Systematic Review

Comparison of Clinical Outcomes and Complications Between Percutaneous Endoscopic and Minimally Invasive Transforaminal Lumbar Interbody Fusion for Degenerative Lumbar Disease: A Systematic Review and Meta-Analysis

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Free full manuscript: www.painphysicianjournal.com **Background:** Percutaneous endoscopic transforaminal lumbar interbody fusion (PE-TLIF) has been increasingly used to treat degenerative lumbar disease in recent years. However, there are still controversies about whether PE-TLIF is superior to minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF).

Objectives: To compare clinical outcomes and complications of PE-TLIF and MIS-TLIF in treating degenerative lumbar disease.

Study Design: A systematic review and meta-analysis.

Methods: A comprehensive search of online databases including PubMed, Embase, and the Cochrane Library was performed to identify related studies reporting the outcomes and complications of PE-TLIF and MIS-TLIF for degenerative lumbar disease. The clinical outcomes were assessed by the Visual Analog Scale and Oswestry Disability Index. In addition, the operative time, intraoperative blood loss, time to ambulation, length of hospital stay, fusion rate, and surgery-related complications were summarized. Forest plots were constructed to investigate the results.

Results: A total of 28 studies involving 1,475 patients were included in this meta-analysis. PE-TLIF significantly reduced operative time, intraoperative blood loss, time to ambulation, and length of hospital stay compared to MIS-TLIF. Moreover, PE-TLIF was superior to MIS-TLIF in the early postoperative relief of back pain. However, there were no significant differences in medium to long-term clinical outcomes, fusion rate, and incidence of complications between PE-TLIF and MIS-TLIF.

Limitations: The current evidence is heterogeneous and most studies included in this metaanalysis are nonrandomized controlled trials.

Conclusions: The present meta-analysis indicates that medium to long-term clinical outcomes and complication rates of PE-TLIF were similar to MIS-TLIF for the treatment of degenerative lumbar disease. However, PE-TLIF shows advantages in less surgical trauma, faster recovery, and early postoperative relief of back pain.

Key words: Percutaneous endoscopic transforaminal lumbar interbody fusion, minimally invasive transforaminal lumbar interbody fusion, degenerative lumbar disease, chronic pain, systematic review, meta-analysis

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umbar degenerative disc disease (LDDD) is a common cause of low back pain. For decades, posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF) have been used as effective surgical methods for LDDD, such as lumbar spinal stenosis, lumbar disc herniation, spondylolisthesis, and lumbar instability (1,2). However, traditional open PLIF and TLIF are associated with iatrogenic injury of paraspinal muscle, which could cause postoperative intractable low back pain (3). To reduce soft tissue injury and intraoperative blood loss, minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) was first proposed by Foley et al (4) in 2002; it has achieved excellent clinical outcomes (5,6). Nevertheless, MIS-TLIF is limited by a narrow operating space and it may be difficult to view the deeper surgical field through the tubular retractor (7).

With the development of surgical techniques and instruments, percutaneous endoscopic transforaminal lumbar interbody fusion (PE-TLIF) has been increasingly used to treat LDDD in recent years (7-9). PE-TLIF can achieve fully endoscopic discectomy, decompression of the spinal canal and foramina, and interbody fusion through the endoscopic and working portal (7-9).

So far, few studies have compared the results of PE-TLIF and MIS-TLIF and it is still uncertain whether PE-TLIF is superior to MIS-TLIF for LDDD. Therefore, the purpose of this systematic review and meta-analysis was to compare clinical outcomes and complications of PE-TLIF and MIS-TLIF in treating LDDD.

METHODS

Literature Search

The systematic review was performed on the basis of Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (10). The language of publication was restricted to English. Articles published from January 2002 through September 2020 in PubMed, Embase, and the Cochrane Library databases were searched. The search strategy was used in 2 separate components. The search terms for PE-TLIF was ((endoscop*) OR (microendoscop*)) AND (lumbar interbody fusion), whereas the search terms for MIS-TLIF was (minimally invasive transforaminal lumbar interbody fusion) OR (MIS-TLIF) OR (MI-TLIF). Articles from the same authors or institutions were examined and duplicate data sets were excluded. The number of articles included and excluded are shown in a flow chart (Fig. 1).

Selection Criteria

Articles included in this systematic review fulfilled the following criteria: 1) patients aged \geq 18 years; 2) a diagnosis of single-level or 2-level LDDD including degenerative lumbar disc herniation, lumbar spinal stenosis, foraminal stenosis and lumbar spondylolisthesis or instability; 3) failed conservative treatment for at least 6 weeks; 4) LDDD treated with PE-TLIF combined with bilateral pedicle screw fixation or MIS-TLIF combined with bilateral pedicle screw fixation; 5) studies simultaneously reporting clinical outcomes including a Visual Analog Scale (VAS) score and/or Oswestry Disability Index (ODI) score and complications; 6) more than 6 months' follow-up; and 7) articles published in SCI or SCIE journals. Studies including less than 5 patients, reporting 2 or more subgroups of patients treated with the same surgical method, involving more than 2-level lumbar degenerative diseases, infection, trauma, tumor or spinal deformity, and reporting selective patients, such as elderly patients or obese patients, were excluded.

Quality and Risk of Bias Assessment

The quality of each individual study included in this meta-analysis was assessed independently by 3 reviewers according to the Interventional Pain Management Techniques-Quality Appraisal of Reliability and Risk of Bias Assessment Tool (IPM-QRB) for randomized controlled trials (11), and Interventional Pain Management Techniques-Quality Appraisal of Reliability and Risk of Bias Assessment for nonrandomized or observational studies (IPM-QRBNR) (12). If inconsistencies occurred, a fourth reviewer would examine the result and a consensus was reached. On the basis of IPM-QRB and IPM-QRBNR criteria, studies scoring between 32 and 48 were assessed as high quality, studies scoring between 16 and 31 were assessed as moderate quality, and studies scoring less than 16 were assessed as low quality.

Data Extraction

The extracted data were as follows: The general data are shown in Supplemental Table 1 and Supplemental Table 2 (author name, publication year, country, study design, sample size, gender, age, follow-up, diagnosis, fusion level, operative time, intraoperative blood loss, time to ambulation, length of hospital stay, and fusion rate). Besides operative time, intraoperative blood loss, time to ambulation, and length of hospital stay in the general data are shown separately in Table 1. Surgery-related complications are shown in Table

2. The clinical outcomes are shown in Figs. 2-7 (VAS-back, VAS-leg, and ODI). Data from articles were extracted and analyzed independently by 3 reviewers and verified by a fourth reviewer when there was a disagreement.

Statistical Analysis

Data are presented as n (%) for categorical variables and mean ± standard deviation (SD) for continuous variables. The SPSS v.16.0 software (Chicago, IL) was used to calculate the weighted mean value of general data (follow-up, fusion level, operative time, intraoperative blood loss, time to ambulation and length of hospital stay). The Review Manager (RevMan) v.5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to merge the preoperative and postoperative clinical outcomes (VAS-back score, VAS-leg score and ODI score) in each study; an overall estimate of the effect is shown in the form of a forest plot. The formulae of Hozo (13) was used to calculate SD through the range of values if clinical data were missing SD. The treatment effect was expressed as mean difference (MD) and 95% confidence interval (CI) (confidence interval). The MD was calculated by the preoperative mean value minus the mean value at the last follow-up from each study. Heterogeneity of clinical outcomes between studies was assessed using the I² value. A sensitivity analysis by eliminating one of each included studies at a time was performed to examine the source of the heterogeneity when heterogeneity existed $(l^2 > 50\%)$. Meta-regression analysis was performed using Stata v.15.1 software (StataCorp LLC, College

Records identified through database Identification searching (n=1836) Records after duplicates removed (n=1007) Screening Records screened Records excluded by title and abstract (n=1007) (n=898) Full-text articles excluded with reasons (n=81) Eligibility Full-text articles assessed for eligibility 19 Non-bilateral pedicle screw fixation (n=109)16 Studies reporting incomplete clinical outcomes and complications 10 Study involving more than two-level Studies included in qualitative lumbar degenerative diseases. spinal synthesis Included deformity or revision (n =28) 9 Articles from the same authors or institutions and reporting duplicate data 9 Articles published in non-SCI or non-SCIE journals 7 Reviews or studies including less than 5 patients 7 Studies reporting 2 or more subgroups of patients treated with the same surgical method 4 Studies reporting other posterior Fig. 1. Flow chart. approaches, such as interlaminar approach

Table 1. Operative time, intraoperative blood loss, time to ambulation and length of hospital stay in the PE-TLIF and MIS-TLIF surgery.

Indon	Mean Pe	r Patient	Mean Per Fusion Level		
Index	PE-TLIF	MIS-TLIF	PE-TLIF	MIS-TLIF	
Operative time (min)	155	181.1	144.8	168.9	
Intraoperative blood loss (mL)	101.1	174	92.9	160.5	
Time to ambulation (day)	1.3	1.7			
Length of hospital stay (day)	3.7	5.2			

Station, TX) to examine the potential effects of followup duration and mean age on the clinical outcomes. A random effects model was used if heterogeneity still

existed. Otherwise, the fixed effects model was used ($l^2 < 50\%$). A value of P < 0.05 was considered statistically significant in all analyses. Funnel plots were construct-

Complication	PE-TLIF (n = 548)	MIS-TLIF (n = 927)
Intraoperative (n)		
Dural tear	7	11
Screw malposition	1	10
Postoperative (n)		
Neurological deficit	17	11
Wound infection	1	17
Hematoma	5	1
Urinary retention	0	17
Urinary tract infection	1	3
Atelectasis	0	8
Pneumonia	0	1
Deep vein thrombosis	0	1
Pulmonary embolus	0	1
Cage subsidence/migration	11	4
Screw loosening	3	0
Pseudarthrosis	0	2
Bone nonunion	0	1
Adjacent segment disease	0	12
Reoperation	3	27
Other	9	4

Table 2. Comparison of	complications	between P	E-TLIF and
MIS-TLIF.			

ed using Stata v.15.1 software to investigate whether there was publication bias for the VAS-back score and ODI score.

RESULTS

Study Description

A total of 28 studies (5-9,14-36) including 13 on PE-TLIF (7-9,14-23), 17 on MIS-TLIF (5-8,24-36), and 2 studies (7,8) reporting the comparison between PE-TLIF and MIS-TLIF fulfilled the inclusion criteria and were investigated in the present meta-analysis. A total of 13 studies (7-9,14-23) involved 548 patients who underwent PE-TLIF surgery. Twelve studies reported patient gender including 224 men (42.3%) and 306 women (57.7%). The mean age and fusion level of 548 patients in 13 studies (7-9,14-23) were 64 years (range 46-71.2 years) and 1.1 segments (L2-S1), respectively. The mean follow-up of 380 patients in 10 studies (7-9,14,15,17-19,21,22) was 19.8 months (range 11-27.9 months). A total of 17 studies (5-8,24-36) involved 927 patients who underwent MIS-TLIF surgery. Seventeen studies (5-8,24-36) reported patient gender including 395 men (42.6%) and 532 women (57.4%), mean age of 59.3 years (range 47.2-67.3 years) and fusion level (mean 1.1 segments, L1-S1). The mean follow-up of



A	p	ге-ор		pc	ost-op			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Ao 2020	6.11	1.83	35	0.82	0.8	35	19.1%	5.29 [4.63, 5.95]	
Heo 2017	8.12	0.63	69	2.79	2.24	69	27.7%	5.33 [4.78, 5.88]	-
Morgenstern 2020	5.5	3	51	1.2	2	51	8.5%	4.30 [3.31, 5.29]	
Quillo-Olvera 2020	7.1	2.3	7	0.86	0.69	7	2.6%	6.24 [4.46, 8.02]	
Yang 2015	5.8	1.5	50	0.8	0.8	50	37.6%	5.00 [4.53, 5.47]	+
Yang 2019	6.14	1.77	7	0.71	0.49	7	4.5%	5.43 [4.07, 6.79]	
Total (95% CI)			219			219	100.0%	5.14 [4.85, 5.43]	•
Hotorogonoity Chiz-	541 df	= 5 (P	= 0.37); I ² = 8%	6				
neterogeneity. Chir –	· J. + I, UI								
Test for overall effect:	Z = 34.8	7 (P <	0.0000	11)					-10 -5 0 5 10
Test for overall effect:	Z= 34.8	7 (P <	0.0000)1)					-10 -5 0 5 10 Favours (no effect) Favours (effect)
Test for overall effect:	Z = 34.8	- 0 (P < 7 (P <	0.0000)1) po	st-op			Mean Difference	-10 -5 U 5 10 Favours (no effect) Favours (effect) Mean Difference
Test for overall effect: B Study or Subgroup	Z = 34.8	re-op	0.0000)1) po Mean	st-op SD	Total	Weight	Mean Difference _IV, Fixed, 95% Cl	-10 -5 U 5 10 Favours (no effect) Favours (effect) Mean Difference IV, Fixed, 95% Cl
Test for overall effect: B Study or Subgroup 40 2020	Z = 34.8 pl <u>Mean</u> 5.65	re-op <u>SD</u>	0.0000 <u>Total</u> 40)1) po <u>Mean</u> 0.79)st-op <u>SD</u> 0.86	<u>Total</u> 40	Weight 27.7%	Mean Difference <u>IV, Fixed, 95% Cl</u> 4.86 [4.31, 5.41]	-10 -5 U 5 10 Favours (no effect) Favours (effect) Mean Difference IV, Fixed, 95% Cl
Test for overall effect: B Study or Subgroup Ao 2020 <uo 2016<="" td=""><td>Z = 34.8 p <u>Mean</u> 5.65 6</td><td>re-op <u>SD</u> 1.55 2.9</td><td>0.0000 <u>Total</u> 40 22</td><td>01) pc <u>Mean</u> 0.79 2.1</td><td>ost-op SD 0.86 2.3</td><td><u>Total</u> 40 22</td><td>Weight 27.7% 3.5%</td><td>Mean Difference <u>IV, Fixed, 95% Cl</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45]</td><td>-10 -5 0 5 10 Favours [no effect] Favours [effect] Mean Difference IV, Fixed, 95% Cl</td></uo>	Z = 34.8 p <u>Mean</u> 5.65 6	re-op <u>SD</u> 1.55 2.9	0.0000 <u>Total</u> 40 22	01) pc <u>Mean</u> 0.79 2.1	ost-op SD 0.86 2.3	<u>Total</u> 40 22	Weight 27.7% 3.5%	Mean Difference <u>IV, Fixed, 95% Cl</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45]	-10 -5 0 5 10 Favours [no effect] Favours [effect] Mean Difference IV, Fixed, 95% Cl
B Study or Subgroup Ao 2020 Kuo 2016 Beng 2013	Z = 34.8 p <u>Mean</u> 5.65 6 5.9	re-op 50 1.55 2.9 2.8	0.0000 <u>Total</u> 40 22 40	01) po <u>Mean</u> 0.79 2.1 0.8	ost-op SD 0.86 2.3 0.4	<u>Total</u> 40 22 40	Weight 27.7% 3.5% 10.9%	Mean Difference <u>IV, Fixed, 95% CI</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98]	-10 -5 0 5 10 Favours [no effect] Favours [effect] Mean Difference IV, Fixed, 95% Cl
B Study or Subgroup Ao 2020 Kuo 2016 Seng 2013 Avu 2018	Z = 34.8 Mean 5.65 6 5.9 7.12	re-op <u>SD</u> 1.55 2.9 2.8 1.33	0.0000 <u>Total</u> 40 22 40 77	01) <u>Mean</u> 0.79 2.1 0.8 1.84	ost-op SD 0.86 2.3 0.4 1.3	<u>Total</u> 40 22 40 77	Weight 27.7% 3.5% 10.9% 48.5%	Mean Difference <u>IV, Fixed, 95% CI</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98] 5.28 [4.86, 5.70]	-10 -5 U 5 10 Favours [no effect] Favours [effect] Mean Difference IV, Fixed, 95% CI
B Study or Subgroup Ao 2020 Kuo 2016 Seng 2013 Wu 2018 Zairi 2013	Mean 5.65 6 5.9 7.12 7.1	re-op <u>SD</u> 1.55 2.9 2.8 1.33 2.5	0.0000 <u>Total</u> 40 22 40 77 40	01) <u>Mean</u> 0.79 2.1 0.8 1.84 2.7	ost-op SD 0.86 2.3 0.4 1.3 1.75	Total 40 22 40 77 40	Weight 27.7% 3.5% 10.9% 48.5% 9.4%	Mean Difference <u>IV, Fixed, 95% C1</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98] 5.28 [4.86, 5.70] 4.40 [3.45, 5.35]	-10 -5 U 5 10 Favours (no effect) Favours (effect) Mean Difference IV, Fixed, 95% Cl
Test for overall effect. B Study or Subgroup Ao 2020 Kuo 2016 Seng 2013 Wu 2018 Zairi 2013 Fotal (95% CI)	Mean 5.65 5.9 7.12 7.1	re-op 50 1.55 2.9 2.8 1.33 2.5	0.0000 <u>Total</u> 40 22 40 77 40 219	01) <u>Mean</u> 0.79 2.1 0.8 1.84 2.7	0.86 2.3 0.4 1.3 1.75	<u>Total</u> 40 22 40 77 40 219	Weight 27.7% 3.5% 10.9% 48.5% 9.4% 100.0%	Mean Difference <u>IV, Fixed, 95% CI</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98] 5.28 [4.86, 5.70] 4.40 [3.45, 5.35] 5.01 [4.72, 5.30]	-10 -5 U 5 10 Favours (no effect) Favours (effect) Mean Difference IV, Fixed, 95% Cl
Test for overall effect B Study or Subgroup Ao 2020 Kuo 2016 Seng 2013 Wu 2018 Zairi 2013 Fotal (95% CI) Heterogeneity: Chi ² =	Z = 34.8 p <u>Mean</u> 5.65 6 5.9 7.12 7.1 5.53, df	re-op re-op <u>SD</u> 1.55 2.9 2.8 1.33 2.5 = 4 (P	0.0000 <u>Total</u> 40 22 40 77 40 219 = 0.24)	01) pc <u>Mean</u> 0.79 2.1 0.8 1.84 2.7 ∶ ² = 28	0.86 2.3 0.4 1.3 1.75	Total 40 22 40 77 40 219	Weight 27.7% 3.5% 10.9% 48.5% 9.4% 100.0%	Mean Difference <u>IV, Fixed, 95% C1</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98] 5.28 [4.86, 5.70] 4.40 [3.45, 5.35] 5.01 [4.72, 5.30]	-10 -5 0 5 10 Favours (no effect) Favours (effect) Mean Difference IV, Fixed, 95% Cl
Test for overall effect B <u>Study or Subgroup</u> Ao 2020 Kuo 2016 Seng 2013 Wu 2018 Zairi 2013 Fotal (95% CI) Heterogeneity: Chi ² = Test for overall effect:	Z = 34.8 p <u>Mean</u> 5.65 6 5.9 7.12 7.1 5.53, dfi Z = 33.9	re-op re-op <u>SD</u> 1.55 2.9 2.8 1.33 2.5 = 4 (P <	0.0000 <u>Total</u> 40 22 40 77 40 219 = 0.24) 0.0000	01) pc <u>Mean</u> 0.79 2.1 0.8 1.84 2.7 (I ² = 28 1)	0.86 2.3 0.4 1.3 1.75	Total 40 22 40 77 40 219	Weight 27.7% 3.5% 10.9% 48.5% 9.4% 100.0%	Mean Difference <u>IV, Fixed, 95% C1</u> 4.86 [4.31, 5.41] 3.90 [2.35, 5.45] 5.10 [4.22, 5.98] 5.28 [4.86, 5.70] 4.40 [3.45, 5.35] 5.01 [4.72, 5.30]	-10 -5 0 5 10 Favours [no effect] Favours [effect] Mean Difference IV, Fixed, 95% Cl

A Mean Difference Mean Difference pre-op post-op IV, Random, 95% Cl Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Ao 2020 53.94 10.87 35 12.94 4.93 35 8.5% 41.00 [37.05, 44.95] He 2017 42.3 5.7 42 28.6 11.1 42 8.5% 13.70 [9.93, 17.47] Heo 2017 8.6% 30.24 [26.51, 33.97] 45.65 12.97 69 15.41 9.07 69 Jin 2020 43.1 4.9 39 12.4 6.5 39 8.7% 30.70 [28.15, 33.25] Kim 2020 68.1 5.4 32 15.6 9.2 32 8.6% 52.50 [48.80, 56.20] Kolcun 2019 29.6 17.2 16.9 79 8.4% 12.40 [7.37, 17.43] 15.3 79 Morgenstern 2020 30.3 8.6 51 8.5 51 8.6% 18.50 [15.18, 21.82] 11.8 Park 2019 8.7% 29.20 [26.89, 31.51] 61.9 8.2 71 32.7 5.6 71 Quillo-Olvera 2020 50.8 9.1 7 7.7 4.5 7 7.9% 43.10 [35.58, 50.62] Shen 2019 48 14 18 13 11 18 7.7% 35.00 [26.77, 43.23] Yang 2015 11.6 6.3 8.5% 39.10 [34.72, 43.48] 50.7 14.5 50 50 Yang 2019 53.57 10.28 7 15.57 7.57 7.4% 38.00 [28.54, 47.46] 7 500 500 100.0% 31.80 [25.26, 38.34] Total (95% CI) Heterogeneity: Tau² = 126.54; Chi² = 369.69, df = 11 (P < 0.00001); I² = 97% -100 -50 50 100 ó Test for overall effect: Z = 9.53 (P < 0.00001) Favours [no effect] Favours [effect] B pre-op post-op Mean Difference Mean Difference Study or Subgroup IV, Random, 95% CI Mean SD Total Mean SD Total Weight IV, Random, 95% Cl Ao 2020 56.9 11.5 40 13.59 5.43 40 7.8% 43.31 [39.37, 47.25] Fan 2010 49.7 11.8 32 24.7 10.1 32 7.6% 25.00 [19.62, 30.38] . Gu 2014 43.7 4.3 44 16.5 2 44 8.1% 27.20 [25.80, 28.60] Kim 2016 7.4% 21.80 [15.23, 28.37] 16.6 50 16.9 51 29.2 50 Kim 2020 69.6 55 55 7.9% 53.30 [49.75, 56.85] 6.2 16.3 11.9 Kuo 2016 23 7.7 22 9.9 7.1 22 7.8% 13.10 [8.72, 17.48] Perez-Cruet 2014 43.1 15.7 304 30.2 20.4 304 8.0% 12.90 [10.01, 15.79] 20.1 40 13.6 2.8 40 7.5% 27.70 [21.41, 33.99] Seng 2013 41.3 Shen 2014 51.58 34 22.84 15.65 34 7.2% 28.74 [21.13, 36.35] 16.38 27.00 [19.51, 34.49] Tsahtsarlis 2012 48 16 34 21 15.5 34 7.2% Wu 2018 35.40 [32.68, 38.12] 60.7 10.6 79 25.3 6.3 79 8.0% Zairi 2013 60 12.5 40 30 11 40 7.7% 30.00 [24.84, 35.16] Zhang 2017 48.6 26 11.8 2.8 26 8.0% 36.80 [33.90, 39.70] 7 800 800 100.0% 29.48 [23.36, 35.61] Total (95% CI) Heterogeneity: Tau² = 120.48; Chi² = 462.15, df = 12 (P < 0.00001); I² = 97% 100 -100 -50 50 Ó Test for overall effect: Z = 9.44 (P < 0.00001) Favours [no effect] Favours [effect] Fig. 4 Preoperative and postoperative ODI scores of PE-TLIF (A) and MIS-TLIF (B).



Fig. 5. Comparison of VAS-back scores before surgery (A), within 2 weeks after surgery (B), 2 to 3 months after surgery (C) and at the last follow-up (D) between PE-TLIF and MIS-TLIF.

	Α	PE	E-TLIF		M	I-TLIF			Mean Difference		Mean Difference
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI
	Ao 2020	6.11	1.83	35	5.65	1.55	40	29.1%	0.46 [-0.31, 1.23]		
	Kim 2020	7.9	0.6	32	7.8	1.7	55	70.9%	0.10 [-0.40, 0.60]		
	Total (95% CI)			67			95	100.0%	0.20 [-0.21, 0.62]		
	Heterogeneity: Chi ² =	0.59, df	= 1 (P	= 0.44); I ² = 09	6				-2	-1 0 1 2
	Test for overall effect	Z = 0.96	i (P = (J.34)							Favours [PE-TLIF] Favours [MI-TLIF]
	R								Maan Difference		Maan Difference
	D Study or Subgroup	Moan	en	Total	Moan	en	Total	Mojaht	Wean Difference		Wean Difference
		1 27	1.02	26	1 40	1 1 1	10121	12.6%	0.111.0.60.0.271		
	A0 2020	1.37	1.03	30	1.48	4.4	40	43.0%	-0.11[-0.59, 0.37]		
	Kim 2020	3.3	0.9	32	3.5	1.1	55	30.4%	-0.20 [-0.63, 0.23]		-
	Total (95% CI)			67			95	100.0%	-0.16[-0.48_0.16]		-
	Heterogeneity Chi ² =	0.07 df	= 1 (P	= 0.78	· F = 0%		35	100.07	-0.10[-0.40, 0.10]	+	
	Taet for overall effect:	7 = 0.00	(P = 0	- 0.70	,1 - 0 x	,				-2	-1 Ó Í 2
	restion overall ellect.	2 = 0.50	(, -)								Favours [PE-TLIF] Favours [MI-TLIF]
	С	PE	-TLIF		м	I-TLIF			Mean Difference		Mean Difference
	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI		IV, Fixed, 95% CI
	Ao 2020	1.14	1.03	35	1.03	0.83	40	47.4%	0.11 (-0.32, 0.54)		
	Kim 2020	2.4	1	32	2.8	0.8	55	52.6%	-0.40 [-0.81, 0.01]		
	Total (95% CI)			67			95	100.0%	-0.16 [-0.45, 0.14]		
	Heterogeneity: Chi ² =	2.88, df:	= 1 (P	= 0.09)); I ² = 65	%				+	
	Test for overall effect:	Z = 1.05	(P = 0).29)						-2	Favoure (PE-TLIE) Eavoure (MI-TLIE)
	D	PF	TLIF		MI	TLIF			Mean Difference		Mean Difference
	Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Fixed. 95% CI		IV. Fixed, 95% Cl
	Ao 2020	0.82	0.8	35	0.79	0.86	40	38.4%	0.03 [-0.35, 0.41]		
	Kim 2020	1.6	0.6	32	1.8	0.8	55	61.6%	-0.20 [-0.50, 0.10]		
				•••							
	Total (95% CI)			67			95	100.0%	-0.11 [-0.34, 0.12]		◆
	Heterogeneity: Chi2=	0.89, df	= 1 (P	= 0.35); F = 09	6				+	
	Test for overall effect	Z=0.94	(P=1	0.35)						-2	-1 U 1 2
											Favours (FE-TEIF) Favours (MI-TEIF)
ig. 6. Comm	urison of VAS-le	g score	es he	fore s	urger	v (A). wi	thin 2	weeks after su	røer	$\mathbf{v}(\mathbf{B}), 2$ to 3 months after surger $\mathbf{v}(\mathbf{C})$ and
	$(\mathbf{D}) 1$		ло осу тт т	E	1 111	c m	,,		weens after su	·80.	, (D), 2 to o months after surgery (O) and
ie iast follou	y-up (D) betweer	1 P E-	ILI.	г ап	a wir,	5-11	LIF.				



666 patients in 11 studies (6-8,24-29,32,35,36) was 34.9 months (range 11-27.9 months).

Methodologic Quality and Risk of Bias Assessment

Based on the IPM-QRB and IPM-QRBNR criteria, 8 studies (4 prospective randomized controlled studies and 4 prospective cohort studies) were assessed as high quality, 13 studies (5 prospective consecutive clinical series and 8 retrospective comparative studies) were assessed as moderate quality, and 7 studies (retrospective case series) were assessed as low quality.

Surgical Trauma

For the PE-TLIF surgery, 11 studies (7-9,14-16,18-20,22,23) involving 470 patients reported mean operative time was 155 minutes (an average of 144.8 minutes per fusion level). Ten studies (8,9,14-17,19,20,22,23) involving 418 patients reported mean intraoperative blood loss was 101.1 mL (an average of 92.9 mL per fusion level). Five studies (7,9,17,22,23) involving 182 patients reported mean time to ambulation was 1.3 days. Nine studies (7-9,15-17,19,20,22) involving 331 patients reported mean length of hospital stay was 3.7 days. For the MIS-TLIF surgery, 17 studies (5-8,24-36) involving 915 patients reported mean operative time was 181.1 minutes (an average of 168.9 minutes per fusion level). Fourteen studies (5,6,8,24-29,31,32,34-36) involving 812 patients reported mean intraoperative blood loss was 174 mL (an average of 160.5 mL per fusion level). Four studies (6,7,31,36) involving 153 patients reported mean time to ambulation was 1.7 days. Fourteen studies (5-8,23,24,26-33) involving 854 patients reported mean length of hospital stay was 5.2 days.

Clinical Outcomes

The mean difference of all clinical outcomes in each study was equal to the preoperative mean value minus the mean value at the last follow-up (Figs. 2-4). For the PE-TLIF surgery, 11 studies (7-9,15,17-23) involving 379 patients reported VAS-back scores with a mean difference of 4.86 (95% CI 4.27, 5.46). Six studies (8,14,17,19,22,23) involving 219 patients (3 studies were excluded for heterogeneity) reported VAS-leg scores with a mean difference of 5.14 (95% CI 4.85, 5.43). Twelve studies (7-9,14-20,22,23) involving 368 patients reported ODI scores with a mean difference of 32.33 (95% CI 25.93, 38.72).

For the MIS-TLIF surgery, 9 studies (5-8,27,28,31,32,35) involving 363 patients (4 studies were excluded for heterogeneity) reported VAS-back scores with a mean difference of 4.26 (95% CI 4.09, 4.42). Five studies (8,28,31,34,35) involving 219 patients (3 studies were excluded for heterogeneity) reported VAS-leg scores with a mean difference of 5.01 (95% CI 4.72, 5.30). Thirteen studies (6-8, 26-29, 31-36) involving 800 patients reported ODI scores with a mean difference of 29.48 (95% CI 23.36, 35.61).

To further investigate the differences in the short and medium long-term clinical outcomes between PE-TLIF and MIS-TLIF, the clinical outcomes of 2 studies (7,8) (a prospective cohort study and a retrospective comparative study) on the comparison of PE-TLIF and MIS-TLIF were separately shown in the form of a forest plot (Figs. 5-7) and the mean difference of clinical outcomes was equal to the mean value in the PE-TLIF group minus the mean value in the MIS-TLIF group.

No statistical difference in preoperative mean VAS-back score was found between PE-TLIF surgery and MIS-TLIF surgery (MD -0.34; 95% CI -0.84, 0.16; I² = 0%; P = 0.18). However, the mean VAS-back score of PE-TLIF surgery was significantly lower than that of MIS-TLIF surgery within 2 weeks (MD -1.11; 95% CI -1.52 , -0.71; I² = 0%; P < 0.05) and 2 to 3 months (MD -0.75; 95% CI -1.45, -0.04; I² = 83%; P = 0.04) after surgery. There was no statistical difference in the mean VAS-back score between PE-TLIF surgery and MIS-TLIF surgery (MD -0.11; 95% CI -0.39, 0.17; I² = 0%; P = 0.43) at the last follow-up. Nevertheless, before surgery, within 2 weeks after surgery, 2 to 3 months after surgery, and the last follow-up, there was no statistical difference in the mean VAS-leg score between PE-TLIF surgery and MIS-TLIF surgery (P > 0.05). In addition, before surgery, 2 to 3 months after surgery, and the last follow-up, there was no statistical difference in the mean ODI score between PE-TLIF surgery and MIS-TLIF surgery (P > 0.05).

FUSION RATE

For the PE-TLIF surgery, 9 studies (7-9,15,16, 8,20,22,23) involving 379 patients reported the mean fusion rate was 95% (360/379). For the MIS-TLIF surgery, 12 studies (5-8,25-28,31-33,35) involving 475 patients reported the mean fusion rate was 94.9% (451/457).

Complications

For the PE-TLIF surgery, 13 studies (7-9, 14-23) involving 548 patients reported the incidence of intraoperative and postoperative complications as 2.2% and 7.8% respectively. The most common intraoperative complication was dural tear (1.3%). However, screw malposition (n = 1), endplate fracture (n = 1), anterior edge of intervertebral disc rupture (n = 1), anterior cortical wall of operated vertebrae rupture (n = 1), and wrong positioning of surgical level (n = 1) were rare. The most common postoperative complications included neurological deficit (3.1%) and cage subsidence/migration (2%). The rare complications included hematoma (n = 5), reoperation (n = 3), sacroiliac joint pain (n = 3), screw loosening (n = 3), wound infection (n = 1), urinary tract infection (n = 1), osteomyelitis (n = 1), and delirium (n=1).

For the MIS-TLIF surgery, 17 studies (5-8,24-36) involving 927 patients reported the incidence of intraoperative and postoperative complications as 2.5% and 10.2% respectively. The most common intraoperative complication was dural tear (1.2%) and screw malposition (1.1%). However, overlong screw (n = 1) and pedicle fracture (n = 1) were rare. The most common postoperative complications included reoperation (2.9%), wound infection (1.8%), urinary retention (1.8%), adjacent segment disease (1.3%), and neurological deficit (1.2%). The rare complications included atelectasis (n = 8), urinary cage subsidence/migration (n = 4), urinary tract infection (n = 3), pneumonia (n = 3), pseudarthrosis (n = 2), pedicle screw breakage (n = 1), bone nonunion (n = 1), hematoma (n = 1), ileus (n = 1), deep vein thrombosis (n = 1), and pulmonary embolus (n = 1).

Meta-Regression Analyses and Publication Bias

For both surgical methods, meta-regression analyses indicated that follow-up duration had no significant effect on VAS-back score, VAS-leg score, and ODI score. In addition, for the PE-TLIF surgery, mean age had no significant effect on VAS-back score, VAS-leg score, and ODI score. For the MIS-TLIF surgery, mean age had no significant effect on VAS-back score and ODI score, but had a significant effect on VAS-leg score and correlated positively with the mean difference of VAS-leg score (Table 3). The publication bias is shown in Fig. 8. For both surgical methods, there was no publication bias for VAS-back score and ODI score.

DISCUSSION

Surgical Trauma

The present meta-analysis showed that PE-TLIF significantly reduced operative time and intraoperative blood loss compared to MIS-TLIF. Ao et al (8) found that postoperative concentrations of C-reactive protein and creatine kinase in the PE-TLIF group was significantly lower than those in the MIS-TLIF group, which demonstrated that PE-TLIF results in less tissue damage than

		Follow	w-up	Mean age					
	PE-TLIF		MIS-TLIF		PE-TLIF		MIS-TLIF		
Variable	Coefficient (95% CI)	<i>P</i> > t	Coefficient (95% CI) $P > t$		Coefficient (95% CI)	<i>P</i> > t	Coefficient (95% CI)	<i>P</i> > t	
VAS-back	0.05 (-0.07, 0.17)	0.40	-0.05 (-0.14, 0.04)	0.30	-0.09 (-0.19, 0.01)	0.09	-0.01 (-0.14, 0.11)	0.83	
VAS-leg	0.06 (-0.13, 0.25)	0.56	-0.01 (-0.05, 0.03)	0.74	-0.05 (-0.20, 0.09)	0.45	0.10 (0.06, 0.14)	0.00*	
ODI	-0.69 (-2.13, 0.76)	-0.58 (-1.62, 0.46)	0.27	-0.01 (-1.18, 1.15)	0.98	0.16 (-1.26, 1.58)	0.82		

Table 3. Meta-regression of potential effect of follow-up and mean age on clinical outcomes.

Abbreviations: PE-TLIF: percutaneous endoscopic transforaminal lumbar interbody fusion; MIS-TLIF: minimally invasive transforaminal lumbar interbody fusion; CI: confidence interval; VAS: visual analog scale; ODI: Oswestry Disability Index.

*P < 0.05 was considered the factor contributing to the heterogeneity of effect. If the coefficient interval crossed both negative and positive values, it indicated that the factor has no significant effect on the heterogeneity of effect.





MIS-TLIF. In addition, this study also found that PE-TLIF significantly reduced time to ambulation and length of hospital stay compared to MIS-TLIF, which was consistent with other studies (7,8). Therefore, PE-TLIF significantly reduced surgical trauma due to conservation of posterior osseous structures including the lamina and facet compared with MIS-TLIF (8).

Clinical Outcomes

The present study shows that both PE-TLIF and MIS-TLIF can obtain satisfactory clinical outcomes after

surgery and there were no significant differences in medium to long-term clinical outcomes. However, the current study also found that PE-TLIF was significantly better than MIS-TLIF in the early postoperative relief of back pain, especially within 3 months after surgery. This result may be related to less invasion of the paraspinal muscle and facet joint in PE-TLIF surgery (8). Nevertheless, there was no significant difference in the early postoperative relief of leg pain, which may be related to the sufficient decompression of the spinal canal and foramina, both by PE-TLIF and MIS-TLIF surgery. In addition, the present study found that PE-TLIF is similar to MIS-TLIF in short and medium long-term improvement of lumbar function. Therefore, both PE-TLIF and MIS-TLIF can obtain medium to long-term satisfactory clinical outcomes.

Fusion Rate

Ao et al (8) found that the fusion rate evaluated by computed tomography image was 85.3% in PE-TLIF surgery and 92.3% in MIS-TLIF surgery at 12 months after surgery; it seemed to have a relatively longer delay to obtain fusion for PE-TLIF surgery. The reason may be concluded to be insufficient bone graft and application of an expandable cage. However, this systematic review indicated that the fusion rate of PE-TLIF surgery is similar to that of MIS-TLIF surgery, both as high as 95%, which is consistent with a previous study (7). Therefore, both PE-TLIF and MIS-TLIF can achieve satisfactory fusion rates.

Complication

The present meta-analysis shows that the overall complication rates of PE-TLIF surgery and MIS-TLIF surgery were 10% and 12.7% respectively. This study also found that the most common intraoperative complication of both PE-TLIF and MIS-TLIF surgery was dural tear, which was consistent with a previous systematic review (37). The present study also found that the incidence of postoperative neurological deficit in PE-TLIF surgery is significantly higher than that of MIS-TLIF surgery. This result may be associated with an included study which reported the incidence of postoperative neurological deficit to be 23.5% (12/51). After excluding this study, the mean incidence of postoperative neurological deficit in PE-TLIF surgery was 1%, which was similar to that of MIS-TLIF surgery (1.2%). This result indicates that neuromonitoring during the operation is necessary, especially in the early stage of PE-TLIF surgery.

The current study discovered that the incidence of postoperative cage subsidence/migration in PE-TLIF surgery is significantly higher than that of MIS-TLIF surgery. This result may be related to the following 3 reasons. Firstly, there were more elderly patients included in PE-TLIF surgery (64 vs 59.3 years), thus there may be more patients with osteoporosis, and osteoporosis was the main pathological basis for postoperative cage subsidence/migration (38). Besides, in the early stage of performing PE-TLIF surgery, it is difficult to implant the cage completely parallel to the endplate under visual endoscopy, which may increase the risk of intraoperative endplate injury. In addition, Ao et al (8) found that PE-TLIF surgery seemed to have a relatively longer delay to obtain fusion compared to MIS-TLIF surgery. Therefore, some patients removed the brace and performed normal activities when bony fusion had not been achieved 3 months after surgery, which causes the cage to migrate slightly, thereby increasing the risk of endplate injury and cage subsidence/migration.

In addition, the present study found that the incidence of wound infection of PE-TLIF surgery is significantly lower than that of MIS-TLIF surgery, which may be associated with less surgical trauma with PE-TLIF. Besides, the incidence of reoperation and adjacent segment degeneration of MIS-TLIF surgery was significantly higher than that of PE-TLIF surgery, which may be related to the longer average follow-up of MIS-TLIF (34.9 vs 19.8 months). In addition, the incidence of other systemic complications including urinary retention, urinary tract infection, pneumonia, pulmonary embolus, and deep vein thrombosis in MIS-TLIF surgery was significantly higher than that of PE-TLIF surgery, which may be associated with longer bed rest after MIS-TLIF surgery.

Limitations

This systematic review has some limitations. First, there is a high degree of statistical heterogeneity among the included studies. Besides, most studies included in this meta-analysis are nonrandomized controlled trials; there are only 2 controlled studies comparing PE-TLIF and MIS-TLIF. Therefore, more randomized controlled trials are needed to further confirm this result.

CONCLUSIONS

The present study demonstrates that PE-TLIF is effective and safe in treating LDDD. PE-TLIF was similar to MIS-TLIF for degenerative lumbar disease regarding medium to long-term clinical outcomes and complication rates. However, PE-TLIF shows advantages with less surgical trauma, faster recovery, and early postoperative relief of back pain.

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