Comparison between minimally invasive and open transforaminal lumbar interbody fusion for the treatment of multi-segmental lumbar degenerative disease: A systematic evaluation and meta-analysis

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Abstract. The present study aimed to compare the differences between minimally invasive transforaminal lumbar fusion (MIS-TLIF) and open transforaminal lumbar fusion (TLIF) for multi-segmental lumbar degenerative disease regarding intraoperative indices and postoperative outcomes. PubMed, Web of Science, Embase, CNKI, Wanfang and VIP databases were searched for literature on MIS-TLIF and open TLIF in treating multi-segmental lumbar degenerative diseases. Of the 1,608 articles retrieved, 10 were included for final analysis. The Newcastle-Ottawa Scale and Review Manager 5.4 were used for quality evaluation and data analysis, respectively. The MIS-TLIF group was superior to the open TLIF group regarding intraoperative blood loss [95% confidence interval (CI): -254.33,-157.86; P<0.00001], postoperative in-bed time (95%CI: -3.49,-2.76; P<0.00001), hospitalization time (95%CI: -5.14,-1.78; P<0.0001) and postoperative leg pain Visual Analog Scale score (95%CI: -0.27,-0.13; P<0.00001). The fluoroscopy frequency for MIS-TLIF (95%CI: 2.07,6.12; P<0.0001) was significantly higher than that for open TLIF. The two groups

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had no significant differences in operation time, postoperative drainage volume, postoperative complications, fusion rate, or Oswestry Disability Index score. In treating multi-segmental lumbar degenerative diseases, MIS-TLIF has the advantages of less blood loss, shorter bedtime and hospitalization time and improved early postoperative efficacy; however, open TLIF has a lower fluoroscopy frequency.

Introduction

Degenerative lumbar diseases are caused by degenerative changes in the lumbar spine and the surrounding tissues. The older the patient, the more prone they are to changes in the lumbar spine structure, causing back pain, spinal dysfunction and other symptoms (1). With the accelerated aging of the Chinese population, the proportion of diagnoses and treatments for lumbar degeneration is increasing and the proportion of lumbar spine surgeries is also increasing annually. Transforaminal lumbar interbody fusion (TLIF) combined with pedicle screw internal fixation is a therapeutic option for patients in whom conservative treatment has failed (2). In lumbar spine surgery, the pedicle screw internal fixation technique can provide fixation of the anterior, middle and posterior columns of the spine in various lumbar fusion procedures and has been widely used in the surgical treatment of various lumbar spine disorders to promote fusion and restore spinal stability. Since Boucher (3) applied the pedicle screw technique in 1959, it has become the standard internal fixation method for the treatment of spinal fractures, degenerative and infectious spinal lesions and spinal deformities. For patients with osteoporosis, cemented reinforcement or cortical bone screws can be used, while for those with cervical osteoporosis or infection, anterior cervical bilateral pedicle screws can be used to enhance stability (4,5). The open TLIF technique was first introduced by Harms and Rolinger in 1982 (6) and has been used since. After >40 years, TLIF has become one of the most commonly used surgical procedures for lumbar degenerative diseases. Conventional TLIF uses an intervertebral foraminal approach

Key words: lumbar degenerative disease, multi-segment, minimally invasive transforaminal lumbar fusion, open transforaminal lumbar fusion, meta-analysis

located on the lateral aspect of the articular eminence, enabling stable intervertebral fusion and effectively reducing the loss of pressure on the neural tissues without the need to enter the spinal canal. This approach can reduce the damage to the spinal dura mater and nerves and has the advantages of easy operation, less trauma and quicker recovery (7). However, extensive stripping of the paravertebral muscles and prolonged pulling may lead to muscle damage, resulting in medically induced muscle injury and chronic postoperative low back pain (8). With the development of minimally invasive concepts and channel technologies, endoscopic technology and robot-assisted surgery have become a current research focus. The minimally invasive TLIF (MIS-TLIF) is precisely used to solve the shortcomings of open TLIF, effectively protecting the attachment of paraspinal muscles to the bone and avoiding interruption of the supraspinous and interspinous ligaments, thus reducing bleeding and postoperative pain. MIS-TLIF, a minimally invasive spinal technique introduced by Foley and Lefkowitz in the early 2000s (9), has been widely used in clinical practice. Common indications for MIS-TLIF and open TLIF include severe degenerative disc disease, low-grade spondylolisthesis (grades 1 and 2), pseudarthrosis and symptomatic spondylolisthesis. Whereas recurrent disc herniation and obese patients are more suited for MIS-TLIF, high-grade vertebral slips (grades 3 and 4) and anatomical variations are more suited for open TLIF and contraindications include extensive epidural scarring, arachnoiditis, active infections, linking of the nerve roots (which may impede access to the intervertebral disc space) and osteoporosis in patients (10-12). Studies have shown that, concerning single-stage surgery, MIS-TLIF reduces intraoperative blood loss, shortens hospitalization and recovery times, reduces complications and has the same clinical outcomes and fusion rates as open TLIF (13,14). However, for multi-segmental lumbar degenerative disease, it remains unclear whether MIS-TLIF still has the advantage of a single-stage surgery. Therefore, the present meta-analysis aimed to explore the similarities and differences between single-stage and multi-segmental treatments by comparing and evaluating the efficacy of MIS-TLIF and open TLIF in treating multi-segmental lumbar degenerative disease.

Materials and methods

Search strategy. The PubMed, Web of Science, Embase, CNKI, Wanfang and VIP databases were searched to identify relevant studies for inclusion. Data on the effectiveness and security of open TLIF and MIS-TLIF for treating lumbar degenerative disorders were collected from the inception of the databases to August 2023. The search keywords used were TLIF, MIS-TLIF and lumbar degenerative diseases. The retrieval strategy was ('MIS-TLIF' OR 'minimally invasive transforaminal lumbar interbody fusion' OR 'TLIF' OR 'transforaminal lumbar interbody fusion') AND ('degenerative disease of the lumbar spine').

Surgical techniques. MIS-TLIF: The patient was placed in the prone position and the C-arm was used to determine the surgical plane preoperatively. A longitudinal incision was made 5-10 mm outside the upper and lower pedicles on the

symptomatic side. The latissimus dorsi fascia was incised and the space between the longest and multifidus muscles (Wiltse approach) was separated from the fingers. The muscles around the facet joints were bluntly separated and a guide needle was placed. A stepwise sleeve was placed to remove the upper and lower joints of the affected intervertebral space and part of the lamina near the spinous process. The intervertebral foramen was exposed, the annulus fibrosus was incised, the nucleus pulposus was removed and the endplate was cleaned. The cage was implanted according to the test model and the bone particles made from the bone block were implanted and compacted. The nerve root was explored and released; no residual pressure or nerve root relaxation was observed. The same decompression and intervertebral bone grafting methods were performed on other segments. Finally, a titanium rod was installed to connect the pedicle screws and a drainage tube was placed in the incision.

TLIF: After general anesthesia, the patient was placed in the prone position and the C-arm was used to locate the surface projection of the fused segment's upper and lower vertebral pedicles. According to the position of the upper and lower pedicles of the fused segment, the median longitudinal incision was made, the skin and lumbar fascia were cut, the paravertebral muscles on both sides were separated, the bone structure behind the lamina was fully exposed, the articular capsule of the upper and lower non-fusion segments was not destroyed and pedicle screws were placed. Decompression and intervertebral bone grafting were the same as those used for MIS-TLIF. Titanium rods were installed, pressurized and tightened and negative-pressure drainage tubes were placed on both sides of the lamina.

Inclusion and exclusion criteria. The inclusion criteria were: i) Patients who underwent open TLIF or MIS-TLIF for degenerative lumbar spine disease; ii) two or more surgical segments; and iii) one of the following reported in the literature: Operative time, intraoperative blood loss, postoperative drainage volume, number of intraoperative radiographs, bed rest time, hospital stay, complications, fusion rate, Oswestry Disability Index (ODI) and Visual Analog Scale (VAS) score (15-24). The exclusion criteria were: i) Comorbidities, such as lumbar infections, neoplastic diseases, or lumbar fractures; ii) history of previous lumbar spine surgeries; iii) reviewed manuscripts, conference papers, expert opinions, case reports and literature not obtained in full text; and iv) animal experiments and biomechanical studies.

Data extraction and literature quality assessment. Articles were independently screened and identified for study inclusion by two researchers through the title, abstract and full text of the article. When there was a difference in opinion regarding the study, it was discussed and resolved by two authors. When necessary, a third researcher was consulted. The quality of the included literature was assessed using the Newcastle-Ottawa Scale (NOS) (25) and categorized as low (<5 points), moderate (5-7 points) and high (8-9 points) quality.

Statistical methods. Review Manager 5.4 (The Cochrane Collaboration) was used to process the collected data. Continuous variables were expressed as mean difference

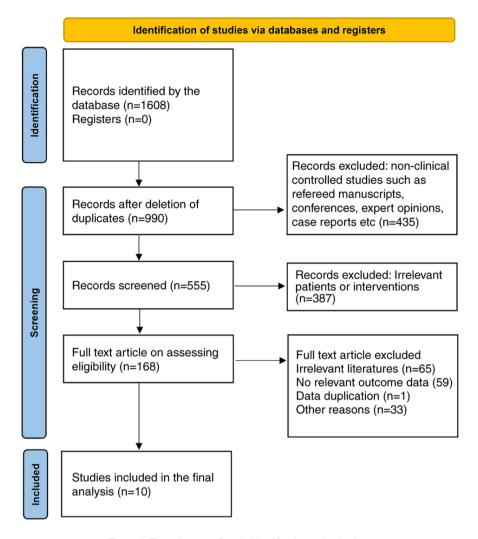


Figure 1. Flow diagram of study identification and selection.

and 95% confidence interval (CI) and dichotomous variables were expressed as odds ratios and 95%CI. The heterogeneity of the included literature was determined using the I^2 statistic, with $I^2 < 50\%$ considered homogeneous studies with less heterogeneity using a fixed-effects model and vice versa using a random-effects model. The literature was removed individually to perform a sensitivity analysis. When the number of included studies was ≥ 10 , a funnel plot or Egger's (Egger's test) test was used to assess for publication bias. P<0.05 was considered to indicate a statistically significant difference.

Results

Basic characteristics of the included literature. In total, 1,608 relevant studies were obtained from the databases based on the search formula and 168 relevant studies were initially screened after excluding non-case controls, duplicates and other irrelevant studies. Finally, the articles were scrutinized; 158 papers with irrelevant content, inconsistent outcome indicators and incomplete critical data were excluded and 10 articles were finally included. The literature screening process and results are shown in Fig. 1 and the basic characteristics of the included studies are listed in Table I.

Quality assessment of included articles. The present study included 10 articles, including zero randomized controlled studies, one prospective study and nine retrospective studies. A total of 864 patients were included: 422 underwent MIS-TLIF and 442 underwent open TLIF. The NOS score table was used for quality evaluation, including three, four and three studies with eight, seven and six points, respectively; three high-quality and seven medium-quality studies. A total of nine studies reported the operation time and intraoperative drainage; however, one article did not report perioperative data because of long-term efficacy. Among them, seven articles involved 2-segment lumbar fusion and two included 2- or 3-segment lumbar fusion.

Outcomes

Perioperative indicators. Perioperative indicators included operation time, blood loss, postoperative drainage volume and fluoroscopy frequency. A total of nine studies compared the time spent performing MIS-TLIF with open TLIF during multi-segmental surgery. The heterogeneity test showed that the heterogeneity of each study was significant (l^2 =97%) and a random-effects model was used for analysis. The results showed no significant difference in operation time between MIS-TLIF and open TLIF in the treatment of multi-segment

Table I. General characteristics of included studies	Table I. Gene	ral charact	eristics of	included	studies.
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First author(s). year	Type of study	Country	MIS-TLIF/ OpenTLIF	Cases	Age (mean)	Sex (M/F)	Outcome	NOS scale	(Refs.)
Cao <i>et al</i> , 2022	Retrospective	China	MIS-TLIF	64	61.80±8.83	30/34	1235	6	(15)
			OpenTLIF	62	60.96±8.48	28/34	6910		
Du et al, 2017	Retrospective	China	MIS-TLIF	16	47.62±13.57	5/8	12679	6	(16)
			OpenTLIF	16	54.38±10.53	5/8			
Gu et al, 2014	Prospective	China	MIS-TLIF	44	66.4±6.7	19/25	12678	8	(17)
			OpenTLIF	38	64.1±7.8	15/23	910		
Hu et al, 2022	Retrospective	China	MIS-TLIF	52	64.18±8.17	28/24	123457	8	(18)
			OpenTLIF	60	66.24±7.16	34/26	8910		
Lee et al, 2015	Retrospective	Korea	MIS-TLIF	27	60.55±13.61	8/19	126789	7	(19)
			OpenTLIF	43	65.06±6.81	16/27			
Modi et al, 2021	Retrospective	India	MIS-TLIF	24	51.2±12.2	NA	(126)	6	(20)
			OpenTLIF	42	51.5±14.0	NA			
Wang <i>et al</i> , 2019	Retrospective	China	MIS-TLIF	67	64.77±7.07	33/34	123567	7	(21)
			OpenTLIF	59	64.92±6.74	25/34	8910		
Wang <i>et al</i> , 2021	Retrospective	China	MIS-TLIF	32	63.3±11.3	15/17	78910	7	(22)
			OpenTLIF	30	66.0±8.4	13/17			
Wang <i>et al</i> , 2022	Retrospective	China	MIS-TLIF	51	64.67±6.17	28/23	123456	8	(23)
			OpenTLIF	55	64.35±5.62	32/23	79		
Zhang et al, 2022	Retrospective	China	MIS-TLIF	45	59.9±6.9	25/20	12789	7	(24)
			OpenTLIF	37	61.8±5.6	21/16			

TLIF, transforaminal lumbar fusion; MIS, minimally invasive; outcomes: 1) Operation time, 2) intraoperative blood loss, 3) postoperative drainage volume, 4) fluoroscopy frequency, 5) postoperative in-bed time, 6) hospitalization time, 7) postoperative complications, 8) fusion rate, 9) Oswestry Disability Index score and 10) Visual Analog Scale score.

lumbar degenerative diseases and the difference was not statistically significant (95%CI: -26.92,20.03; P=0.77; Fig. 2). A total of nine studies compared intraoperative blood loss; the heterogeneity test showed significant heterogeneity ($I^2=92\%$) and continued to use the random effect model, demonstrating that the intraoperative blood loss was considerably lower in the MIS-TLIF group compared with the open TLIF group (95%CI: -254.33,-157.86; P<0.00001; Fig. 3). A total of four studies compared the postoperative drainage volume and the heterogeneity test showed significant heterogeneity in each study ($I^2=99\%$); therefore, the random-effects model was used. The results showed no significant difference in postoperative drainage between the MIS-TLIF and open TLIF surgery groups (95%CI: -259.91,8.58; P=0.07; Fig. 4). Only two articles compared the frequency of fluoroscopy; the heterogeneity of the two studies was apparent ($I^2=92\%$) and the random-effects model was used. The results showed that the fluoroscopy frequency in the MIS-TLIF group was significantly higher than that in the open TLIF group and the difference was statistically significant (95%CI: 2.07,6.12; P<0.0001; Fig. 5). The results showed that in the perioperative indices of multi-segment lumbar spine surgery, the bleeding in the MIS-TLIF group was less than that in the open TLIF group, while the number of radiations was higher than that in the open group and the difference was statistically significant; the operative time and postoperative drainage did not differ significantly.

Postoperative bedtime and hospitalization time. A total of four studies compared postoperative bedtime and the heterogeneity test showed I^2 =78%. After sensitivity analysis, one study was excluded; the heterogeneity test result was $I^2=0\%$ and the fixed-effects model was used. The results suggested a statistically significant difference between the postoperative bed rest times in the MIS-TLIF and open TLIF surgery groups (95%CI: -3.49,-2.76; P<0.00001; Fig. 6). A total of seven studies compared the length of hospitalization time and the heterogeneity of each study was significant $(I^2=95\%)$ using a random effect model, showing that the postoperative hospitalization time in the MIS-TLIF group was significantly shorter than that in the open TLIF group (95%CI: -5.14,-1.78; P<0.0001; Fig. 7). The outcomes indicated that the postoperative bed and hospitalization times in the MIS-TLIF group were significantly shorter than those in the open TLIF group. This indicated that minimally invasive surgery causes less tissue damage and patients recover more quickly postoperatively.

Postoperative complications. A total of eight studies compared the postoperative complications of MIS-TLIF and open TLIF for multi-segment lumbar degenerative diseases. The heterogeneity of each study was low (I^2 =48%) and a fixed-effects model was used. The results showed no significant difference in postoperative complications between MIS-TLIF and open TLIF (95%CI: 0.41,1.14; P=0.15; Fig. 8). The MIS-TLIF and open TLIF groups did not differ

	Mis Open						Mean difference					
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rano	lom, 95% C	<u>я </u>	
Cao2022	150.06	27.19	64	197.27	32.18	62	11.4%	-47.21 [-57.63, -36.79]				
Du2017	151.9	29.8	16	195	39.9	16	10.4%	-43.10 [-67.50, -18.70]				
Gu2014	195.5	28	44	186.6	23.4	38	11.4%	8.90 [-2.23, 20.03]		+		
Hu2022	287.74	32.17	52	232.96	42.56	60	11.2%	54.78 [40.91, 68.65]			_	
Lee2015	167.33	37.54	27	216.58	40.41	43	10.9%	-49.25 [-67.86, -30.64]				
Modi2021	181.5	18.9	24	139.4	15.6	42	11.5%	42.10 [33.19, 51.01]		-	-	
Wang2019	325.59	43.74	67	331.81	74.81	59	10.6%	-6.22 [-27.99, 15.55]				
Wang2022	213.8	15.89	51	198.56	17.36	55	11.6%	15.24 [8.91, 21.57]				
Zhang2022	136.33	35.51	45	148.4	40.91	37	11.0%	-12.07 [-28.85, 4.71]		+		
Total (95% CI)			390			412	100.0%	-3.45 [-26.92, 20.03]				
Heterogeneity: Tau ² =			,	df = 8 (F	P < 0.00	001); l²	= 97%	⊢ −10	00 –50	0	50	100
Test for overall effect:	Z = 0.29	(P = 0.7)	()						Mi	s Open		

Figure 2. Forest plot for the operation time. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

		Mis Open						Mean difference		Mean d	ifference	
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% (CI	IV, Rando	om, 95% Cl	
Cao2022	270.07	66.38	64	442.14	75.82	62	13.6%	-172.07 [-196.98, -147.16]		-		
Du2017	265.4	68.9	16	450	182.6	16	9.1%	-184.60 [-280.23, -88.97]				
Gu2014	248.4	94.3	44	576.3	176.2	38	11.4%	-327.90 [-390.47, -265.33]		_		
Hu2022	537.62	112.78	52	574.97	134.26	60	12.5%	-37.35 [-83.11, 8.41]			†	
Lee2015	527.41	219.66	27	865.81	525.09	43	4.8%	-338.40 [-515.87, -160.93]				
Modi2021	165.2	40.7	24	304.4	53.1	42	13.6%	-139.20 [-162.07, -116.33]		-		
Wang2019	328.76	196.55	67	716.29	343.76	59	8.8%	-387.53 [-487.07, -287.99]				
Wang2022	229.6	101.03	51	450.9	125.7	55	12.6%	-221.30 [-264.57, -178.03]				
Zhang2022	254.15	40.4	45	450	66.41	37	13.6%	-195.85 [-220.29, -171.41]		-		
Total (95% CI)			390			412	100.0%	-206.09 [-254.33, -157.86]		•		
Heterogeneity: Tau ² =			,	= 8 (P <	0.00001); I² = 9	2%	• / •	-500	-250	0 250	
Test for overall effect:	Test for overall effect: Z = 8.37 (P < 0.00001)										Open	

Figure 3. Forest plot for the blood loss. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

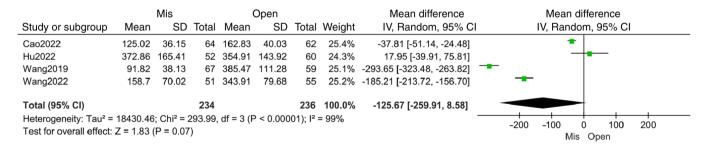


Figure 4. Forest plot for the postoperative drainage volume. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

significantly in the incidence of postoperative complications in multi-segmental lumbar degenerative disease.

Fusion rate. A total of six studies reported the fusion rate, of which four studies divided the fusion situation into four grades according to the Bridwell criterion (26): grades I and II were fusion and grades III and IV were non-fusion. Subgroup analysis was performed for Bridwell grades I and II. The heterogeneity test results ($l^2=0\%$) indicated that heterogeneity was small and a fixed-effects model was used. The findings revealed no discernible difference between open TLIF and MIS-TLIF regarding the fusion rate (95%CI: 0.77,1.32; P=0.96; Fig. 9). Two articles only reported the overall fusion rate.

Heterogeneity in each study was low ($l^2=0\%$). A fixed-effects model was used. The results showed no significant difference in the overall fusion rate between the two groups and the statistics did not support the difference (95%CI: 0.60,2.62; P=0.54) (Fig. 10). The results demonstrated that MIS-TLIF and open TLIF can provide excellent fusion results for multi-segmental lumbar spine diseases.

Postoperative functional score. Postoperative functional scores included the ODI and VAS scores. A total of nine studies compared ODI scores based on the last follow-up. The overall heterogeneity test was high (I^2 =89%) and a random-effects model was used. The results showed no significant difference

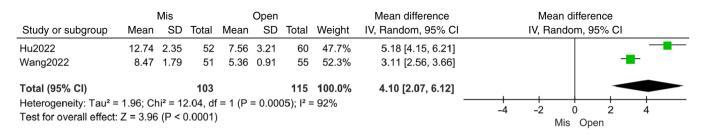


Figure 5. Forest plot for the fluoroscopy frequency. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

		Mis		C	Open			Mean difference		Ν	Mean di	fference	,	
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		١١	V, Fixed	, 95% C	1	
Cao2022	3.85	0.84	64	7.95	1.42	62		Not estimable						
Hu2022	3.18	1.08	52	6.24	1.34	60	65.6%	-3.06 [-3.51, -2.61]						
Wang2019	1.23	1.05	67	4.8	3.18	59	18.3%	-3.57 [-4.42, -2.72]						
Wang2022	4.75	0.44	51	7.64	3.4	55	16.1%	-2.89 [-3.80, -1.98]						
Total (95% CI)			170			174	100.0%	-3.13 [-3.49, -2.76]	•					
Heterogeneity: $Chi^2 = 1.39$, $df = 2$ (P = 0.50); $l^2 = 0\%$ Test for overall effect: Z = 16.86 (P < 0.00001)														

Figure 6. Forest plot for the postoperative in-bed time. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

		Mis Open						Mean difference		Mea	n differe	nce	
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Ra	ndom, 9	5% CI	
Cao2022	7.9	1.94	64	11.96	2.71	62	15.9%	-4.06 [-4.89, -3.23]					
Du2017	7.8	2.1	16	12	5	16	11.7%	-4.20 [-6.86, -1.54]			-		
Gu2014	9.3	3.7	44	12.1	3.6	38	14.4%	-2.80 [-4.38, -1.22]			-		
Lee2015	10.3	5.4	27	11.12	5.42	43	11.8%	-0.82 [-3.42, 1.78]					
Modi2021	5.3	0.9	24	5.7	1.3	42	16.3%	-0.40 [-0.93, 0.13]					
Wang2019	5.21	2.31	67	15.24	7.41	59	13.5%	-10.03 [-12.00, -8.06]	_				
Wang2022	7.08	0.44	51	9.55	1.65	55	16.4%	-2.47 [-2.92, -2.02]		-			
Total (95% CI)			293			315	100.0%	-3.46 [-5.14, -1.78]		•	•		
• •	Heterogeneity: Tau ² = 4.43; Chi ² = 129.17, df = 6 (P < 0.00001); l ² = 95%										0		——————————————————————————————————————
lest for overall effect:	Test for overall effect: $Z = 4.04$ (P < 0.0001)										Mis Ope	en	

Figure 7. Forest plot for the hospitalization time. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

in postoperative ODI scores between the two groups (95%CI: -2.05,-0.24; P=0.12; Fig. 11). The MIS-TLIF and open TLIF groups did not differ significantly in postoperative dysfunction index scores and both procedures resulted in excellent decompression. The six papers (15,17,18,21,22,24) returned the reported results of postoperative VAS scores, but because the results of one of them were expressed as mean and maximum-minimum and could not be calculated for conversion to standardized data, this article was discarded; with the exclusion of postoperative VAS scores for low back pain from one study ($I^2=35\%$) and overall ($I^2=47\%$), using a fixed-effects model, the findings revealed a statistically significant difference between the postoperative VAS values for leg pain in the MIS-TLIF and open TLIF groups (95%CI: -0.27,-0.13; P<0.00001; Fig. 12). The MIS-TLIF and open TLIF groups showed no significant differences in postoperative lower back pain; however, there was a difference in postoperative leg pain, with lower VAS scores for postoperative leg pain in the MIS-TLIF group.

Publication bias and sensitivity analysis. Publication bias and sensitivity of intraoperative operative time, blood loss, postoperative drainage volume, fluoroscopy frequency, postoperative bedtime, hospitalization time, complications, fusion rate and ODI and VAS scores were assessed using Review Manager 5.4. The funnel plots of the items were mostly symmetrical, indicating no overt publication bias and that the data were consistent and dependable (Fig. 13). Studies with (I^2 >50%) were analyzed for sensitivity and we found that (I^2 =78%) became (I^2 =0%) by excluding one of the studies on bedtime; (I^2 =74%) became (I^2 =35%) after excluding one of the studies related to the VAS score of postoperative low back pain. The heterogeneity of the rest of the studies did not change significantly after excluding the literature one by one, indicating the stability of the results.

Study or subgroup	Mis Events	Total	Oper Events		Weight	Odds ratio M-H, Fixed, 95% Cl	Odds ratio M-H, Fixed, 95% Cl
Study of Subgroup	Events	Total	Events	TOLA	weight	M-H, Fixed, 95 % Ci	
Du2017	0	16	0	16		Not estimable	
Gu2014	5	44	4	38	10.9%	1.09 [0.27, 4.39]	
Hu2022	12	52	8	60	16.3%	1.95 [0.73, 5.22]	+
Lee2015	0	27	0	43		Not estimable	
Wang2019	5	67	8	59	22.5%	0.51 [0.16, 1.67]	
Wang2021	4	32	5	30	12.9%	0.71 [0.17, 2.96]	
Wang2022	1	51	3	55	8.1%	0.35 [0.03, 3.44]	
Zhang2022	0	45	9	37	29.4%	0.03 [0.00, 0.59]	
Total (95% CI)		334		338	100.0%	0.68 [0.41, 1.14]	•
Total events	27		37				
Heterogeneity: Chi ² =	9.61, df = 5	5 (P = 0	0.09); l ² =	48%			
Test for overall effect:	Z = 1.45 (F	P = 0.1	5)			0.001	0.1 1 10 1000 Mis Open
			-				Mis Open

Figure 8. Forest plot for the postoperative complications. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval; M-H, Mantel-Haenszel.

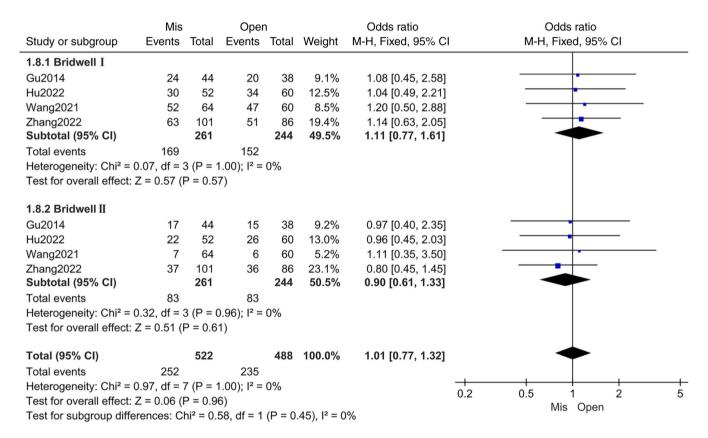


Figure 9. Forest plot for the fusion rate. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval; M-H, Mantel-Haenszel.

Discussion

Lumbar degenerative diseases are prevalent in older individuals and multi-segmental lumbar degenerative diseases are common in clinical practice. Patients with ineffective conservative treatment and severe neurological symptoms require surgical treatment to restore the original stable structure of the lumbar spine and decompress the compressed spinal cord and nerve roots. A number of surgical methods exist, including posterior LIF (PLIF), TLIF, oblique LIF, extreme lateral LIF and various minimally invasive methods. TLIF, a mature technique, is a common surgical method for treating lumbar degenerative diseases (27). Compared to PLIF, TLIF causes less disturbance to the dural sac and nerve root, less chance of injury and less damage to the ligamentous complex, which is conducive to spinal stability (28). However, traditional TLIF still has the common problem of requiring open surgery. Due to the large skin incision, hooks pulling the soft tissue during the operation may cause liquefaction and necrosis of the soft tissue, leading to postoperative low back pain. MIS-TLIF uses spinal surgical channel technology, which causes less surgical trauma to the muscle of the patient and can achieve unilateral

	Mis		Ope	n		Odds ratio		Odds ratio			
Study or subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	I	Ν	/I-H, Fixed, 95%	- CI	
Gu2014	41	44	35	38	19.9%	1.17 [0.22, 6.18]		-			
Hu2022	52	52	60	60		Not estimable					
Lee2015	22	27	36	43	39.9%	0.86 [0.24, 3.03]					
Wang2019	67	67	59	59		Not estimable					
Wang2021	59	64	53	60	33.2%	1.56 [0.47, 5.21]				_	
Zhang2022	100	101	84	86	7.0%	2.38 [0.21, 26.72]		-			_
Total (95% CI)		355		346	100.0%	1.26 [0.60, 2.62]			-		
Total events	341		327								
Heterogeneity: Chi ² =	0.75, df = 3	3 (P = 0	0.86); I² =	0%			0.02	0.1	1		 50
Test for overall effect:	Test for overall effect: $Z = 0.61$ (P = 0.54)							0.1	Mis Open	10	50

Figure 10. Forest plot for the overall fusion rate. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval; M-H, Mantel-Haenszel.

		Mis		(Dpen			Mean difference	Mean difference
Study or subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Cao2022	10.89	2.91	64	13.31	3.57	62	11.4%	-2.42 [-3.56, -1.28]	
Du2017	19.9	1.8	16	20.2	2.3	16	10.7%	-0.30 [-1.73, 1.13]	
Gu2014	16.5	2	44	16.5	1.9	38	12.0%	0.00 [-0.85, 0.85]	
Hu2022	12.46	4.31	52	14.14	3.37	60	10.7%	-1.68 [-3.13, -0.23]	
Lee2015	5.73	3.45	27	4.3	2.83	43	10.4%	1.43 [-0.12, 2.98]	
Wang2019	7.4	2.2	67	7.94	3.33	59	11.7%	-0.54 [-1.54, 0.46]	
Wang2021	11.3	4.42	32	12.1	3.06	30	9.5%	-0.80 [-2.68, 1.08]	
Wang2022	23.9	1.7	51	27.4	1.86	55	12.3%	-3.50 [-4.18, -2.82]	_ - _
Zhang2022	4.8	2.4	45	4.8	2.9	37	11.3%	0.00 [-1.17, 1.17]	
Total (95% CI)			398			400	100.0%	-0.91 [-2.05, 0.24]	
Heterogeneity: Tau ² = 2.66; Chi ² = 74.41, df = 8 (P < 0.00001); I ² = 89%									<u>-4 -2 0 2 4</u>
Test for overall effect: $Z = 1.55$ (P = 0.12)									Mis Open

Figure 11. Forest plot for the Oswestry Disability Index scores. MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

and bilateral decompression, less stimulation to soft tissue, less inflammatory response than open surgery and faster functional recovery. Current trends in surgery favor minimally invasive procedures. The ongoing development of various procedures aims to achieve improved clinical outcomes and fewer postoperative complications.

There was no significant difference in the operative time between the two groups in this meta-analysis, probably because minimally invasive surgery requires numerous fluoroscopies to determine the location of anatomical structures such as pedicles and articular eminences of the responsible segment and requires multiple intraoperative adjustments of the access and direction, making the operation process more complicated and the instruments used more complex. Previous studies found that the operative time was longer in the MIS-TLIF group than in the open TLIF group (29,30). However, a significant correlation exists between operative time and operator proficiency. Garcia et al (31) concluded that the operator needs to perform at least 58 procedures to become proficient in MIS-TLIF and then the operative time decreases gradually. MIS-TLIF requires the operator to be experienced in open surgery and proficient in using minimally invasive surgical instruments, which explains the longer and steeper learning curve of the MIS-TLIF procedure (32). There was no significant difference in the postoperative drainage volume. Blood loss was lower in the MIS-TLIF group compared with the open TLIF group. This may be because MIS-TLIF adopts the intermuscular approach, using the working sleeve to expand step-by-step without extensive soft tissue separation and with less damage to muscle fibers. By comparison, open TLIF involves a large incision and more tissue damage, resulting in increased intraoperative bleeding. There was no significant difference in the fusion rates in the present study. There was no difference between the two groups regarding Bridwell grades I and II or overall fusion rate. The fusion rate is an important index for testing the effect of surgery, which shows whether open TLIF or MIS-TLIF, complete nerve decompression and stable fusion of surgical segments can be achieved in two-segment lumbar surgery. This is similar to the results of the single-stage surgery (33). It has also been suggested that open surgery has a higher fusion rate than minimally invasive surgery, arguing that open surgery provides cleaner handling of the disc tissue under direct vision, adequate handling of the implant bed and more bone grafting (34). There were no significant differences in postoperative complications in the present study, suggesting that minimally invasive maneuvers in two-segment lumbar spine surgery did not reduce postoperative complications. This may be related to the long duration

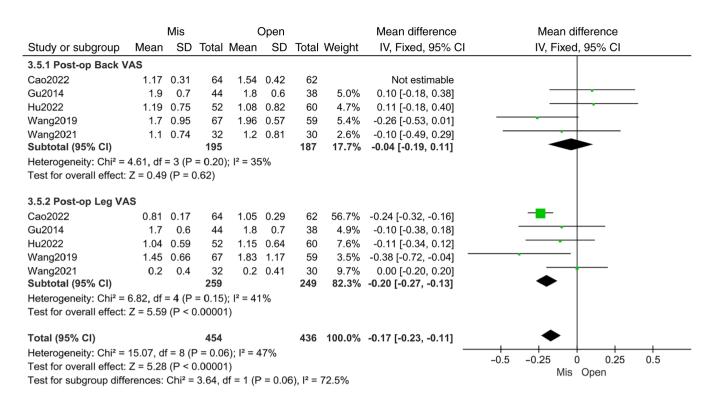


Figure 12. Forest plot for the VAS scores. VAS, Visual Analog Scale; MIS, minimally invasive transforaminal lumbar fusion; Open, Open, transforaminal lumbar fusion; SD, standard deviation; CI, confidence interval.

and high risk of injury associated with multi-segmental surgery. According to one investigation, MIS-TLIF has a higher rate of postoperative complications in multiple segments than in single segments (35). MIS-TLIF also has the disadvantage of requiring a significantly higher number of intraoperative radiations compared with the open TLIF group. MIS-TLIF requires multiple intraoperative fluoroscopies to locate the channel and reposition surgical segments. The increase in the number or duration of fluoroscopy prolongs the duration of the procedure and increases radiation exposure to the patient, which was confirmed in a study by Qin et al (36). A study found that the fluoroscopy time increased by 22.9 sec compared with the open TLIF group. By detecting the exposure dose used by the physician, it was found that the radiation dose in the MIS-TLIF group was 30 μ Sv higher than that in the open TLIF group (37). In the present study, the bed and hospitalization times of the MIS-TLIF group were shorter than those of the open-TLIF group, indicating that patients undergoing MIS-TLIF left bed and were able to be discharged from the hospital earlier. This also indirectly reflects the theoretical advantage of reduced soft tissue injury in the MIS-TLIF group. A more direct manifestation of this is lower hospitalization costs. Regarding postoperative functional indicators, the postoperative ODI and low back pain VAS scores were not statistically significant; only the postoperative leg pain VAS score was significant. Although both groups demonstrated effectively reduced postoperative symptoms, the minimally invasive group outperformed the open group regarding the postoperative leg pain VAS score. As for postoperative pain scores, postoperative opioid use may affect postoperative pain scores; however, Claus et al (38) showed that low-dose ketochromic acid and opioid use can achieve the same analgesic effect. Only Wang et al (22) studied the long-term efficacy. The ODI and VAS scores were similar between the minimally invasive and open surgery groups at 24 months and the final follow-up. This is similar to single-stage surgery, with both procedures achieving equally safe and satisfactory results while overall favoring MIS-TLIF (39). Although there are a number of articles related to open TLIF and MIS-TLIF surgeries, they all compared single-stage fusion and there are no meta-analyses on multiple segments. The common limitations of these studies include the lack of long-term follow-up, the fact that the majority of the research countries are concentrated in China and the lack of comparison between multi-segmental surgery (14,40); regarding single-stage surgery, MIS-TLIF is superior to open TLIF concerning intraoperative blood loss, shortened hospitalization and recovery times and reduced complications. However, multi-segmental surgery has no clear conclusion, which remains controversial. The present study focused on multi-segmental surgery and is the first meta-analysis to analyze the efficacy of minimally invasive open TLIF in treating multi-segmental lumbar degenerative diseases.

The present study discovered that patients with multi-segmental lumbar degenerative disorders can achieve effective relief of their postoperative symptoms, regardless of whether they undergo open-TLIF or MIS-TLIF. MIS-TLIF has the advantages of less intraoperative blood loss, shorter bedtime and shorter hospitalization time in multi-segment surgery; however, it had a significantly higher frequency of fluoroscopic surgery than open surgery. In the postoperative ODI and VAS scores, the VAS score of leg pain after MIS-TLIF was superior than that of open TLIF. There was no difference in the operative time and fusion rate. Therefore,

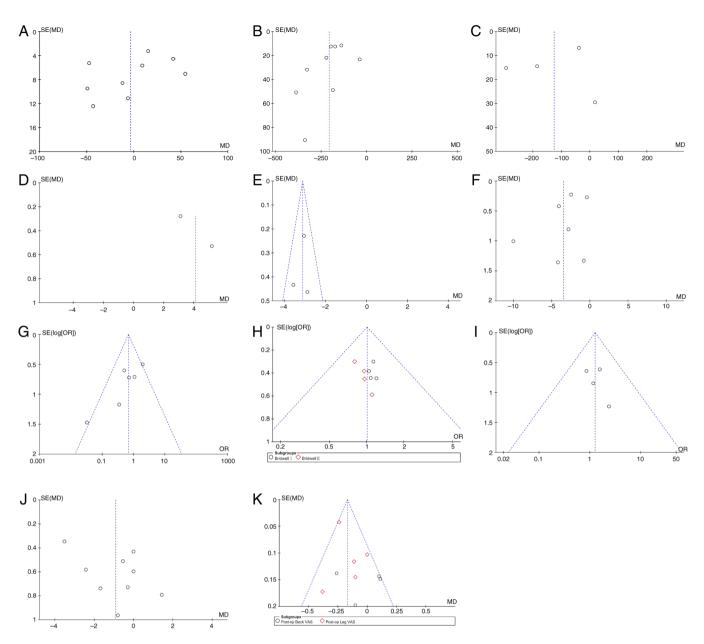


Figure 13. Funnel plots created to assess publication bias for (A) operation time, (B) intraoperative blood loss, (C) postoperative drainage volume, (D) fluoroscopy frequency, (E) postoperative in-bed time, (F) hospitalization time, (G) postoperative complications, (H) fusion rate, (I) overall fusion rate, (J) Oswestry Disability Index scores, (K) Visual Analog Scale scores. SE, standard error; MD, mean difference; CI, confidence interval.

for patients with lumbar degenerative disorders requiring multi-segment fusion surgery, MIS-TLIF is preferable to open TLIF.

The limitations of the present study included: i) The literature included in the present study lacked randomized controlled studies and high-quality articles; ii) the follow-up time of the included studies was inconsistent, which may have impacted the results and caused a lack of long-term follow-up; iii) the minimum number of included studies in the outcome indicators was two, which may have introduced some bias; iv) the countries of the researchers were relatively concentrated, with most studies conducted in China and a few studies in Europe, America and other countries; therefore, it is unknown whether the conclusion applies to other countries. Due to the quality of the articles and the high heterogeneity of some of the indicators, the results of the present study may be somewhat different from the actual results. Nevertheless, the results of the present study provide some clinical references in this field; however, more randomized controlled trials with larger sample sizes are needed to obtain more reliable results.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WJZ and ZKW were accountable for the design of the present study and both performed the statistical analyses. WJZ and ZKW confirm the authenticity of all the raw data. HLL and SLQ conducted the study and collected important background information. PFH and YFX drafted the manuscript and performed the interpretation of data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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