



Full-Endoscopic versus Minimally Invasive Lumbar Interbody Fusion for Lumbar Degenerative Diseases : A Systematic Review and Meta-Analysis

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Objective : Although full-endoscopic lumbar interbody fusion (Endo-LIF) has been tried as the latest alternative technique to minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) since mid-2010, the evidence is still lacking. We compared the clinical outcome and safety of Endo-LIF to MIS-TLIF for lumbar degenerative disease.

Methods : We systematically searched electronic databases, including PubMed, EMBASE, and Cochrane Library to find literature comparing Endo-LIF to MIS-TLIF. The results retrieved were last updated on December 11, 2020. The perioperative outcome included the operation time, blood loss, complication, and hospital stay. The clinical outcomes included Visual analog scale (VAS) of low back pain and leg pain and Oswestry disability index (ODI), and the radiological outcome included pseudoarthrosis rate with 12-month minimum follow-up.

Results : Four retrospective observational studies and one prospective observational study comprising 423 patients (183 Endo-LIF and 241 MIS-TLIF) were included, and the pooled data analysis revealed low heterogeneity between studies in our review. Baseline characteristics including age and sex were not different between the two groups. Operation time was significantly longer in Endo-LIF (mean difference [MD], 23.220 minutes; 95% confidence interval [CI], 10.669–35.771; $p=0.001$). However, Endo-LIF resulted in less perioperative blood loss (MD, -144.710 mL; 95% CI, 247.941–41.478; $p=0.023$). Although VAS back pain at final (MD, -0.120; $p=0.586$), leg pain within 2 weeks (MD, 0.005; $p=0.293$), VAS leg pain at final (MD, 0.099; $p=0.099$), ODI at final (MD, 0.141; $p=0.093$) were not different, VAS back pain within 2 weeks was more favorable in the Endo-LIF (MD, -1.538; 95% CI, -2.044 to -1.032; $p<0.001$). On the other hand, no statistically significant group difference in complication rate (relative risk [RR], 0.709; $p=0.774$), hospital stay (MD, -2.399; $p=0.151$), and pseudoarthrosis rate (RR, 1.284; $p=0.736$) were found.

Conclusion : Relative to MIS-TLIF, immediate outcomes were favorable in Endo-LIF in terms of blood loss and immediate VAS back pain, although complication rate, mid-term clinical outcomes, and fusion rate were not different. However, the challenges for Endo-LIF include longer operation time which means a difficult learning curve and limited surgical indication which means patient selection bias. Larger-scale, well-designed study with long-term follow-up and randomized controlled trials are needed to confirm and update the results of this systematic review.

Key Words : Lumbar vertebrae · Intervertebral disc degeneration · Endoscopy · Minimally invasive surgical procedures · Systematic review.

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INTRODUCTION

Lumbar interbody fusion combined with screw fixation is a representative surgical technique for various lumbar degenerative disease such as spondylolisthesis, spinal stenosis, foraminal stenosis, disc herniation, symptomatic degenerative disc disease or degenerative scoliosis²⁷⁾. Lumbar interbody fusion can be carried via the anterior, direct lateral, oblique, or posterior approach, with each approach having distinct benefits and risks²⁸⁾. Among them, posterior approach has been accepted as a classic familiar approach and surgical technique has evolved over the past few decades²³⁾.

Posterior lumbar interbody fusion (PLIF) has been performed since mid-1950s, and the transforaminal lumbar interbody fusion (TLIF) was introduced in 1982^{7,22)}. In the 21st century, the trend of minimally invasive surgery (MIS) has been a major issue among many spine surgeons, leading to the development of several types of novel equipment¹⁵⁾. In particular, percutaneous transpedicular screw fixation and MIS-TLIF or MIS-PLIF using tubular retractors has become a popular alternative technique to conventional open surgery⁵⁾.

Recently, the concept and technology of full-endoscopic spine surgery has shown dramatic developments¹⁾. With the introduction of a large working cannula system, full-endoscopic lumbar interbody fusion (Endo-LIF) was suggested since the mid-2010s. In addition, the development of biportal endoscopic techniques using an arthroscope has allowed Endo-LIF to be performed through a biportal system has in the same era^{11,25)}. Endo-LIF using a single-portal or biportal endoscopic system has become the sensational trend among some experts of full-endoscopic spine surgeons as one of the latest MIS techniques for lumbar interbody fusion³³⁾.

Since late-2010s, many previous literatures have reported about the technical trials and success of Endo-LIF, as well as its favorable outcome in terms of minimized soft tissue injury, less blood loss, improvement of pain, and rapid recovery^{13,14,17,19,24,31,32,35,37)}. Furthermore, several comprehensive reviews about the development, clinical outcome, and complications of Endo-LIF have been published, providing more evidence in support of the new technique^{3,9)}. The debate over which of the two surgical methods, MIS-TLIF/PLIF or Endo-LIF, is more effective and safer has not yet been established. Several clinical observational studies have directly compared the two techniques, but the results are inconclusive and con-

troversial³⁾.

To our knowledge, no meta-analysis has been published on direct comparative study between Endo-LIF and MIS-TLIF/PLIF. Therefore, the objective of the present systematic review and meta-analysis is to compare the effectiveness and safety of Endo-LIF to MIS-TLIF/PLIF in terms of perioperative surgical, clinical, and radiological outcomes.

MATERIALS AND METHODS

Institutional Review Board submission and approval was not required for this study. We strictly followed the Cochrane Handbook for Systematic Reviews of Interventions protocol, and this study was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses^{12,21)}.

Search strategy

We searched Medline using PubMed, EMBASE, and the Cochrane Library databases on December 11, 2020, without restricting the region, publication type, or language. The following search strategy was used : percutaneous endoscopic AND minimally invasive AND fusion AND lumbar.

Eligibility criteria

Only English-language articles were included in this study. First, duplicated articles were deleted, and the remaining articles were assessed by the title and abstracts. We excluded articles about air-based micro-endoscopic technique using a tubular retractor system, laparoscopic anterior lumbar interbody fusion, and endoscopy-assisted oblique lumbar interbody fusion. Second, systematic reviews, meta-analyses, cadaveric studies, laboratory articles, expert opinions, case reports, and technical reports without an analysis of cases were excluded. Finally, after the screening process, full texts were reviewed and excluded if they met any of the following exclusion criteria : 1) non-comparative study, 2) articles about stand-alone endoscopic fusion without percutaneous screw fixation, and 3) not related to clinical outcome including pain, complication, operation time, blood loss, or fusion rate. Two authors independently extracted and reviewed relevant articles according to the eligibility criteria, and a consensus was established about any inconsistencies found during the selection process.

Methodological evaluation and quality assessment

The methodological quality of each study included in the meta-analysis was assessed based on the Cochrane Handbook for Systematic Reviews of Interventions (version 6.1.0). Risk of bias and quality of studies was assessed using Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) guidelines⁶⁾. Based on the study characteristics as a non-randomized controlled study, the quality of each selected study was evaluated using the modified Newcastle-Ottawa scale³⁰⁾ which consists of three factors: patient selection, comparability of the study groups, and assessment of outcomes.

Data analysis and statistical methods

We investigated the following baseline parameters: publication area, publication period, patient number, patient age, gender, follow-up period, indications of surgery, surgical approach (Endo-LIF or MIS-TLIF/PLIF). A database of the selected studies was created for the meta-analysis. We analyzed the Visual analog scale (VAS) scores of back pain or leg pain and changes in the Oswestry disability index (ODI) to evaluate the clinical efficacy of each surgical technique. Operation

time, blood loss, hospital stay, and surgery-related complication rate were analyzed to evaluate perioperative outcomes indicating the difficulty or invasiveness of each surgical technique. In addition, the fusion rate at the final follow-up was analyzed to compare the radiological outcome between the two surgical techniques.

All meta-analyses were performed using open meta analyst and Review Manager 5.4.1 (Cochrane Collaboration, London, UK); publication bias was checked using the Beg and Egger test in Stata 11.0 (Stata Corporation, College Station, TX, USA) via⁸⁾. A random-effects model was applied to derive robust results in all analyses. All results were presented as the weighted mean difference (MD) in continuous variables and odds ratio (OR) or risk ratio (RR) in dichotomous variables with 95% confidence interval (CI). Statistical heterogeneity among different studies was evaluated using the chi square test, and values of $I^2 > 50\%$ or $p < 0.10$ indicated significant heterogeneity.

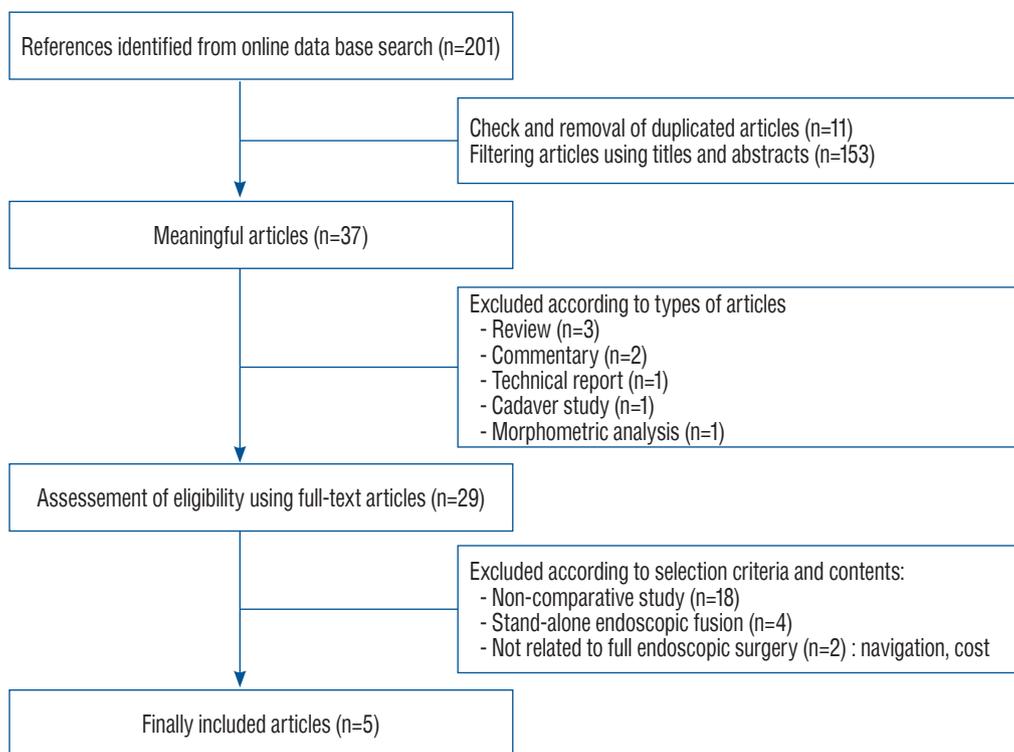


Fig. 1. Study selection process.

RESULTS

Study selection

The database search resulted in the identification of 201 studies. After the removal of duplications (n=11) and screening of titles and abstracts (n=153), a total of 37 articles remained. Among them, review articles, simple commentaries, technical reports, cadaver studies, and morphometric analyses

were excluded, and 29 articles remained for full text review. After thorough review of the text, 24 articles were excluded according to the aforementioned exclusion criteria (18 non-comparative studies, four stand-alone endoscopic fusions, and two unrelated to clinical outcome). A total of five studies were included in final study selection (Fig. 1).

Table 1. Study characteristics

Study	Number of patients			Age (years)		Follow-up duration (months)	Endo-LIF technique	Diagnosis, Endo-LIF/MIS-TLIF, PLIF	Surgery level, Endo-LIF/MIS-TLIF, PLIF
	Total (male/female)	Endo-LIF (male/female)	MIS-TLIF/PLIF (male/female)	Endo-LIF	MIS-TLIF/PLIF				
Park et al. ²⁶⁾ (2019) (n=141)	141 (46/95)	71 (26/45)	70 (20/50)	68±8	66±9	12	Biportal, posterolateral	Stenosis : 7/11	L3-4 : 13/8 L4-5 : 50/56 L5-S1 : 8/6
Heo et al. ¹⁰⁾ (2019) (n=69)	69 (26/43)	23(7/16)	46 (19/27)	61.4±9.4	63.5±10.5	12	Biportal, posterolateral	Not available	L3-4 : 3/4 L4-5 : 17/19 L5-S1 : 3/13
Ao et al. ⁴⁾ (2020) (n=75)	75 (38/37)	35(16/19)	40 (22/18)	52.80±7.50	53.68±7.24	12	Uniportal, transKambin	Not available	L3-4 : 1/1 L4-5 : 25/19 L5-S1 : 9/20
Li et al. ²⁰⁾ (2020) (n=52)	52 (30/22)	22 (12/10)	30 (18/12)	52.0±8.38	50.7±8.9	12	Uniportal, posterolateral	Disc herniation : 6/4 Stenosis : 12/18 Spondylolisthesis : 4/8	L4-5 : 14/20 L5-S1 : 8/10
Kim et al. ¹⁸⁾ (2021) (n=87)	87 (42/45)	32 (17/15)	55 (25/30)	70.5±8.26	67.3±10.7	14	Biportal, posterolateral	Spondylolisthesis : 32/55	L2-3 : 1/0 L3-4 : 3/2 L4-5 : 20/46 L5-S1 : 8/7

Endo-LIF : endoscopic lumbar interbody fusion, MIS-TLIF/PLIF : minimally invasive surgery-transforaminal lumbar interbody fusion/posterior lumbar interbody fusion

Table 2. Grading of quality clinical studies based on GRADE guidelines

Study	Country	Study design	Risk of bias	Indirectness	Imprecision	Publication bias	Large effect	Plausible residual confounding	Total	Quality of evidence
Park et al. ²⁶⁾ (2019) (n=141)	Korea	Non-RCT	-2	0	0	0	1	0	-1	Moderate
Heo et al. ¹⁰⁾ (2019) (n=69)	Korea	Non-RCT	-2	0	0	0	0	0	-2	Low
Ao et al. ⁴⁾ (2020) (n=75)	China	Non-RCT	-1	0	0	0	0	0	-1	Moderate
Li et al. ²⁰⁾ (2020) (n=52)	China	Non-RCT	-2	0	0	0	0	0	-2	Low
Kim et al. ¹⁸⁾ (2021) (n=87)	Korea	Non-RCT	-2	0	0	0	0	0	-2	Low

GRADE : Grading of Recommendations, Assessment, Development, and Evaluation, RCT : randomized controlled trial

Characteristics of eligible studies

One article was a prospective non-randomized controlled trial (non-RCT) and other four reports were retrospective studies. The publication periods were between 2019 and 2020, and all studies were performed in East-Asian countries. The patient number ranged from 52 to 141 patients, and minimum follow-up duration of all studies ranged from 12 to 14 months. Three studies performed biportal surgeries and two studies performed single-portal surgeries^{4,10,18,20,26}.

All studies specified the indication as lumbar degenerative disease including disc herniation, stenosis, or spondylolisthesis. Also, all studies reported clinical outcome including pre-

operative and postoperative VAS of back/leg or ODI, surgical outcomes including operation time, blood loss, hospital stay, or incidence of complication, and radiological outcome including fusion rates (Table 1).

Risk of bias and quality of study

Because all five studies were classified as non-RCT, the risk for selection bias of the studies was considered high. There was a high risk of performance bias due to a lack of allocation concealment and blinding of participants. Attrition bias was high in all studies due to patient selection process, follow-up loss, and other excluding factors not mentioned. Consequent-

Table 3. Risk of bias and quality of studies considering non-RCT based on modified Newcastle-Ottawa scale

Study	Data collection	Level of evidence	Risk of bias	Modified Newcastle-Ottawa scale			
				Selection	Comparability	Outcome	Sum of quality score
Park et al. ²⁶ (2019) (n=141)	Retrospective	4	High	3	4	3	10
Heo et al. ¹⁰ (2019) (n=69)	Retrospective	4	High	2	4	3	9
Ao et al. ⁴ (2020) (n=75)	Prospective	4	High	3	4	3	10
Li et al. ²⁰ (2020) (n=52)	Retrospective	4	High	3	4	3	10
Kim et al. ¹⁸ (2021) (n=87)	Retrospective	4	High	3	4	3	10

RCT : randomized controlled trial

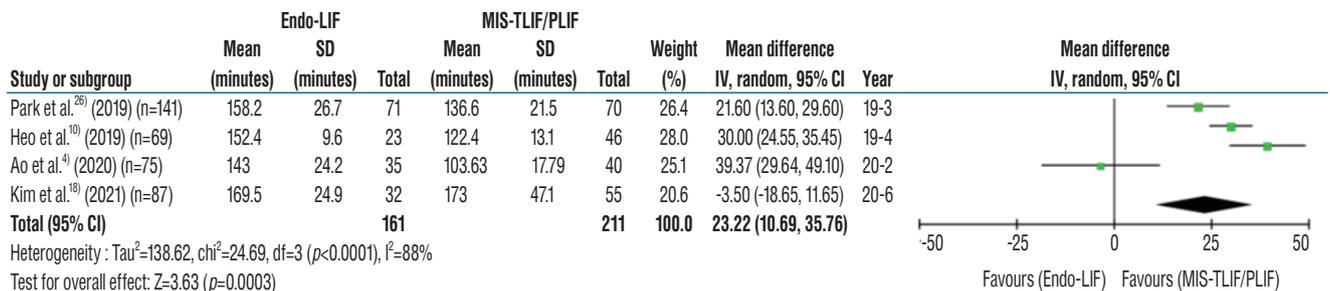


Fig. 2. Operation time. Endo-LIF : endoscopic lumbar interbody fusion, MIS-TLIF/PLIF : minimally invasive surgery-transforaminal lumbar interbody fusion/posterior lumbar interbody fusion, SD : standard deviation, CI : confidence interval.

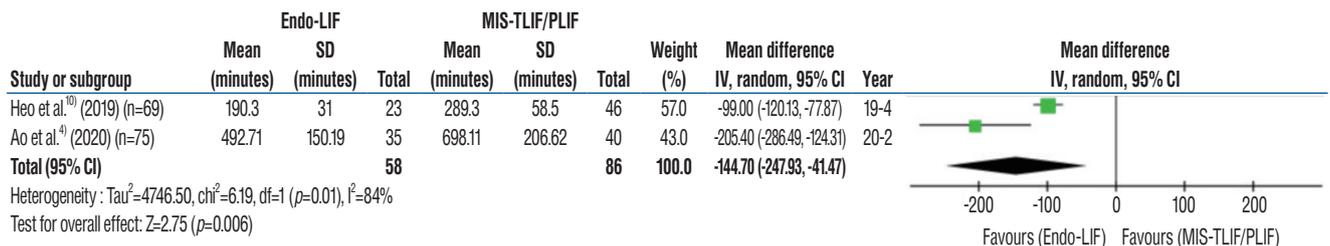


Fig. 3. Estimated blood loos during surgery. Endo-LIF : endoscopic lumbar interbody fusion, MIS-TLIF/PLIF : minimally invasive surgery-transforaminal lumbar interbody fusion/posterior lumbar interbody fusion, SD : standard deviation, CI : confidence interval.

ly, according to GRADE guidelines, two studies were considered as moderate-quality evidence and the other three studies were low-quality evidence (Table 2).

However, considering that all studies were non-RCTs, meth-

odological quality of the evidence was high in all studies based on modified Newcastle-Ottawa scale (Table 3).

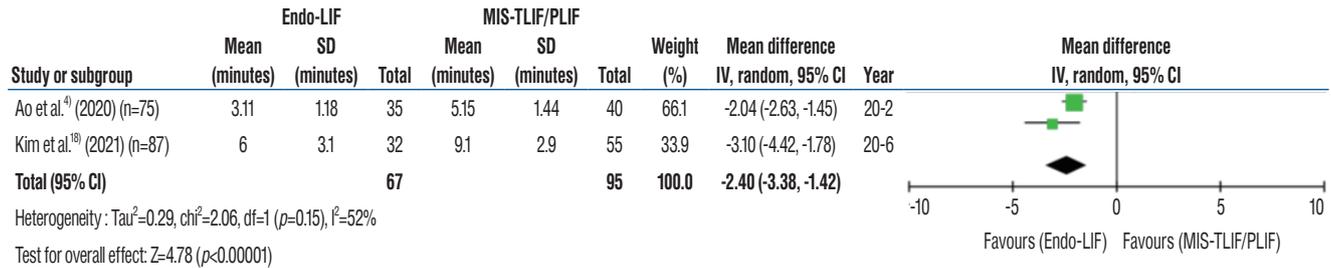


Fig. 4. Hospital stay after surgery. Endo-LIF : endoscopic lumbar interbody fusion, MIS-TLIF/PLIF : minimally invasive surgery-transforaminal lumbar interbody fusion/posterior lumbar interbody fusion, SD : standard deviation, CI : confidence interval.

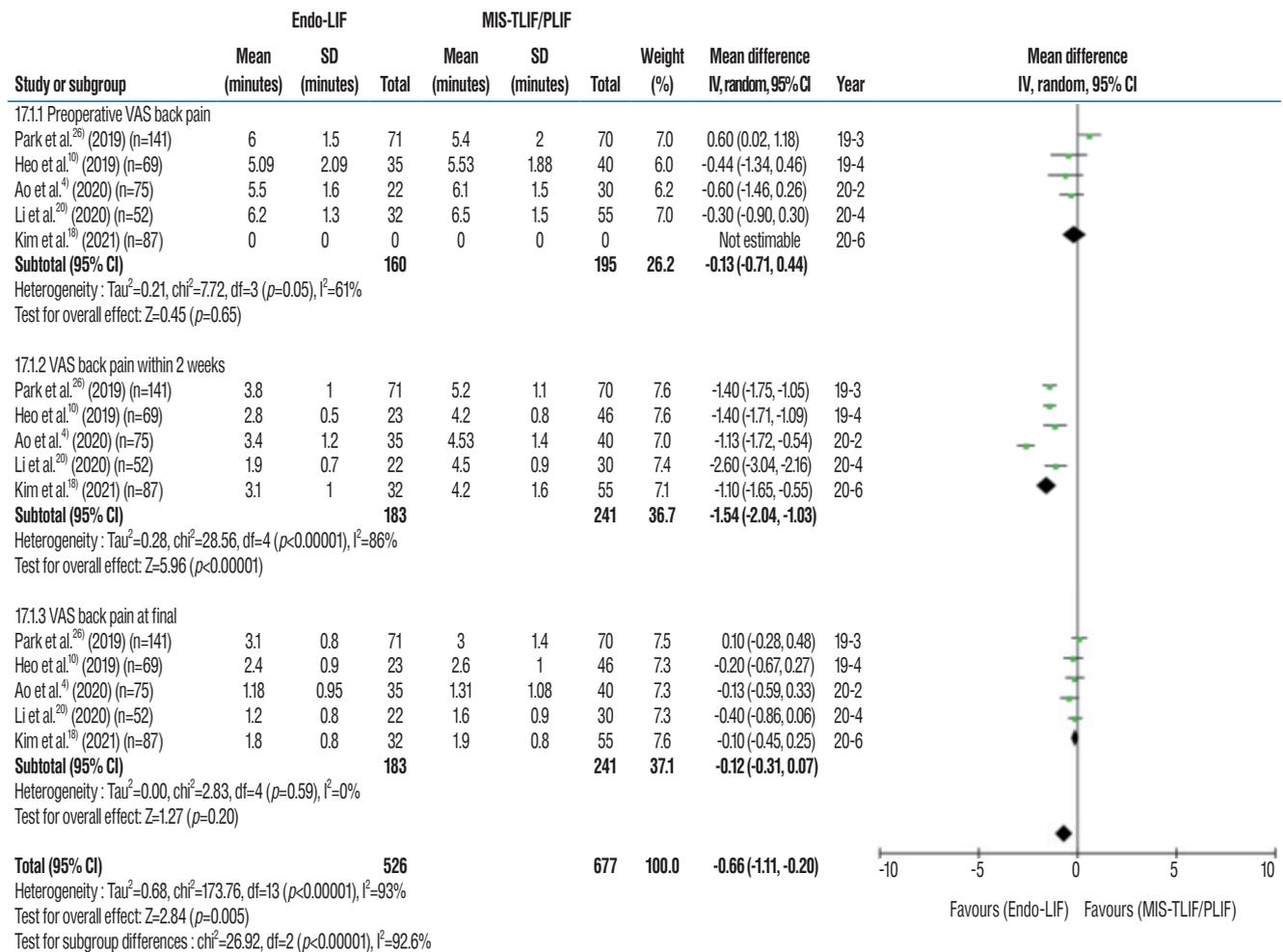


Fig. 5. Preoperative and postoperative VAS scores of back pain. Endo-LIF : endoscopic lumbar interbody fusion, MIS-TLIF/PLIF : minimally invasive surgery-transforaminal lumbar interbody fusion/posterior lumbar interbody fusion, SD : standard deviation, CI : confidence interval, VAS : Visual analog scale.

Results of studies

Baseline characteristics

In total, 424 adult patients (183 endo-LIF and 241 MIS-TLIF/PLIF) were included, with an average age of 60.62 years (95% CI, 55.907–65.327) at the time of surgery. There was no intergroup difference in the mean age (MD, 0.92; 95% CI, -0.84 to 2.68; $p=0.31$) and male ratio (OR, 1.01; 95% CI, -0.68 to 1.52; $p=0.95$).

Perioperative surgical outcomes

In terms of operation time, Endo-LIF group revealed significantly longer operation time compared to MIS-TLIF/PLIF group (MD, 23.22 minutes; 95% CI, 10.29–35.76; $p=0.0003$) (Fig. 2). However, the estimated blood loss during surgery was significantly less in the Endo-LIF group than in the MIS-TLIF group (MD, -144.70 minutes; 95% CI, -247.93 to -41.47; $p=0.006$) (Fig. 3). In addition, the mean hospital stay was significantly shorter in the Endo-LIF group than in the MIS-group (MD, -2.40 days; 95% CI, -335 to -1.42; $p=0.00001$) (Fig. 4). Meanwhile, the overall complications related to surgery was not different between the two groups (RR, 0.71; 95% CI, 0.32–1.57; $p=0.40$).

Clinical outcomes

Preoperative back pain VAS scores were not significantly different between the two groups (MD, -0.13; 95% CI, -0.71 to 0.44; $p=0.65$). Back pain VAS scores at final follow-up were, also, not significantly different between the two groups (MD, -0.12; 95% CI, -0.31 to 0.07; $p=0.20$). However, postoperative back pain VAS scores within 2 weeks after surgery was significantly favorable in the Endo-LIF group compared to MIS-TLIF/PLF group (MD, -1.54; 95% CI, -2.04 to -1.03; $p<0.00001$) (Fig. 5).

Leg pain VAS scores were not significantly different between the two groups at the preoperative period, within 2 weeks after surgery, and at the final follow-up (MD, 0.01; 95% CI, -0.32 to 0.35; $p=0.94$; MD, 0.08; 95% CI, -0.13 to 0.29; $p=0.45$; and MD, 0.09; 95% CI, -0.11 to 0.30; $p=0.37$, respectively).

ODIs were also not significantly different between two groups at preoperative period and final follow-up (MD, -0.46; 95% CI, -3.86 to 2.93; $p=0.79$; and MD, 0.14; 95% CI, -1.42 to 1.70; $p=0.86$, respectively).

Radiological outcomes

The overall fusion failure rates at the final follow-up were not significantly different between the two groups (RR, 1.29; 95% CI, 0.77–2.16; $p=0.33$).

DISCUSSION

Two surgical techniques are available for water-based full-endoscopic interbody fusion : single-portal surgery using a large-diameter working cannula through a single portal and biportal surgery using two arthroscopes through two portals. Full-endoscopic fusion also has two surgical trajectories : the trans-Kambin approach, which is similar to percutaneous endoscopic transforaminal lumbar discectomy³²⁾ and the posterolateral approach which is similar to classic MIS-TLIF using a tubular retractor^{11,16)}. In terms of invasiveness to surrounding anatomical structures and risk of traversing nerve root injury, trans-Kambin approach is more favorable than posterolateral approach³⁴⁾. However, in terms of risk of exiting nerve root injury and feasibility of decompression of the central canal and lateral recess, the posterolateral approach is more favorable than trans-Kambin approach³⁴⁾. The trans-Kambin approach can be performed using the single-portal endoscopic system, whereas the posterolateral approach can be performed using both single-portal and biportal endoscopic instruments⁹⁾.

In terms of literature evidence, Endo-LIF has a very short history and lacks high-quality clinical studies; whereas MIS-TLIF/PLIF has a legacy spanning two decades along with abundant amount of high-quality clinical studies. However, recent reports including five comparative studies and one review article have suggested similar or superior results in Endo-LIF compared to MIS-TLIF/PLIF in terms of clinical outcome and complication rates^{4,9,10,18,20,26)}. In the present systematic review and meta-analysis, the overall clinical outcomes and surgical outcomes were not significantly different between the two groups. Interestingly, intraoperative blood loss, duration of hospital stay, and immediate postoperative back pain within 2 weeks after surgery were more favorable in the Endo-LIF group than in the MIS-TLIF/PLIF group. These results seem to be attributable to the less invasive nature of Endo-LIF, such as a smaller incision and less dissection of the paraspinal muscles.

The representative pitfalls of full-endoscopic spine surgery compared with microscopic surgery include unfamiliarity with the two-dimensional endoscopic view and anatomical orientation, difficult learning curve, and major surgery-related complications, such as dura tearing or nerve injury^{2,29)}. According to this systematic review, the Endo-LIF group had a significantly longer operation time than the MIS-TLIF/PLIF group. Nevertheless, the overall complication rates did not differ between the two groups. Although Endo-LIF has a more difficult learning curve than microscopic surgery, its surgical safety is comparable to that of MIS-TLIF/PLIF in terms of complication rates. However, novice endoscopic surgeons can face issues such as serious complications, surgical failure, conversion to microscopic surgery, or an unreasonably long operation time²⁹⁾. Sufficient education and training are mandatory to overcome this difficult learning curve.

One of the major concerns about Endo-LIF compared to MIS-TLIF/PLIF is the issue of fusion rate. Intuitively, Endo-LIF seems to be at a disadvantage compared to MIS-TLIF/PLIF in terms of end-plate preparation during procedure and insertion of a sufficiently large cage. However, according to this study, the fusion failure rates at final follow-up were not significantly different between the two groups. Considering the detailed surgical procedure, end-plate preparation without osseous endplate injury tends to be more effective in Endo-LIF because endplate preparation is more meticulous under a clear magnified endoscopic view^{4,11,26)}. In addition, the technical inefficiency of cage insertion has been overcome with technological advances including development of surgical tubular retractor for cage insertion, invention of specified instrument for endplate preparation, introduction of expandable cages and support of percutaneous pedicle screw^{9,36)}.

Although the Endo-LIF technique is one of the most cutting-edge and effort-demanding surgical approaches, it has been performed by some expert spine endoscopic surgeons without major obstacles. This bias in surgeon proficiency may affect the outcome of Endo-LIF, possibly leading to underestimation of complications or overestimation of clinical outcomes. There were no high-quality studies including randomized controlled prospective studies. It was impossible to avoid various biases, including patient selection bias from the different surgical indications between the two groups, performance bias from non-blinding of participants, and outcome assessment bias. In particular, unlike MIS-TLIF/PLIF, the applica-

tion of Endo-LIF can be limited in severe cases, such as high-grade spondylolisthesis or bilateral foraminal stenosis, and these different surgical indications can cause patient selection bias.

In addition, the numbers of studies and patients were too small (241 patients in five studies). Consequently, reporting bias cannot be avoided. Further, the overall follow-up period was too short (ranging from 12 to 14 months) to determine the clinical efficacy of Endo-LIF. However, this study offers a meaningful general comparison of Endo-LIF and MIS-TLIF/PLIF. Randomized controlled prospective studies or comparative studies with a larger sample size and longer follow-up period are required to confirm the results of the present study.

CONCLUSION

According to this meta-analysis, the overall outcome including about 1-year clinical outcome, surgical complication, and fusion rate were not different significantly between the two groups. However, in terms of rapid recovery after surgery with less invasiveness, less bleeding, and diminished surgery-related back pain, Endo-LIF is more favorable compared to MIS-TLIF/PLIF, despite a disadvantages of difficult learning curve and longer operation time.

AUTHORS' DECLARATION

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Informed consent

This type of study does not require informed consent.

Author contributions

Conceptualization : SS, BRY; Data curation : SS, BRY; Formal analysis : SS, BRY; Funding acquisition : SS; Methodology : SS, BRY, SGL, WKK, JMJ; Project administration : SS, BRY; Visualization : SS, BRY, SGL, WKK, JMJ; Writing - original draft : SS, BRY; Writing - review & editing : SGL, WKK, JMJ

Data sharing

None

Preprint

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