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Original Article

Comparison of unilateral versus bilateral pedicle screw fixation in transforaminal lumbar interbody fusion: a systematic review and meta-analysis of twelve randomized controlled trials

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Abstract: Background: Transforaminal lumbar interbody fusion (TLIF) is one of the surgical options used for the treatment of lumbar degenerative disease. However, it still remains unknown whether TLIF with unilateral pedicle screw (PS) fixation is superior to that with bilateral PS fixation. This meta-analysis was performed to compare the relative benefits and risks of unilateral and bilateral PS fixation in TLIF for the treatment of lumbar degenerative disease. Methods: Medline, Embase, and the Cochrane Central Register of Controlled Trials databases were searched to identify relevant randomized controlled trials (RCTs). All data were analyzed by Review Manager 5.3 software. A random effect model was used for heterogeneous data; otherwise, a fixed effect model was used. Results: Eleven randomized and one quasi-randomized controlled trials were retrieved in the meta-analysis. Overall, there were significant differences between the two groups for operative time and blood loss. No significant differences were detected regarding fusion rate, total complication rate, dura tear, superficial wound infection, screw-related complications, reoperation rate, visual analog scale (VAS), Oswestry Disability Index (ODI), Japanese Orthopedic Association (JOA), the Short Form (36) Health Survey (SF-36) scores, and hospital stay. Conclusions: This meta-analysis showed that unilateral fixation group was superior to bilateral fixation group regarding operative time and blood loss. However, the results of fusion rate, total complication rate, specific complications, reoperation rate, functional outcomes and hospital stay were similar in the two groups. Therefore, the results of this study indicate that unilateral PS fixation in TLIF is a good alternative to bilateral PS fixation for the treatment of lumbar degenerative disease.

Keywords: Transforaminal lumbar interbody fusion, unilateral, bilateral, pedicle screw fixation, lumbar degenerative disease, meta-analysis

Introduction

Transforaminal lumbar interbody fusion (TLIF), initially described by Harms and Jeszenszky in the early 1990s [1], is increasingly popular as a surgical option to treat various lumbar degenerative diseases. It has the advantages of reducing the risk of excessive neural tissue retraction and epidural fibrosis when compared with a wider posterior lumbar interbody fusion (PLIF) approach [2, 3], as well as avoiding the potential complications associated with anterior lumbar interbody fusion (ALIF), such as iatrogenic damage to the great vessels or presacral sympathetic plexus [4, 5]. Generally, TLIF supplemented with bilateral pedicle screw (PS) fixation is a widely accepted method [6-12]. It provides stable environment of the fused segment for further interbody fusion and many studies have shown excellent clinical outcomes [6-10]. However, some studies have reported increased stiffness of bilateral fixation results in undesired adverse effects, including adjacent segment degeneration [13, 14] and implant-associated osteoporosis [15, 16]. Moreover, bilateral fixation carries the disadvantages of destruction of the contralateral elements, elevation in blood loss, operative time, and costs of implants. To reduce these adverse effects, many authors have advocated unilateral PS fixation and they have reported favorable clinical outcomes [17-21]. It remains unknown whether

unilateral or bilateral PS fixation with TLIF is more effective in the treatment of lumbar degenerative disease. Therefore, we performed a meta-analysis of the available literature to gain a better understanding of comparative effectiveness of unilateral and bilateral PS fixation in TLIF for lumbar degenerative disease.

Methods

Search strategy

The study was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) [22]. Medline (1946 to present), Embase (1974 to present), and the Cochrane Central Register of Controlled Trials databases were searched through April 2016 using combinations of such key terms as 'unilateral', 'transforaminal lumbar interbody fusion', 'posterior lumbar interbody fusion', 'TLIF', and 'PLIF' with the Boolean operators 'AND', 'NOT', and 'OR'. No linguistic restriction was imposed on the search as recommended by the Cochrane Back Review Group editorial board. The reference lists of selected articles and relevant reviews were also reviewed to identify studies not identified in the original search. Two investigators independently reviewed all subjects, abstracts, and the full text of articles that were potentially eligible based on abstract review. The eligible studies were then selected based on the eligibility criteria. Inconsistencies between investigators' data were resolved through discussion until a consensus was reached.

Inclusion and exclusion criteria

The following inclusion criteria were applied: (1) Randomized controlled trials (RCTs) or quasi-RCTs; (2) Subjects who had undergone transforaminal lumbar interbody fusion for lumbar degenerative disease; (3) The different interventions were unilateral and bilateral PS fixation; (4) At least one desirable outcome should be reported. Articles were excluded if they had any of following characteristics: (1) Subjects suffering from spinal trauma, tumor, deformities or systematic disorders, such as infectious disease, metabolic pathology, severe osteoporosis, and symptomatic vascular disease; (2) Subjects in unilateral PS fixation group were implanted with contralateral facet screw, interspinous process plate or other related implants simultaneously; (3) Studies in which unilateral group performed MIS-TLIF approach while bilateral group used open TLIF approach; (4) Biomechanical study, cadaveric study, comment, and case report; (5) Repeated studies.

Quality assessment

The methodological quality of all articles that met the eligibility criteria were assessed independently by two reviewers using a 12-item scale recommended by the Cochrane Back Review Group [23]. For each criterion, the reviewer's rating was categorized as "yes", "no", or "unsure". The studies were rated as having "low risk of bias" if at least 6 of the 12 criteria were met without serious flaws. Otherwise, the studies were rated as having "high risk of bias".

Data extraction

The data extracted included the following items: (1) Basic characteristics: study country, study year, study design, included diseases, enrolled and followed number, follow-up duration; (2) Baseline characteristics: mean age, gender proportion, mean height and weight, BMI, duration of symptoms, preoperative pain and functional scores; (3) Surgical information: surgical approach, fused level and level numbers, and graft use; (4) Primary outcomes: fusion rate, complication rate and reoperation rate; (5) Secondary outcomes including visual analog scale (VAS), Oswestry Disability Index (ODI), Japanese Orthopedic Association (JOA), and the Short Form (36) Health Survey (SF-36) scores; (6) Other outcomes: operative time, blood loss, hospital stay. The data were independently extracted by two reviewers and any discrepancies between the reviewers were discussed and resolved by consensus.

Data analysis

The analysis was carried out using Review Manager 5.3 software (Cochrane Collaboration, Oxford, UK). For dichotomous variables, the relative risk (RR) and 95% confidence intervals (CIs) were calculated. For continuous variables, the weighted mean differences (WMD) and 95% CIs were calculated. The level of significance was set at $P<0.05$. Standard errors, *P* values for differences in means, and interquartile ranges were transformed into standard deviation (SD), where necessary, according to

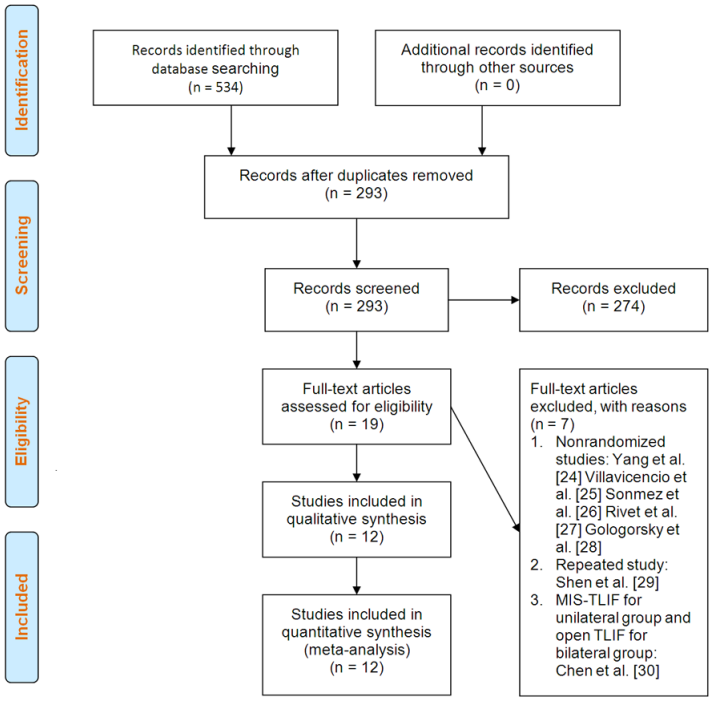

Figure 1. Study search and selection.

the method described by Cochrane Handbook for Systematic Reviews of Interventions. Heterogeneity was evaluated using I^2 statistics. An I^2 value<25% was considered to be homogeneous, between 25 and 50% to be of low heterogeneity, between 50 and 75% to be of moderate heterogeneity, and above 75% to be of high heterogeneity. A fixed effects model was used if there was no evidence of heterogeneity (I^2 value<25%) between studies. If there was evidence of heterogeneity (I^2 value ≥25%), a random effects model was used.

Results

Literature search

The details of literature search and selection are discussed in the **Figure 1**. A total of 534 articles were identified through three electronic database searches. After removal of duplicate and irrelevant articles by title and abstract review, 19 potential articles were retrieved for further full-text assessment. Among them, 7 articles were excluded because of not meeting the eligibility criteria [24-30]. Finally, 11 RCTs and 1 quasi-RCT involving 797 patients were included in the meta-analysis [31-42]. The details of demographic and clinical characteristics of patients are shown in **Tables 1** and **2**. No significant differences between the two groups were found in the baseline characteristics among these included studies (**Table 3**). For the unilateral group, the mean age ranged from 53.39 to 67 years, compared to 53.2 to 66.1 years for the bilateral group. The proportion of female patients ranged from 42.4% to 75% and 28.6% to 70% for unilateral and bilateral groups, respectively.

Quality assessment

The methodological quality of all included studies was presented in **Figure 2**. All thirteen studies were rated as having "low risk of bias".

Primary outcomes: fusion rate, complication rate, and reoperation rate

The fusion rate data was available in ten studies [32-38, 40-42]. No nonunion case was reported in four studies [37, 38, 40, 42] at the last follow-up assessment. Among them, nine studies [32, 33, 35-38, 40-42] had more than 24 months follow-up duration. Overall, there was no significant difference between the two groups (RR = 0.97; 95% CI: 0.94, 1.01; P=0.12; **Figure 3**). No heterogeneity was detected between these studies (I^2=0%; P=0.71). Sensitivity analysis with the removal of the study [34] of 12-month follow-up also revealed a similar trend (P=0.11). Ten studies [32-39, 41, 42] reported the complication data. The overall rate of total complications was similar between the unilateral (11.2%) and bilateral (10.2%) groups (RR=1.12; 95% CI: 0.74, 1.70; P=0.59; **Figure 4**). No statistical heterogeneity was detected among these studies (I^2=0%; P=0.68).As for specific complications, the data of dura tear, superficial wound infection, and screw-related complications were extracted. There were no significant differences between the two groups regarding dura tear (RR=0.86; 95% CI: 0.36, 2.06; P=0.73; **Figure 5**) [32, 33, 36-38, 42], superficial wound infection (RR=0.87;95% CI: 0.36, 2.11; P=0.75; **Figure 5**) [33, 34, 36, 38, 41, 42], and screw-related complications (RR=0.91; 95% CI: 0.27, 3.09; P=0.89; **Figure 5**) [33, 36-38]. No statistical heterogeneity was detected in these data. As for reoperation rate, our analysis showed there was no significant difference without sig-

Table 1. Characteristics of all included studies

Articles	Country	Year	Mean Age (Years)		Gender (% Female)		Followed / Enrolled Patients		Follow-up (Months)		Surgical Approach	Fused Levels	
			Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral	Unilateral	Bilateral		Unilateral	Bilateral
Feng et al.	China	2011	53.75	53.2	0.6	0.5	20/20	20/20	3		TLIF	1 level: L3-4: 1, L4-5: 11, L5-S1: 8	1 level: L3-4: 2, L4-5: 12, L5-S1: 6
Aoki et al.	Japan	2012	66.2	65.6	0.68	0.52	24/25	23/25	31	31.2	TLIF	1 level: L3-4: 4, L4-5: 21	1 level: L3-4: 5, L4-5: 20
Xue et al.	China	2012	57.1	58.2	0.541	0.581	37/37	43/43	25.3		TLIF	1 level: L3-4: 2, L4-5: 14, L5-S1: 13, 2 levels: L3-5: 3, L4-S1: 5	1 level: L3-4: 4, L4-5: 15, L5-S1: 12 2 levels: L3-5: 5, L4-S1: 7
Dahdaleh et al.	USA	2013	62.2	57.3	0.75	0.7	16/20	20/21	12.4	11.4	MIS-TLIF	1 level: L3-4: 1, L4-5: 12, L5-S1: 7	1 level: L3-4: 1, L4-5: 12, L5-S1: 3
Choi et al.	South Korea	2013	53.39	56.22	0.538	0.667	26/26	27/28	27.52	28.85	MIS-TLIF	1 level: L4-5: 20, L5-S1: 6	1 level: L3-4: 2, L4-5: 18, L5-S1: 7
Zhang et al.	China	2013	59.4	55.7	0.424	0.286	33/33	35/35	25.6		TLIF	2 levels: L2-4: 1, L3-5: 12, L4-S1: 20	2 levels: L2-4: 2, L3-5: 10, L4-S1: 23
Shen et al.	China	2013	57.3	58.9	0.452	0.529	31/31	34/34	26.6		MIS-TLIF	1 level: L4-5: 15, L5-S1: 16	1 level: L4-5: 15, L5-S1: 19
Gu et al.	China	2015	64.5	66.1	0.514	0.462	35/35	39/39	32.1	31.7	MIS-TLIF	2 levels: L3-5: 15, L4-S1: 20	2 levels: L3-5: 16, L4-S1: 23
Duncan et al.	USA	2012	53.5	55.7	0.565	0.642	46/57	56/59	25.1		TLIF	NA	NA
Dong et al.	China	2014	54	56.6	0.7	0.684	20/20	19/19	36		MIS-TLIF	1 level: L4-5: 13, L5-S1: 7	1 level: L4-5: 14, L5-S1: 5
Lin et al.	China	2013	67	65.5	0.442	0.476	43/43	42/42	26		MIS-TLIF	1 level: L3-4: 9, L4-5: 18, L5-S1: 16	1 level: L3-4: 9, L4-5: 19, L5-S1: 14
Xie et al.	China	2012	56.2	55	0.571	0.538	56/56	52/52	36-48		TLIF	1 level: L3-4: 10, L4-5: 20, L5-S1: 12 2 levels: L3-5: 6, L4-S1: 8	1 level: L3-4: 10, L4-5: 18, L5-S1: 12 2 levels: L3-5: 5, L4-S1: 7

MIS-TLIF: minimally invasive approach for transforaminal lumbar interbody fusion. NA: not available.

Table 2. The included diseases, outcomes, and definition of fusion

Articles	Included diseases	Significant outcomes	Insignificant outcomes	Definition of fusion
Feng et al.	LSS	NA	Operative time, Blood loss	NA
	LS (Grade I or II)		Hospital stay, JOA	
Aoki et al.	LS (Grade I or II)	Operative time, Blood loss	Fusion rate, Total complications	The presence of continuous trabecular bone formation through or outside the cages,<3° movement radiolucent on lateral flexion and extension radiographs, and the absence of lines around more than 50 % of the implant
		VAS-BP, VAS-LP	Dura tear, JOA, Reoperation rate	
Xue et al.	LSS, LS, LDH	NA	Fusion rate, Total complications, Dura tear, Screw-related complications	Continuous osseous trabeculations bridging the graft- transverse interface or stable fusion of the segment with between standards<4 mm of translation or<10° of angular motion adjacent end plates on lateral flexion-extension radiographs
	RLDH, DLBP		Superficial wound infection, VAS, ODI, Reoperation rate	
Dahdaleh et al.	LS (Grade I or II)	Blood loss	Fusion rate, Total complications, Superficial wound infection	Absence of angulation on dynamic flexion-extension radiographs, evidence of bridging bone, and absence of hardware lucency or migration
			VAS, ODI	
Choi et al.	LSS, LS, LDH	Operative time, Blood loss	Fusion rate, Total complications, Reoperation rate	The Bridwell system is composed of the following categories and grades: fused with remodeling and trabeculae present (Grade I); graft intact, not fully remodeled and incorporated, but no lucency present (Grade II); graft intact, potential lucency present at top and bottom of graft (Grade III); and fusion absent with collapse/resorption of the graft (Grade IV)
	RLDH			
Zhang et al.	LSS, LS, SDDD	Operative time, Blood loss	Fusion rate, Total complications, Screw-related complications	Bone bridging the disk space without lucency and<4° of angular motion on flexion-extension views between the fused segments
	FBS		Dura tear, Superficial wound infection, VAS, ODI, SF-36, Hospital stay	
Shen et al.	LDH, LSS, DLBP	Operative time, Blood loss	Fusion rate, Total complications, Dura tear	An absence of radiolucent lines covering>50% of either implant, translation of ≤3 mm and angulation<5° on flexion-extension bone radiographs, and continuous trabecular growth connecting the vertebral bodies on CT scan cut
		Hospital stay	Screw-related complications, VAS, ODI, Reoperation rate	
Gu et al.	LSS, LS	Operative time, Blood loss	Fusion rate, Total complications, Dura tear, Screw-related complications	Formation of trabecular bony bridges between contiguous vertebral bodies at the instrumented levels
			Superficial wound infection, VAS, ODI, Hospital stay	
Duncan et al.	LSS, LS, LDH	NA	Total complications	NA
Dong et al.	LS (Grade I or II)	Operative time, Blood loss	Fusion rate, Hospital stay	Formation of continuous trabecular bone observed in and around the fusion cage, or lumbar dynamic images showing<5° of intervertebral movement at the fused segment
	SDDD			
Lin et al.	LSS, LS, LDH	Operative time, Blood loss	Fusion rate, Total complications, Superficial wound infection, VAS, ODI	At least 3 of 4 criteria achieved: bony bridging, bony continuity between endplates, trabecular structure in the anterior bone bridge, and lack of radiolucent lines around implants.
Xie et al.	LSS, RLDH, SDDD	Operative time, Blood loss	Total complications, Dura tear, JOA, Superficial wound infection, SF-36	Radiographic evidence existed of bone bridging the disk space without lucency and the motion between the fused segments motion was<4° on flexion and extension views. >4° of motion or the presence of translation was considered a failure of fusion.
		Hospital stay		

LSS: lumbar spinal stenosis. LS: lumbar spondylolisthesis. LDH: lumbar disc herniation. RLDH: recurrent lumbar disc herniation. SDDD: symptomatic degenerative disc disease. DLBP: discogenic low back pain. FBS: failed back surgery. NA: not available.

Table 3. Comparison of baseline characteristics between unilateralgroup and bilateral group

Articles	Mean age	Gender	Follow-up time	Fused level	Preoperative diagnosis	Preoperative VAS	Preoperative functional scores (ODI, JOA, or SF-36 scores)	BMI	Mean height	Mean weight	Duration of symptoms
Feng et al.	*	*	*	*	*	*	*	NA	NA	NA	NA
Aoki et al.	*	*	*	*	NA	*	*	NA	NA	NA	NA
Xue et al.	*	*	NA	*	*	*	*	NA	NA	NA	NA
Dahdaleh et al.	*	*	*	*	NA	*	*	*	NA	NA	NA
Choi et al.	*	*	*	*	NA	*	*	NA	NA	NA	NA
Zhang et al.	*	*	NA	*	*	*	*	NA	NA	NA	*
Shen et al.	*	*	NA	*	*	*	*	NA	*	*	NA
Gu et al.	*	*	*	*	*	*	*	*	NA	NA	*
Duncan et al.	*	*	NA	NA	NA	NA	NA	NA	NA	NA	NA
Dong et al.	*	*	NA	*	*	NA	NA	NA	NA	NA	NA
Lin et al.	*	*	NA	*	*	*	*	NA	NA	NA	NA
Xie et al.	*	*	NA	*	*	*	*	NA	NA	NA	NA

VAS: Visual analog score. ODI: Oswestry Disability Index. JOA: Japanese Orthopedic Association. SF-36: the Short Form (36) Health Survey. BMI: Body Mass Index. *: Statistically insignificant (P>0.05). NA: not available.

	Feng et al.	Aoki et al.	Xue et al.	Dahdaleh et al.	Choi et al.	Zhang et al.	Shen et al.	Gu et al.	Duncan et al.	Dong et al.	Lin et al.	Xie et al.
Adequate randomization	Yes	Yes	Yes	Unsure	Unsure	Yes	Yes	No	Yes	Yes	Unsure	Yes
Allocation concealment	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Yes	Unsure	Unsure
Blinding of patients	No	No	No	No	No	No	No	No	No	No	No	No
Blinding of care providers	No	No	No	No	No	No	No	No	No	No	No	No
Blinding of outcome assessors	Unsure	Unsure	No	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Yes
Acceptable drop-out rate	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Intention-to-treatment analysis	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes
Free of selective reporting	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Similar baseline	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Avoided or similar co-interventions	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes
Acceptable compliance	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Similar timing of outcome assessment	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Total scores	8	6	8	6	6	8	8	7	6	8	6	9

Figure 2. Methodological quality assessment of all included studies.

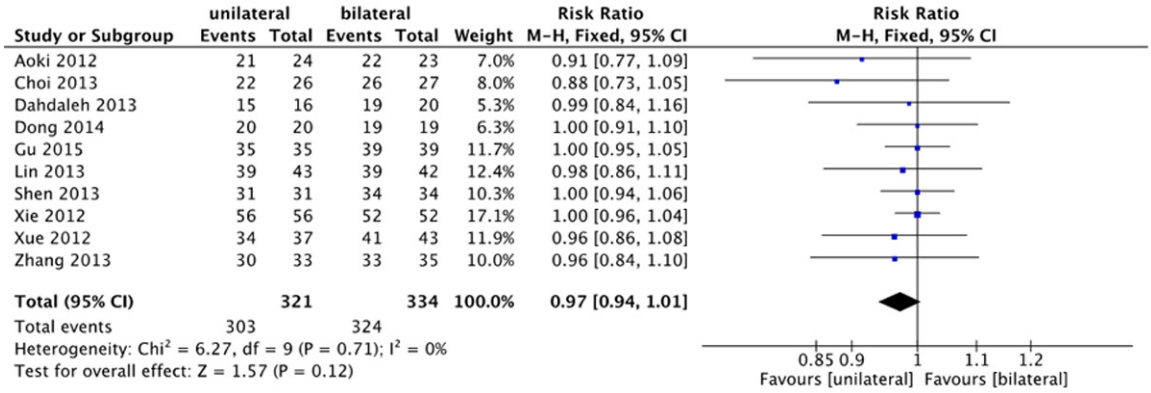

Figure 3. The forest plot for fusion rate.

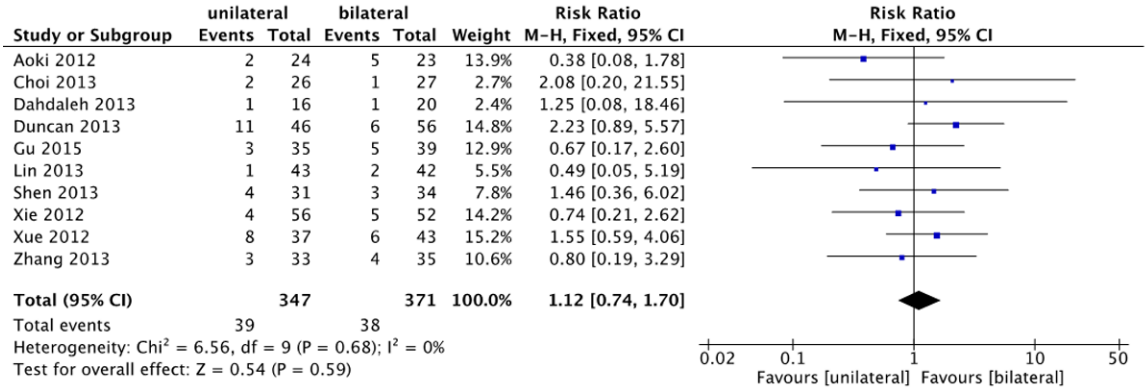

Figure 4. The forest plot for total complication rate.

nificant heterogeneity (RR=0.83; 95% CI: 0.21, 3.23; P=0.78; I^2=0%, P=0.70; **Figure 6**) [32, 33, 35, 37].

Secondary outcomes: VAS, ODI, JOA, and SF-36

Seven studies [32-34, 36-38, 41] reported VAS for back pain (VAS-BP) with adequate mean and corresponding SD. There was no significant difference between the two groups (WMD=0.03; 95% CI: -0.19, 0.24; P=0.81; **Figure 7**). VAS for leg pain (VAS-LP) was available in four studies [32, 34, 36, 38]. Pooled analysis revealed no significant difference (WMD=0.43; 95% CI: -0.26, 1.12; P=0.22; **Figure 7**). JOA scores were reported in three studies that performed open TLIF [31, 32, 42]. Overall, there was no significant difference with moderate heterogeneity (WMD=0.17; 95% CI: -0.73, 1.07; P=0.71; I2=59%; P=0.09; **Figure 7**). Six studies [33, 34, 36-38, 41] reported ODI values. There was no significant difference between the two groups (WMD=0.03; 95% CI: -0.36, 0.42; P=0.89) with no heterogeneity (I^2=0%; P=0.43; **Figure 8**). In addition, two studies [36, 42] reported the SF-36 scores. Pooled analysis showed no significant differences in physical function score (WMD=0.70; 95% CI: -3.19, 4.59; P=0.72; **Figure 8**), mental health score (WMD=1.12; 95% CI: -3.41, 5.64; P=0.63; **Figure 8**), and general health score (WMD=-0.62; 95% CI: -4.58, 3.35; P=0.76; **Figure 8**). No heterogeneity was detected among these data.

Other outcomes: operative time, blood loss, and hospital stay

Ten studies [31-37, 39-41] reported operative time. Pooled estimate revealed that unilateral group achieved significantly shorter operative time than bilateral group (WMD=-39.72; 95% CI: -58.12, -21.31; P<0.0001). The analysis of heterogeneity showed high heterogeneity

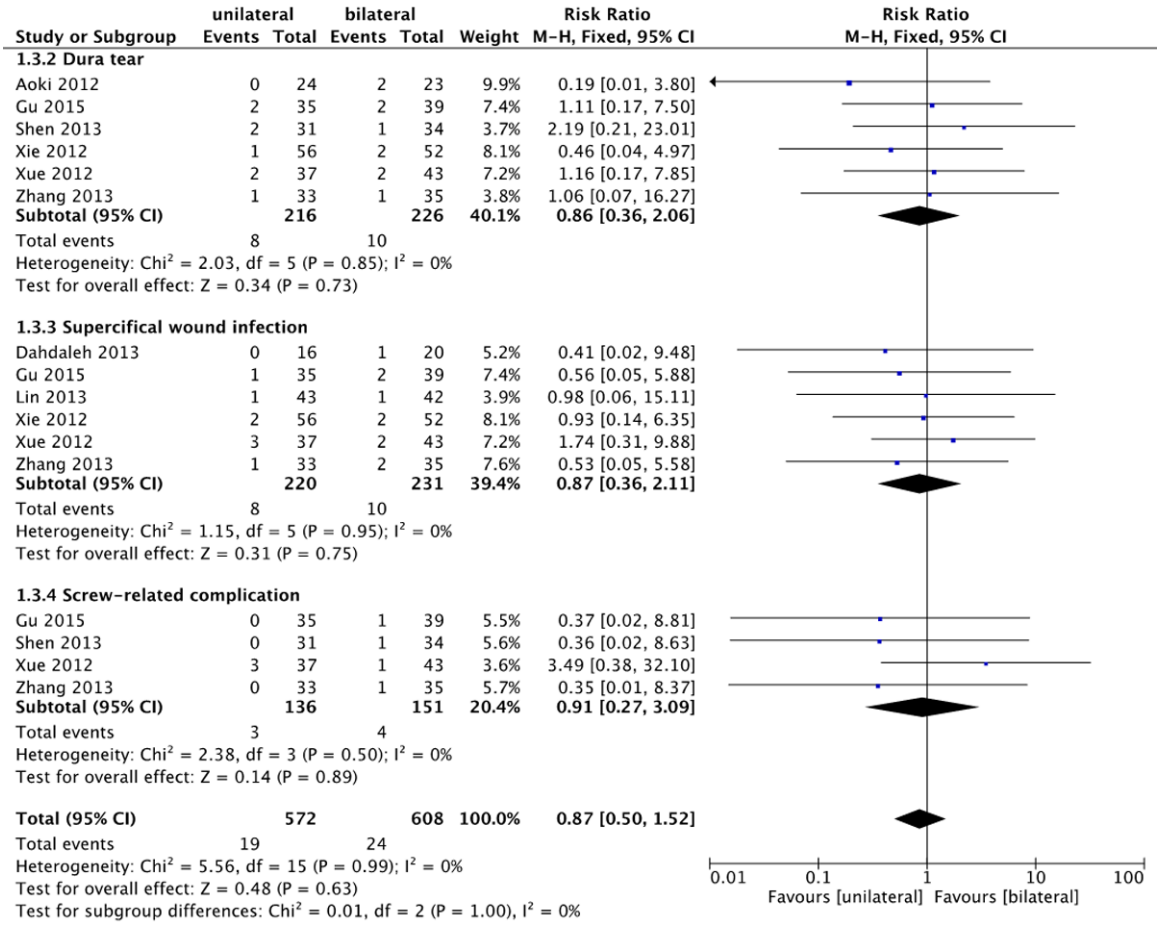

Figure 5. The forest plots for the rate of specific complications.

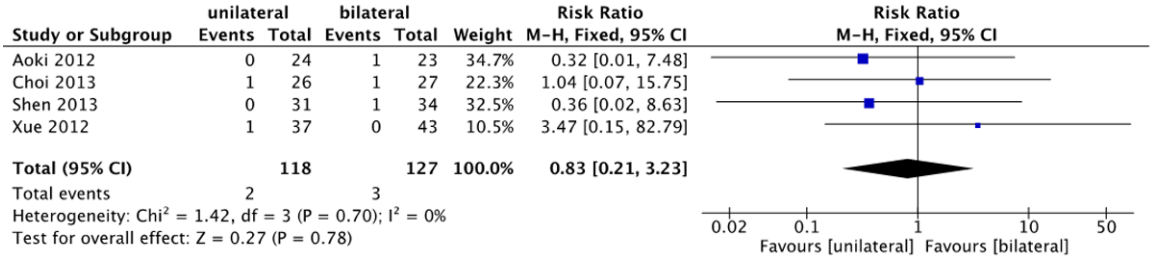

Figure 6. The forest plot for reoperation rate.

(I^2=94%; P<0.00001; **Figure 9**). Eleven studies [31-38, 40-42] reported blood loss. Pooled analysis revealed significantly reduced blood loss in unilateral group with high heterogeneity. (WMD=-133.38; 95% CI: -206.26, -60.50; P=0.0003; I^2=96%; P<0.00001; **Figure 10**). Data regarding hospital stay were available in eight studies [31, 33, 34, 36-38, 40, 42]. Pooled estimate showed no significant difference between the two groups with high heterogeneity (WMD=-1.74; 95% CI: -3.90, 0.41; P=0.11; I^2=94%; P<0.00001; **Figure 11**).

Subgroup analysis and publication bias

We performed subgroup analysis on patients that underwent MIS-TLIF or patients with only 1-level lumbar degenerative disease. The results were shown on **Table 4**. We utilized funnel plots to assess the possibility of publication bias. The funnel plot showed a fairly symmetrical distribution of the studies that reported total complication rate (**Figure 12**). All studies lied within the 95%CI and were distributed evenly about the vertical, implying minimal publication bias.

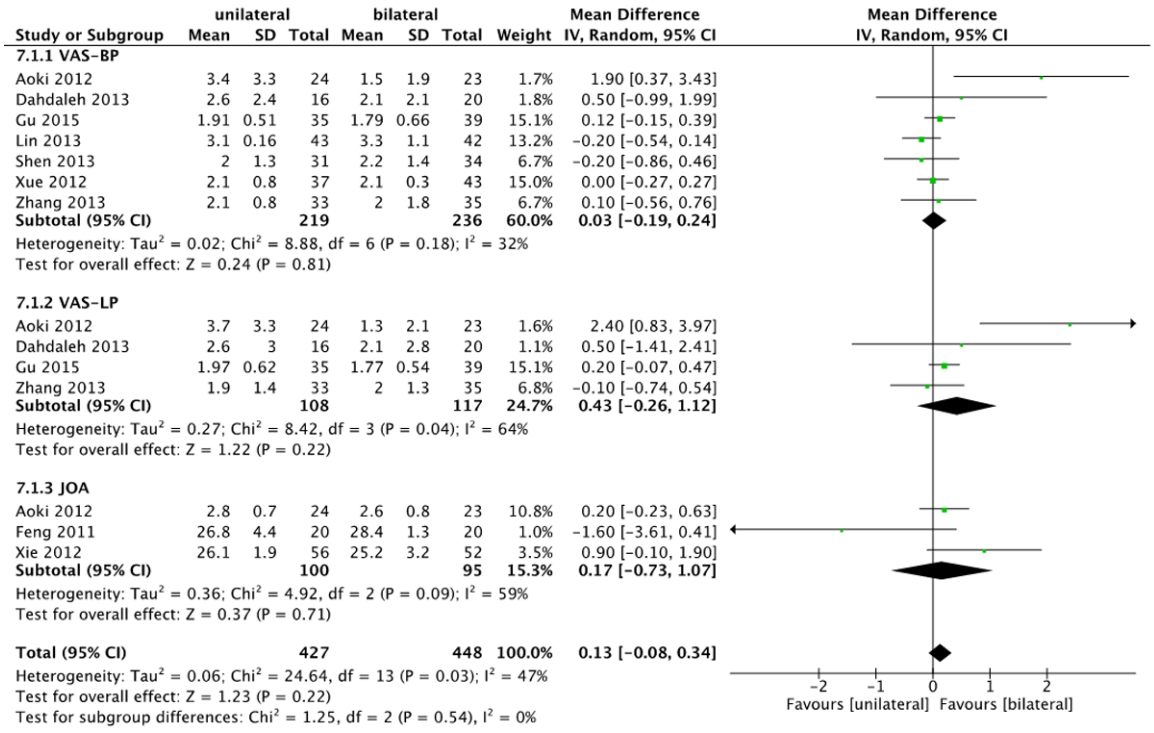

Figure 7. The forest plots for VAS and JOA. VAS-BP: visual analog score for back pain; VAS-LP: visual analog score for leg pain; JOA: Japanese Orthopedic Association.

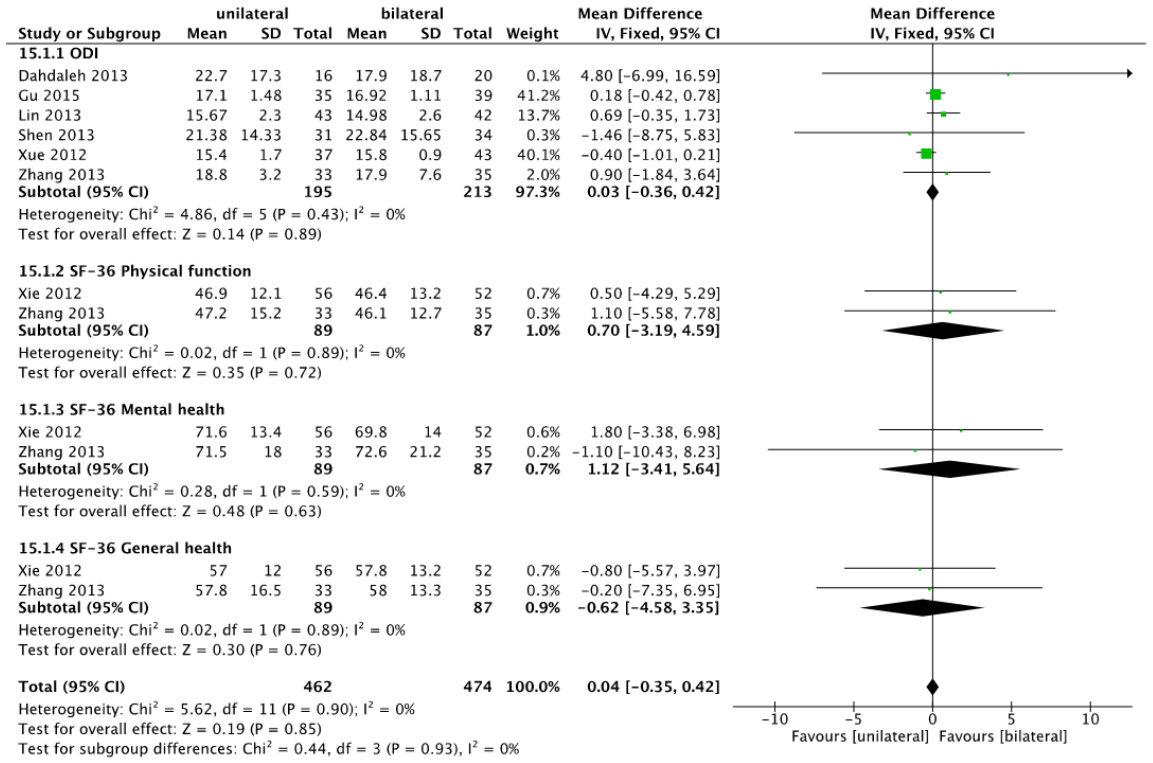

Figure 8. The forest plots for ODI and SF-36. ODI: Oswestry Disability Index; SF-36: the Short Form (36) Health Survey scores.

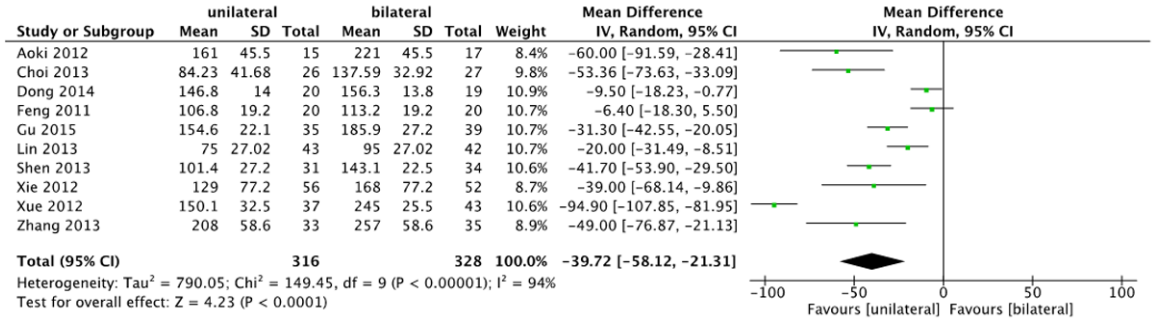

Figure 9. The forest plot for operative time.

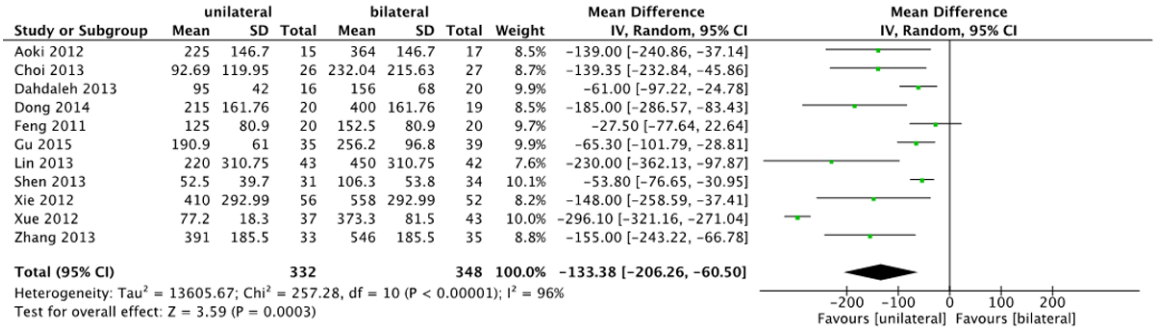

Figure 10. The forest plot for blood loss.

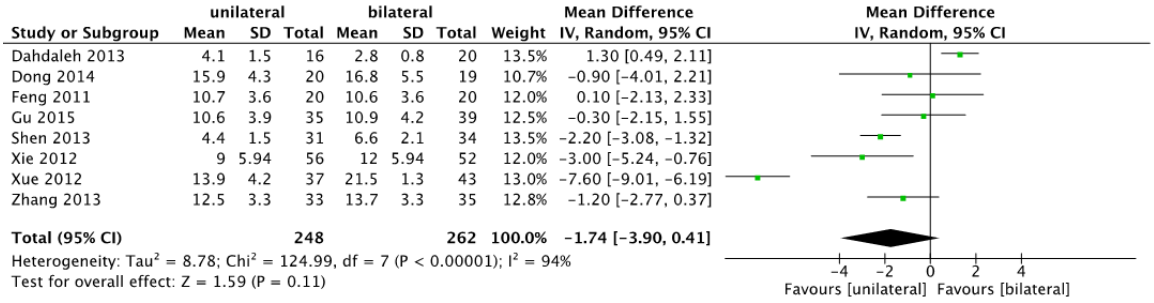

Figure 11. The forest plot for hospital stay.

Discussion

Transforaminal lumbar interbody fusion (TLIF) is increasingly popular as a surgical option to treat various degenerative lumbar diseases. However, it remains unknown whether TLIF with unilateral pedicle screw fixation is superior to that with bilateral pedicle screw fixation for the treatment of lumbar degenerative disease. Our meta-analysis pooled data from 11RCTs [31-37, 39-42] and 1 quasi-RCT [38] and found that unilateral group was associated with less blood loss and shorter operative time compared to bilateral group. However, there were no significant differences between the two groups regarding the fusion rate, complication rate, reoperation rate, pain (VAS) or functional (ODI, JOA, SF-36) outcomes, and hospital stay.

Internal fixation is employed to provide stable environment in the fused segments and promote further interbody fusion. Numerous previous biochemical studies have demonstrated that unilateral PS fixation provides less stability than bilateral PS fixation [43-49]. Through a finite element study, Ambati DV, et al [43] found unilateral PS fixation resulted in increased segmental motion as compared to bilateral fixation, especially in lateral bending and axial rotation. Slucky AV, et al [45] found unilateral con-

Table 4. Subgroup analyses of patients that underwent MIS-TLIF and patients with 1-level lumbar degenerative disease

Outcomes	No. Studies	No. Patients	Statistical method	Effect estimate	P	X^2	I^2 (%)
Fusion rate							
MIS TLIF	6	352	Risk Ratio (M-H, Fixed, 95% CI)	0.98 (0.93, 1.02)	0.29	3.13	0%
1-level	6	325	Risk Ratio (M-H, Fixed, 95% CI)	0.96 (0.91, 1.02)	0.16	3.82	0%
Total complication rate							
MIS TLIF	5	313	Risk Ratio (M-H, Fixed, 95% CI)	1.00 (0.46, 2.19)	1	1.37	0%
1-level	5	286	Risk Ratio (M-H, Fixed, 95% CI)	0.87 (0.39, 1.92)	0.72	2.44	0%
Dura tear							
MIS TLIF	2	139	Risk Ratio (M-H, Fixed, 95% CI)	1.48 (0.34, 6.36)	0.6	0.19	0%
1-level	2	112	Risk Ratio (M-H, Fixed, 95% CI)	0.74 (0.15, 3.52)	0.7	1.61	0%
Superficial wound infection							
MIS TLIF	3	195	Risk Ratio (M-H, Fixed, 95% CI)	0.61 (0.13, 2.83)	0.53	0.18	0%
1-level	2	121	Risk Ratio (M-H, Fixed, 95% CI)	0.65 (0.09, 4.93)	0.68	0.17	0%
Screw-related complications							
MIS TLIF	2	139	Risk Ratio (M-H, Fixed, 95% CI)	0.37 (0.04, 3.45)	0.38	0	0%
1-level	1	65	Risk Ratio (M-H, Fixed, 95% CI)	0.36 (0.02, 8.63)	0.53	NA	NA
Reoperation rate							
MIS TLIF	2	118	Risk Ratio (M-H, Fixed, 95% CI)	0.64 (0.09, 4.72)	0.66	0.24	0%
1-level	3	165	Risk Ratio (M-H, Fixed, 95% CI)	0.51 (0.10, 2.73)	0.44	0.39	0%
VAS-BP							
MIS TLIF	4	260	Mean Difference (IV, Fixed, 95% CI)	-0.01 (-0.21, 0.18)	0.9	2.91	0%
1-level	4	233	Mean Difference (IV, Random, 95% CI)	0.17 (-0.48, 0.82)	0.61	7.6	61%
VAS-LP							
MIS TLIF	2	110	Mean Difference (IV, Fixed, 95% CI)	0.21 (-0.06, 0.47)	0.13	0.09	0%
1-level	2	83	Mean Difference (IV, Random, 95% CI)	1.53 (-0.32, 3.39)	0.11	2.26	56%
ODI							
MIS TLIF	4	260	Mean Difference (IV, Fixed, 95% CI)	0.31 (-0.21, 0.83)	0.25	1.47	0%
1-level	3	186	Mean Difference (IV, Fixed, 95% CI)	0.68 (-0.35, 1.71)	0.2	0.8	0%
Operative time							
MIS TLIF	5	316	Mean Difference (IV, Random, 95% CI)	-29.86 (-44.22, -15.51)	<0.0001	28.76	86%
1-level	6	314	Mean Difference (IV, Random, 95% CI)	-28.89 (-44.36, -13.43)	0.0003	39.18	87%
Blood loss							
MIS TLIF	6	352	Mean Difference (IV, Random, 95% CI)	-88.87 (-124.62, -53.13)	<0.00001	14.72	66%
1-level	7	350	Mean Difference (IV, Random, 95% CI)	-92.01 (-131.56, -52.47)	<0.00001	18.92	68%
Hospital stay							
MIS TLIF	4	214	Mean Difference (IV, Random, 95% CI)	-0.49 (-2.64, 1.66)	0.65	32.81	91%
1-level	4	180	Mean Difference (IV, Random, 95% CI)	-0.40 (-2.64, 1.83)	0.72	32.94	91%

M-H: Mantel-Haenszel. MIS TLIF: minimally invasive approach for transforaminal lumbar interbody fusion. VAS-BP: visual analog score for back pain. VAS-LP: visual analog score for leg pain. ODI: Oswestry Disability Index. CI: confidence interval. NA: not available.

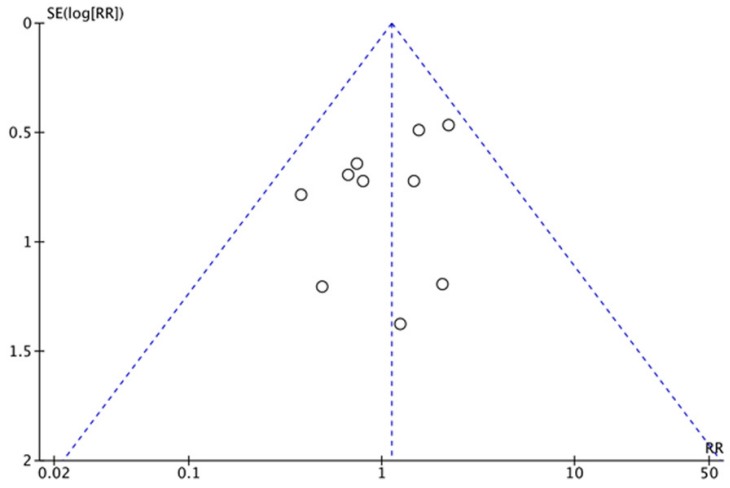

Figure 12. The funnel plot for total complication rate.

structs could only provide 50% the stiffness of bilateral constructs and produce off-axis movement, which could be detrimental to stability. Luo B, et al [46] found that in all movement directions, unilateral fixation achieved larger range of motion after short- and long-term loading compared to bilateral fixation. Theoretically, deceased construct stiffness and increased segmental motion in unilateral fixation might negatively impose on the fusion rate. However, our analysis found there was no significant difference (unilateral: 94.4%, bilateral: 97.0%; P=0.12). A possible explanation for this is unilateral fixation reserves the intact contralateral elements, which may be a contributor for spinal stability. Hu et al. reported no significant difference regarding rate of non-union between the two groups [50]. However, they only included seven studies. Our finding was also in agreement with some biomechanical studies [51-53], which demonstrated unilateral PS fixation could provide enough stability for interbody fusion.

Our meta-analysis found no superiority existed between the two groups in terms of total complication rate, which suggested unilateral group was as safe as bilateral group. However, this finding was inconsistent with results from many previous studies where unilateral fixation provided insufficient stability to prevent cage migration in some patients [39, 54]. Moreover, We collected the specific complications data (dura tear, superficial wound infection, and screw-related complications) among the included studies. This meta-analysis found that there were no significant differences regarding these specific complications. However, these results should be interpreted cautiously because of the relatively small sample size, especially screw-related complications. Therefore, randomized controlled trials of large sample size are warranted to clarify these outcomes.

As for operative time and blood loss, this meta-analysis showed the significant differences in favor of unilateral group. The reason for this might be that unilateral fixation used a less invasive approach without causing destruction of the contralateral elements and thus it took less operative time and caused less blood loss [35, 36]. Moreover, our analysis found there was no significant difference regarding hospital stay between the two groups. We observed high heterogeneity in these outcomes. It might be related to the differences of the proficiency of the surgeons. The potentially different criteria for defining these outcomes among these studies might also lead to this level of heterogeneity. In addition, we took VAS, ODI, JOA, and SF-36 to assess the clinical functional outcomes. In our meta-analysis, both unilateral and bilateral fixations achieved significantly improved functional results. In this regard, unilateral fixation was as effective as bilateral fixation for the treatment of lumbar degenerative disease.

We also performed subgroup analysis on patients that underwent MIS-TLIF approach. There were six studies that performed MIS-TLIF approach, including 352 patients. Subgroup analysis showed the similar trends. Similar to our results, Wang et al. reported that unilateral fixation with MIS-TLIF approach had less blood loss compared to bilateral fixation, and no significant differences were detected in functional outcomes, fusion rate and complication rate [55]. However, their study was underpowered by the fact that only three studies were included.

There were several limitations in this meta-analysis that needed to be taken consideration. First, all of the RCTs occurred at a single center and only twelve small studies with 797 patients in total were included. Further multicenter studies with more patients should be performed.

Second, all studies had follow-up duration that was less than 48 months. A longer-term follow-up was necessary to confirm these results. Third, among these studies, some baseline characteristics were different, such as surgical approach and cage use. For instance, six studies [31-33, 36, 39, 42] performed traditional open TLIF and the other six studies [34, 35, 37, 38, 40, 41] employed MIS-TLIF. Aoki et al. implanted one cage in the unilateral group, but employed two cages in the bilateral group [32]. Dahdaleh et al. added rhBMP as bone fusion enhancer [34]. In Duncan's study, bone morphogenetic protein, allograft or synthetic calcium phosphate were applied as a graft material [39]. These differences might potentially impose on the clinical or radiological pooled outcomes. Finally, theses studies lacked a uniform standard definition of interbody fusion, which might be susceptible to bias.

Conclusions

In conclusion, this meta-analysis indicates that unilateral group is associated with less blood loss and shorter operative time. The results of fusion rate, complication rate, reoperation rate, functional outcomes, and hospital stay are similar in the two groups. Based on current literature, unilateral pedicle screw fixation is a good alternative to bilateral pedicle screw fixation in TLIF for the treatment of lumbar degenerative disease. However, large multicenter randomized controlled trials with long-term follow-up are warranted to further confirm these outcomes.

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Disclosure of conflict of interest

None.

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