

# A Bayesian network meta-analysis of 5 different fusion surgical procedures for the treatment of lumbar spondylolisthesis

Linjun Tang, MS\*, Yong Wu, MS, Daping Jing, BM, Yong Xu, MS, Cheng Wang, MD, Jingjing Pan, MS

## Abstract

Lumbar fusion has been widely used to treat lumbar spondylolisthesis, which can be classified into 5 types according to its approach, including posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), posterolateral fusion plus anterior lumbar interbody fusion (PLFplusALIF), and posterolateral fusion plus posterior lumbar interbody fusion (PLFplusPLIF). Theoretically, each approach has its own advantages and disadvantages, however, no studies are available to compare them.

A network meta-analysis (NMA) was performed in this study and the results were illustrated by the mean difference (MD) or odds ratio (OR). Meanwhile, the preferable treatments were indicated using the surface under the cumulative ranking curve (SUCRA). All data were analyzed and graphs were plotted using R 3.4.1.

A total of 28 literatures were included in this meta-analysis. PLIF was the most effective treatment for pain relief. Conversely, TLIF was the most effective method for reducing vertebral slippage. For patients with isthmic spondylolisthesis (IS), PLIF performed the best in terms of Visual Analogue Scale (VAS) score, Oswestry Disability Index (ODI) score, fusion rate, blood loss, and complication rate. For patients with degenerative spondylolisthesis (DS), TLIF was the best from the points of view of VAS, complication rate, and vertebral slippage reduction.

PLIF and TLIF are identified as the optimal treatments for all lumbar spondylolisthesis cases, among which, PLIF may be the preferred choice for pain relief, while TLIF can offer the best outcomes in terms of vertebral slippage reduction. Furthermore, TLIF has displayed the best clinical outcomes and tolerability for DS patients.

**Abbreviations:** CI = confidence interval, DS = degenerative spondylolisthesis, IS = isthmic spondylolisthesis, MD = mean difference, NMA = network meta-analysis, ODI = Oswestry Disability Index, OR = odds ratio, PLF = posterolateral fusion, PLFplusALIF = posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF = posterolateral fusion plus posterior lumbar interbody fusion, PLIF = posterior lumbar interbody fusion, RCTs = randomized controlled trials, SUCRA = surface under the cumulative ranking curve, TLIF = transforaminal lumbar interbody fusion, VAS = Visual Analogue Scale.

**Keywords:** network meta-analysis, posterolateral fusion, posterior lumbar interbody fusion, spondylolisthesis, transforaminal lumbar interbody fusion

## 1. Introduction

Spondylolisthesis, defined as the forward slippage of one vertebra on another, has the most common types of degenerative

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spondylolisthesis (DS) and isthmic spondylolisthesis (IS). Typically, spondylolisthesis is associated with the symptoms of low back pain and leg pain, decreasing walking ability, and neurogenic claudication. The primary treatments for lumbar spondylolisthesis are non-surgical physiotherapy, motion restriction (by means of a lumbar brace) or analgesics. Moreover, surgical interventions are recommended when the symptoms cannot be relieved through conservative treatment. Among them, surgical fusion for lumbar spondylolisthesis is an important method for spinal stabilization, which can also reduce pain and alleviate disability in patients with chronic lower back pain.

Notably, a variety of surgical procedures have been extensively used to treat lumbar spondylolisthesis in adults with the development of surgical techniques, including posterolateral fusion (PLF), posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), posterolateral fusion plus anterior lumbar interbody fusion (PLFplusALIF), and posterolateral fusion plus posterior lumbar interbody fusion (PLFplusPLIF).<sup>[1–5]</sup> Typically, each surgical approach possesses their own merits and demerits. For example, PLFplusALIF has adopted a retroperitoneal approach to expose the anterior spine, which is thereby associated with increased risks of direct vascular injury and ureteral injury.<sup>[6]</sup> By contrast, PLIF is advantageous in preventing the vascular complications associated with PLFplusALIF, which also allows for better surgical exposure for neural

element decompression. However, PLIF will result in neurological complications due to the risk of retraction on thecal sac and nerve roots, with the reported postoperative neurological deficit rate of 9.0% to 24.6%.<sup>[17]</sup> With regard to TLIF, its transforaminal approach contributes to avoiding significant vascular complications, and has lower rates of neurological complications than those of PLIF. Nonetheless, TLIF will lead to extensive muscle retraction and dissection, potentially resulting in postoperative pain, delayed rehabilitation, and spinal impairment.<sup>[18]</sup>

Pairwise meta-analyses have been performed,<sup>[9–12]</sup> nevertheless, systematic summaries of the efficacy and safety of various fusion approaches for spondylolisthesis, as well as the discrepancies among these approaches are lacking. Network meta-analysis (NMA), also known as a comparison among multiple treatments, allows for synchronous data extraction and analysis from medical trials. Unlike conventional meta-analysis, NMA can simultaneously compare at least 3 interventions and provide strong evidence for the relative efficacy of each treatment based on the direct and indirect evidence.<sup>[13]</sup> This method has recently been utilized in many studies, aiming to assess and compare the effectiveness of various therapeutic interventions.<sup>[14–16]</sup> Importantly, it can provide a useful and comprehensive summary for treatment determination.

To select the optimal treatment, NMA was employed in this study to compare these treatments, and the total sample size was also expanded through combining relevant statistics from other trials to minimize bias. Noteworthy, Bayesian NMA is superior to the traditional analyses in comparing multiple treatments, since it combines both direct and indirect comparisons while providing a posterior probability distribution for distinguishing the subtle differences among treatments.<sup>[17]</sup> Thus, this study aimed to compare the radiological, operative, and clinical outcomes of PLIF, TLIF, PLF, ALIF, PLFplusPLIF, and PLFplusALIF in treating lumbar spondylolisthesis through a NMA.

## 2. Patients and methods

### 2.1. Retrieval strategy

The electronic databases, including PubMed, Web of Science, and the Cochrane database, were retrieved until June 2019, using the terms of spondylolisthesis, posterior interbody fusion, posterolateral fusion, anterior lumbar interbody fusion, posterior lumbar interbody fusion, transforaminal lumbar interbody fusion, randomized controlled trial, and comparative study. Typically, only the English-language citations were considered. In addition, each step of pooled analysis was conducted by 2 investigators independently, and any disagreement was settled by mutual discussion.

### 2.2. Eligibility Criteria

The literature inclusion criteria were as follows, studies enrolling 18-year-old or above subjects who underwent spinal fusion for lumbar spondylolisthesis, studies comparing any  $\geq 2$  of PLF, TLIF, PLIF, ALIF, PLFplusALIF, and PLFplusPLIF, studies reporting any of the following areas, including radiological outcomes (such as fusion rates and vertebral slippage reduction), clinical outcomes (like clinical satisfaction, Visual Analogue Scale [VAS], and Oswestry Disability Index [ODI] scores), operative outcomes (such as blood loss and operation time) and complications, and studies in which all included patients were

followed up for at least 1 year after surgery. At the same time, the study exclusion Criteria were as follows, duplicated studies, meta-analysis or NMA, and reviews, abstracts, or case reports.

### 2.3. Data extraction

Data, including name of the first author, year of publication, location of the study, year of the study, type of intervention, demographic characteristics (number, sex, and age), follow-up period, and outcomes, were extracted by 2 reviewers independently. Any disagreement between them was solved by the opinion from a third reviewer.

### 2.4. Statistical analysis

All statistical analyses and graphical procedures were conducted using the R software Version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria) in conjunction with the *gemtc* package. Bayesian NMA and the random-effects model were adopted throughout our analysis, due to the heterogeneity of the included studies with respect to study design, population selection, and follow-up period.<sup>[18]</sup> Dichotomous results were expressed as odds ratio (OR) with 95% confidence interval (CI), as for continuous outcomes, the mean difference (MD) was used to evaluate the treatment effects. Subsequently, network plots were graphed to describe the scale of published studies, meanwhile, the number of studies, including a direct comparison between 2 specific interventions, was also labeled. In addition, each therapy at each endpoint was ranked according to their surface under the cumulative ranking curve (SUCRA), which indicated the performance of each treatment.

### 2.5. Ethical consideration

This is a Bayesian network meta-analysis article, does not involve ethical review, and ethical approval is not necessary after inquiring the ethical review committee in our hospital.

## 3. Results

### 3.1. Baseline characteristics of the included studies

The flow diagram of literature selection was shown in Fig. 1. A total of 855 potentially relevant studies were retrieved from the above-mentioned databases. Among them, 798 references were removed, and the remaining 57 records were further screened according to their titles, abstracts, and contents. Finally, 6 randomized controlled trials (RCTs) and 22 observational studies involving 2494 participants were included in NMA.<sup>[1–5,19–40]</sup> The detail information was summarized in Table 1. These studies were published between 1997 and 2019. Moreover, the network of the enrolled trials comparing different interventions of sciatica treatments was shown in Fig. 2. Typically, the thickness of solid lines was proportional to the number of direct comparisons between 2 therapies, whereas the size of nodes was in proportion to the sample size involved in each therapy.

### 3.2. NMA

All eligible studies, including observational studies and RCTs, were included in NMA. The results were shown in Table 2 and Fig. 3. As could be observed, patients in PLIF group achieved better fusion rate than that in PLF group (OR = 3, 95% CI = 1.3–

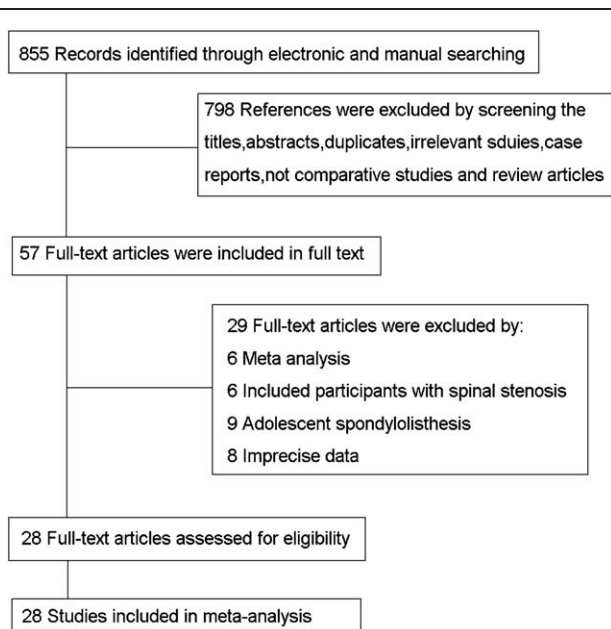


Figure 1. The flow diagram of study selection for the meta-analysis.

7.5). As for complication, TLIF group had a lower rate than that in PLF group (OR=0.22, 95% CI=0.065–0.78). With regard to VAS, both PLIF and TLIF group were superior to PLF group in reducing total pain (MD=−0.49, 95% CI=−0.91 to −0.11, MD=−0.61, 95% CI=−1.3 to −0.056, respectively). However, both PLFplusPLIF and PLFplusALIF groups had evidently increased operation time compared with that in PLF group (MD=80, 95% CI=37–120, MD=66, 95% CI=6.3–130, respectively). Meanwhile, comparison between interventions other than PLF group suggested that, TLIF was superior to PLFplusPLIF and PLFplusALIF in shortening the operation time (MD=−89, 95% CI=−150 to −28, MD=−75, 95% CI=−150 to −2.5, respectively). In addition, PLIF was also better than PLFplusPLIF in lessening the operation time (MD=−68, 95% CI=−120 to −12). Additionally, the complication rate was higher in TLIF group than in PLFplusPLIF group (OR=0.19, 95% CI=0.036–0.94). Besides, no statistically significant differences were observed in outcome clinical satisfaction, ODI, blood loss, and vertebral slippage reduction.

The evidence acquired from these RCTs showed high reliability, as a result, RCTs were selected from eligible studies using the same method (Table 2). Only 3 treatments were analyzed in the RCTs, including PLF, PLIF, and TLIF. However, there were no statistically significant differences among them.

On the other hand, subgroup analysis stratified by entity was also performed, and DS and IS were selected from eligible studies using the same method (Table S1, <http://links.lww.com/MD/E3>). For IS patients, the operation time in PLFplusALIF group was markedly longer than that in PLF group (MD=66, 95% CI=0.039–130). For DS patients, no statistically significant differences were observed among all outcomes.

### 3.3. Ranking results

NMA has one distinctive advantage based on the Bayesian Framework, which is its ability to rank the corresponding interventions using their corresponding SUCRA values (Fig. 4).

SUCRA results were presented in Table 3. Typically, a higher SUCRA value indicated a better result for clinical satisfaction, fusion rate, and vertebral slippage reduction. In contrast, a higher SUCRA value would suggest a worse result for complication rate, ODI, VAS, blood loss, and operation time. Results from observational studies and RCTs showed that PLIF was the most efficacious treatment for pain relief, which could acquire the best VAS results and the lowest complication rate. In comparison, TLIF had the most beneficial effects on daily function ODI, fusion rate, blood loss, and vertebral slippage reduction. Moreover, PLF would require the shortest operation time. PLFplusALIF ranked the first in terms of satisfaction rate. On the other hand, TLIF also exhibited good performance in VAS, blood loss, operation time, and satisfaction. However, results from RCTs alone were different. Specifically, PLIF ranked the first in VAS, ODI, satisfaction, fusion rate, and vertebral slippage reduction, while TLIF ranked the first in blood loss, and PLF would achieve the best effects on complication rate and operation time.

For IS patients, PLIF performed the best in VAS, ODI, fusion rate, blood loss, and complication rate, while TLIF had the most beneficial effect on vertebral slippage reduction. For DS patients, TLIF achieved the best effects on VAS, complication rate, and vertebral slippage reduction. Meanwhile, PLIF still had a higher fusion rate, and PLFplusPLIF ranked the first in ODI, while PLF was the best in blood loss and operation time.

### 3.4. Publication bias

Funnel plots were plotted to assess the publication bias, and the results indicated no publication bias among the eligible studies (Fig. 5).

## 4. Discussion

The most concerning aspects of patients include pain relief, quality of life, and ODI. Results from our NMA indicate that PLIF may be the preferred choice over other fusions for pain relief. Meanwhile, TLIF may be the best choice for vertebral slippage reduction. Furthermore, TLIF may display both the best clinical outcomes and tolerability for DS patients.

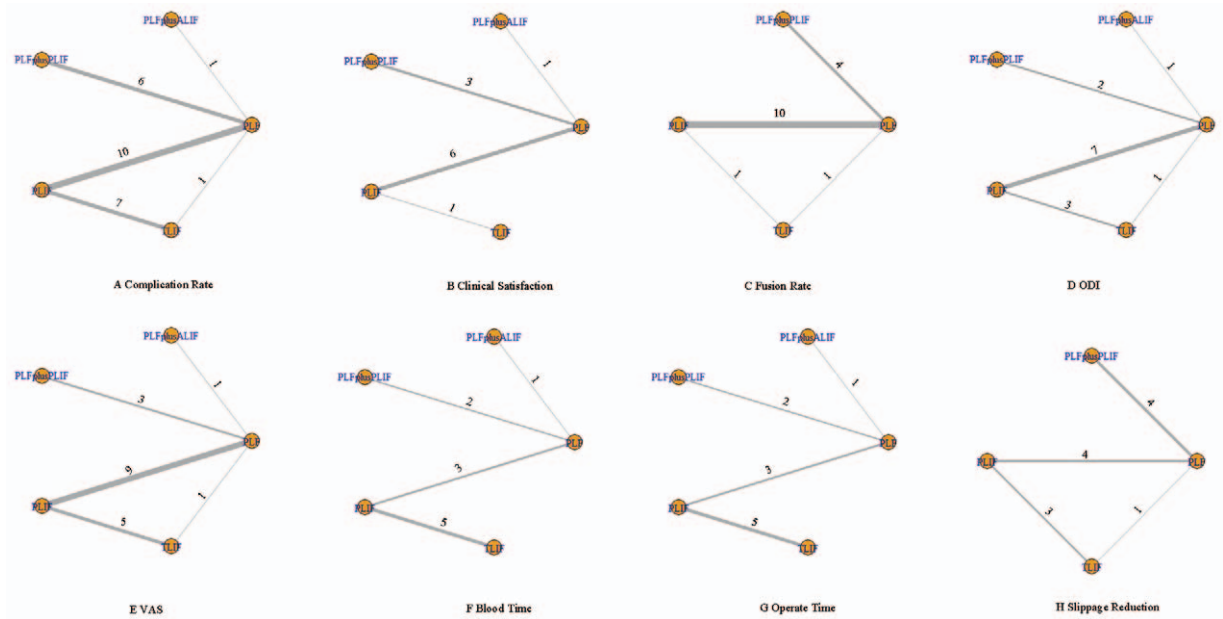
Adult spondylolisthesis is a radiographically identifiable condition, which can be revealed by the motion in lumbar segments. It is important to isolate the specific symptoms, signs, and functional disabilities to distinguish spondylolisthesis from other types of low-back pain and sciatica. Fusion is frequently performed to prevent potential further vertebral slippage and to stabilize the associated degenerative disc and arthritic facets, so as to improve or prevent back pain and possible instability. Traditional factors favoring fusion are improved spinal stability, minimized long-term back pain from the operated degenerative levels, and concern for recurrent leg pain from spondylolisthesis progression in the absence of fusion. An effective surgery for spondylolisthesis involves fusion of the fewest possible segments, minimized dislocation, adequate decompression, sagittal axis correction, and fusion accomplishment. To achieve these goals, the anterior, posterior, and combined approaches have been used. With the development of surgical techniques and instrumentation, many reduction procedures have been developed to reduce the spondylolisthetic deformity and restore the spinal balance. Our NMA discovers that PLIF and TLIF, which are more biomechanically stable since the bone graft is placed along the spine weight-bearing axis, are more effective on pain

**Table 1****Baseline characteristics of included studies.**

References	Country	Design	Diagnose	Group	Cases	Age, y	female	Duration of follow-up	Main outcomes
Mulsman 2011	Turkey	RCT	IS	PLF	25	47.3	16	3.3 yrs	①②③④⑤⑥⑦
				PLIF	25	50.6	17	3.3 yrs	
Lee 2014	Korea	RCT	IS	PLF	39	53.4	18	39.7 mos	①③④⑤⑥⑦
				PLIF	42	53.7	19	36.4 mos	
Farrokhi 2012	Iran	RCT	IS	PLF	40	49.66	30	1 yr	①③④⑤⑥
				PLIF	40	50.35	31	1 yr	
Inamdar 2006	India	RCT	DS+IS+TS	PLF	11	44.7	–	1 yr	①②③④⑧
				PLIF	11	41.4	–	1 yr	
Cheng 2009	China	RCT	DS+IS	PLF	68	48	32	4 yrs	①②③④⑥
				PLIF	70	49	31	4 yrs	
Yang 2016	China	RCT	IS	PLIF	32	43.4	20	30.5 mos	①④⑤⑥⑦⑧
				TLIF	34	43.4	19	30.5 mos	
de Kunder 2016	Netherlands	nRCT	DS+IS	PLIF	48	48	25	2 yrs	①⑥⑦
				TLIF	48	48	31	2 yrs	
Han 2016	China	nRCT	DS+IS	PLIF	26	57.31	10	20.81 mos	④⑤⑥⑦
				TLIF	36	59.69	16	18.73 mos	
Sakeb 2013	Bangladesh	nRCT	DS+IS	PLIF	52	46	41	1 yr	①⑤⑧
				TLIF	50	49	36	1 yr	
Fariborz 2016	Iran	nRCT	DS+IS	PLIF	30	35	–	1 yr	①
				TLIF	30	35	–	1 yr	
Yan 2008	China	nRCT	DS	PLIF	85	58.73	44	2 yrs	①⑤⑧
				TLIF	91	57.51	45	2 yrs	
Liu 2016	China	nRCT	DS	PLIF	125	55.05	85	2 yrs	①⑤⑥⑦
				TLIF	101	54.1	59	2 yrs	
Abdu 2009	USA	nRCT	DS	PLF	213	67.2	144	4 yrs	①③④⑥⑦
				PLFplusPLIF	63	59.7	50	4 yrs	
Ekman 2007	Sweden	nRCT	IS	PLF	77	39	39	2 yrs	①②⑧
				PLFplusPLIF	86	40	53	2 yrs	
Swan 2006	USA	nRCT	IS	PLF	46	43	23	2 yrs	①②④⑤⑥⑦⑧
				PLFplusALIF	47	42	25	2 yrs	
Madan 2002	United Kingdom	nRCT	SS	PLF	21	42.2	8	3.5 yrs	①②③④⑤⑧
				PLFplusPLIF	23	41.15	9	2.4 yrs	
Wang 2006	China	nRCT	DS+IS	PLF	24	53.4	16	34.8 mos	①②⑥⑦
				PLFplusPLIF	21	52.7	13	24.3 mos	
Suk 1997	Korea	nRCT	SS	PLF	40	44.4	29	5.4 yrs	①②③⑧
				PLFplusPLIF	36	–	–	3.3 yrs	
La Rosa 2003	Italy	nRCT	IS	PLF	18	58.6	7	5.2 yrs	⑤⑧
				PLFplusPLIF	21	57.2	7	2 yrs	
Dehoux 2004	France	nRCT	IS	PLF	25	42.4	11	6 yrs	①②③⑤⑦
				PLIF	27	39.5	12	6 yrs	
Zhao 2009	China	nRCT	DS+IS	PLF	14	71.3	–	16 mos	①③⑧
				PLIF	16	72.4	–	16 mos	
La Rosa 2001	Italy	nRCT	DS+IS	PLF	16	57	9	18 mos	①②③⑤⑧
				PLIF	14	57.4	7	18 mos	
Dantas 2007	Brasil	nRCT	DS+IS	PLF	30	52.4	13	2 yrs	①②⑤
				PLIF	30	47.6	20	2 yrs	
Cunningham 2013	Australia	nRCT	IS	PLF	21	46	4	121 mos	⑤
				PLIF	31	43	17	76 mos	
Gottschalk 2015	USA	nRCT	DS	PLF	68	69.9	40	2 yrs	①③④⑤
				PLFplusPLIF	111	64.9	65	2 yrs	
Fujimori 2015	USA	nRCT	DS	PLF	32	61	21	2 yrs	①③④⑤⑧
				TLIF	24	59	18	1.8 yrs	
Ha 2008	Korea	nRCT	DS	PLF	21	57.8	15	2 yrs	③④⑤⑧
				PLIF	19	57.8	14	2 yrs	
Barbanti 2010	Italy	nRCT	IS	PLF	43	49.3	24	62.1 mos	①③④⑤
				PLIF	28	55.1	14	62.1 mos	

DS = degenerative spondylolisthesis, IS = isthmic spondylolisthesis, nRCT = nonrandomized controlled trials, PLF = posterolateral fusion, PLFplusALIF = posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF = posterolateral fusion plus posterior lumbar interbody fusion, PLIF = posterior lumbar interbody fusion, RCT = randomized controlled trials, SS = spondylolytic spondylolisthesis, TLIF = transforaminal lumbar interbody fusion, TS = traumatic spondylolisthesis.

Main outcomes: ① complication rate ② clinical satisfaction ③ fusion rates ④ Oswestry disability index ⑤ back pain- Visual analog scale ⑥ blood loss ⑦ operative time. ⑧ reduction of slippage.



**Figure 2.** The network of the included trials comparing different interventional treatments for spondylolisthesis. Each node corresponded to a surgical procedure. Arrows indicated studies directly comparing between the agents shown using yellow circles. The numbers above the lines represented direct comparisons between 2 interventions. PLF = posterolateral fusion, PLIF = posterior lumbar interbody fusion, PLFplusALIF = posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF = posterolateral fusion plus posterior lumbar interbody fusion, RCTs = randomized controlled trials, TLIF = transforaminal lumbar interbody fusion.

**Table 2**  
**Results of network comparison.**

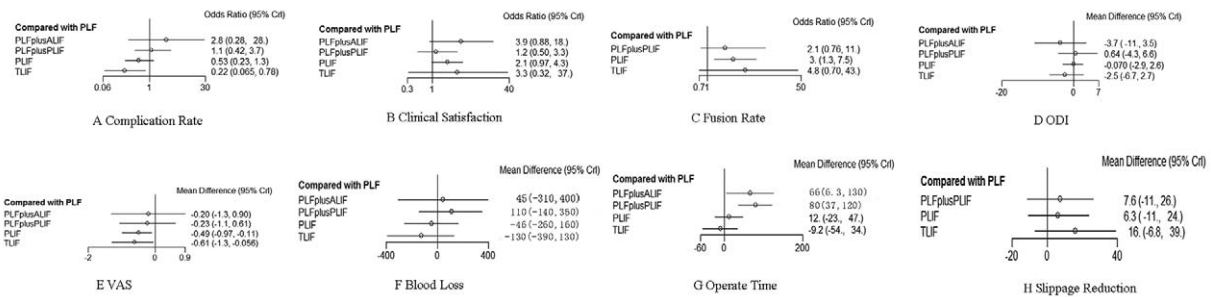
Complication rate						
nRCT+RCT	PLF	1.3 (0.25,10)	0.99 (0.015,90)	–	–	RCT
	0.53 (0.23,1.3)	PLIF	0.75 (0.015,36)	–	–	
	0.22 (0.065,0.78)	0.42 (0.16,1.1)	TLIF	–	–	
	1.1 (0.42,3.7)	2.1 (0.57,8.9)	5.2 (1.1,28)	PLFplusPLIF	–	
	2.8 (0.28,28)	5.3 (0.45,59)	13 (0.92,170)	2.5 (0.18,29)	PLFplusALIF	
Clinical satisfaction						
nRCT+RCT	PLF	1.6 (0.44,5.5)	–	–	–	RCT
	2.1 (0.97,4.3)	PLIF	–	–	–	
	3.3 (0.32,37)	1.6 (0.17,16)	TLIF	–	–	
	1.2 (0.5,3.3)	0.57 (0.19,2.2)	0.36 (0.029,4.8)	PLFplusPLIF	–	
	3.9 (0.88,18)	1.9 (0.36,10)	1.2 (0.073,19)	3.3 (0.52,19)	PLFplusALIF	
Fusion rates						
nRCT+RCT	PLF	2.3 (0.83,5.9)	–	–	–	RCT
	3 (1.3,7.5)	PLIF	–	–	–	
	4.8 (0.7,43)	1.6 (0.22,14)	TLIF	–	–	
	2.1 (0.76,11)	0.72 (0.19,4.4)	0.45 (0.042,5.9)	PLFplusPLIF	–	
ODI						
nRCT+RCT	PLF	–0.33 (–4.9,3.7)	–1.6 (–13,9.3)	–	–	RCT
	–0.07 (–2.9,2.6)	PLIF	–1.2 (–12,9)	–	–	
	–2.5 (–6.7,2.7)	–2.3 (–5.8,2.3)	TLIF	–	–	
	0.64 (–4.3,6.6)	0.72 (–4.8,7.5)	3 (–3.8,10)	PLFplusPLIF	–	
	–3.7 (–11,3.5)	–3.6 (–11,4.2)	–1.2 (–10,6.8)	–4.3 (–14,3.9)	PLFplusALIF	
VAS						
nRCT+RCT	PLF	–0.11 (–0.69,0.46)	0.82 (–3.3,4.9)	–	–	RCT
	–0.49 (–0.97,–0.11)	PLIF	0.94 (–3.2,5)	–	–	
	–0.61 (–1.3,–0.056)	–0.13 (–0.61,0.36)	TLIF	–	–	
	–0.23 (–1.1,0.61)	0.26 (–0.64,1.2)	0.38 (–0.6,1.5)	PLFplusPLIF	–	
	–0.2 (–1.3,0.9)	0.28 (–0.83,1.5)	0.41 (–0.79,1.7)	0.027 (–1.4,1.4)	PLFplusALIF	
Blood loss						
nRCT+RCT	PLF	–46 (–280,180)	–130 (–590,320)	–	–	RCT
	–46 (–260,160)	PLIF	–88 (–480,300)	–	–	
	–130 (–390,130)	–81 (–240,74)	TLIF	–	–	

(continued)

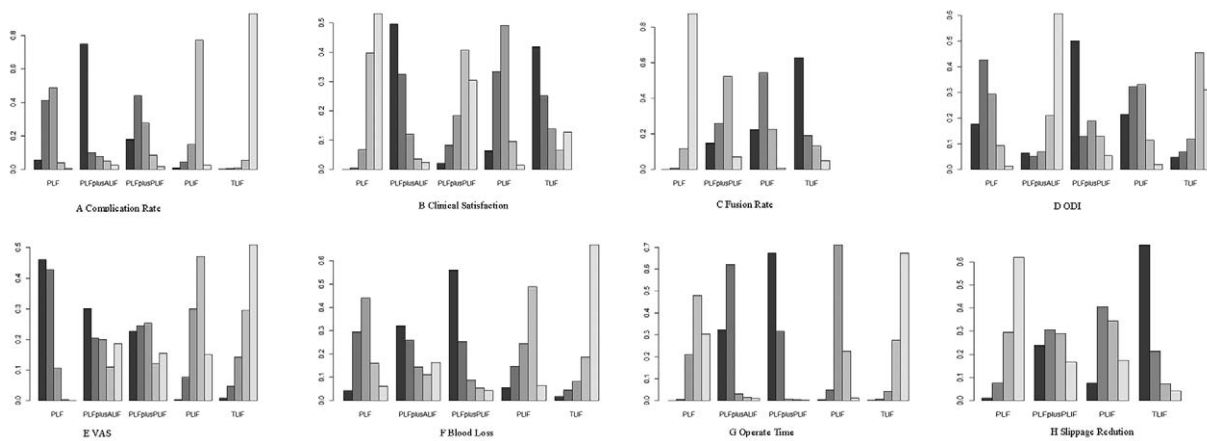
**Table 2**  
**(continued).**

	110 (-140,350)	160 (-170,470)	240 (-120,590)	PLFplusPLIF	-
	45 (-310,400)	90 (-320,500)	170 (-260,610)	-69 (-490,370)	PLFplusALIF
Operate time					
nRCT+RCT	PLF	13 (-15,40)	1.5 (-52,53)	-	-
	12 (-23,47)	PLIF	-12 (-56,33)	-	-
	-9.2 (-54,34)	-22 (-48,4.7)	TLIF	-	-
	80 (37,120)	68 (12,120)	89 (28,150)	PLFplusPLIF	-
	66 (6.3,130)	53 (-14,120)	75 (1.5,150)	-14 (-86,59)	PLFplusALIF
Vertebral slippage reduction					
nRCT+RCT	PLF	10 (-2.7,23)	6.6 (-12,25)	-	-
	6.3 (-11,24)	PLIF	-3.7 (-17,9.4)	-	-
	16 (-6.8,39)	9.7 (-9.7,29)	TLIF	-	-
	7.6 (-11,26)	1.3 (-24,27)	-9.7 (-29,9.7)	PLFplusPLIF	-

nRCT = nonrandomized controlled trials, ODI = Oswestry disability index scores, PLF = posterolateral fusion, PLFplusALIF = posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF = posterolateral fusion plus posterior lumbar interbody fusion, PLIF = posterior lumbar interbody fusion, RCT = randomized controlled trials, TLIF = transforaminal lumbar interbody fusion, VAS = visual analog scale.



**Figure 3.** Forest plots of all outcomes based on the observational studies and RCTs. A forest plot regarding the estimates of odds ratios (ORs, mean difference) between each treatment and the PLF group. ODI=Oswestry Disability Index scores, PLF=posterolateral fusion, PLIF=posterior lumbar interbody fusion, PLFplusALIF=posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF=posterolateral fusion plus posterior lumbar interbody fusion, RCTs= randomized controlled trials, TLIF=transforaminal lumbar interbody fusion, VAS=Visual Analogue Scale.



**Figure 4.** Rank probabilities of the clinical efficacy and performance status. The size of each bar corresponded to the probability of each treatment with a specific rank. A rank plot illustrating the empirical probabilities, in which each treatment was ranked as 1st through 5th (left to right). ODI=Oswestry Disability Index scores, PLF=posterolateral fusion, PLIF=posterior lumbar interbody fusion, PLFplusALIF=posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF= posterolateral fusion plus posterior lumbar interbody fusion, TLIF=transforaminal lumbar interbody fusion, VAS=Visual Analogue Scale.

relief and vertebral slippage reduction. The graft is therefore under maximal compression, with both the anterior and posterior columns under tension, thus enhancing the opportunity of arthrodesis.

Surgical techniques have been continuously modified and refined within the past several decades, such as minimizing the neural retraction level required and avoiding broad dissection of the paraspinal musculature during PLIF. These have contributed

**Table 3**  
**Surface under the cumulative ranking curve (SUCRA).**

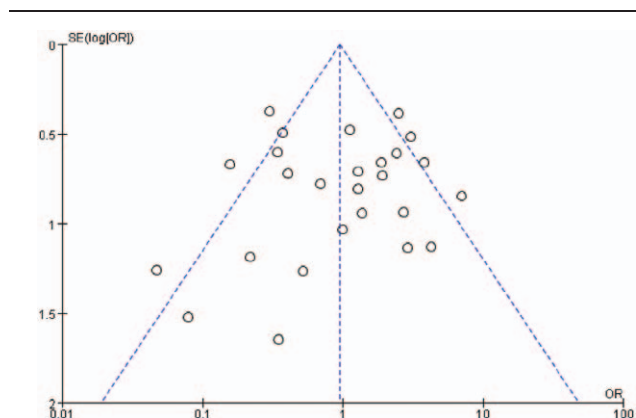
nRCT + RCT								
Complication	Satisfaction	Fusion rate	ODI	VAS	Blood loss	Time	Slippage reduction	
PLF	0.05792	0.00033	0.00015	0.17593	0.46145	0.04285	0.00005	0.01095
PLIF	0.00990	0.06458	0.22372	0.21375	0.00218	0.05620	0.00338	0.07620
TLIF	0.18065	0.41803	0.62867	0.04761	0.00845	0.01767	0.00128	0.67395
PLFplusPLIF	0.18065	0.02127	0.14745	0.50008	0.22650	0.56062	0.67211	0.23890
PLFplusALIF	0.75031	0.49576	–	0.06261	0.30141	0.32265	0.32316	–
RCT								
Complication	Satisfaction	Fusion rate	ODI	VAS	Blood loss	Time	Slippage reduction	
PLF	0.25237	0.20491	0.04863	0.42757	0.25322	0.56953	0.13491	0.03823
PLIF	0.35746	0.79508	0.95136	0.25781	0.10650	0.22632	0.59908	0.76572
TLIF	0.39016	–	–	0.31461	0.64027	0.20413	0.26600	0.19603
IS								
Complication	Satisfaction	Fusion rate	ODI	VAS	Blood loss	Time	Slippage reduction	
PLF	0.01346	0.00496	0.04462	0.49488	0.22613	0.22026	0.00416	0.01173
PLIF	0.00381	0.22922	0.95537	0.11902	0.01636	0.12472	0.05907	0.07601
TLIF	0.03511	–	–	0.23347	0.50685	0.13882	0.06918	0.66705
PLFplusPLIF	0.51376	0.05807	–	–	0.05916	–	–	0.24520
PLFplusALIF	0.43385	0.70773	–	0.15261	0.19148	0.51618	0.86757	–
DS								
Complication	Satisfaction	Fusion rate	ODI	VAS	Blood loss	Time	Slippage reduction	
PLF	0.68071	–	0.00091	0.18375	0.50195	0.01108	0.01032	0.05623
PLIF	0.28717	–	0.89266	0.31866	0.13710	0.07522	0.07592	0.23126
TLIF	0.00352	–	0.10167	0.41643	0.09218	0.67272	0.67358	0.71250
PLFplusPLIF	0.02858	–	0.00475	0.08115	0.26876	0.24096	0.24016	–

DS=degenerative spondylolisthesis, IS=isthmic spondylolisthesis, nRCT=nonrandomized controlled trials, ODI=Oswestry disability index scores, PLF=posterolateral fusion, PLFplusALIF=posterolateral fusion plus anterior lumbar interbody fusion, PLFplusPLIF=posterolateral fusion plus posterior lumbar interbody fusion, PLIF=posterior lumbar interbody fusion, RCT=randomized controlled trials, TLIF=transforaminal lumbar interbody fusion, VAS=visual analog scale.

to a reduction in the operation risks, operation time, and blood loss during PLIF.<sup>[37]</sup> During a PLF procedure, the broad dissection that exceeds the facet joint may lead to a transiently aggravated postoperative pain, which can further influence patient satisfaction on the procedure. Specifically, PLIF can overcome these drawbacks and provide anterior column support, which helps to restore lumbar lordosis, intervertebral space height, and increase fusion rate. However, a pairwise meta-analysis by de Kunder et al<sup>[10]</sup> showed that TLIF was

advantageous over PLIF in terms of complication rate, blood loss, and operation time.

The TLIF technique was described by Harms and Jenzszky<sup>[41]</sup> as a modification of the well-established PLIF procedure. Research by Humphreys et al<sup>[42]</sup> indicated that blood loss, length of stay, and operation time were lower in TLIF surgery than in PLIF. TLIF uses a posterior approach that runs through the distal lateral portion of the vertebral foramen and accesses the disc space. It provides the surgeon with a fusion procedure that may reduce many risks and limitations associated with PLIF, yet produce similar spinal stability. This contributes to reducing the incidence of postoperative radiculitis. Since the discovery of TLIF, spinal surgeons are endeavoring to decline the invasiveness of surgery, and to lessen the postoperative pain and recovery time. TLIF is usually performed through a unilateral approach preserving the contralateral interlaminar surface, which can be used as a site for additional fusion. As a minimally invasive technique, TLIF may result in a lower ODI score due to the less invasive approach and reduction of iatrogenic injury, which may be ascribed to the minimized surgical trauma through the use of tubular retractors and decreased dissection of paraspinal musculature.<sup>[43]</sup> However, results of RCTs alone show that PLIF may be more suitable than the other fusions for spondylolisthesis patients. TLIF and PLIF are 2 frequently used techniques for the surgical treatment of lumbar spondylolisthesis. Nowadays, the selection of technique is still greatly based on the surgeon preference and experience, since the evidence for superiority of one technique over the other is sparse.



**Figure 5.** Funnel plot to detect publication bias. No significant funnel asymmetry indicating publication bias was observed.

Nonetheless, our results should be interpreted with caution due to the limitations of the study. Firstly, comparisons between different treatments are mostly derived from indirect evidence, which can thereby hardly assess the consistency of results. Secondly, the random-effects model is used for NMA, and studies with relatively small populations may have disproportionate influence on the results, compared with others that have larger study populations. In addition, heterogeneities caused by the performance bias and reporting bias may also limit the reliability of our conclusions. Moreover, the long follow-up intervals among the included studies may lead to bias in this study. Thirdly, only 7 RCTs are included in this analysis, which is too small in number. Therefore, more RCTs on the effectiveness and safety would be needed. Fourthly, the follow-up period of 14 studies is not long enough, which is mostly <2 years. Fifthly, the included publications are from 1997 to 2019, and many factors that may influence the outcome of surgical treatment may have been changed during such a period of 22 years. TLIF appears at a relatively late time, which leads to the relatively small number of cases. Sixthly, pedicle stabilization is decisive in the amount of slippage reduction. However, no sufficient data about the role of pedicular screw stabilization can be obtained from the included studies. Other limitations also include the heterogeneity of techniques and the variability when it comes to surgical indication and surgeon experience.

## 5. Conclusion

This is the first study that applies NMA to compare the efficacy and safety of these 5 different approaches for treating spondylolisthesis. Our results suggest that PLIF and TLIF are identified as the optimal treatments for all lumbar spondylolisthesis. Concretely, PLIF may be the best option for pain relief, while TLIF may offer the best outcomes in vertebral slippage reduction. Furthermore, TLIF may display the best clinical outcomes and tolerability for DS patients. Nonetheless, well designed RCTs evaluating the safety, functional outcomes, and quality-of-life of patients following spondylolisthesis are needed, so as to make any practice recommendations.

## Author contributions

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**Investigation:** Daping Jing.

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**Supervision:** Cheng Wang.

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