</b>
Subtotal (95% CI)		36		37	19.1%	1.03 [0.43, 2.44]	<b>•</b>
Total events	8		8				
Heterogeneity: Not a	oplicable						
Test for overall effect	Z = 0.06 (P = 0.06)	95)					
1.7.2 Observational	studies						
Chan 2021	10	104	9	102	22.0%	1.09 [0.46, 2.57]	<b>_</b>
Fan 2016	3	41	2	37	5.1%	1.35 [0.24, 7.66]	
Heo 2019	0	32	1	33	3.6%	0.34 [0.01, 8.13]	
Scheer 2015	36	162	18	120	50.1%	1.48 [0.89, 2.48]	
Subtotal (95% CI)		339		292	80.9%	1.32 [0.86, 2.01]	•
Total events	49		30				
Heterogeneity: Chi <sup>2</sup> =	= 1.08, df = 3 (P =	= 0.78); I <sup>2</sup>	= 0%				
Test for overall effect	Z = 1.28 (P = 0.1)	20)					
Total (95% CI)		375		329	100.0%	1.26 [0.86, 1.84]	●
Total events	57	_	38				
Heterogeneity: Chi <sup>2</sup> =	= 1.36, df = 4 (P =	= 0.85); I <sup>2</sup>	= 0%				
Test for overall effect	Z = 1.20 (P = 0.1)	23)		_			Reduction and Fusion In-situ Fusion
Test for subgroup dif	ferences: Chi <sup>2</sup> = (	).25, df =	1 (P = 0.6)	51), $ ^2 =$	0%		

Fig. 8 Forest plot illustrating complication rate of reduction and fusion group and in situ fusion group

#### Sensitivity analysis

For all outcomes, a leave-one-out sensitivity analysis was performed. A substantial change in outcome was observed in the overall pooled leg pain after the omission of Chan et al. [36]. Additionally, a significant change in the overall pooled operating time was found after removing the study by Lian et al. [12], Chan et al. [36], or Scheer et al. [16]. No significant changes were found in the other outcomes analyzed. The detailed results are listed in the Supplementary Materials (pp. 7–15).

## **Publication bias**

Publication bias for all outcomes was statically tested using Egger's linear regression test [33]. There is no evidence of publication bias according to the test (P > 0.05). The detailed results are summarized in the Supplementary Materials (pp. 16–22).

	Deduction and D		In site F			Diel Datie	Dial Datia
	Reduction and F	usion	In-situ Fi	usion		RISK RATIO	RISK RATIO
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.8.1 RCT							
Lian 2013	36	36	37	37	30.4%	1.00 [0.95, 1.05]	+
Subtotal (95% CI)		36		37	30.4%	1.00 [0.95, 1.05]	<b>♦</b>
Total events	36		37				
Heterogeneity: Not ap	oplicable						
Test for overall effect	Z = 0.00 (P = 1.0)	0)					
1.8.2 Observational	studies						
Chan 2021	102	104	97	102	30.4%	1.03 [0.98, 1.09]	
Fan 2016	38	41	30	37	17.3%	1.14 [0.96, 1.37]	
Scheer 2015	137	162	85	120	21.9%	1.19 [1.05, 1.36]	_ <b>_</b>
Subtotal (95% CI)		307		259	69.6%	1.11 [0.95, 1.29]	
Total events	277		212				
Heterogeneity: Tau <sup>2</sup> =	= 0.01; Chi <sup>2</sup> = 10.1	7, df =	2 (P = 0.00)	$(16); I^2 =$	80%		
Test for overall effect	Z = 1.37 (P = 0.1)	7)					
Total (95% CI)		343		296	100.0%	1.07 [0.96, 1.20]	◆
Total events	313		249				
Heterogeneity: Tau <sup>2</sup> =	= 0.01; Chi <sup>2</sup> = 20.3	88, df =	3 (P = 0.00)	001); I <sup>2</sup> =	= 85%		
Test for overall effect	: Z = 1.30 (P = 0.1	9)					Peduction and Eusion In-situ Eusion
Test for subaroup dif	ferences: $Chi^2 = 1$ .	66. df =	1 (P = 0.2)	$(20), 1^2 =$	39.9%		Neudelion and Fusion III-Silu Fusion

Fig. 9 Forest plot illustrating fusion rate of reduction and fusion group and in situ fusion group

	Reduction and I	Fusion	In-situ F	usion		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Chan 2021	4	104	5	102	50.6%	0.78 [0.22, 2.84]	
Heo 2019	0	32	1	33	14.8%	0.34 [0.01, 8.13]	
Scheer 2015	4	162	3	120	34.6%	0.99 [0.23, 4.33]	<b>+</b>
Total (95% CI)		298		255	100.0%	0.79 [0.32, 1.98]	-
Total events	8		9				
Heterogeneity: Chi <sup>2</sup> =	= 0.35, df = 2 (P =	0.84); I <sup>2</sup>	= 0%				
Test for overall effect	Z = 0.50 (P = 0.6)	51)					Reduction and Fusion In-situ Fusion

Fig. 10 Forest plot illustrating reoperation rate of reduction and fusion group and in situ fusion group

#### Grading the evidence

According to the assessment results of the GRADE approach [34], the strength of evidence was found to be moderate for complication rate and operating time; low for back pain intensity, JOA score, and reoperation rate; very low for leg pain, ODI, EBL, and fusion rate. Figure 11 summarizes the overall recommendation for each outcome.

## Discussion

No consensus has been reached regarding the surgical methodology for DLS. Several published reviews have compared the prognosis of fusion surgery with and without reduction procedure, but none restricted the pathology of DLS [37–40]. To our best knowledge, this is the first meta-analysis to evaluate the effect of reduction procedure on clinical outcomes focusing on patients with DLS by analyzing the findings of five comparative studies (one RCT and four observational studies), with a total of 704 patients enrolled. From the currently available data, this meta-analysis does not show significant superiority of reduction and fusion as compared with in situ fusion for the treatment of DLS.

Very low/Low-quality evidence supported that back/leg pain intensity, ODI, and JOA score were not statistically different between the reduction and fusion and in situ fusion groups (Fig. 11). Reduction during surgery is appealing as it may contribute to indirect decompression by restoring the spinal anatomy and disc space, but this alteration may be minimal since the degree of slippage was grade I or II in the majority of DLS patients [5]. The improvement of clinical outcomes still relies more on the decompression procedure during surgery in those patients, which may further mask the potential benefits of the reduction procedure [41, 42]. Published studies with various types of lumbar spondylolisthesis have also reported no clear association between the reduction of slippage and improved clinical outcomes [22, 37, 38]. However, the availability of the outcome data is limited in this meta-analysis. Pain intensity and ODI were reported in four studies, while the JOA score was mentioned in only three. Furthermore, different pain assessment tools (NRS and VAS) were used across studies, and in two studies [12, 35], it was not explicitly specified whether the pain

		Certainty a	issessment			N₂ of p	atients	Effec	t	
N₂ of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Reduction and Fusion	In-situ Fusion	Relative (95% CI)	Absolute (95% CI)	Certainty
Back pain										
4	not serious	not serious	not serious	very serious	none	213	209	-	MD <b>0.04</b> higher (0.17 lower to 0.26 higher)	
Leg pain										
2	not serious	very serious	not serious	serious	none	136	135	-	MD <b>0.41</b> lower (0.87 lower to 0.06 higher)	OCO Very low
ODI	•		•			•				
4	not serious	serious	not serious	very serious	none	213	209	-	MD <b>3.64</b> lower (8.1 lower to 0.82 higher)	HOOO Very low
JOA score										
2	not serious	serious	not serious	serious	none	77	74	-	MD 0.01 lower (0.64 lower to 0.62 higher)	
Estimated b	lood loss	•	•							
4	not serious	very serious	not serious	serious	none	343	296	-	MD <b>14.42</b> higher (43.81 lower to 72.65 higher)	⊕OOO Very low
Operating ti	me									
4	not serious	not serious	not serious	serious	none	343	296	-	MD <b>7.2 higher</b> (0.19 higher to 14.21 higher)	⊕⊕⊕⊖ Moderate
Complicatio	n rate	•	•			•				
5	not serious	not serious	not serious	serious	none	57/375 (15.2%)	38/329 (11.6%)	<b>RR 1.26</b> (0.86 to 1.84)	<b>30 more per</b> <b>1,000</b> (from 16 fewer to 97 more)	Hoderate
Fusion rate										
4	not serious	very serious	not serious	serious	none	313/343 (91.3%)	249/296 (84.1%)	<b>RR 1.07</b> (0.96 to 1.20)	<b>59 more per</b> <b>1,000</b> (from 34 fewer to 168 more)	Usery low
Reoperation	n rate									
3	not serious	not serious	not serious	very serious	none	8/298 (2.7%)	9/255 (3.5%)	<b>RR 0.79</b> (0.32 to 1.98)	7 fewer per 1,000 (from 24 fewer to 35 more)	
CI: confiden	ce interval: MD: n	hean difference: RE	risk ratio							

Fig. 11 Grading the strength of evidence according to GRADE approach

assessment referred to leg or back pain. The corresponding data was taken as the result of back pain assessment in this meta-analysis after meticulous evaluation of the full-text. Overall, solid conclusions on differences in clinical scores for reduction and fusion in situ cannot be drawn with such limited data.

Very low-quality evidence suggested that the reduction procedure did not result in higher EBL, while moderatequality evidence showed that the mean operating time was 7.2 min longer in the reduction and fusion group (Fig. 11). We think the additional steps of distracting and lifting during the reduction technique may be responsible for the discrepancy in operating time [12, 43–45], but this statistically significant difference is likely not clinically significant. Furthermore, different surgical procedures were conducted in the enrolled studies, including PLIF, TLIF, ALIF, and LLIF, which increased clinical heterogeneity and therefore limited generalizability of the pooled results. Future systematic reviews with subgroup analyses based on these factors are exceedingly desired. Moderate-quality evidence indicated that the overall complication rate was not statistically different between the reduction and fusion and in situ fusion groups (Fig. 11). The reduction-related complication was only mentioned in the study by Lian et al. [12], in which the pedicle screws in the slipped vertebra were pulled out during intraoperative reduction, and bone cement had to be used to support the screws in two patients. Moreover, very low-quality evidence revealed that the reduction and fusion group had no significant advantage in improving the fusion rate (Fig. 11). Considering the difference in documenting postoperative complication, assessing degree of fusion, and surgical techniques among the included studies, the reported results should be interpreted with caution.

Low-quality evidence exhibited that the reoperation rate was not significantly different between groups (Fig. 11). Patients underwent reoperation because of adjacent segment disease [36], surgical site infection [14, 36], and suture granuloma [36]. The reason of reoperation was not explicitly stated in the study by Scheer et al. [16]. Therefore, no definite association between reduction procedure and reoperation can be drawn based on the current result.

There are multiple other factors that may lead to biased results. First, the degree of slippage before surgery was limited to Meyerding grade I in the study by Chan et al. [36], while it was not restrained or described in detail in the other studies. Second, the follow-up duration of the included studies was not sufficient to assess long-term clinical outcomes. Third, bone mineral density (BMD) was mentioned in none of the included studies. In a retrospective study involving 81 patients older than 60 years diagnosed with DLS or spinal stenosis, Andersen et al. [46] proposed that low BMD was associated with the development of DLS. Another research by Okuyama et al. [47] revealed that low BMD suggested a potentially increased risk of instability of the inserted pedicle screws. Furthermore, BMD is a frequently used and reliable indicator for diagnosing osteoporosis in clinical work [48]. As common comorbidity of patients with DLS, osteoporosis may have a negative effect on postoperative clinical outcomes and should be highly valued during the perioperative management [49, 50]. Thus, whether the slip should be reduced in patients with low BMD or even osteoporosis needs to be further investigated in future studies.

The present study is also restricted by few limitations. First, the majority of the included studies were observational studies, and the indicators assessed varied from one study to another. The limited articles and incomplete data might downgrade the evidence. Second, three of nine meta-analyses had  $I^2$  values of > 50% (ODI, EBL, and fusion rate), indicating substantial heterogeneity. Such results should be interpreted with caution. Third, the reviewers were not blinded to the authors and institutions during the quality assessments, which might have resulted in potential bias and might have affected the grading.

#### Implications for clinical practice

Though this meta-analysis indicates comparable clinical outcomes between the two cohorts, this does not imply that the additional reduction step is not worthwhile. Indeed, the reduction procedure leads to spinal canal and foramen widening, contributing to indirect decompression. Moreover, reduction and fusion maintains superior spinal sagittal alignment over in situ fusion, containing higher intervertebral disc height, segmental lordosis (SL), and lumbar lordosis (LL) [12–14]. In a prospective study enrolling 57 patients with DLS who underwent lumbar fusion surgery, Kuhta et al. [51] reported that obtaining adequate SL was correlated with favorable ODI 5 years postoperatively. Similarly, Takahashi et al. [52] showed that DLS patients with a higher increase in SL and LL were predisposed to a higher JOA recovery rate after lumbar fusion surgery for DLS. Furthermore, biomechanical analysis by Senteler et al. [53] revealed that a postoperative higher LL contributed to reducing shear stresses of the adjacent levels to prevent adjacent segment degeneration. Therefore, given the benefits of spinal sagittal realignment and the absence of increased adverse events, the application of the reduction procedure in treating DLS remains a viable consideration.

#### **Directions for future research**

While the current meta-analysis uncovered some nonsignificant differences between the two groups, it is important to acknowledge that these negative findings could be influenced by the substantial heterogeneity among the included primary studies. To minimize these inherent differences and enhance the reliability of future research, it is imperative to establish standardized protocols for patient selection, surgical procedures, and outcome assessment. Moreover, previous studies have highlighted a strong correlation between spinal sagittal alignment and clinical outcomes in patients with DLS [52, 54–56]. Therefore, future analysis should place greater emphasis on the radiographic assessment of DLS patients and investigate the impact of reduction and fusion on the restoration of spinal alignment and its subsequent effect on clinical prognosis. By exploring these aspects, we can further elucidate the potential benefits and limitations of reduction and fusion procedures and optimize their application in the management of DLS.

# Conclusion

The present study represents the first meta-analysis to specifically compare the clinical effectiveness of reduction and fusion versus in situ fusion in patients with preoperative pathology limited to DLS. Our analysis revealed that the operating time for the reduction procedure was longer compared to in situ fusion, although this difference may not hold significant clinical relevance. Based on the currently available data, our findings suggest no substantial superiority of reduction and fusion over in situ fusion in terms of improving the prognosis of DLS patients.

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#### Declarations

**Conflict of interest** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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