Balancing Benefits and Risks of the Use of Cage in Lumbar Spondylolisthesis Surgery: A Meta-Analysis

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ABSTRACT

Lumbar spondylolisthesis is a prevalent spinal disorder for which the primary treatment approach involves surgical intervention, including reduction, decompression, internal fixation, and bone graft fusion. This systematic review evaluated and compared the clinical efficacy of posterior lumbar interbody fusion (PLIF)/transforaminal lumbar interbody fusion (TLIF) procedures using a cage, as opposed to posterolateral fusion (PLF) procedures without a cage, for the treatment of lumbar spondylolisthesis. The use of a cage has been shown to improve fusion rate and reduce functional disability. Patients who underwent inter-lumbar fusion with a cage experienced lower scores for postoperative lower back pain, with no significant difference in leg pain scores. Additionally, the use of a cage led to a decrease in postoperative complications, although there was no significant difference in operation time. The incorporation of a cage during lumbar spondylolisthesis surgery has been found to augment the efficacy of pedicle screw fixation through the simultaneous management of nerve decompression and pedicle screw fixation, resulting in significant enhancements in patient prognosis.

Key Words: *Spondylolisthesis, Pain, Fusion, Cage, Meta-analysis*.

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INTRODUCTION

Lumbar spondylolisthesis, a common spinal disease, used to describe the anterior, lateral, or posterior slippage of one vertebral body over another.[1] Degenerative lumbar spondylolisthesis is more common in middle-aged and elderly people, peaking in the population around 60 years of age, and accounts for about 5% of patients with lumbar and leg pain. The incidence varies by race and region. The disorder commonly affects L4-L5, or L5-S1, and the incidence in the L5 vertebra accounts for 82-90% of such cases.

Surgery options include reduction, decompression, internal fixation, and bone graft fusion. Various fusion modes and locations are reset fusion, *in situ* fusion, posterolateral fusion (PLF), and lumbar interbody fusion (LIF). LIF can be further divided into posterior lumbar interbody fusion (PLIF), trans-anterior lumbar intervertebral fusion (ALIF), and trans-foraminal lumbar intervertebral body fusion (TLIF).

Surgery without a cage includes PLF with pedicle screws, PLF without pedicle screws, and decompression alone. PLIF, TLIF, and PLF aimed at nerve decompression and using pedicle screw fixation are the most commonly used methods.

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These three mainstream surgical methods differ in surgical approach and interbody fusion device. Previous studies have not clearly defined the significance of cage.[2,3] The question of whether using a cage enhances the surgical efficacy of the pedicle screw system remains to be investigated. Consequently, a rigorous systematic evaluation and meta-analysis is needed to clarify the value of the cage. The aim of this study was to conduct a meta-analysis of published literature to compare the cage interbody-fusion with the pedicle screw system for lumbar spondylolisthesis.

METHODOLOGY

The research was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) and assessing the methodological quality of systematic reviews (AMSTAR) guidelines.[4] A systematic review of the literature was conducted by searching MEDLINE (PubMed), Cochrane, Embase, WanFang, and manual search of various journals of spinal disorder up to December 2023 for prospective studies comparing the functional and surgical outcomes of PLIF/TLIF using cage and PLF without cage for lumbar spondylolisthesis. The search terms used were spondylolysis or spondylolisthesis or spondyloschisis or vertebral sliding; fusion or Cage or PLIF or TLIF or PLF or spondylodesis; pain; (randomised controlled trial or controlled clinical trial or randomised or trial title/abstract). The analytical framework, including the research question, compared interventions, and desired outcomes, is presented in Figure 1. The research question was the necessity of cage usage in interbody fusion for lumbar spondylolisthesis. Eligibility criteria were defined by the PICO question, including types of participants, types of intervention, controls, and desired

outcomes. Participants were patients with lumbar spondylolisthesis, and intervention was cage interbody fusion *versus* pedicle screw system. The outcomes assessed were separated into primary outcomes and secondary outcomes. Primary outcomes were back pain intensity (visual analogue scale, VAS score), specific quality of life dedicated to the lumbar spine (Oswestry Disability Index, ODI), and fusion rate. Secondary outcomes were those relating to surgical trauma, including blood loss, operation time, and complication rate. Types of studies evaluated included clinical prospective and randomised studies and any type of comparative study evaluating the desired interventions. Inclusion criteria were clinical randomised controlled trials, original studies on the efficacy of the use of a cage related to pain having patients with lumbar spondylolisthesis >18 years, with data on clinical efficacy (pain). Exclusion criteria were non-clinical, absence of controls, retrospective studies, no outcome measures defined, less than three months follow-up, studies on cervical or thoracic vertebrae, studies restricted to unilateral pedicle screw, dynamic fusion cage or conservative treatment, conference papers, and literature reviews.

The authors imported all the literature retrieved from searches into Mendeley Desktop 1.19.8 and removed any duplicates. Two reviewers independently completed the title and abstract screening, followed by full-text screening. Any disagreement was settled through discussion. Data regarding study characteristics (including authors and study location), patient population (including age and gender), and primary and secondary outcomes were extracted into a pre-piloted Excel sheet. The meta-analysis was carried out using the RevMan version 5.4. The Cochrane Collaboration, Copenhagen, Denmark). The count data were analysed using the odds ratio (OR), while the measurement data with the same measurement unit were analysed using weighted mean difference (WMD), and the measurement data with different measurement units were analysed using standardised mean difference (SMD). The above effect sizes were expressed as 95% confidence intervals (95% CI). Statistical heterogeneity was analysed using Q-tests and I2 tests. When Q-tests showed p >0.10 and I^2 >50%, it was considered that there is a certain degree of heterogeneity. Analysing the sources of heterogeneity, and for heterogeneity originating from statistics, the authors used a random effects model analysis to exclude heterogeneity before conducting subgroup analysis. Finally, using the RevMan version 5.4 software to draw forest plots.

RESULTS

Nine studies, including 781 patients participating in randomised controlled trials, were included. Three hundred and sixty-six patients were treated with PLF with pedicle screw and 415 underwent interbody fusion with cage. Three studies performed TLIF and six studies performed PLIF. The mean patient age was 65.9 years, and the follow-up period was six months to three years in among all studies (Table I).[6-11,14]

Figure 2 shows the risk of bias in the randomised controlled trials in terms of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and others.

All nine studies reported differences between preoperative and postoperative pain intensity, including four with valid data, three with VAS score, and one with Japanese Orthopaedic Association (JOA) score.[5-8] JOA scores were converted into VAS scores (10 points) for analysis. Differences were not significant based on the standardised mean difference (SMD) and 95% CI (SMD = -0.25; 95% CI: -0.52 to 0.02; p = 0.07; Figure 3A), indicating that surgery with the use of a cage did not significantly improve the back pain of patients.[8] However, the data from the reference represented a conversion from the JOA score, which introduced some errors. Removing the data from the reference reduced the p-value to 0.04 (<0.05), making the difference significant. In conclusion, examination of postoperative lower back pain scores shows that the cage interbody fusion may be superior.

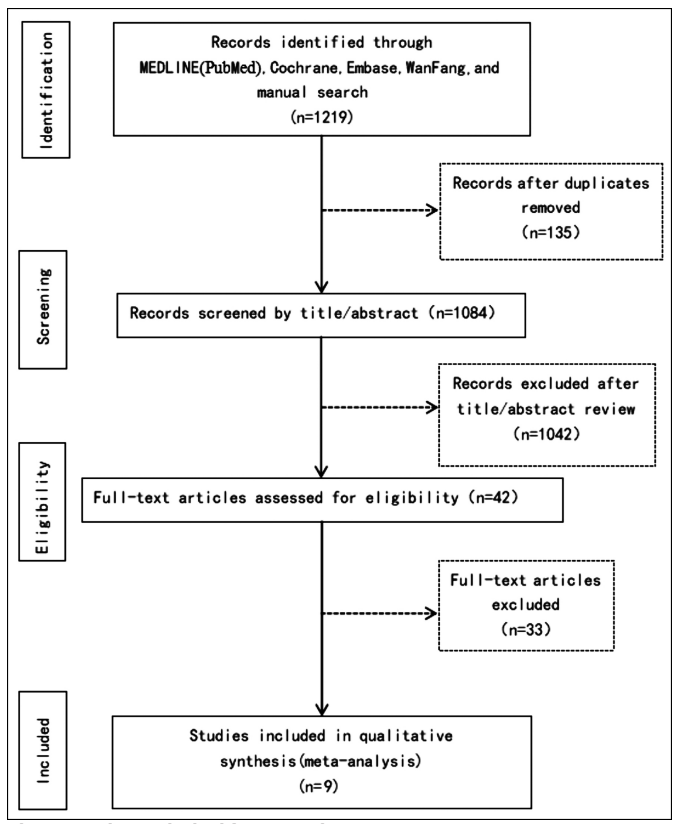

Figure 1: The analytical framework.

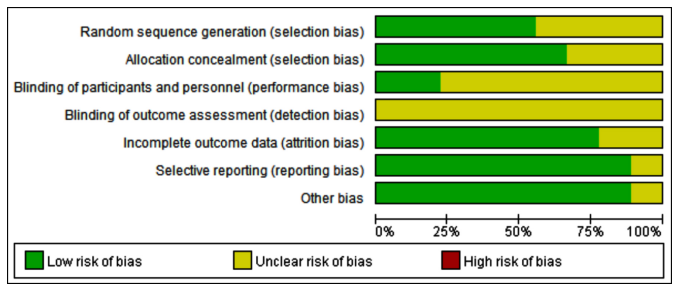

Figure 2: Risk of bias.

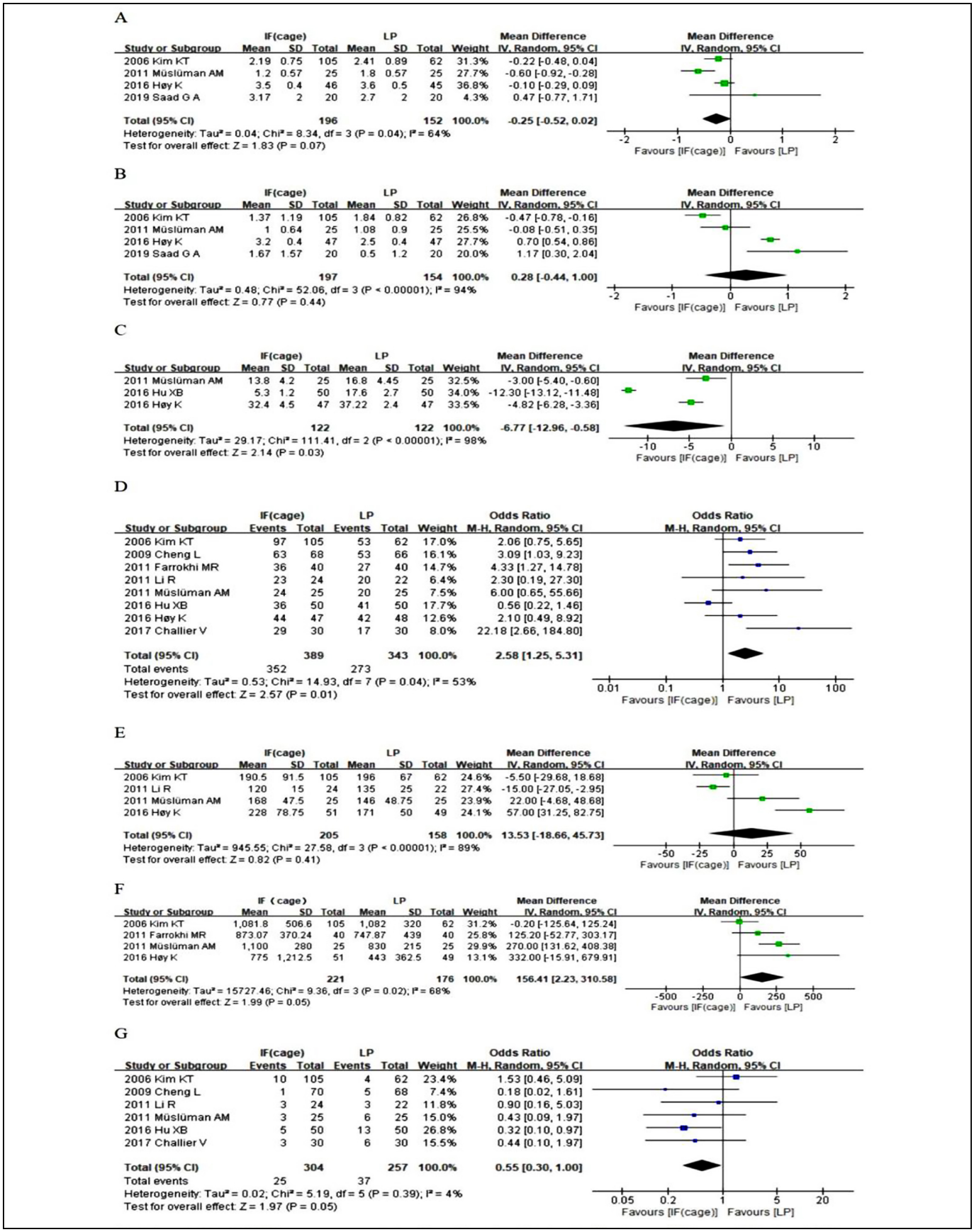

Figure 3: Forest plots.

Table I: Characteristics of studies included in the current meta-analysis.

Lead Authors	Years of Publication	Countries	Study Type	Types of Interventions		No. of Participants	Males	Females	Average Follow-up Time (years)	Mean age (years)	Outcome
				F1	F2						
Cheng L[3]	2009	China	RCT	PLF+PLIF	PLF	138	72	66	2	48.5	4,7
Challier V[7]	2017	France	MRCT	PLF+TLIF	PLF	60	18	42	2	64.5	4,6,7
Farrokhi MR[2]	2011	Iran	RCT	PLIF	PLF	80	19	61	2	50	4,6
Mlislurnan AM[9]	2011	Turkiye	RCT	PLIF	PLF	50	17	33	3.3	49	1,2,3,4,5,6,7
Kim KT[10]	2006	Korea	RCT	PLIF and PLF+PLIF	PLF	167	45	122	3	56	1,2,4,5,7
Hu XB[8]	2016	China	RCT	TLIF	PLF	100	54	46	0.5	54	3,4,7
Hoy K[6]	2016	Denmark	RCT	TLIF	PLF	100	41	59	2	58	1,2,3,4,5,6
Abdelkader GA[11]	2019	Egypt	RCT	PLIF	PLF	40	11	29	2	44	1,2
Li R[14]	2011	China	RCT	PLIF	PLF	46	17	29	1.5	37	4,5,7

1. Back pain (VAS), 2. Leg pain (VAS), 3. ODI, 4. Fusion rate, 5. Operatoin time. 6. Blood loss, 7. Complications.

No significant difference was found for leg pain scores, based on SMD and 95% CI (SMD = 0.28; 95% CI: -0.44 to 1.00; p = 0.44; Figure 3B). The ODI is a condition-specific outcome measure used in the management of spinal disorders.[9] A total score of 5 points is possible for each section and a total of 50 points for the full index. Higher scores indicated a worse condition.[10] Four studies evaluated the effect of surgery on the ODI, but one study was excluded due to incomplete data.[6,11,12] Significant changes from the baseline values were observed for all procedures (SMD = -6.77; 95% CI: -12.96 to -0.58; p = 0.03; Figure 3C). Consequently, regardless of using a cage, intervertebral fusion improved functional disability status. Eight studies reported differences in fusion rate between PLF and cage interbody fusion with the latter producing higher fusion rates than PLF with pedicle screw alone (OR = 2.58; 95% CI: 1.25 to 5.31; p = 0.01; Figure 3D). Using the cage enhanced the fusion efficiency of the pedicle screw fixation.[2,3,6,7,11,14] Four studies reported differences in operation time between PLF and cage interbody fusion.[6,9,12,14] Using the cage did not significantly affect operation time. (SMD = 13.53 95% CI: -18.66 to 45.73; p = 0.41; Figure 3E). Five studies reported differences in blood loss between PLF and cage interbody fusion patients. Four studies had valid data,[2,6,7,12] blood losses from using cage were significantly higher than fixation with pedicle screw only (SMD = 156.41 95% CI: 2.23 to 310.58; p = 0.05; Figure 3F). The main complications included pedicle screw fracture, deep incision infection, nerve paralysis, and pain at the bone grafting site. Six studies had data on surgical complication rates and showed that the use of a cage had a lower complication rate than fixation with pedicle screw only (OR = 0.55; 95% CI: 0.30 to 1.00; p = 0.05; Figure 3G).[3,7-11,14]

DISCUSSION

Lumbar spondylolisthesis is common and causes a huge clinical and economic burden on society, largely concerning elderly patients.[15] It results from degeneration and isthmic fissure, combined with lumbar intervertebral disc herniation and lumbar spinal stenosis. The pedicle screw treats lumbar spondylolisthesis by decompression on both sides which relieves nerve compression and retains the integrity of the posterior ligament complex. Thus, nerve tissue in the spinal canal is protected, maintaining the biomechanical function of the lumbar spine and reducing trauma. This is a successful surgical method which produces reliable reduction and long-term stability. The use of a cage in the surgery strengthened the surgical efficacy of pedicle screw fixation from an aspect of nerve decompression and pedicle screw fixation, significantly improving patient prognosis.

All nine studies analysed were prospective, but the sample size was small. The VAS pain score is determined by the patients' subjective feelings, as individual perceptions of pain is different. During the relief of postoperative radiation pain, preoperative nerve compression, intraoperative nerve pull, and postoperative nerve injury recovery are closely related, increasing the heterogeneity of the data. No significant difference was found in surgical duration, but study heterogeneity was relatively large (I^2 = 83%) due to methods of recording duration and adeptness of the surgeon. Surgical proficiency varies widely, and surgical conditions vary greatly from hospital to hospital and in different years. All of the above may be responsible for the heterogeneity in surgical duration, making it difficult to obtain statistically significant results. Cage augmentation has been shown to enhance the surgical effectiveness of pedicle screw fixation by addressing nerve decompression and pedicle screw fixation, leading to improved patient prognosis. However, it is important to note that this approach also results in increased surgical trauma. The present meta-analysis is constrained by the scarcity of relevant publications, highlighting the need for additional high-quality clinical randomised controlled trials to establish reliable conclusions and provide guidance for clinical practices in the surgical management of lumbar spondylolisthesis. The authors look forward to more extensive research for different lumbar spondylolisthesis patients to provide individualised advice, such as: Different ages, genders, different segments of the lesions, *etc*.

CONCLUSION

The present meta-analysis demonstrates that the utilisation of a cage in inter-lumbar fusion procedures enhances fusion rate and positively influences functional disability, *albeit* at the expense of increased blood loss. Patients who under-

went inter-lumbar fusion with a cage experienced a decrease in postoperative lower back pain scores, while no significant difference was observed in leg pain scores. Furthermore, the implementation of a cage resulted in a reduction in postoperative complication rate, while procedure duration remained unaffected.

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The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
YM: Contribution to the conception and design of the work.
FY, CX, XW: Acquisition, analysis, and interpretation of data.
YM, FY, YY: Drafting of the work and critical revision of the manuscript for important intellectual content.
FZ: Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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