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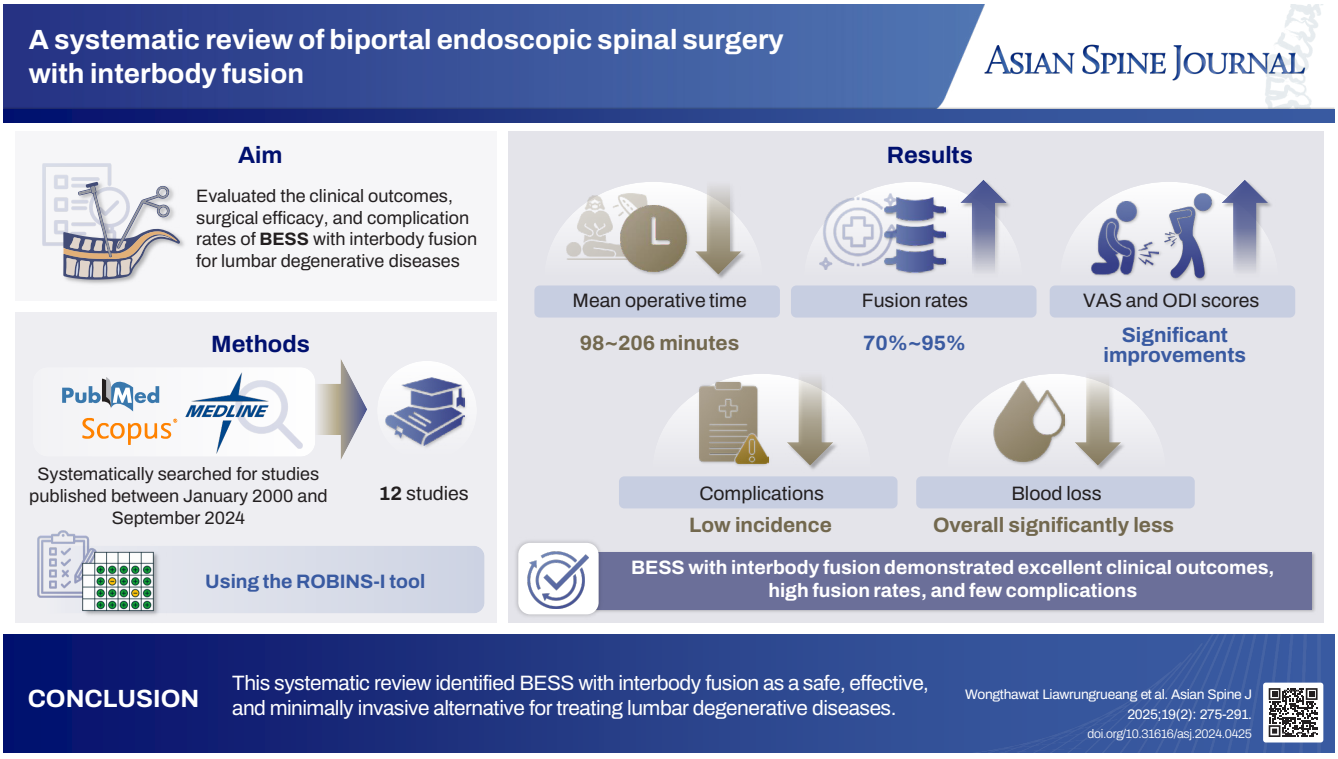

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A systematic review of biportal endoscopic spinal surgery with interbody fusion

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Biportal endoscopic spinal surgery (BESS) with interbody fusion is a relatively novel minimally invasive technique that was developed to reduce soft tissue trauma and intraoperative blood loss and shorten recovery time while achieving comparable clinical outcomes for lumbar degenerative diseases. Despite the growing interest in BESS, a comprehensive analysis of its effectiveness, complication rates, and long-term outcomes remains lacking. This systematic review evaluated the clinical outcomes, surgical efficacy, and complication rates of BESS with interbody fusion for lumbar degenerative diseases. Recent literature on endoscopic lumbar interbody fusion was included to expand the scope and gain new perspectives, thereby, providing a comparative analysis that highlighted the advantages, limitations, and emerging trends in minimally invasive spine surgery. This review synthesized current evidence to guide future research and clinical applications. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and using a combination of MeSH (Medical Subject Headings) terms and relevant keywords, PubMed/Medline and Scopus databases were systematically searched for studies published between January 2000 and September 2024. The studies were assessed using the ROBINS-I (Risk of Bias in Non-randomized Studies of Interventions) tool to determine the risk of bias. From the 12 studies that provided clinical evidence, the data extracted were patient demographics; operative time; blood loss; clinical outcomes, such as Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores and fusion rates; and complications. The mean operative time ranged from 98 to 206 minutes, with fusion rates between 70% and 95%. Most studies reported significant improvements in VAS scores for back and leg pain and ODI scores. Complications, including dural tears (2.9%–6.4%) and hematomas (1.4%–4.3%), were infrequent but notable. BESS with interbody fusion demonstrated excellent clinical outcomes, high fusion rates, and few complications. Although these results are promising, more randomized controlled trials and long-term studies are required to confirm the broader applicability, particularly in more complex or multilevel spinal pathologies.

Keywords: Endoscopy; Lumbar vertebrae; Spinal fusion; Minimally invasive surgery; Degeneration

Introduction

Lumbar degenerative diseases, such as degenerative disc disease, lumbar spinal stenosis, and spondylolisthesis, are the leading causes of chronic back pain and disability worldwide [1,2]. Given the expected increase in the prevalence of these conditions in the aging population, the increasing demand for effective surgical treatments that minimize morbidity and optimize patient outcomes has been underscored [3,4]. Traditional open fusion techniques, such as posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF), have long been the standard surgical intervention when conservative treatment fails [4-6]. However, despite their efficacy in spinal stability and decompression, these traditional techniques are associated with significant drawbacks, including extensive soft tissue disruption, prolonged recovery time, high complication rates, and postoperative pain [7].

To overcome the current challenges in minimally invasive spine surgery (MISS), techniques have been developed over the past 2 decades, aiming to reduce the physiological impact of spinal fusion surgery while maintaining or improving clinical outcomes [8,9]. Biportal endoscopic spinal surgery (BESS) with interbody fusion has emerged as a promising alternative to traditional open techniques. BESS uses two small portals to allow simultaneous decompression and interbody fusion, minimize muscle dissection, and preserve the posterior musculature and ligamentous structures. This approach has been reported to reduce intraoperative blood loss, decrease postoperative pain, and lead to faster recovery and shorter hospital stays [8,10,11]. The BESS technique offers several theoretical advantages, including enhanced operative field visualization through endoscopic magnification, which allows precise decompression and placement of interbody cages. This technique is particularly advantageous in patients with comorbidities, such as obesity and osteoporosis, which increase surgical risks [11-14].

Over the past decade, minimally invasive techniques have become increasingly popular for treating lumbar degenerative diseases. Although BESS has shown promising results in reducing surgical trauma and facilitating faster recovery, its comparison with emerging techniques, such as endoscopic lumbar interbody fusion (EndoLIF), remains underexplored. Incorporating recent findings on EndoLIF can provide an in-depth context for understanding the outcomes of BESS and will highlight the current landscape and clinical implications of minimally invasive approaches [15,16]. This review aimed to bridge this gap by providing an updated systematic analysis of the current literature on BESS and its newer alternatives, offering a unique contribution to the field. We comprehensively evaluated the clinical outcomes, surgical efficacy, and complications of BESS with interbody fusion. By synthesizing available evidence, we aimed to better understand the role of BESS in treating lumbar degenerative diseases and its potential advantages and limitations compared with traditional spinal fusion methods. In addition, we explored the current technological advancements and future directions of BESS in the field of spinal surgery.

Methods

Literature search strategy

A systematic literature search was conducted using the PubMed/Medline and Scopus databases, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The goal of this study was to identify relevant studies on BESS with interbody fusion. A combination of the following MeSH (Medical Subject Headings) terms and keywords was used to ensure comprehensive topic coverage: "unilateral," "biportal," "endoscopic," "fusion," "endoscopic spinal fusion," "endoscopic lumbar interbody fusion," "lumbar interbody fusion," and "minimally invasive spine surgery." The search was restricted to studies published in English between January 2000 and September 2024. In addition, the bibliographies of the included articles were manually searched to identify additional relevant studies. Only peer-reviewed full-text studies were considered for inclusion. This systematic review was conducted in accordance with the PRISMA guidelines [17]. Although ideal for quantitative synthesis, a meta-analysis was not feasible because of the heterogeneity in study design, patient selection, surgical techniques, and outcome reporting among the included studies. Therefore, a narrative review approach was adopted for in-depth qualitative synthesis. When more homogeneous datasets become available in the future, meta-analyses will be valuable for ensuring robust data pooling and analysis.

Inclusion and exclusion criteria

The inclusion criteria focused on original research articles, including randomized controlled trials (RCTs), prospective or retrospective cohort studies, and case-control studies, published in peer-reviewed journals. Eligible studies provided quantitative data on the clinical outcomes of BESS with interbody fusion, such as Visual Analog Scale (VAS), Oswestry Disability Index (ODI), fusion rates, and follow-up duration. Only studies in English published between January 2000 and September 2024 were considered. The exclusion criteria were narrative reviews, meta-analyses, letters to the editor, conference abstracts, case reports, studies that focused solely on decompression without interbody fusion or with incomplete data on patient demographics or outcomes, and articles on cervical or thoracic spine procedures.

Data extraction

Two reviewers independently extracted the data using a standardized form to ensure consistency. The extracted variables included study characteristics (design, sample size, year, and country); patient demographics (age, sex, diagnosis, and operative levels); and surgical details (operative time, blood loss, type of interbody cage, and instrumentation). Clinical outcomes, including preoperative and postoperative VAS scores for back and leg pain, ODI, and radiological fusion rates, were recorded. Complications, such as dural tear, infection, hematoma, and hardware-related issues; reoperations; and revisions were systematically noted. Data on follow-up duration were also collected. Discrepancies in extraction were resolved through discussion, and a third reviewer was consulted if necessary. All data were compiled into a spreadsheet for subsequent analysis, ensuring comprehensive evaluation of BESS with interbody fusion across the included studies.

Assessment of risk of bias

Risk of bias was assessed using appropriate tools based on the study design. For nonrandomized studies, the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool evaluated seven domains to rate the risk of bias as low, moderate, serious, or critical [18]. For RCTs, the RoB 2 tool (Cochrane, London, UK) as-

sessed five domains to categorize the risk of bias as low, some concerns, or high [19]. Two reviewers conducted independent assessments, and disagreements were resolved through discussion and consultation with a third reviewer.

Ethics statement

This study received ethical approval for this systematic review article from the ethical committees in accordance with the Declaration of Helsinki. Approval was granted by the Ethics Committee and Institutional Review Board (IRB) of the University of Phayao (IRB no., HREC-UP-HSST 1.1/006/68).

Results

A total of 4,972 records were identified from the PubMed/Medline and Scopus databases; 3,470 duplicate records and 410 non-English articles were removed, leaving 1,092 records for screening. After removing 301 records based on title and abstract screening, 791 reports underwent full-text retrieval and eligibility assessment. Following a thorough review, 64 reports were evaluated for eligibility; 52 reports were excluded because they were unrelated to endoscopic surgery, focused on decompression without fusion, or involved fusion without interbody fusion. The 12 studies that best matched the inclusion criteria were included in this review. These studies provided data on patient outcomes, surgical efficacy, and complication rates. Fig. 1 shows the details of the study selection process according to the PRISMA flow diagram.

Study characteristics and patient demographics

The 12 studies in this systematic review included a combined sample of (total number) patients, were published between 2017 and 2024, and were primarily conducted in South Korea and China, with one study conducted in Indonesia. Most used a retrospective cohort design, although some had a prospective design. The sample size

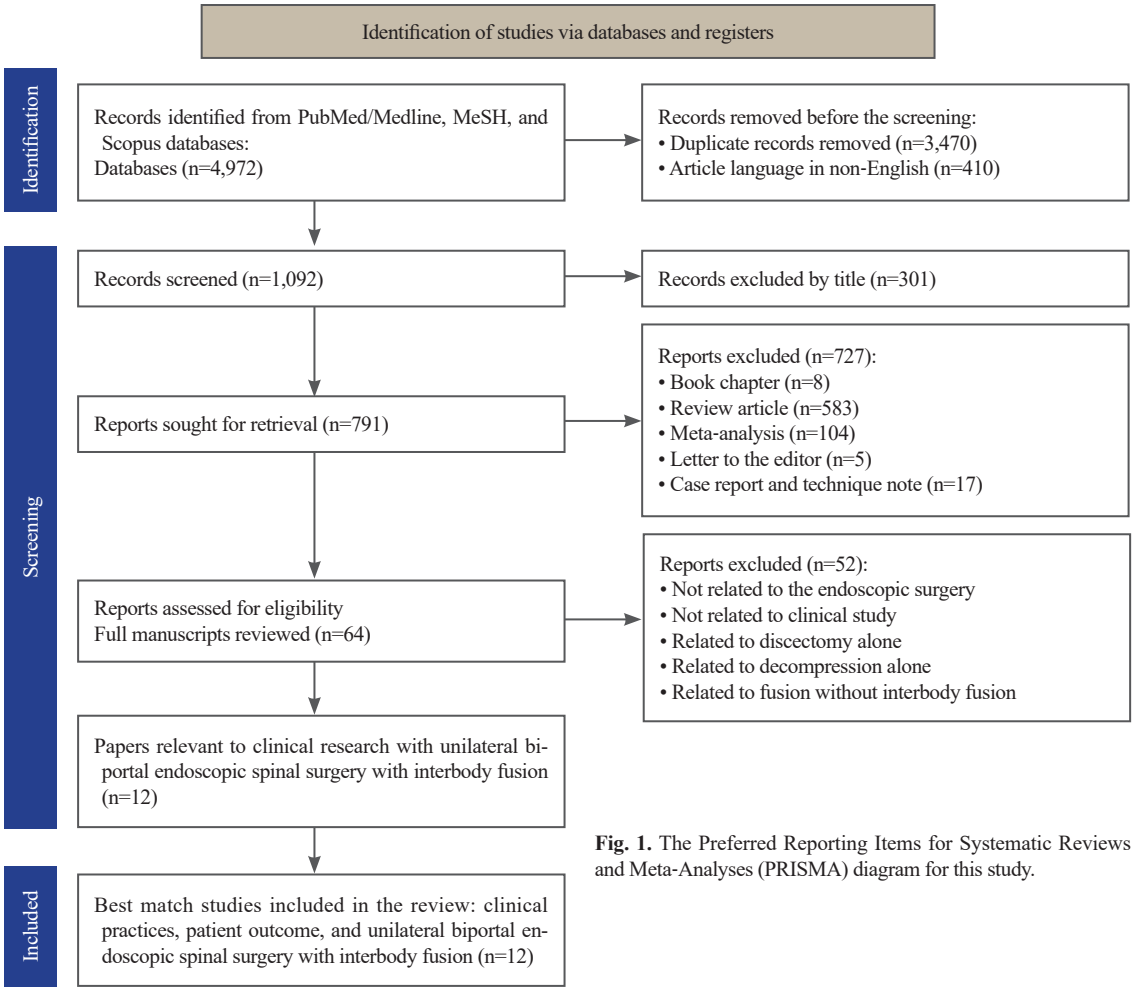

Fig. 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram for this study.

Table 1. Demographics and characteristics of studies

No.	Study	Nationality	Study design	No. of sample size	Age (yr)	Gender (M/F)	Diagnosis	Operative level	Follow-up duration (mo)
1	Heo et al. [20] (2017)	South Korea	Prospective	69	71.2±7.8	24/45	Degenerative spondylolisthesis: (n=51); isthmic spondylolisthesis: (n=9); central stenosis with segmental instability: (n=6); central stenosis with concomitant foraminal stenosis: (n=3)	L3/L4a) (n=9); L4/L5 (n=48); L5/S1 (n=12)	13.5±7.1
2	Park et al. [21] (2019)	South Korea	Retrospective	71 (ULIF); 70 (PLIF)	68±8 (ULIF); 66±9 (PLIF)	26/45 (ULIF); 20/50 (PLIF)	• ULIF group: spinal stenosis (7 [9.9%]); spondylolisthesis (62 [87.3%]): grade 1 (62 [100%]), HNP: 2 (2.8%) • PLIF group: spinal stenosis (11 [15.7%]), spondylolisthesis (57 [81.4%]): grade 1 (49 [86%]), grade 2 (8 [14%]); HNP (2 [2.9%])	• ULIF group: L3/L4 (13 [18.3%]); L4/L5 (50 [70.4%]); L5/S1 (8 [11.3%]) • PLIF group: L3/L4 (8 [11.4%]); L4/L5 (56 [80%]); L5/S1 (6 [8.6%])	17.1±4.9 (ULIF) 20.4±7.2 (PLIF)
3	Heo et al. [22] (2019)	South Korea	Retrospective	23 (ERAS); 46 (non-ERAS)	61.4±9.4 (ERAS); 63.5±10.5 (non-ERAS)	7/16 (ERAS); 19/27 (non-ERAS)	Low-grade degenerative spondylolisthesis (grade 1); low-grade isthmic spondylolisthesis (grade 1); central stenosis with instability; central stenosis with concomitant foraminal stenosis	• ERAS group: L3/L4 (n=3); L4/L5 (n=17); L5/S1 (n=3) • Non-ERAS group: L3/L4 (n=4); L4/L5 (n=29); L5/S1 (n=13)	13.4±2.5
4	Kim et al. [23] (2021)	South Korea	Retrospective	32 (BE-TLIF); 55 (MI-TLIF)	70.5±8.26 (BE-TLIF); 67.3±10.7 (MI-TLIF)	17/15 (BE-TLIF); 25/30 (MI-TLIF)	• BE-TLIF group: degenerative spondylolisthesis (26 [81.2%]); lytic spondylolisthesis (6 [18.7%]) • MI-TLIF group: degenerative spondylolisthesis (48 [87.2%]); lytic spondylolisthesis (7 [10.9%])	• BE-TLIF group: L2/L3 (1 [3%]); L3/L4 (3 [9.3%]); L4/L5 (20 [62.5%]); L5/S1 (8 [25%]) • MI-TLIF group: L2/L3 (0 [0%]); L3/L4 (2 [2.0%]); L4/L5 (46 [68.5%]); L5/S1 (7 [8.5%])	27.2±5.4 (BE-TLIF); 31.5±7.3 (MI-TLIF)
5	Kang et al. [24] (2021)	South Korea	Retrospective	47 (BE-TLIF); 32 (MT-TLIF)	66.87±10.41 (BE-TLIF); 66.38±9.45 (MT-TLIF)	17/30 (BE-TLIF); 17/15 (MT-TLIF)	• Spinal stenosis with or without low-grade degenerative • Spondylolisthesis (grade ≤2), low-grade isthmic spondylolisthesis (grade ≤2), and segmental instability	• BE-TLIF group: L2/L3 (4 [6.2%]); L3/L4 (7 [10.8%]); L4/L5 (34 [52.3%]); L5/S1 (20 [30.8%]) • MT-TLIF group: L2/L3 (1 [2.3%]); L3/L4 (9 [20.9%]); L4/L5 (22 [51.2%]); L5/S1 (11 [25.6%])	14.5±2.3 (BE-TLIF); 15.78±3.16 (MT-TLIF)
6	Gatam et al. [9] (2021)	Indonesia	Retrospective	72 (ULIF); 73 (MIS-TLIF)	55.1±5.12 (ULIF); 52.3±6.13 (MIS-TLIF)	26/46 (ULIF); 28/45 (MIS-TLIF)	Single-level degenerative lumbar spondylolisthesis (grade 1 and grade 2)	• ULIF group: L3/L4 (8 [10.52%]); L4/L5 (56 [81.57%]); L5/S1 (8 [7.89%]) • MIS-TLIF group: L3/L4 (10 [11.542%]); L4/L5 (48 [65.71%]); L5/S1 (15 [22.85%])	12
7	Xie et al. [25] (2022)	China	Retrospective	30 (BLIF); 30 (uni-LIF)	49.1±6.11 (BLIF); 51.2±6.49 (uni-LIF)	17/13 (BLIF); 16/14 (uni-LIF)	Symptomatic L4/L5 spinal stenosis	L4/L5	12
8	Peng et al. [26] (2023)	China	Retrospective	53 (ULIF); 53 (O-TLIF)	54.79±8.54 (ULIF); 54.92±12.03 (O-TLIF)	23/30 (ULIF); 30/23 (O-TLIF)	• Lumbar spinal stenosis: 47 (ULIF), 51 (O-TLIF) • Spondylolisthesis: 6 (ULIF), 2 (O-TLIF)	• ULIF group: L2/L3 (n=1); L3/L4 (n=3); L4/L5 (n=29); L5/S1 (n=20) • O-TLIF group: L2/L3 (n=0); L3/L4 (n=3); L4/L5 (n=29); L5/S1 (n=21)	12

(Continued on the next page)

Table 1. Continued

No.	Study	Nationality	Study design	No. of sample size	Age (yr)	Gender (M/F)	Diagnosis	Operative level	Follow-up duration (mo)
9	Cao et al. [27] (2023)	China	Retrospective	38 (static cages); 46 (expandable cages)	56.69±12.39 (static cages); 56.83±12.15 (expandable cages)	15/23 (static cages); 18/28 (expandable cages)	Degenerative lumbar spondylolisthesis (grade 1 and grade 2)	• ULIF (static cages): L4/L5 (n=25); L5/S1 (n=13) • ULIF (expandable cages): L4/L5 (n=32); L5/S1 (n=14)	27.45±3.47 (static cages); 26.30±4.23 (expandable cages)
10	Cao et al. [28] (2023)	China	Retrospective	45 (OLIF); 62 (ULIF)	59.43±10.26 (OLIF); 61.28±9.41 (ULIF)	20/25 (OLIF); 28/34 (ULIF)	Degenerative lumbar spondylolisthesis: grade 1: 26 (OLIF), 33 (ULIF); grade 2: 19 (OLIF), 29 (ULIF)	• OLIF group: L2/L3 (n=9); L3/L4 (n=14); L4/L5 (n=22) • ULIF group: L2/L3 (n=8); L3/L4 (n=23); L4/L5 (n=31)	26.62±3.57 (OLIF); 27.45±4.96 (ULIF)
11	You et al. [29] (2024)	China	Retrospective	31	64.45±10.49	13/18	Lumbar spondylolisthesis with spinal scoliosis: slippage grades: grade 1 (n=23), grade 2 (n=8)	L4/L5 (n=20); L5/S1 (n=11)	13.52±3.94
12	Ha et al. [30] (2024)	South Korea	Retrospective	104	67.5±9.0	38/66	Lumbar spondylolisthesis, spinal stenosis, herniated disc, adjacent segment disease	• ULIF: L3/4 (18 [17.3%]); L4/5 (48 [46.1%]); L5/S1 (18 [17.3%]); L3/4/5 (2 [1.9%]); L4/5/S1 (12 [11.5%]) • Revisional ULIF: L4/5 (2 [1.9%]) • ULIF extension: L2 to S1 (2 [1.9%]); L3 to S1 (2 [1.9%])	12

Values are presented as mean±standard deviation or number (%) unless otherwise stated.

M, male; F, female; ULIF, unilateral biportal endoscopic lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; HNP, herniated nucleus pulposus; ERAS, enhanced recovery after surgery (non-ERAS, microscopic TLIF; ERAS, endoscopic TLIF); BE-TLIF, biportal endoscopic transforaminal lumbar interbody fusion; MI-TLIF, minimally invasive transforaminal lumbar interbody fusion; MT-TLIF, microscopic transforaminal lumbar interbody fusion; MIS-TLIF, minimally invasive surgical transforaminal lumbar interbody fusion; BLIF, biportal lumbar interbody fusion; Uni-LIF, uniportal lumbar interbody fusion; O-TLIF, open transforaminal lumbar interbody fusion; OLIF, oblique lateral interbody fusion.

[a]L3/L4, L4/L5, L5/S1: Lumbar vertebrae and sacral segments involved in the surgical procedure.

ranged from 23 to 104 patients per study, and the mean follow-up duration was 12–31 months. The patient population primarily comprised individuals diagnosed with degenerative lumbar conditions, such as degenerative spondylolisthesis, lumbar spinal stenosis, and herniated disc disease; in most patients, the treated spinal levels were L3/L4, L4/L5, and L5/S1. The detailed characteristics of the included studies and patient demographics are summarized in Table 1 [9,20-30].

Risk of bias analysis

The risk of bias was evaluated using the ROBINS-I tool for nonrandomized studies and the RoB 2 tool for RCTs [18]. Most studies were found to have a moderate risk of bias, mainly due to confounding factors and participant selection among the retrospective studies. The risk of bias related to missing data and measurement of outcomes was generally low, because most studies reported comprehensive follow-up data. Studies with prospective designs had relatively low risk of bias, particularly when the inclusion/exclusion criteria and outcome assessments were clearly defined. However, the lack of RCTs and reliance on observational data limited the strength of the conclusions. A detailed breakdown of the risk of bias across studies is provided in Fig. 2 and Table 2 [9,20-30].

Summary of biportal endoscopic spinal surgery outcomes

Our analyses indicated that BESS with interbody fusion offered several benefits, including reduced operative time, less intraoperative blood loss, substantial improvements in pain and functional outcomes, and high rates

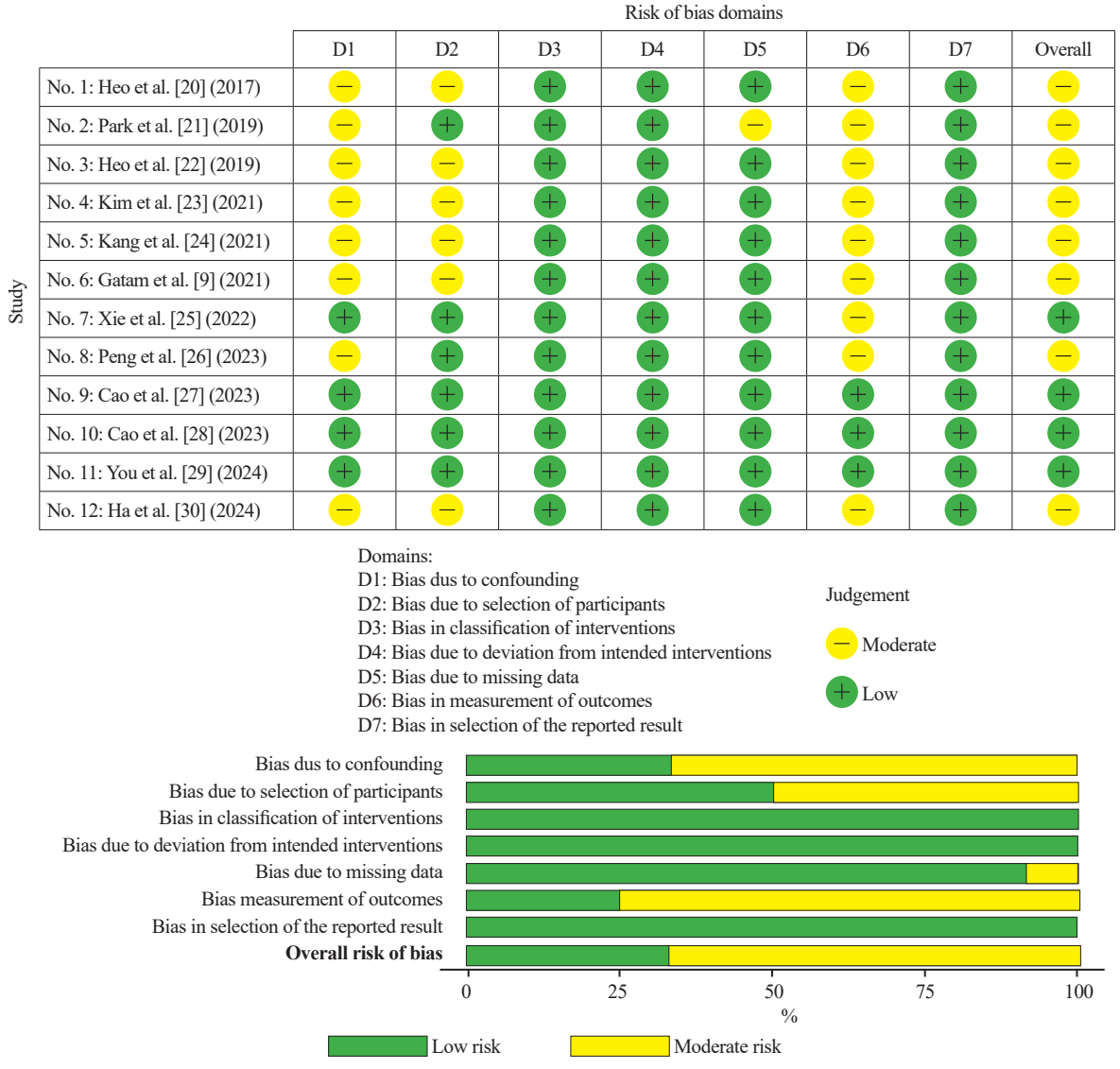

Fig. 2. Summary report of risk of bias tool for non-randomized trial (ROBINS-I).

Table 2. Summary of risk of bias (ROBINS-I) of all studies

No.	Study	Bias due to confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported result	Overall risk of bias
1	Heo et al. [20]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
2	Park et al. [21]	Moderate	Low	Low	Low	Moderate	Moderate	Low	Moderate
3	Heo et al. [22]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
4	Kim et al. [23]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
5	Kang et al. [24]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
6	Gatam et al. [9]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate
7	Xie et al. [25]	Low	Low	Low	Low	Low	Moderate	Low	Low
8	Peng et al. [26]	Moderate	Low	Low	Low	Low	Moderate	Low	Moderate
9	Cao et al. [27]	Low	Low	Low	Low	Low	Low	Low	Low
10	Cao et al. [28]	Low	Low	Low	Low	Low	Low	Low	Low
11	You et al. [29]	Low	Low	Low	Low	Low	Low	Low	Low
12	Ha et al. [30]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate

ROBINS-I, Risk of Bias in Non-randomized Studies of Interventions.

of radiological fusion. There were complications, such as dural tears and hematoma, but these were generally minor and manageable. The high fusion rates and improved clinical outcomes support the efficacy of BESS as a minimally invasive alternative to traditional open fusion techniques for treating lumbar degenerative conditions. The outcomes of BESS with the interbody fusion technique are summarized in Table 3 [9,20-30].

Surgical outcomes

The operative time varied significantly among the studies, reflecting differences in pathology, patient cohorts, procedural complexity and techniques, and surgeon experience. In particular, the mean operative time for BESS procedures was 165.8±25.5 minutes, according to Heo et al. [20], and was longer at 206.35±35.23 minutes, according to You et al. [29]; whereas Cao et al. [28] observed a shorter operative time of 108.23±25.69 minutes for oblique lateral interbody fusion (OLIF) procedures. Notably, the studies consistently indicated that the operative time tended to be shorter as the technical experience of the surgeon increased, reflecting the steep learning curve of BESS. Moreover, surgical complexity, observed in patients with multilevel disease or those requiring revision, was associated with operative time. Kang et al. [24] reported a notably longer mean operative time for biportal endoscopic transforaminal lumbar interbody fusion (BE-TLIF) than for microscopic transforaminal lumbar interbody fusion (MT-TLIF) (170.46±34.81 minutes versus 135.70±42.88 minutes). These differences emphasized the technical demands of BESS, particularly in complex cases, and the importance of surgeon proficiency in achieving optimal efficiency.

Clinical outcomes

All studies consistently demonstrated significant and substantial improvements in clinical outcomes after BESS with interbody fusion, based on reductions in VAS scores for back and leg pain and improved functional recovery (ODI). Heo et al. [20] reported a dramatic reduction in VAS leg pain from 8.12±0.63 preoperatively to 2.79±1.24 on final follow-up, along with a comparable decrease in ODI scores from 45.65±12.97 to 15.41±9.07. Similarly, Park et al. [21] demonstrated significant pain relief in both the unilateral biportal endoscopic lumbar interbody fusion (ULIF) and PLIF cohorts. In the ULIF group, the VAS back pain decreased from 6.0±1.5 preoperatively to 3.1±0.8 on final follow-up, and the ODI scores improved from 61.9±8.2 to 32.7±5.6. The PLIF cohort experienced parallel improvements, with ODI scores decreasing from 55.7±12.1 to 29.2±10.1. Notably, enhanced recovery after surgery (ERAS) protocols were associated with superior outcomes, compared with non-ERAS protocols. On day 1 and at 1 year postoperatively, Heo and Park [22] observed that the VAS scores were lower in the ERAS cohort (4.2±1.0 and 2.4±0.9, respectively) than in the non-ERAS group (4.9±1.3 and 2.6±1.0, respectively) and that the ODI scores improved from 57.8±6.3 to 21.8±2.9, respectively, in the ERAS group and from 59.4±5.9 to 22.6±3.1, respectively, in the non-ERAS group. These results highlighted the additional benefit of ERAS protocols in optimizing recovery. Studies compar-

Table 3. This systematic review summarises clinical and surgical outcomes with complication rates

No.	Study	Operative time (min)	Blood loss (mL)	VAS back pain	VAS leg pain	ODI	Fusion rate (%)	Complications
1	Heo et al. [20]	165.8±25.5	85.5±19.4	Not specified	Preop to final FU: 8.12±0.63 to 2.79±1.24	Preop to final FU: 45.65±12.97 to 15.41±9.07	Not specified	• Dural tear: 2 (2.9%) • Hematoma: 3 (4.3%)
2	Park et al. [21]	158.2±26.7 (ULIF); 136.6±21.5 (PLIF)	Not specified in blood loss (transfusion: 0 [0%] ULIF, 13 [18.6%] PLIF)	Preop, postop 1 wk, final FU: 6.0±1.5, 3.8±1.0, 3.1±0.8 (ULIF); 5.4±2, 5.2±1.1, 3.4±1.4 (PLIF)	Preop, postop 1 wk, final FU: 6.6±1.3, 3.6±1.3, 3.6±1.0 (ULIF); 7.0±1.7, 3.3±1.1, 3.3±1.4 (PLIF)	Preop to final FU: 61.9±8.2 to 32.7±5.6 (ULIF); 55.7±12.1 to 29.2±10.1 (PLIF)	Definite and probable bony fusion: 58 (95.1%) (ULIF); 63 (90.0%) (PLIF)	• Dural tear: 3 (4.2%) (ULIF), 2 (2.9%) (PLIF) • Nerve root injury: 0 (0%) (ULIF), 1 (1.4%) (PLIF) • Hematoma: 1 (1.4%) (ULIF), 1 (1.4%) (PLIF) • Infection: 1 (1.4%) (ULIF), 2 (2.9%) (PLIF) • Cage subsidence: 5 (8.2%) (ULIF), 4 (5.7%) (PLIF) • Screw loosening: 3 (4.9%) (ULIF), 3 (4.3%) (PLIF)
3	Heo et al. [22]	152.4±9.6 (ERAS); 122.4±13.1 (non-ERAS)	190.3±31.0 (ERAS); 289.3±58.5 (non-ERAS)	Postop 1 day, 2 days, 1 yr: 4.2±1.0, 2.8±0.5, 2.4±0.9 (ERAS); 4.9±1.3, 4.2±0.8, 2.6±1.0 (non-ERAS)	Preop, postop 1 yr: 8.1±1.2, 2.5±0.8 (ERAS); 7.7±1.0, 2.2±0.9 (non-ERAS)	Preop, 1 yr FU: 57.8±6.3, 21.8±2.9 (ERAS); 59.4±5.9, 22.6±3.1 (non-ERAS)	18/23 (78.3%) (ERAS); 34/46 (73.9%) (non-ERAS)	• Symptomatic epidural hematoma: 1 (ERAS), 1 (non-ERAS) • Dural tear: 1 (non-ERAS) • Superficial wound infection: 1 (non-ERAS) • Deep vein thrombosis: 1 (non-ERAS)
4	Kim et al. [23]	169.5±24.9 (BE-TLIF); 173±47.1 (MI-TLIF)	Not specified	Preop, postop 2 wk, 2 mo, final FU: 6.2±1.3, 3.1±1.0, 2.4±0.9, 1.8±0.8 (BE-TLIF); 6.5±1.5, 4.2±1.6, 3.5±0.9, 1.9±0.8 (MI-TLIF)	Preop, postop 2 wk, 2 mo, final FU: 7.9±0.6, 3.3±0.9, 2.4±1.0, 1.6±0.6 (BE-TLIF); 7.8±1.7, 3.5±1.1, 2.8±0.8, 1.8±0.8 (MI-TLIF)	Preop, 1 yr FU: 68.1±5.4, 15.6±9.2 (BE-TLIF); 69.6±6.2, 16.3±11.9 (MI-TLIF)	30/32(93.7%) (BE-TLIF) 51/55(92.7%) (MI-TLIF)	• Complication: 2(6.3%)(BE-TLIF), 3 (5.5%) (MI-TLIF) • Transient palsy: 1 (BE-TLIF), 2 (MI-TLIF) • Epidural hematoma: 1 (BE-TLIF), 1 (MI-TLIF)
5	Kang et al. [24]	170.46±34.81 (BE-TLIF); 135.70±42.88 (MT-TLIF)	185.74±172.51 (BE-TLIF); 395.31±180.36 (MT-TLIF)	Decrease VAS in both groups: preop, postop 1 mo, 6 mo, 1 yr: not specified	Decrease VAS in both groups: preop, postop 1 mo, 6 mo, 1 yr: not specified	Decrease ODI in both groups: preop, postop 1 mo, 6 mo, 1 yr; not specified	57 (87.7%) (BE-TLIF); 38 (88.4%) (MT-TLIF)	• Incomplete decompression: 1 (2.1%) (BE-TLIF), 2 (6.3%) (MT-TLIF) • Dural tear: 3 (6.4%) (BE-TLIF), 1 (3.1%) (MT-TLIF) • Hematoma: 2 (4.3%) (BE-TLIF), 1 (3.1%) (MT-TLIF) • Infection: 1 (3.1%) (MT-TLIF)
6	Gatam et al. [9]	Not specified	Not specified	Preop, postop 3 mo, 6 mo, 1 yr: 5.7, 1.9, 1.7, 0.8 (ULIF); 5.4, 2.4, 1.6, 0.9 (MIS-TLIF)	Preop, postop 3 mo, 6 mo, 1 yr: 4.6, 3.7, 2.1, 0.7 (ULIF); 4.5, 3.6, 1.8, 0.8 (MIS-TLIF)	Preop, postop 3 mo, 6 mo, 1 yr: 60, 12, 8, 6 (ULIF); 62, 16, 12, 8 (MIS-TLIF)	92.7% (ULIF); 93.3% (MIS-TLIF)	• Dural tear: 3 (ULIF) • Infection: 2 (MIS-TLIF) • Cage subsidence: 2 (MIS-TLIF)
7	Xie et al. [25]	98.07±4.65 (BLIF); 134.53±7.36 (uni-LIF)	Not specified	Not specified	Preop, postop 1 yr: 7.40±0.50, 2.73±0.45 (BLIF); 7.43±0.50, 2.80±0.41 (uni-LIF)	Preop, postop 1 yr: 43.17±1.95, 5.70±0.92 (BLIF); 43.10±2.11, 5.63±0.81 (uni-LIF)	26 (86.7%) (BLIF); 21 (70%) (uni-LIF) (definite fusion)	• Nerve root injury: 2 (BLIF) • CSF leakage: 1 (uni-LIF)
8	Peng et al. [26]	176.32±32.89 (ULIF); 130.87±24.54 (O-TLIF)	326.86±223.45 (ULIF); 427.97±280.52 (O-TLIF)	Not specified	Not specified	Not specified	Not specified	No major complications reported

(Continued on the next page)

Table 3. Continued

No.	Study	Operative time (min)	Blood loss (mL)	VAS back pain	VAS leg pain	ODI	Fusion rate (%)	Complications
9	Cao et al. [27]	169.25±28.37 (static cages); 158.39±31.26 (expandable cages)	Preop/last FU: 138.25±25.91 (static cages); 126.17±31.85 (expandable cages)	Preop, last FU: 6.55±1.78, 1.73±0.96 (static); 6.49±1.84, 1.65±1.02 (expandable)	Preop, last FU: 6.23±1.45, 1.43±0.87 (static); 6.41±1.65, 1.61±1.13 (expandable)	Preop, last FU: 64.72±12.63, 15.18±7.34 (static); 66.18±13.52, 18.21±9.15 (expandable)	Fusion at 1 yr: grade 1 (29 static cage, 38 expandable cage); grade 2 (9 static cage, 8 static cage)	• Dural laceration: 1 (expandable) • Cage settlement: 1 (static)
10	Cao et al. [28]	108.23±25.69 (OLIF); 142.34±35.81 (ULIF)	63.49±12.18 (OLIF); 91.23±24.65 (ULIF)	Preop, last FU 2 yr: 6.71±1.89, 1.34±0.96 (OLIF); 6.58±1.64, 2.13±1.17 (ULIF)	Preop, last FU 2 yr: 7.23±2.14, 1.26±0.83 (OLIF); 6.92±1.87, 1.43±0.92 (ULIF)	Preop, last FU 2 yr: 56.91±12.38, 13.26±6.72 (OLIF); 58.42±13.25, 17.41±7.52 (ULIF)	93.33 (OLIF); 91.94 (ULIF)	• Complications: 7/45 (15.6%) (OLIF), 10/62 (16.1%) (ULIF) • Endplate injury: 2 (OLIF), 3 (ULIF) • Numbness: 2 (OLIF) • Sympathetic trunk nerve injury: 3 (OLIF) • Screw malposition: 2 (ULIF) • Radicular symptoms postop: 2 (ULIF)
11	You et al. [29]	206.35±35.23	94.97±9.85	Preop, last FU: 9.52±0.92, 0.75±0.44	Preop, last FU: 8.94±0.81, 0.85±0.48	Preop, last FU: 63.54±12.57, 12.13±4.12	28/31 (90.32%)	No major complications reported
12	Ha et al. [30]	103.5±24.0	Not specified	Preop, last FU 1 yr: 7.1±0.4, 0.9±0.4	Preop, last FU 1 yr: 6.7±0.5, 0.8±0.4	Preop, last FU 1 yr: 39.8±2.1, 15.2±1.6	Interbody fusion at 1 yr (Bridwell criteria): 92 (grade 1), 11 (grade 2), 1 (grade 3)	• Dural tears: 3 • Foot drop: 1 • Cage subsidence (grade 0): 4

Values are presented as mean±standard deviation or number (%) unless otherwise stated.
VAS, Visual Analog Scale (used to measure pain levels); ODI, Oswestry Disability Index (used to measure disability); Preop, preoperative; Postop, postoperative; FU, follow-up; ULIF, unilateral biportal endoscopic lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; ERAS, enhanced recovery after surgery (non-ERAS, microscopic TLIF; ERAS, endoscopic TLIF); BE-TLIF, biportal endoscopic transforaminal lumbar interbody fusion; MI-TLIF, minimally invasive transforaminal lumbar interbody fusion; MT-TLIF, microscopic transforaminal lumbar interbody fusion; MIS-TLIF, minimally invasive surgical transforaminal lumbar interbody fusion; BLIF, biportal lumbar interbody fusion; Uni-LIF, uniportal lumbar interbody fusion; O-TLIF, open transforaminal lumbar interbody fusion; CSF, cerebrospinal fluid; OLIF, oblique lateral interbody fusion.

ing BESS with other minimally invasive techniques, such as minimally invasive surgical transforaminal lumbar interbody fusion (MIS-TLIF) and MT-TLIF, further underscored the efficacy of the former. Comparing the preoperative and final follow-up assessments, Kim et al. [23] reported a greater reduction in VAS back pain after BESS (from 6.2±1.3 to 1.8±0.8) than after MIS-TLIF (from 6.5±1.5 to 1.9±0.8) and better functional recovery or steeper decline in ODI scores after BESS (from 68.1±5.4 to 15.6±9.2) than after MIS-TLIF (from 69.6±6.2 to 16.3±11.9). In addition, BESS demonstrated promising outcomes in older and high-risk populations. Kang et al. [24] showed sustained pain and disability improvements over 1 year among patients with degenerative spondylolisthesis treated by BESS, based on the significant decline in VAS and ODI scores postoperatively. Similarly, Ha et al. [30] observed remarkable functional recovery, with ODI scores improving from 39.8±2.1 preoperatively to 15.2±1.6 on follow-up after 1 year.

Blood loss measurement

Intraoperative blood loss is a critical measure of the safety and efficacy of surgical techniques, particularly minimally invasive procedures, such as BESS. Across the studies, BESS consistently demonstrated significantly less blood loss, compared with conventional techniques, emphasizing its minimally invasive nature. In particular, Heo et al. [20] reported an average blood loss of 85.5±19.4 mL after BESS, whereas Peng et al. [26] observed markedly less blood loss in the ULIF group than in the open TLIF group (326.86±223.45 mL versus 427.97±280.52 mL). Similarly, Cao et al. [28] reported mean blood loss of 63.49±12.18 mL after OLIF and 91.23±24.65 mL after ULIF, highlighting the advantages of minimally invasive techniques. The methods used to quantify blood loss varied among the studies. Most studies relied on estimated blood loss (EBL), which was calculated based on suction volume and gauze weight.

However, some studies only provided qualitative observations by the surgical team, limiting data precision. For example, Park et al. [21] did not report absolute values for blood loss but indicated that no patients in the ULIF group required blood transfusions, but 13 patients (18.6%) in the PLIF group required blood transfusions. However, Heo and Park [22] provided detailed quantification, reporting significantly lower mean blood loss in the ERAS cohort than in the non-ERAS cohort (190.3±31.0 mL versus 289.3±58.5 mL), further corroborating the benefits of ERAS protocols in conjunction with BESS. Despite the overall trend of reduced blood loss after BESS, surgical complexity and surgeon experience varied among the studies. Multilevel procedures or revisions, as reported by Kang et al. [24] and Ha et al. [30], occasionally resulted in more blood loss. Kang et al. [24] reported a mean blood loss of 185.74±172.51 mL in the BE-TLIF group and 395.31±180.36 mL in the MT-TLIF group, emphasizing the impact of technique and surgeon expertise on outcomes.

Fusion rates

Radiographic fusion rates were consistently high across the studies. Fusion was assessed using interval computed tomography scans or plain radiographs during 6–12 months of follow-up. In 2017, Heo et al. [20] reported a fusion rate of 95.1%. In 2019, Park et al. [21] observed a similar rate of 95.1% in their ULIF cohort, with slightly lower rates in the PLIF group (90.0%). In 2023, Cao et al. [27] reported fusion rates of 93.3% and 88.9% in patients treated with expandable and static cages, respectively, suggesting that implant design may influence fusion success. Overall, the high fusion rates observed after BESS procedures demonstrated its ability to achieve fusion outcomes that were at par with or exceeded those of open fusion techniques; therefore, BESS is a highly viable option for lumbar degenerative pathologies.

Complications

The overall complication rate of BESS was relatively low. Dural tears were the most frequently reported, with rates ranging from 2.9% to 6.4%. In particular, dural tears occurred at rates of 2.9%, according to Heo et al. [20] in 2017, and 6.4% in the BE-TLIF cohort of Kang et al. [24] in 2021 and were managed intraoperatively without long-term neurological sequelae. Hematomas were observed in 4.3% of patients, according to Heo et al. [20] in 2017, and had an incidence of 1.4% in both the ULIF and PLIF cohorts in the study by Park et al. [21] in 2019. Cage subsidence was noted by Park et al. [21] in 2019 at rates of 8.2% in the ULIF group and 5.7% in the PLIF group. Cao et al. [27] in 2023 reported dural laceration in one patient and cage settlement in another patient. No life-threatening complications or significant neurological deficits were reported across the studies. These findings suggested that BESS is a relatively safe procedure with manageable complication rates.

Learning curve

The learning curve associated with BESS was a recurring theme in several studies, reflecting its impact on operative time, complication rates, and surgical outcomes. Studies have consistently demonstrated relatively long operative times and high complication rates during the initial phase of adopting the BESS technique. Kang et al. [24] noted that compared with more experienced surgeons, less experienced surgeons required significantly more time to complete the procedures, particularly in complex cases. Similarly, Park et al. [21] reported that the rates of complications, such as dural tears, initially increased in the learning phase and gradually decreased as proficiency improved. Evidence from Heo and Park [22] showed that as surgeons became more familiar with the biportal approach, operative times decreased significantly and outcomes improved. In particular, the mean operative time decreased by 20% after a surgeon performed over 20 cases, underscoring the steep but manageable learning curve of BESS. Furthermore, Cao et al. [28] found a correlation between surgeon experience and improved precision in cage placement and decompression, which contributed to better clinical outcomes. The technical demands of BESS, including navigating the narrow operative field and maintaining precise instrument control, were frequently cited as challenges during the learning phase. Compared with those transitioning from traditional open approaches, surgeons with prior experience in MISS adapted more quickly to BESS. Some studies highlighted simulation-based training and mentorship programs as effective strategies to accelerate skill acquisition and reduce the learning curve.

Discussion

This systematic review showed that BESS with interbody fusion is a minimally invasive alternative to traditional open lumbar fusion techniques and has the potential for broad application in degenerative spine conditions. The studies reviewed consistently demon-

strated significant improvements in clinical outcomes, high fusion rates, and low complication rates, compared with conventional methods [9,28]. The main advantages of BESS include reduced surgical trauma, less intraoperative blood loss, and faster recovery times. Previous studies have consistently reported reduced blood loss and rapid postoperative recovery, highlighting the significant advantages of the minimally invasive nature of BESS [20,31,32]. These findings are especially important for elderly patients and those with comorbidities, for whom minimizing surgical risks and improving recovery times are critical. From a clinical outcomes perspective, BESS has been shown to provide comparable or superior results in pain relief and functional recovery compared with traditional fusion methods [22]. Across studies, the VAS scores for both back and leg pain consistently decreased and the ODI scores reflecting functional restoration significantly improved postoperatively [14,21]. These outcomes implied that BESS had substantial benefits in routine clinical practice by effectively reducing pain and improving patient mobility with fewer complications. Another significant advantage of BESS was its high fusion rate (95.1%) [20,21], which is generally comparable with those reported after minimally invasive techniques, such as PLIF and TLIF; this further supported the use of BESS as a reliable alternative. However, concerns remained when BESS was compared with conventional open fusion methods. The relatively high definite fusion rates after PLIF highlighted the potential superiority of open procedures over BESS in certain cases [21]. In addition, although the use of expandable cages has improved fusion success, particularly in patients with challenging anatomical structures or poor bone quality, the fusion outcomes remain inconsistent in more complex cases, such as those with osteoporosis. Therefore, the need for further technological advancements to optimize outcomes and address these limitations is underscored.

Across studies, BESS was found to be favorable and associated with low complication rates. Dural tears were the most common but were effectively managed without long-term neurological consequences [20,30,33]. The narrow operative field during BESS predisposes to more frequent dural tears and emphasizes the importance of surgeon experience and careful tissue handling. Hematomas were reported in 1.4% to 4.3% of patients but did not require major interventions [21,24]. Cage subsidence, particularly in patients with osteoporosis or poor bone quality, was another reported complication, but it generally did not necessitate further surgical intervention. These findings indicated that although BESS carries some risks, the benefits of reduced surgical trauma and fast recovery outweighed the complications observed, especially when performed by experienced surgeons [34]. The steep learning curve poses a challenge for surgeons transitioning to this technique, because a high skill level in manipulating instruments within a narrow operative field is required [35]. Furthermore, although BESS offers excellent visualization, depth perception and manual control can be

Table 4. Advantages, limitations, and future trends of BESS with interbody fusion

Category	Advantages	Limitations	Future trends
Minimally invasive	Less tissue disruption, reduced postoperative pain, faster recovery, and shorter hospital stays	Steep learning curve; suboptimal outcomes in complex anatomy or severe degeneration.	Technological advances such as robotics and AR will simplify the technique and increase its adoption in complex cases.
Enhanced visualization	High-resolution, magnified view for precise decompression and fusion, reducing the risk of neurovascular damage	Restricted depth perception and demanding manual control of instruments can lead to longer operative times for inexperienced surgeons.	AR and AI-enhanced visualization tools will improve precision and intraoperative safety.
High fusion rates	Consistently high fusion rates (70%–95%), comparable to traditional methods like PLIF and TLIF	Variable fusion outcomes in complex cases increase subsidence risk in patients with poor bone quality.	Custom 3D-printed implants and enhanced biologics will optimize fusion, especially in complex or osteoporotic patients.
Reduced blood loss	Significantly reduced intraoperative bleeding, minimizing the need for transfusions	Complex multilevel cases may still present a risk for higher blood loss, especially in revision surgeries.	Improved endoscopic tools and hemostatic agents will improve bleeding control during complex procedures.
Lower postoperative pain	Reduced tissue damage leads to faster recovery and lower opioid requirements postsurgery.	Transient nerve irritation and variable pain relief may occur, particularly in more complex decompressions.	Integration of nerve monitoring and optimized pain management protocols will further minimize postoperative pain.
Potential for complex cases	BESS is expanding to treat multilevel degenerative diseases and revisions of failed surgeries.	Higher technical demands in complex cases, with a greater risk of incomplete decompression or intraoperative complications.	Robotic-assisted systems and AI-guided tools will enhance precision and broaden the application of UBSS in multilevel and complex spinal pathologies.

BESS, biportal endoscopic spinal surgery; AR, augmented reality; AI, artificial intelligence; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; 3D, three-dimensional; UBSS, unilateral biportal spinal surgery.

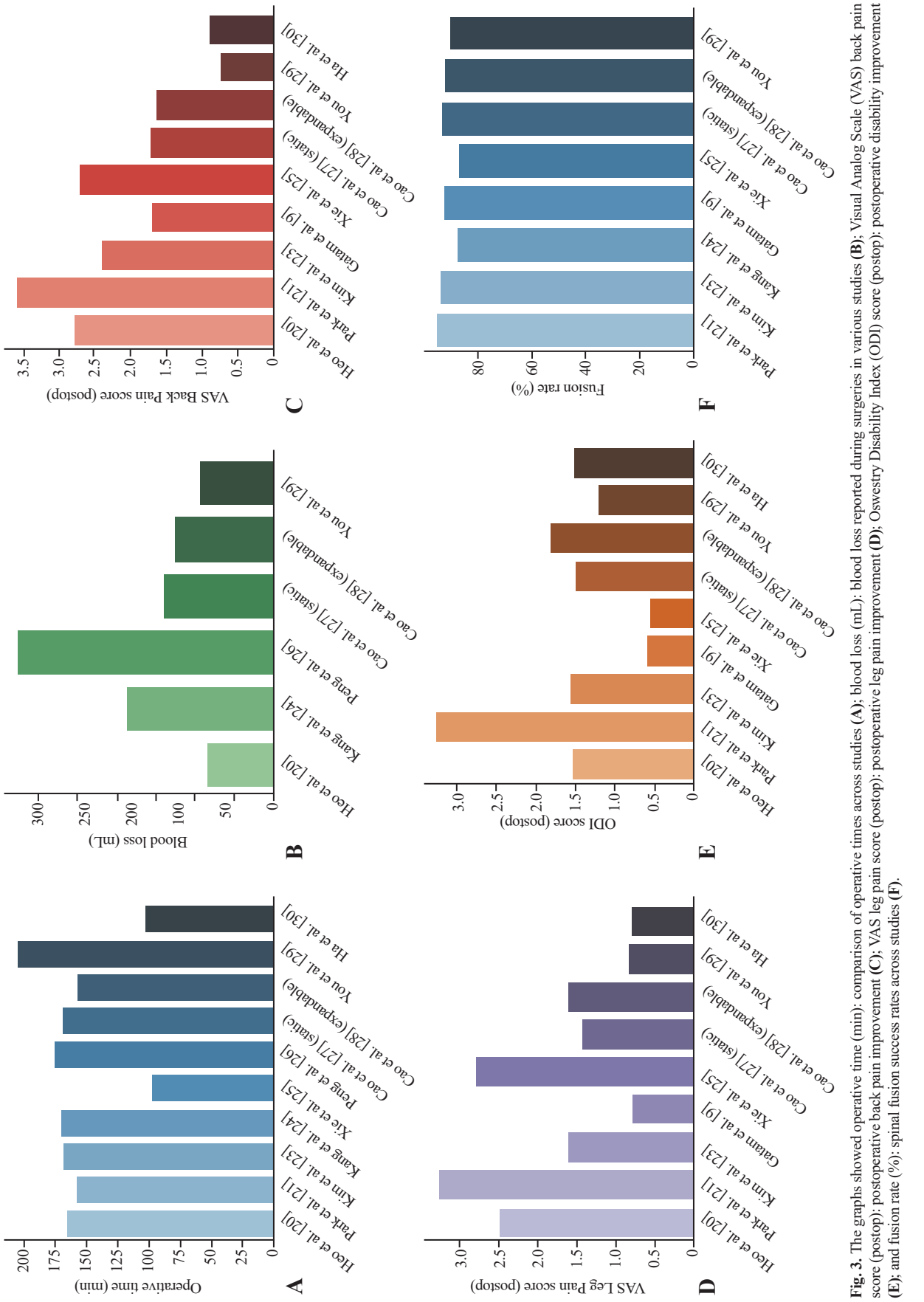

Fig. 3. The graphs showed operative time (min): comparison of operative times across studies (**A**); blood loss (mL): blood loss reported during surgeries in various studies (**B**); Visual Analog Scale (VAS) back pain score (postop): postoperative back pain improvement (**C**); VAS leg pain score (postop): postoperative leg pain improvement (**D**); Oswestry Disability Index (ODI) score (postop): postoperative disability improvement (**E**); and fusion rate (%): spinal fusion success rates across studies (**F**).

challenging, particularly for less experienced surgeons, leading to prolonged operative time and increased risk of intraoperative complications. In addition, complex multilevel cases and revisions of failed surgery have higher technical demands, which may result in suboptimal outcomes in specific patient populations.

Integration of recent literature on EndoLIF enriched this review and offered a comparative discussion on the relative strengths and challenges of BESS [12,36]. Both techniques aim to minimize soft tissue disruption and improve postoperative recovery, but BESS allows superior visualization and reduced muscle dissection. However, EndoLIF has shown potential for optimized outcomes in specific patient cohorts, including those with complex spinal pathologies [15,36,37]. The reviewed studies affirmed that BESS consistently delivered significant improvements in VAS and ODI scores, with high fusion rates and manageable complications. However, outcomes may be affected by challenges, such as steep learning curve and variability in surgeon expertise [20,22]. This underscores the importance of further training and development of standardized protocols to maximize surgical success. As the current technology develops, navigation and artificial intelligence (AI) systems become increasingly important during BESS. Navigation systems can enhance the precision of endoscopic procedures and facilitate accurate placement of screws and cages, and augmented reality (AR) could improve the surgeon's spatial awareness of complex anatomical regions [38-40]. Further developments in AI-driven surgery may refine patient-specific approaches and tailor implant selection and surgical techniques based on predictive models that analyze anatomy and pathology [41-44]. These innovations could mitigate the risks associated with the steep learning curve of BESS and expand its use to more complex cases, such as multilevel degenerative diseases and scoliosis. The advantages, limitations, and future directions of BESS with interbody fusion are summarized in Table 4. All factors related to operative time, blood loss, VAS for back and leg pain, ODI score, and fusion rates among the studies are compared and summarized in a diagram (Fig. 3) [9,20,21,23-30].

BESS was associated with reduced intraoperative blood loss, although the variability in measurement methods limited the comparison of the results among the studies. Most studies relied on EBL from suction volume and gauze weight, whereas some used qualitative observations. Given the absence of standardized protocols, such as hemoglobin-based methods, consistent and objective measurement methods need to be evaluated in future research to better assess the advantages of BESS. The steep learning curve of BESS significantly affected operative time and complication rates. Early-phase surgeons often reported relatively long operative times and more complications. Training programs, mentorship, and advanced technologies, such as AR and AI-guided tools, can help mitigate these challenges. Structured pathways for skill development will be essential for broader adoption and optimized outcomes of BESS.

The limitations of this systematic review include the absence of pooled data from a meta-analysis, because the methodologies and outcomes varied among the studies. Future research should standardize reporting measures to facilitate a meta-analysis approach, which can confirm the findings of this study. Nevertheless, this review showed that BESS with interbody fusion has emerged as a transformative approach for treating lumbar degenerative diseases and offers substantial benefits over traditional open techniques. The ability of BESS to reduce surgical trauma, improve clinical outcomes, and maintain high fusion rates makes it a highly effective option for patients requiring spinal fusion. Refinements of technique and further research, particularly RCTs with long-term follow-up, are necessary to fully define the role of BESS in the evolving landscape of MISS. As technology advances, BESS will likely become a more refined, accessible, and essential tool in the armamentarium of spine surgeons.

Conclusions

This systematic review identified BESS with interbody fusion as a safe, effective, and minimally invasive alternative for treating lumbar degenerative diseases. By incorporating recent insights on EndoLIF, this review expanded the context and highlighted the advantages and limitations of BESS within the evolving spine surgery landscape. Despite the limitations posed by data heterogeneity, which precluded a meta-analysis, the findings provided valuable qualitative insights into the clinical outcomes, high fusion rates, and manageable complications associated with BESS. Continued research, particularly RCTs with standardized data, will be crucial to further validate these findings and support future meta-analyses, ultimately refining clinical guidelines and surgical practice.

Key Points

- Biportal endoscopic spinal surgery (BESS) with interbody fusion is an advanced minimally invasive technique that reduces tissue damage, blood loss, and recovery time while delivering excellent clinical outcomes for lumbar degenerative diseases.
- A systematic review of 12 studies confirmed that BESS provides significant pain relief (Visual Analog Scale, Oswestry Disability Index), high fusion rates (70%–95%), and a low incidence of complications, with dural tears (2.9%–6.4%) and hematomas (1.4%–4.3%) being rare and manageable.
- Compared to traditional fusion techniques (posterior lumbar interbody fusion, transforaminal lumbar interbody fusion), BESS offers less blood loss, shorter hospital stays, and greater surgical precision through endoscopic magnification.
- As a leading minimally invasive spine surgery, BESS continues to evolve, with ongoing advancements expected to broaden its applications and enhance patient outcomes.

Conflict of Interest

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

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Author Contributions

Conceptualisation: WL, HJL. Methodology: WL, WC, HJL. Data curation: WL, WC, HJL, SBK, SMP, HJP. Formal analysis: WL. Visualisation: WL. Project administration: WL. Writing–original draft preparation: WL, WC, HJL, SBK, SMP, HJP. Writing–review and editing; WL, HJP. Supervision: WL, HJL. Final approval of the manuscript: all authors.

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