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Minimally Invasive Lumbar Spinal Fusion Is More Effective Than Open Fusion: A Meta-Analysis

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Purpose: To evaluate the efficacy of minimally invasive spinal fusion in comparison to open fusion for adult lumbar spondylolisthesis or spondylosis.

Materials and Methods: The present study was conducted as a meta-analysis of all estimates from studies that were selected after comprehensive literature search by two independent reviewers.

Results: Of 745 articles, nine prospective cohort studies were identified. The quality of evidence was downgraded because of study design, inconsistency, imprecision, and publication bias. Greater Oswestry Disability Index score improvement [weighted mean difference (WMD), 3.2; 95% confidence interval (CI), 1.5 to 5.0; p=0.0003] and a lower infection rate (odds ratio, 0.3; 95% CI, 0.1 to 0.9; p=0.02) were observed in the minimally invasive group (low-quality evidence). The minimally invasive group had less blood loss (WMD, 269.5 mL; 95% CI, 246.2 to 292.9 mL; p<0.0001), a shorter hospital stay (WMD, 1.3 days; 95% CI, 1.1 to 1.5 days, p<0.0001), and longer operation time (WMD, 21.0 minutes; 95% CI, 15.9 to 26.2 minutes; p<0.0001) and radiation exposure time (WMD, 25.4 seconds; 95% CI, 22.0 to 28.8 seconds, p<0.0001) than the open group (low-quality evidence). There were no significant differences in pain improvement, fusion rate, complications, or subsequent surgeries between the two treatment groups (low-quality evidence).

Conclusion: Although present findings are limited by insufficient evidence and there is a lack of adequately powered high-quality randomized controlled trials to address this gap in evidence, our results support that minimally invasive lumbar fusion is more effective than open fusion for adult spondylolisthesis and other spondylosis in terms of functional improvement, reducing infection rate, and decreasing blood loss and hospital stay.

Key Words: Minimally invasive, percutaneous pedicle screw, spinal fusion, lumbar spine, efficacy, meta-analysis

INTRODUCTION

Pedicle screw instrumented fusion is used as a safe and effective treatment for adult lumbar spondylolisthesis and other spondylosis.[1,2] However, it is associated with extensive blood loss, a lengthy hospital stay, significant cost, and high reoperation rates.[3,4] Standard instrumented fusion requires extensive tissue dissection to expose entry points that provide the lateral-to-medial orientation for optimal screw trajectory. Extensive injury to the back muscles during surgery has been shown to correlate with poor long-term outcomes.[5,6]

To overcome these problems, minimally invasive instrumented fusion through small, separate wounds without extensive tissue dissection has been introduced.[7] This technique significantly reduces back muscle injury and blood loss, which leads to better trunk muscle performance and faster recovery and rehabilitation.[8] However, the potential benefits of minimized tissue disruption, reduced blood loss, and shorter hospital stay must be weighed against the increased rate of neurological complications associated with this technique.[9] Moreover, hardware-related complications and pseudarthrosis have been re-

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ported in recent studies.[10,11]

Evidence regarding the efficacy of minimally invasive lumbar spinal fusion employing percutaneous pedicle screws exclusively for posterior augmentation has not been synthesized, while plenty of meta-analyses have explored mixed data from studies that utilized conventional pedicle screws for mini-open instrumentation as an alternative to percutaneous pedicle screws. The primary purpose of the current study was to investigate the efficacy of minimally invasive instrumented fusion for adult lumbar spondylolisthesis and other spondylosis. We compared minimally invasive and open pedicle screw instrumented lumbar fusion, especially with respect to 1) pain and functional improvements and fusion rate, 2) complications and subsequent surgeries, and 3) perioperative outcomes (blood loss, hospital stay, operation time, and radiation exposure time).

MATERIALS AND METHODS

We conducted a thorough and comprehensive review of the literature according to the guidelines for performance and reporting of systematic reviews and meta-analyses outlined in the Meta-analysis of Observational Studies in Epidemiology (MOOSE)[12] and Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).[13] This study was exempt from Institutional Review Board review. We searched the literature comparing minimally invasive lumbar spinal fusion with open fusion, including transforaminal lumbar interbody fusion (TLIF), posterior lumbar interbody fusion (PLIF), or posterolateral fusion (PLF), for the treatment of spondylolisthesis and other spondylosis. The literature searches were restricted to randomized controlled trials (RCTs), controlled clinical trials (or quasi-RCTs), and prospective cohort studies published in English. The searches were also limited to studies in which percutaneous pedicle screws were exclusively utilized for posterior spinal fixation in the intervention group. Studies with instrumented conventional pedicle screws instead of percutaneous pedicle screws and a mini-open approach were excluded. We also identified articles with overlapping populations and sought to determine the extent of overlap. In the case of substantial overlap (patients in one article were a subset of those in a larger study), the smaller study was excluded. Our detailed eligibility criteria are listed in Table 1.

For inclusion in the present analysis, studies must have reported the following primary outcomes: postoperative back pain and leg pain improvement measured via a visual analogue scale (VAS); functional improvement measured via Oswestry Disability Index (ODI) score; fusion rate; complications (neurological, hardware-related, and surgical-site complications); subsequent surgeries (revision, removal, reoperation, and supplemental fixation); and perioperative outcomes (blood loss, length of hospital stay, operation time, and radiation exposure time).

Literature search and study selection

Two authors independently performed a comprehensive literature search of PubMed, Embase, and the Cochrane Library database for relevant studies published up to December 2017 using derivatives of the following Medical Subject Headings (MeSH): percutaneous pedicle screw, minimally invasive fusion, minimally invasive arthrodesis, mini-open fusion, mini-open arthrodesis, minimal access fusion, and minimal access arthrodesis. The detailed search strategy is illustrated in Supplementary Table 1 (only online). The reference lists of included articles were also systematically checked to identify additional eligible articles.

One reviewer (SOS) screened titles and abstracts to determine potential inclusion, with a 10% random sample of records independently screened by a second reviewer (SBL). Articles were double blind coded. Inclusion was subsequently confirmed by a team of three reviewers (SOS, SBL, and JWH) who independently checked the full text of all retrieved articles. Uncertainties and disagreements were resolved through team discussion and/or contact with study authors.

Data extraction and analysis

The study reviewers then used a custom data extraction form to extract relevant study data in duplicate. Data elements extracted included methodology data to confirm study eligibility, study design, patient demographics, performed interventions, outcomes of interest, statistical methods, and study results. One reviewer (SOS) then entered extracted data into a spreadsheet (Microsoft Excel 2013, Microsoft Corp., Redmond, WA, USA) with the accuracy of data entry confirmed by the second reviewer (SBL).

We pooled data from each included study and performed meta-analyses (both fixed-effect and random-effects methods) using Comprehensive Meta-Analysis software package Version 2 (Biostat, Englewood, NJ, USA) and STATA Version 14.0 (Stata Corp., College Station, TX, USA). The odds ratio (OR) for the intervention group and the accompanying 95% confidence interval (CI) were calculated for dichotomous outcomes, and the weighted mean difference (WMD) and 95% CI were calculated for continuous outcomes. We reported outcome measures according to the length of follow up: short (<1 year), intermediate (1 to 5 years), and long-term (≥5 years). Pain and functional improvements were analyzed using data from baseline to last follow-up. Fusion rate, complications, and subsequent surgeries were analyzed using data from the last follow-up visit.

The overall quality of evidence for each outcome was categorized as high, moderate, low, or very low according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) protocol.[12,13] Five specific domains were used for grading study quality: risk of bias, inconsistency, indirectness, imprecision, and publication bias. We downgraded the evidence by 1 point when fewer than three domains were judged "serious or unclear" or when the study design was not

Table 1. Inclusion and Exclusion Criteria

Study components	Inclusion	Exclusion
Participants	Adults	Children (age ≤18 years)
Pathology	A pathology of spondylolisthesis, spondylosis (degenerative disease)	A pathology of deformity, trauma, infection, inflammatory disease, or tumor
Interventions	Posterior lumbar/lumbosacral spinal fusion (including transforaminal/posterior lumbar interbody fusion and posterolateral fusion) utilizing percutaneous pedicle screw fixation	Decompression only without fusion Fusions extended to cervical and thoracic spine Stand-alone anterior or posterior fusion Presacral (axial) anterior fusion Posterior instrumentation with facet screws or interspinous process devices Unilateral instrumentation Robot-assisted instrumentation Mini-open instrumentation* Mixed instrumentation
Comparator	Conventional open pedicle screw instrumented fusion	
Study outcomes	Clinical outcomes for pain and function, fusion rate, subsequent surgery, complications, and perioperative surgical data	Other radiographic measures (excluding fusion): alignment, range of motion, etc. Nonclinical outcomes
Study design	Randomized controlled trials Controlled clinical trials Prospective cohort studies	Retrospective cohort studies Case-control studies Case series Case reports Nonclinical studies
Publication	Studies published in English in peer-reviewed journals	Abstracts, editorials, letters Duplicate publications of the same study that do not report on different outcomes Single-center reports from multicenter trials Studies reporting on the technical aspects of the surgery White papers or narrative reviews Articles identified as preliminary reports when results are published in later versions

*Conventional pedicle screws were instrumented through a mini-open approach without use of percutaneous pedicle screw systems.

an RCT. We downgraded the evidence by 2 points when four or more domains were judged "serious or unclear."

Risk of bias

Two independent authors assessed the risk of bias and other major methodological flaws in the included studies using the checklist for RCTs[12,13] or the checklist for cohort studies by Cowley.[14] We defined high-quality studies as those that fulfilled ≥6 of the 12 criteria for RCTs or ≥9 of the 17 criteria of Cowley. We downgraded the quality of evidence by 1 point when risk of bias was serious or when major methodological flaws were noted. Disagreements were resolved by discussion.

Inconsistency

We evaluated statistical heterogeneity with the Q-test and I^2 value. We defined substantial statistical heterogeneity as a Q-test with a *p*-value lower than 0.1 or an I^2 value greater than 75%.[15,16] We downgraded the quality of evidence by 1 point when heterogeneity was substantial.

Indirectness

We assessed whether the question being addressed in this meta-analysis varied from the available evidence with regard to population, intervention, comparators, or outcomes.

Imprecision

Results were considered imprecise when trials included relatively few patients and few events and thus had wide CIs around the estimate of the effect.

Publication bias

We downgraded the quality of evidence by 1 point when a funnel plot suggested publication bias. The possibility of publication bias was not evaluated for statistical significance if a small number (<10) of studies was assessed.[13,17]

RESULTS

We identified 745 potentially relevant citations from the elec-

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tronic database and reference searches after duplicates were eliminated. Sixty-seven studies were selected for full-text assessment after the initial title and abstract screening. Forty articles were excluded because of the study design (27 retrospective, 12 case series, and 1 unclear), and nine (including 1 RCT[18]) were excluded because open pedicle screws were used in the intervention group instead of percutaneous screws.

A total of 11 studies[19-29] met the inclusion criteria and two[20,28] were removed because of overlapping populations: 1) a study population published in 2009 by Peng, et al.[28] was determined to be a subset of those in another study published in 2012 by Lee, et al.[22] The prior study by Peng, et al.[28] overlapped their case-enroll period with the later larger one by Lee, et al.[22] Therefore, the study by Peng, et al.[28] was excluded. 2) A subset of patients in the study published in 2014 by Wang, et al.[20] were judged to be overlapped with those of two other studies published in 2010[26] and 2011[25] by the same authors. The other two studies[25,26] did not have overlapping populations with each other. Consequently, the study published in 2014 by Wang, et al.[20] was excluded.

Finally, nine studies[19,21-27,29] were selected for analysis (Fig. 1). Characteristics of all included studies are summarized in Table 2 and Supplementary Table 2 (only online). A total of 707 participants (363 in the minimally invasive group and 344 in the open group) were included in the nine prospective cohort studies. Mean duration of follow-up was 22.2±6.8 months in the minimally invasive group and 24.1±7.6 months in the open group. Detailed demographic and surgical data at baseline are illustrated in Table 3. The baseline data were similar between the two groups (all $p>0.05$).

Quality assessment

All studies had a Cowley score of 9 or more, and we judged these studies to have a low risk of bias (Table 4). Serious inconsistency was noted in all perioperative outcome measures (blood loss, hospital stay, operation time, and radiation exposure time) with substantial heterogeneity ($I^2>75\%$, $p<0.1$). Serious imprecision was noted in the primary outcome measures for pain and functional improvement, as well as in all perioperative outcome measures (effect size of mean difference crosses 0.5). Publication bias was judged to be unclear because it could not be quantified due to the small number of studies analyzed.

Based on the GRADE protocol, all studies suffered from methodological flaws (limitations in the design and implementation), leading us to downgrade their quality by 1 point (Table 5). We downgraded the evidence for primary outcomes of back pain, leg pain, and functional improvement by 2 points (low-quality evidence) because of study design and because two domains (imprecision and publication bias) were judged "serious or unclear." The evidence for primary outcomes of fusion rate, complications, and subsequent surgeries was also downgraded by 2 points (low-quality evidence) because of the design and because one domain (publication bias) was judged "serious or unclear." Moreover, the evidence for perioperative outcomes (blood loss, hospital stay, operation time, and radiation exposure time) was downgraded by 2 points (low-

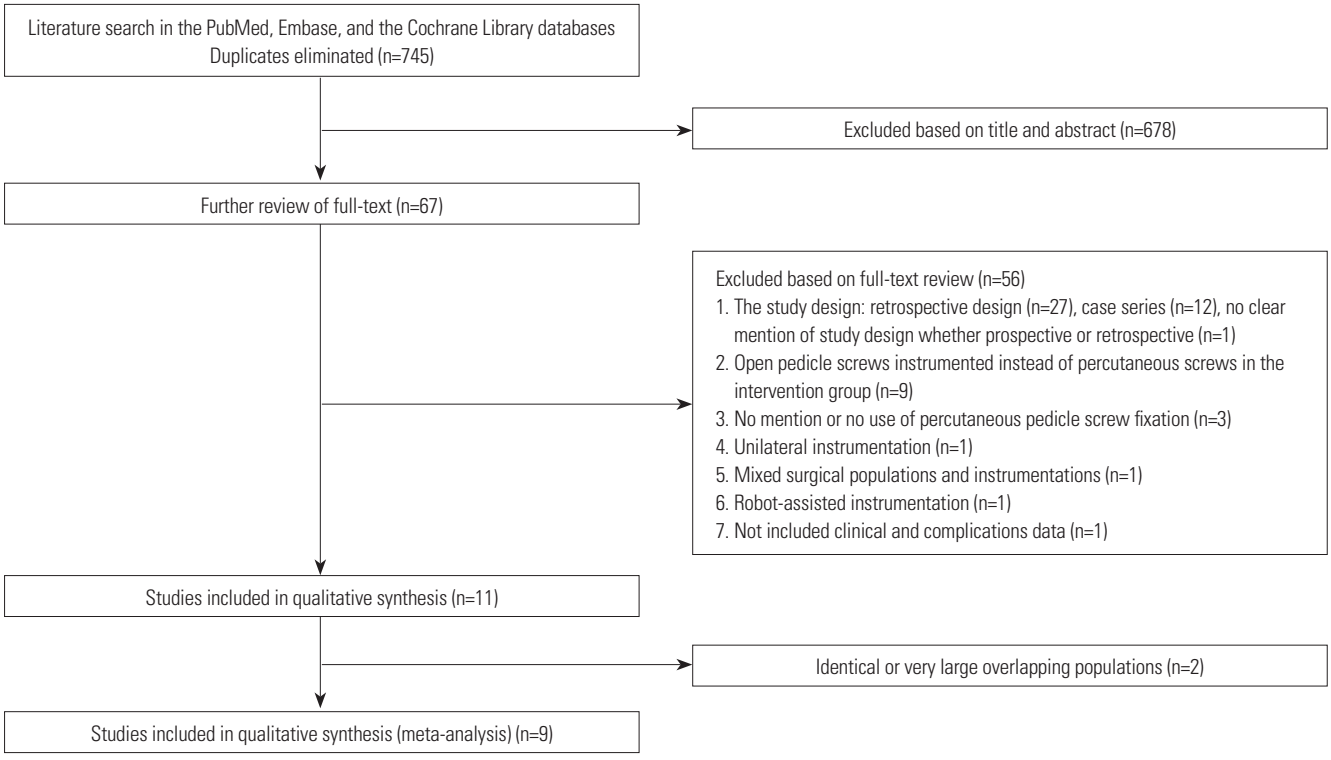

Fig. 1. Flow diagram demonstrating the individual steps in the literature-selection process.

Table 2. Characteristics of All Included Comparative Observational Studies

Studies	Study design, year published, year enrollment, intervention	Comparison group	N	Age (yr)	Gender Male (%)	Fusion level	Diagnoses (number of patients in percutaneous group, open group)	Instrumentations including cage and pedicle screw	Bone graft	Follow-up (month)
Parker, et al.[19]	Prospective cohort study, 2014, NR, Single-level TLIF	Minimally invasive group	50	53.5±12.5	16 (32)	L3–4; 4 L4–5; 32 L5–S1; 14	Degenerative spondylolisthesis grade I (50, 50)	A single PEEK interbody cage and percutaneous pedicle screw system (implants NR)	Local autogenous bone with or without bone extensors (i.e., DBM)	24, % followed: NR
		Open group	50	52.6±11.6	18 (36)	L3–4; 3 L4–5; 30 L5–S1; 17		A single PEEK interbody cage and conventional pedicle screw system (implants NR)	Local autogenous bone with or without bone extensors (i.e., DBM)	24, % followed: NR
Gu, et al.[21]	Prospective cohort study, 2013, 2010–2011, Two-level TLIF	Minimally invasive group	44	66.4±6.7	19 (43.2)	L3–5; 13 L4–S1; 31	Degenerative disc disease (15, 11) Spinal stenosis (18, 14) Spinal stenosis with segmental instability (11, 13)	A single PEEK interbody cage (Capstone; Medtronic, Memphis, TN, USA) and percutaneous pedicle screw system (Sextant; Medtronic)	Local autologous bone	20.6±4.5, % followed: NR
		Open group	38	64.1±7.8	15 (39.5)	L3–5; 14 L4–S1; 24		NR	NR	20.0±3.3, % followed: NR
Lee, et al.[22]	Prospective cohort study, 2012, 2002–2008, Single-level TLIF	Minimally invasive group	72	52.2±13.8	20 (27.8)	L3–4; 6 L4–5; 49 L5–S1; 17	Spondylolisthesis (Grade 1 and 2) Recurrent disc herniation Spinal stenosis requiring resection of more than 50% of either facet joint	A single PEEK interbody cage (Capstone; Medtronic) and percutaneous pedicle screw system (Sextant; Medtronic)	Local autogenous bone with DBM (Osteofil; Medtronic)	24, 95.8% (69/72) followed for 24 months
		Open group	72	56.6±14.6	22 (30.6)	L3–4; 4 L4–5; 54 L5–S1; 14	Degenerated collapsed disc requiring disc-space height restoration (Specific number; NR)	A single PEEK interbody cage (Capstone; Medtronic) and conventional pedicle screw system (implants NR)	Local autogenous bone with DBM (Osteofil; Medtronic) and one case with rhBMP-2 (Infuse; Medtronic)	24, 91.7% (66/72) followed for 24 months
Mobbs, et al.[23]	Prospective cohort study, 2011, 2006–2010, Single- or multi-level PLIF	Minimally invasive group	37	68.56±12.99	19 (51.4)	T11–12; 0 L2–3; 1 L3–4; 2 L4–5; 20 L5–S1; 6 Multi-level; 8	Isthmic spondylolisthesis (4, 9) Degenerative spondylolisthesis (18, 9) Degenerative scoliosis (1, 4) Degenerative disc disease with foraminal stenosis (14, 8)	A single rotatable interbody cage (implants NR) and percutaneous pedicle screw systems (Denali/ Serengeti system; K2M, Leesburg, VA, USA and MANTIS; Stryker, Kalamazoo, MI, USA)	Local autogenous bone with or without synthetic bone	11.5 (5.4–20.1), % followed: NR
		Open group	30	67.48±13.19	16 (53.3)	T11–12; 1 L2–3; 0 L3–4; 0 L4–5; 15 L5–S1; 9 Multi-level; 5		A single rotatable interbody cage and conventional pedicle screw system (implants NR)	Local autogenous bone with or without synthetic bone	18.7 (8.1–40.0), % followed: NR

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Table 2. Characteristics of All Included Comparative Observational Studies (continued)

Studies	Study design, year published, year enrollment, intervention	Comparison group	N	Age (yr)	Gender Male (%)	Fusion level	Diagnoses (number of patients in percutaneous group, open group)	Instrumentations including cage and pedicle screw	Bone graft	Follow-up (months)
Kotani, et al.[24]	Prospective cohort study, 2011, 2005–NR, Single-level PLF	Minimally invasive group	43	63±9	14 (32.6)	L3–4; 4 L4–5; 76 (no specific declaration between groups)	Degenerative spondylolisthesis (43, 37)	Percutaneous pedicle screw system (Sextant; Medtronic)	Autogenous posterior iliac crest bone	32 (24–49), % followed: NR
		Open group	37	66±9	12 (32.4)			Conventional polyaxial pedicle screw and rod system (implants NR)	Autogenous posterior iliac crest bone	40 (24–60), % followed: NR
Wang, et al.[25]	Prospective cohort study, 2011, 2006–2008, Single- or two-level TLIF	Minimally invasive group	25	54.8±10.9	13 (52.0)	L3–4; 2 L4–5; 11 L5–S1; 9 Two-level; 3	Recurrent disc herniation (7, 8) Postsurgical foraminal stenosis (10, 9) Postsurgical segmental instability (5, 7)	A single PEEK interbody cage (OIC; Stryker) and percutaneous pedicle screw system (Sextant; Medtronic)	Local autogenous bone with or without autogenous iliac crest bone	Overall, 27.5 (12–38), % followed: NR
		Open group	27	56.2±13.6	15 (55.6)	L3–4; 2 L4–5; 11 L5–S1; 10 Two-level; 4	Postsurgical spondylolisthesis grade 1 (3, 3)	A single PEEK interbody cage (OIC; Stryker) and conventional pedicle screw system (implants NR)	NR	
Wang, et al.[26]	Prospective cohort study, 2010, 2006–2008, Single-level TLIF	Minimally invasive group	42	47.9±8.5	13 (30.1)	L3–4; 3 L4–5; 21 L5–S1; 18	Degenerative spondylolisthesis (24, 22)	A single PEEK interbody cage (OIC, Stryker) and percutaneous pedicle screw system (Sextant; Medtronic)	Local autogenous bone	Overall, 26.3 (13–35), % followed: NR
		Open group	43	53.2±10.6	16 (37.2)	L3–4; 3 L4–5; 23 L5–S1; 17	Isthmic spondylolisthesis (18, 21)	NR	NR	
Schizas, et al.[27]	Prospective cohort study, 2008, NR, Single-level TLIF	Minimally invasive group	18	45.5±NR	NR	L5–S1; 12 Other level (specific level;NR); 6	Isthmic spondylolisthesis (15, 6) Degenerative disc disease with foraminal stenosis (2, 12) Iatrogenic spondylolysis (1, 0)	A single PEEK interbody cage (Medtronic) and percutaneous pedicle screw system [Sextant (11 cases); Medtronic and Viper (7 cases); DePuy Spine, USA]	Local autologous bone with autogenous iliac crest bone	22, % followed: NR
		Open group	18	48.1±NR	NR	L5–S1; 11 Other level (specific level; NR); 7		NR	Local autologous bone with autogenous iliac crest bone	24, % followed: NR
Park and Ha[29]	Prospective cohort study, 2007, 2003–2004, Single-level PLIF	Minimally invasive group	32	62.1±9.6	8 (25)	L3–4; 2 L4–5; 23 L5–S1; 7	Isthmic spondylolisthesis (6, 7) Degenerative spondylolisthesis (7, 5) Lumbar disc herniation (1, 3)	A single PEEK interbody cage (Telamon; Medtronic) and percutaneous pedicle screw system (Sextant; Medtronic)	Local autogenous bone	12, % followed: NR
		Open group	29	59.0±12.2	13 (44.8)	L3–4; 3 L4–5; 18 L5–S1; 8	Spinal stenosis with segmental instability (18, 14)	A single PEEK interbody cage (Telamon; Medtronic) and conventional pedicle screw system (implants NR)	Local autogenous bone	12, % followed: NR

TLIF, transforaminal lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; PLF, posterolateral fusion; PEEK, polyetheretherketone; NR, not reported; DBM, demineralized bone matrix, and rhBMP-2, recombinant human bone morphogenetic protein-2.

Table 3. Demographic and Surgical Data between the Two Surgical Groups

Overall	Minimally invasive group	Open group
Number of patients	363	344
Age (yr)	57.1±8.2	58.1±6.6
Gender, male (%)	122 (33.6)	127 (36.9)
Diagnosis		
Spondylolisthesis (low-grade)	188	169
Degenerative	142	123
Isthmic	43	43
Postsurgical	3	3
Other spondylosis	103	103
Degenerative disc disease	15	11
Lumbar disc herniation	1	3
Spinal stenosis	18	14
Foraminal stenosis	16	20
Spinal stenosis with segmental instability	29	27
Recurrent lumbar disc herniation	7	8
Postsurgical foraminal stenosis	10	9
Postsurgical segmental instability	5	7
Degenerative scoliosis	1	4
Iatrogenic spondylolysis	1	0
Number of each separate diagnosis NR	72	72
Fusion modalities		
TLIF	251	248
Single-level	204	206
Two-level	47	42
PLIF	69	59
Single-level	61	54
Multi-level	8	5
PLF		
Single-level	43	37
Fusion level		
Single-level	308	297
T11–12	0	1
L2–3	1	0
L3–4	19	15
L4–5	156	151
L5–S1	83	86
Level NR	49	44
Two-level	47	42
L3–L5	13	14
L4–S1	31	24
Level NR	3	4
Multi-level		
Level NR	8	5
Follow-up periods	22.2±6.8	24.1±7.6

TLIF, transforaminal lumbar interbody fusion; PLIF, posterior lumbar interbody fusion; PLF, posterolateral fusion; NR, not reported.
The differences of all baseline data were not significant. $p>0.05$.

quality evidence) because of the design and because three domains (inconsistency, imprecision, and publication bias) were judged "serious or unclear."

Pain and functional improvements

Low-quality evidence from five studies[19,22,23,25,26] revealed that improvement in VAS back pain score was not significantly different between the minimally invasive spinal fusion and open fusion groups (WMD, 0.2; 95% CI, -0.2–0.6; p=0.3; mean follow-up, 20.9±7.2 months). Likewise, low-quality evidence from two studies[19,22] revealed that improvement in VAS leg pain score did not differ significantly between the two groups (WMD, 0.3; 95% CI, -0.5–1.0; p=0.5; mean follow-up, 25.2±2.0 months). In contrast, there was low-quality evidence from five studies[19,22,23,25,26] in which the minimally invasive group had significantly greater improvement in ODI score than the open group (WMD, 3.2; 95% CI, 1.5–5.0; p=0.0003; mean follow-up, 24.2±4.8 months) (Fig. 2). The detailed clinical outcome scores of all included studies are summarized in Supplementary Tables 3 and 4 (only online).

Fusion rate

Fusion rates were reported in all studies, with overall rates of 96.7% in the minimally invasive group (351/363 patients; mean follow-up, 22.2±6.8 months) and 97.4% in the open group (335/344 patients; mean follow-up, 24.1±7.6 months) (Supplementary Tables 5 and 6, only online). Eight of nine studies were eligible for the meta-analysis; one study was not eligible because the fusion rate was 100% in both groups.[19] We found low-quality evidence from eight studies in which there was no statistically significant difference in the overall fusion rate between the two groups (OR, 0.9; 95% CI, 0.3–2.1; p=0.7). Low-quality evidence was obtained from subgroup analyses according to the fusion method (5 studies for TLIF,[21,22,25-27] two studies for PLIF,[23,29] and a single study for PLF[24]), which revealed no significant difference in the fusion rate between the two groups (Fig. 3).

Complications

The detailed complications of all included studies are summarized in Supplementary Table 7 (only online).

Neurological complications

Seven studies[19,21-23,25-27] addressed neurological complications, including dural tear, CSF leakage, nerve root injury, and postoperative radiculopathy (Table 6). The overall rates of neurological complications were 4.5% in the minimally invasive group (13/288 patients; mean follow-up, 22.3±5.3 months) and 4.7% in the open group (13/278 patients; mean follow-up, 23.5±3.2 months). We found low-quality evidence from these studies that there was no statistically significant difference in the overall rate of neurological complications between the two groups (OR, 0.8; 95% CI, 0.4–1.8; p=0.7) (Fig. 4).

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Table 4. Risk of Bias Assessment of Included Comparative Observational Studies

	Parker, et al.[19]	Gu, et al.[21]	Lee , et al.[22]	Mobbs, et al.[23]	Kotani, et al.[24]	Wang, et al.[25]	Wang, et al.[26]	Schizas, et al.[27]	Park and Ha[29]
1 Method of selection of patients identified and appropriateness	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2 Number of patients deceased or lost to follow-up reported or included in appropriate statistical analysis	No	No	Yes	No	No	No	No	No	No
3 Follow-up period range and mean given (minimum=n)	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
4 Prosthesis models specified	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5 Clearly defined criteria for measuring outcomes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6 Valid statistical analysis undertaken	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7 Data given for deceased patients (information)	No	No	Yes	No	No	No	No	No	No
8 Age range and mean age reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
9 Numbers of males and females given	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
10 Weight range and mean weight given	No	No	No	No	No	No	No	No	Yes
11 Preoperative diagnoses with percentages of patients given	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
12 Clinical evaluation independent of operating surgeon	Yes	Unclear	Yes	Unclear	Unclear	No	No	Unclear	Unclear
13 Radiological evaluation independent and blinded to clinical results	No	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	Unclear
14 Results given for specific models	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
15 Quantification of outcomes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
16 Follow-up data compared with preoperative data (mean and range)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
17 Independence of investigators (no vested interest) stated	No	Yes	No	Unclear	Yes	Yes	Yes	No	Yes
Scores	9	13	14	12	12	13	13	9	11

A positive answer (Yes) to any question counts as 1 point.

Table 5. The Quality Assessment of Evidence for Each Outcome

Number of studies	Study design	Risk of bias*	Inconsistency	Indirectness	Imprecision	Publication bias‡‡	Quality
Back pain improvement: 5	No RCTs	No serious	No serious†	No serious	Serious**	Unclear	Low
Leg pain improvement: 2	No RCTs	No serious	No serious†	No serious	Serious**	Unclear	Low
Functional improvement: 5	No RCTs	No serious	No serious†	No serious	Serious**	Unclear	Low
Fusion rate: 8	No RCTs	No serious	No serious†	No serious	No serious††	Unclear	Low
Neurological complications: 7	No RCTs	No serious	No serious†	No serious	No serious††	Unclear	Low
Harware complications: 6	No RCTs	No serious	No serious†	No serious	No serious††	Unclear	Low
Surgical-site complications: 7	No RCTs	No serious	No serious†	No serious	No serious††	Unclear	Low
Subsequent surgeries: 6	No RCTs	No serious	No serious†	No serious	No serious††	Unclear	Low
Blood loss: 6	No RCTs	No serious	Serious‡	No serious	Serious**	Unclear	Low
Hospital stay: 6	No RCTs	No serious	Serious§	No serious	Serious**	Unclear	Low
Operation time: 7	No RCTs	No serious	Serious‖	No serious	Serious**	Unclear	Low
Radiation exposure time: 4	No RCTs	No serious	Serious¶	No serious	Serious**	Unclear	Low

RCTs, randomized controlled trials; df, degrees of freedom.
*All studies fulfilled 9 or more criteria of checklist by Cowley and these studies were judged at low risk of bias, †Heterogeneity: I^2=0%, ‡Heterogeneity: χ^2=89.096, df=5 (p<0.0001); I^2=94.4%, §Heterogeneity: χ^2=91.483, df=5 (p<0.0001); I^2=94.5%, ‖Heterogeneity: χ^2=42.123, df=6 (p<0.0001); I^2=85.8%, ¶Heterogeneity: χ^2=44.986, df=3 (p<0.0001); I^2=93.3%, **Weighted mean difference effect size crosses 0.5, ††Odds ratio effect size did not cross 2.5, ‡‡Publication bias was not calculated due to the small number of studies analyzed.

Hardware complications

Six studies[19,21,22,26,27,29] described hardware-related complications, including screw malposition, screw loosening, screw breakage, overlong screw, cage migration, cage fracture, and graft dislodgement (Table 6). The overall rates of hardware complications were 5.4% in the minimally invasive group (14/258 patients; mean follow-up, 21.8±5.4 months) and 3.6% in the open group (9/250 patients; mean follow-up, 22.3±5.2 months). There was low-quality evidence that the overall rate of hardware complications did not differ significantly between the two groups (OR, 1.2; 95% CI, 0.5–2.6; p=0.7) (Fig. 4).

Surgical-site complications

Seven studies[19,21-23,25,26,29] reported surgical-site complications, including surgical-site infection, superficial infection, deep infection, and hematoma (Table 6). The overall rates of surgi-

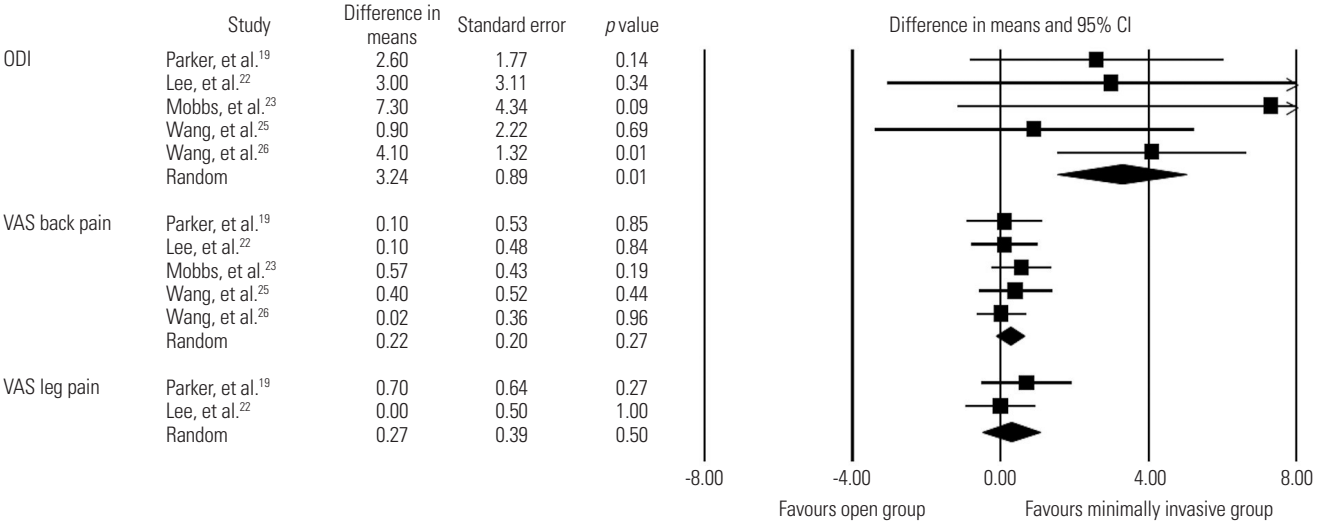

Fig. 2. Comparisons of ODI scores for functional improvement and VAS scores for back pain and leg pain between minimally invasive and open lumbar spinal fusion. Heterogeneity: ODI score [τ^2=0.000; χ^2=2.549, df=4 (p=0.636); I^2=0.0%], VAS back pain [τ^2=0.000; χ^2=1.192, df=4 (p=0.879); I^2=0.0%], and VAS leg pain [τ^2=0.000; χ^2=0.748, df=1 (p=0.387); I^2=0.0%]. ODI, Oswestry Disability Index; VAS, visual analogue scale; df, degrees of freedom; CI, confidence interval.

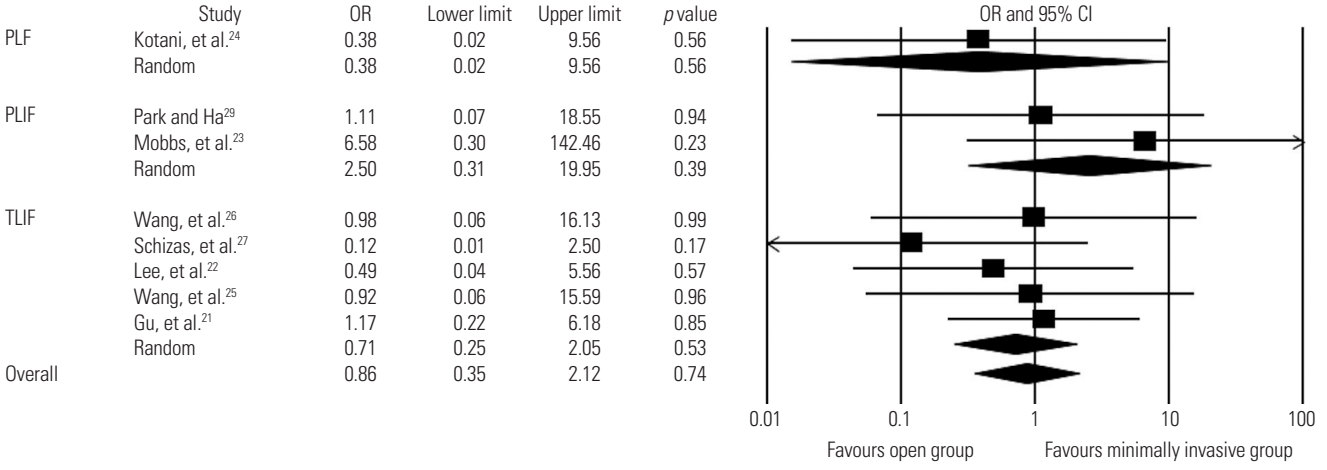

Fig. 3. Comparison of fusion rates between minimally invasive and open lumbar spinal fusion. Heterogeneity: fusion rates for PLF [τ^2=0.000; χ^2=0.000, df=0 (p=1.000); I^2=0.0%], fusion rates for PLIF [τ^2=0.000; χ^2=0.701, df=1 (p=0.402); I^2=0.0%], fusion rates for TLIF [τ^2=0.000; χ^2=1.836, df=4 (p=0.766); I^2=0.0%], and overall fusion rates [τ^2=0.000; χ^2=3.925, df=7 (p=0.788); I^2=0.0%]. PLF, posterolateral fusion; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; df, degrees of freedom; OR, odds ratio; CI, confidence interval.

cal-site complications were 1.7% in the minimally invasive group (5/302 patients; mean follow-up, 20.9±6.9 months) and 4.5% in the open group (13/289 patients; mean follow-up, 22.6±4.0 months). Low-quality evidence from these seven studies revealed that the overall rate of surgical-site complications did not differ significantly between the two groups (OR, 0.4; 95% CI, 0.2–1.1; p=0.1) (Fig. 4). The overall rates of infection (including surgical-site infection, superficial infection, and deep wound infection) were 1.2% in the minimally invasive group (3/260 patients; mean follow-up, 19.9±6.7 months) and 5.3% in the open group (13/246 patients; mean follow-up, 21.0±5.4 months). There was low-quality evidence from six studies[19,21-23,25,29] in which the minimally invasive group had a significantly lower rate of infection than the open group (OR, 0.3; 95% CI, 0.1–0.9; p=0.02) (Fig. 5).

Subsequent surgeries

Six studies included information about subsequent surgeries,[19,22,23,26,27,29] and a total of 493 patients (251 in the minimally invasive group and 242 in the open group) were analyzed (Table 6). We found low-quality evidence suggesting that the overall rate of subsequent surgeries did not differ significantly between the two groups (4.4% in the percutaneous group and 3.7% in the open group; OR, 0.9; 95% CI, 0.4–2.3; p=0.9; mean follow-up, 20.2±6.8 months). Revisions, removals, and reoperations were also analyzed in four studies,[19,22,26,29] three studies,[23,27,29] and four studies,[19,22,26,29] respectively. The overall rates of revisions were 2.6% in the minimally invasive group (5/196 patients;

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Table 6. Complications and Subsequent Surgeries between the Two Surgical Groups

Outcomes	N of studies	Minimally invasive group		Open group		OR (95% CI)
		N of events (%)	Total N of patients	N of events (%)	Total N of patients	
Surgical-site complications						
Overall	7	5 (1.7)	302	13 (4.5)	289	0.4 (0.2 to 1.1)
Infection	6	3 (1.2)	260	13 (5.3)	246	0.3 (0.1 to 0.9)*
Surgical-site infection	3	0 (0.0)	159	5 (3.3)	152	0.2 (0.02 to 0.9)†
Superficial wound infection	3	2 (2.0)	101	7 (7.4)	94	0.3 (0.02 to 1.4)
Deep wound infection	1	1 (3.1)	32	1 (3.4)	29	0.9 (0.05 to 15.1)
Hematoma	2	2 (2.5)	79	0 (0.0)	73	2.8 (0.3 to 27.6)
Neurological complications						
Overall	7	13 (4.5)	288	13 (4.7)	278	0.8 (0.4 to 1.8)
Dural tear/CSF leak	7	12 (4.2)	288	11 (4.0)	278	0.9 (0.4 to 2.1)
Nerve root injury (L5 root paresis)	1	1 (5.6)	18	0 (0.0)	18	3.2 (0.1 to 83.2)
Postoperative radiculopathy (transient L3 radicular pain)	2	0 (0.0)	55	2 (4.2)	48	0.3 (0.03 to 2.9)
Hardware complications						
Overall	6	14 (5.4)	258	9 (3.6)	250	1.2 (0.5 to 2.6)
Screw-related complications	6	8 (3.1)	258	2 (0.8)	250	1.8 (0.6 to 5.8)
Screw malposition	4	4 (2.0)	196	2 (1.0)	194	1.1 (0.3 to 5.1)
Screw loosening	1	2 (11.1)	18	0 (0.0)	18	5.6 (0.3 to 125.4)
Screw breakage	1	1 (5.6)	18	0 (0.0)	18	3.2 (0.1 to 83.2)
Overlong screw	1	1 (2.3)	44	0 (0.0)	38	2.7 (0.1 to 67.1)
Cage-related complications	3	5 (4.1)	122	7 (5.9)	119	0.7 (0.2 to 2.2)
Cage migration	2	5 (4.8)	104	6 (5.9)	101	0.8 (0.2 to 2.7)
Cage fracture during insertion	1	0 (0.0)	18	1 (5.6)	18	0.3 (0.01 to 8.3)
Graft dislodgement	1	1 (2.4)	42	0 (0.0)	43	3.1 (0.1 to 79.4)
Pseudarthrosis	9	12 (3.3)	363	9 (2.6)	344	1.2 (0.5 to 2.9)
Other complications						
Overall	3	3 (2.4)	127	7 (5.8)	120	0.6 (0.2 to 1.9)
Deep vein thrombosis	1	0 (0.0)	37	1 (3.3)	30	0.3 (0.01 to 6.7)
Myocardial infarction	1	0 (0.0)	72	1 (1.4)	72	0.3 (0.01 to 8.2)
Pneumonia	1	1 (1.4)	72	1 (1.4)	72	1.0 (0.06 to 16.3)
Paralytic ileus	1	0 (0.0)	37	3 (10)	30	0.1 (0.005 to 2.1)
Urinary tract infection	1	1 (2.7)	37	0 (0.0)	30	2.5 (0.1 to 63.8)
Postoperative anemia	1	0 (0.0)	72	1 (1.4)	72	0.3 (0.01 to 8.2)
Brachial plexus injury due to positioning	1	1 (5.6)	18	0 (0.0)	18	3.2 (0.1 to 83.2)
Subsequent surgeries‡						
Overall	6	11 (4.4)	251	9 (3.7)	242	0.9 (0.4 to 2.3)
Revision	4	5 (2.6)	196	2 (1.0)	194	1.1 (0.3 to 4.5)
Revision for malpositioned screw	4	4 (2.0)	196	2 (1.0)	194	
Revision for migrated cage	1	1 (3.1)	32	0 (0.0)	29	
Removal for pseudarthrosis	3	3 (3.4)	87	3 (3.9)	77	1.3 (0.2 to 7.9)
Reoperation	4	3 (1.5)	196	4 (2.1)	194	0.6 (0.1 to 2.8)
Reoperation for graft dislodgement	1	1 (2.4)	42	0 (0.0)	43	
Reoperation for surgical-site infection	2	0 (0.0)	122	3 (2.5)	122	
Reoperation for deep wound infection	1	1 (3.1)	32	1 (3.4)	29	
Reoperation for hematoma	1	1 (2.4)	42	0 (0.0)	43	
Supplemental fixation	0	0 (0.0)	0	0 (0.0)	0	

N, number; OR, odds ratio; CI, confidence interval; CSF, cerebrospinal fluid.

*p=0.02, †p=0.04, ‡Complications lead to a subsequent surgical intervention. Subsequent surgical intervention was categorized as follows: a revision is a procedure that adjusts or in any way modifies or removes part of the original implant configuration, with or without replacement of a component; a revision may also include adjusting the position of the original configuration (revision for migrated cage, removal of screws, etc.). A removal is a procedure where all of the original system configuration are removed with or without replacement (removal for pain at operative site but after fusion, for pseudarthrosis, etc.). A reoperation is any surgical procedure at the involved level(s) that does not removal, modification, or addition of any components to the system. A supplemental fixation is a procedure in which additional instrumentation not under study in the protocol is implanted.

mean follow-up, 21.9±6.8 months) and 1.0% in the open group (2/194 patients; mean follow-up, 21.9±6.8 months). Overall, 3.4% underwent removals in the minimally invasive group (3/87 patients; mean follow-up, 15.2±5.9 months) and 3.9% in the open group (3/77 patients; mean follow-up, 18.2±6.0 months). The overall rates of reoperations were 1.5% in the minimally invasive group (3/196 patients; mean follow-up, 21.9±6.8 months) and 2.1% in the open group (4/194 patients; mean follow-up, 21.9±6.8 months). Low-quality evidence revealed that the two groups did not differ significantly in rates

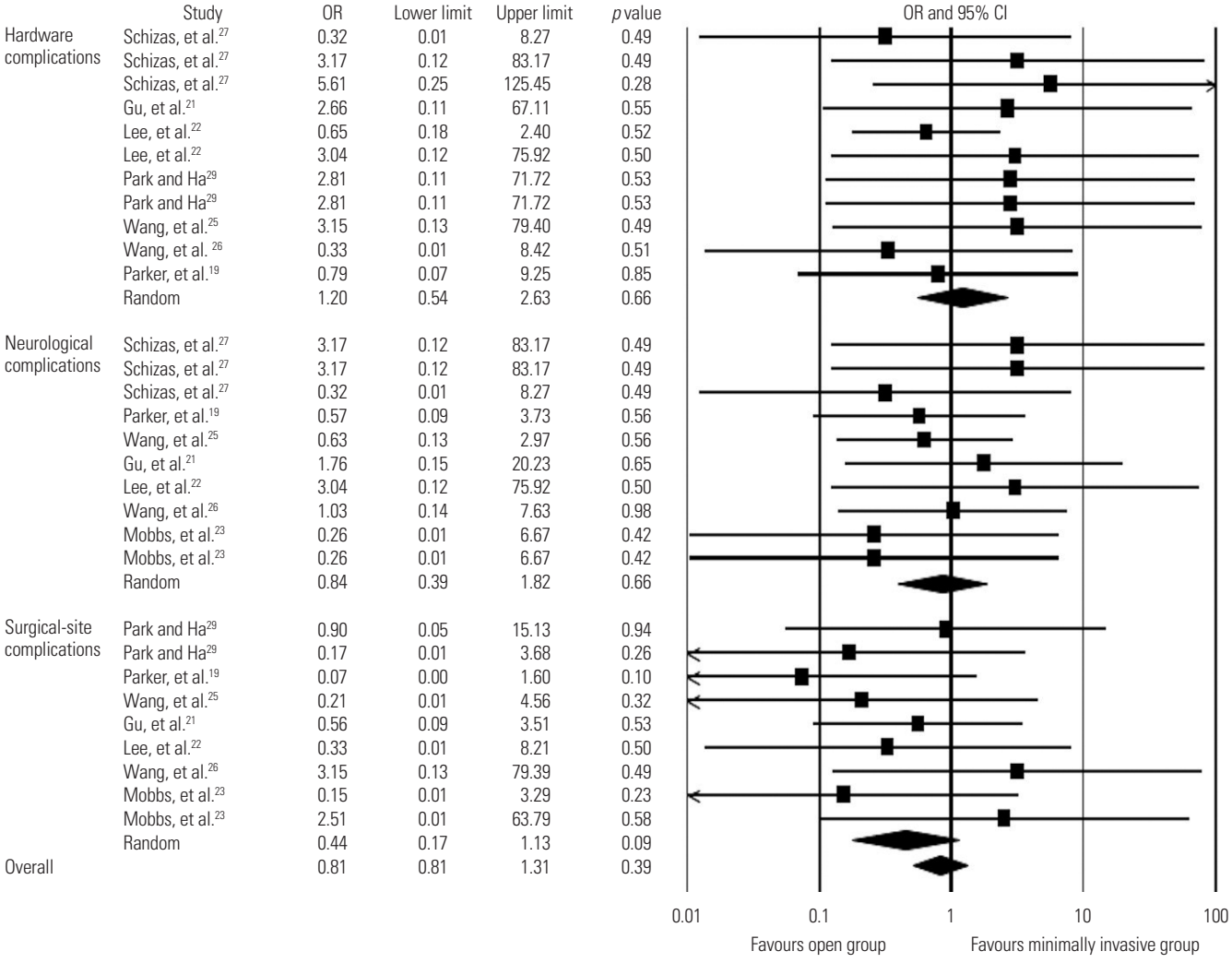

Fig. 4. Comparison of complications rates (hardware-related, neurological, and surgical-site complications) between minimally invasive and open lumbar spinal fusion. Heterogeneity: hardware-related complications [τ^2=0.000; χ^2=4.922, df=10 (p=0.896); I^2=0.0%], neurological complications [τ^2=0.000; χ^2=3.909, df=9 (p=0.917); I^2=0.0%], surgical-site complications [τ^2=0.000; χ^2=5.232, df=8 (p=0.732); I^2=0.0%], and overall complication rates [τ^2=0.000; χ^2=16.605, df=29 (p=0.968); I^2=0.0%]. df, degrees of freedom; OR, odds ratio; CI, confidence interval.

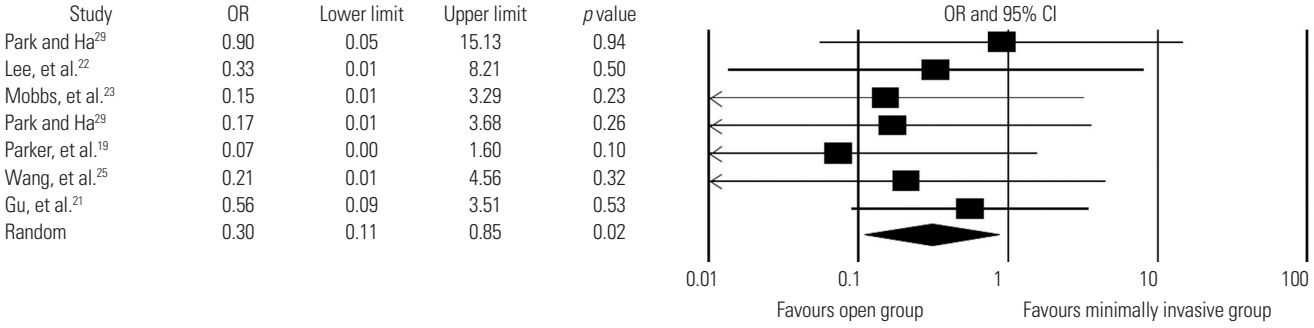

Fig. 5. Comparison of infection rates between minimally invasive and open lumbar spinal fusion. Heterogeneity: τ^2=0.000; χ^2=2.197, df=6 (p=0.901); I^2=0.0%. df, degrees of freedom; CI, confidence interval; OR, odds ratio.

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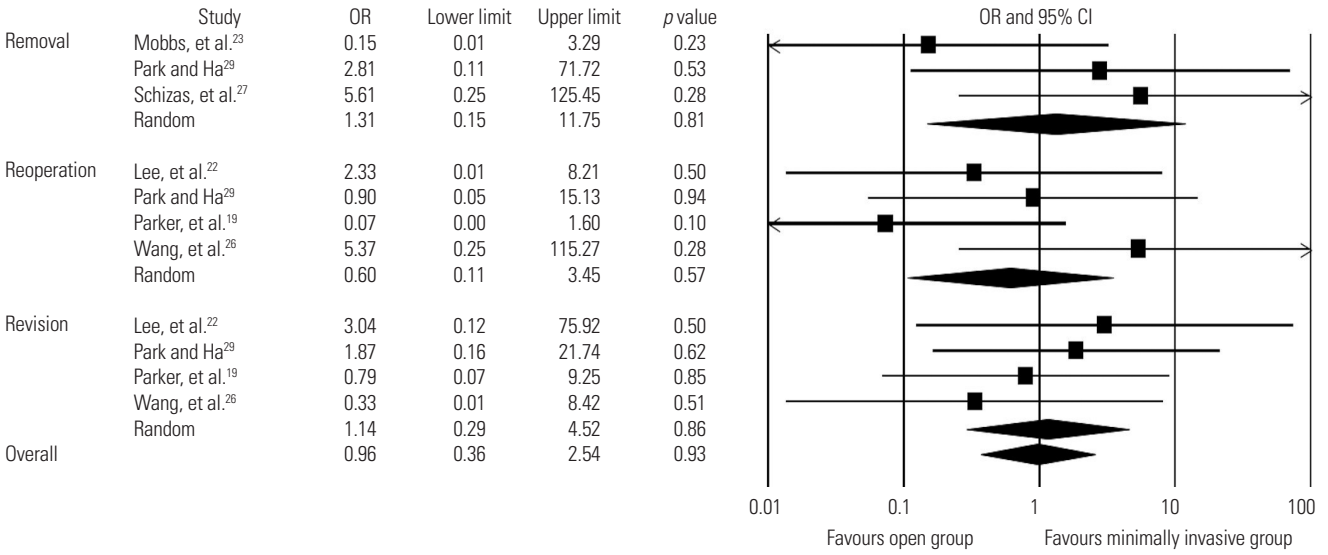

Fig. 6. Comparison of subsequent surgery rates between minimally invasive and open lumbar spinal fusion. Heterogeneity: Removal [τ^2=1.204; χ^2=2.938, df=2 (p=0.230); I^2=31.9%], reoperation [τ^2=0.774; χ^2=3.965, df=3 (p=0.265); I^2=24.3%], revision [τ^2=0.000; χ^2=1.154, df=3 (p=0.764); I^2=0.0%], overall subsequent surgery rates [τ^2=0.000; χ^2=8.565, df=10 (p=0.574); I^2=0.0%]. df, degrees of freedom; OR, odds ratio; CI, confidence interval.

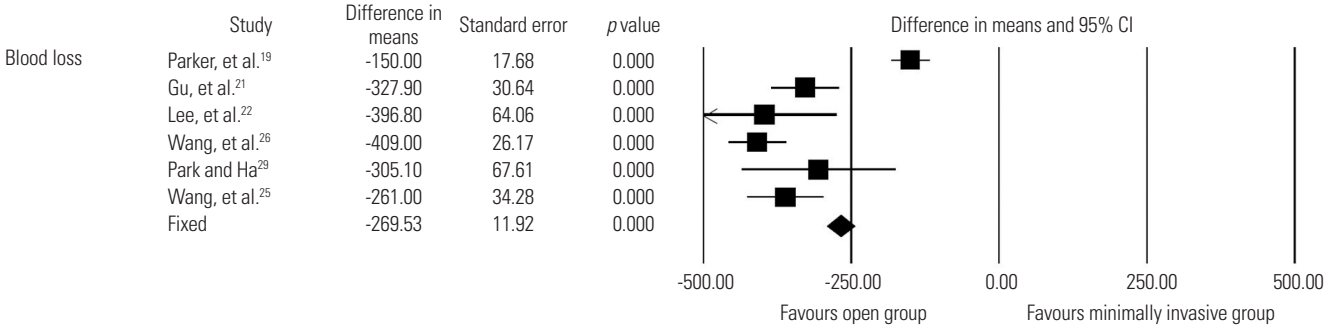

Fig. 7. Comparison of blood loss between minimally invasive and open lumbar spinal fusion. Heterogeneity: τ^2=0.747; χ^2=57.666, df=5 (p<0.0001); I^2=91.3%. df, degrees of freedom; CI, confidence interval.

of revision (OR, 1.1; 95% CI, 0.3– 4.5; p=0.9), removal (OR, 1.3; 95% CI, 0.2–11.8; p=0.8), and reoperation (OR, 0.6; 95% CI, 0.1–3.5; p=0.6) (Fig. 6).

Perioperative outcomes

The detailed perioperative outcome data are summarized in Supplementary Tables 8, 9, and 10 (only online).

Blood loss

Six studies[19,21,22,25,26,29] reported estimated blood loss during surgery, with 265 patients in the minimally invasive group and 259 in the open group. Low-quality evidence indicated that the minimally invasive group had significantly less blood loss than the open group (WMD, 269.5 mL; 95% CI, 246.2–292.9 mL; p<0.0001) (Fig. 7).

Hospital stay

Six studies[19,21-23,26,29] reported length of hospital stay, with 277 patients in the minimally invasive group and 262 in the open group. Low-quality evidence suggested that the minimally invasive group had a significantly shorter hospital stay than the open group (WMD, 1.3 days; 95% CI, 1.1–1.5 days; p<0.0001) (Fig. 8).

Operation time

Seven studies[19,21,22,24-26,29] reported operation time, with 302 patients in the minimally invasive group and 289 in the open group. There was low-quality evidence indicating that the minimally invasive group had a significantly longer operation time than the open group (WMD, 21.0 minutes; 95% CI, 15.9–26.2 minutes; p<0.0001) (Fig. 8).

Radiation exposure time

Four studies[21,22,25,26] reported radiation exposure time, with 183 patients in the minimally invasive group and 180 in the open group. Low-quality evidence suggested that the minimally invasive group had a significantly longer radiation exposure time than the open group (WMD, 25.4 seconds; 95% CI, 22.0–28.8 seconds; p<0.0001) (Fig. 8).

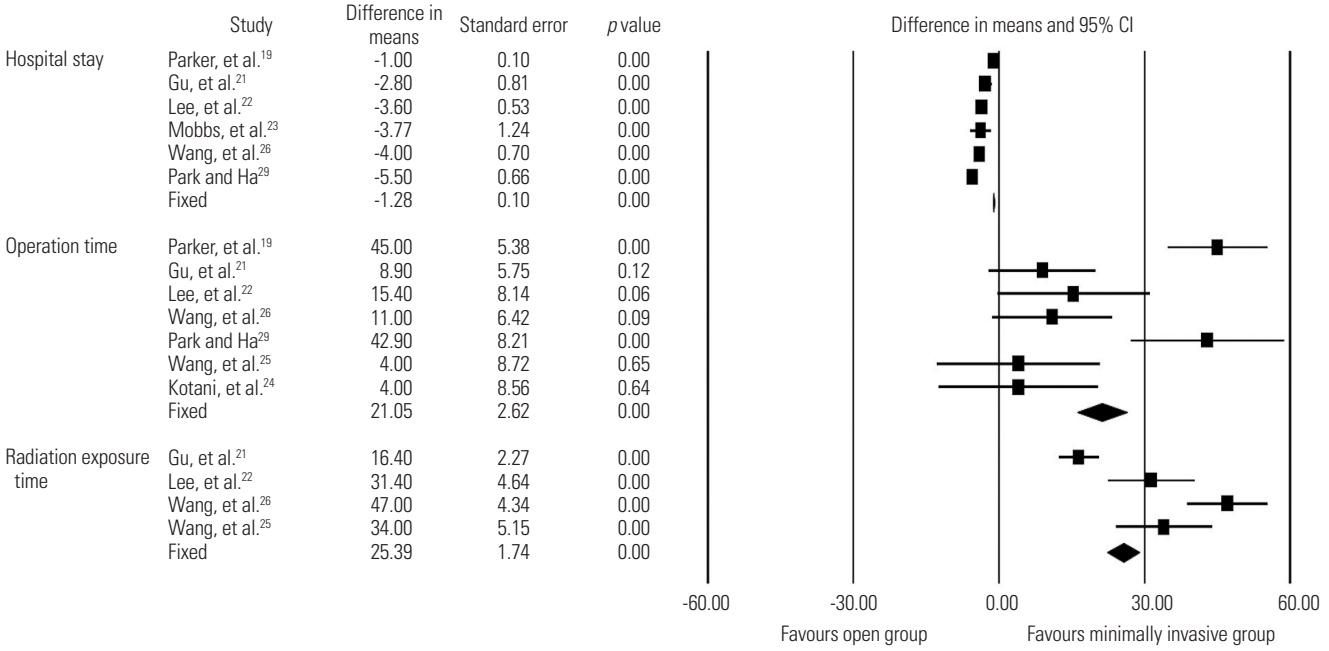

Fig. 8. Comparison of hospital stay, operation time, and radiation exposure time between minimally invasive and open lumbar spinal fusion. Heterogeneity: hospital stay [τ^2=0.236; χ^2=26.011, df=5 (p<0.0001); I^2=80.8%], operation time [τ^2=0.297; χ^2=40.069, df=6 (p<0.0001); I^2=85.0%], and radiation exposure time [τ^2=0.240; χ^2=14.309, df=3 (p=0.003); I^2=79.0%]. df, degrees of freedom; CI, confidence interval.

DISCUSSION

This meta-analysis highlights low-quality evidence that indicates minimally invasive lumbar spinal fusion for the treatment of adult spondylolisthesis and spondylosis is more effective than open fusion with regard to functional improvement and reduced infection rate in the intermediate term. The two fusion methods showed similar results in terms of pain relief, fusion rate, complications, and subsequent surgeries, although the evidence was low quality. In addition, we noted low-quality evidence indicating that minimally invasive fusion is associated with decreased blood loss and length of hospital stay, but was less advantageous in terms of operation time and radiation exposure time than open fusion.

Although screw- or cage-related nerve root injuries and secondary radiculopathies were reported, most studies indicated resolution of any neurological deficits and pain with subsequent surgery. These complications also showed an equivalent incidence with open fusion. There were no reports of visceral or vascular injury associated with percutaneous pedicle screw instrumentation. Significant reduction of paraspinal muscle injury via minimally invasive surgery and subsequent preservation of trunk muscle performance are thought to result in greater functional improvement, a lower risk of infection, and better perioperative surgical outcomes (less blood loss, quicker recovery, and shorter hospital stay).

To our knowledge, this study is the first systematic review evaluating the efficacy of minimally invasive lumbar spinal fusion exclusively employing percutaneous pedicle screw instrumentation. The strengths of our study include the exhaustive search strategy, reproducible protocols, and strict adherence to systematic review methodology. The use of standardized and validated data collection and extraction tools limited bias and increased inter-rater reliability.

The major limitations of the present study are the lack of RCTs and the small number of included articles. These weaknesses prevented synthesis of higher-quality evidence. In particular, there were very few studies comparing multi-level instrumented fusion in adult spondylosis patients. Overall, the quality of the evidence was "low" in our comparison of primary outcomes between minimally invasive fusion and open fusion. The magnitude of the effect sizes was small. All studies had attrition bias with no reported number of dropouts, and the mean follow-up duration was less than two years.

Another weakness was variation in the type of arthrodesis (e.g., TLIF, PLIF, or PLF) and bone graft material (e.g., local autogenous bone, autogenous iliac crest bone, or synthetic bone extensor). Variation in preoperative diagnosis (e.g., spondylolisthesis, other spondylosis, and mixed diagnoses) and fusion assessment methods was another drawback of this analysis. Computed tomography (CT) to evaluate screw placement was not routinely performed in all studies. The scarcity of CT imaging data may have led to underestimation of screw malposition, implant loosening, implant breakage, and pseudarthrosis in the reviewed studies.

On intermediate-term follow-up, our results showed low-quality evidence that percutaneous pedicle screw instrumented fusion is more effective at improving ODI score, reducing infection rate, and decreasing blood loss and hospital stay, but less effective at reducing operation and radiation expo-

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sure time than open fusion. Furthermore, the two methods were comparable with regard to pain relief, fusion rate, complications, and subsequent surgeries based on low-quality evidence. Several methodological flaws and weaknesses limited the reported results. In particular, there were no well-designed RCTs from which to synthesize high-quality evidence.

The ambiguity in these findings could lead to major alterations of the results derived from our analyses and highlights the need for adequately powered RCTs that will assess the long-term efficacy of minimally invasive lumbar spinal fusion. Future studies should compare subgroups based on fusion modality (e.g., TLIF, PLIF, PLF), spine disorder (e.g., spondylolisthesis, other spondylosis, deformity, trauma), and surgery level (e.g., single or multi-level fusion).

Although the findings are limited by insufficient evidence and lack of adequately powered high-quality RCTs to address this gap in evidence, our results support that minimally invasive lumbar spinal fusion is more effective than open fusion for adult spondylolisthesis and other spondylosis in terms of functional improvement, reducing infection rate, and decreasing blood loss and hospital stay.

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