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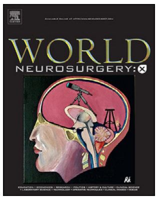

A meta-analysis of risk factors for cage migration after lumbar fusion surgery

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ABSTRACT

Objective: Cage migration is a rare complication after lumbar fusion surgery, and it is also the cause of lumbar revision surgery. Previous studies have reported that many influencing factors can increase the incidence of cage migration. However, there still remains controversial. The current study was conducted to investigate the risk factors influencing incidence of cage migration.

Methods: A systematic database search of PubMed, Embase, Web of Science, Cochrane Library and Clinical Trials was performed for relevant articles published until July 2022. According to the inclusion and exclusion criteria, two evaluators independently conducted literature screening, data extraction and quality evaluation of the obtained literature. The Newcastle–Ottawa Scale (NOS) score was used for quality evaluation, and meta-analysis was performed by STATA 16.0 software.

Results: A total of 2126 relevant articles were initially identified, and 7 articles were finally included in this study for data extraction and meta-analysis. The results of meta-analysis showed that the bony endplate injury, pear-shaped disc, and screw loosening are significantly correlated with cage migration. The OR values (95%CI) of the three factors were 7.170 (3.015, 17.051), 8.056 (4.050, 16.023), and 12.840 (3.570, 46.177) respectively.

Conclusion: Bony endplate injury, pear-shaped disc, and screw loosening are the current risk factors for cage migration postoperatively.

1. Introduction

Posterior lumbar interbody fusion (PLIF) and transforaminal lumbar interbody fusion (TLIF) have been widely used in the surgical treatment of lumbar degenerative diseases (LDDs).[1–4] The purpose of interbody fusion is to obtain the stability of the spine by fusing two adjacent vertebral bodies, restore the normal intervertebral height, and prevent spinal deformity.[5] The common complications of TLIF or PLIF include nerve root injury, screw extraction, adjacent segment disease, and the change of fusion cage position.[6,7] Among these complications, the cage displacement is relatively rare, and may lead to progressive spinal deformity, neurological deterioration, and non-fusion.[8] At present, some studies have reported the factors that affect the cage displacement after lumbar interbody fusion surgery, however, there still remains controversial. In order to provide reliable evidence for clinical work, we performed meta-analysis to study the risk factors of cage migration after PLIF or TLIF.

2. Materials and methods

2.1. Study selection and inclusion criteria

We conducted a systematic search of the scientific literature on cage migration after lumbar fusion surgery and performed a meta-analysis of the pooled data from the eligible studies. Case-control studies or cohort studies were searched from PUBMED, EMBASE, Web of Science, Cochrane Library and Clinical Trials independently by two authors. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[5] Fig. 1 showed the specific retrieval strategy for PubMed in the current study. Two assessors independently screened the literature by adopting uniform inclusion criteria. If there is any disagreement, it is resolved through discussion or with the assistance of a third researcher. The eligibility criteria were specified using the Population, Intervention, Criteria, Outcome and Study design (PICOS) framework. The selected literatures must meet the following conditions: 1) the subjects were patients with LDD who underwent PLIF or TLIF surgery; 2) The postoperative follow-up time was more than 24 months;

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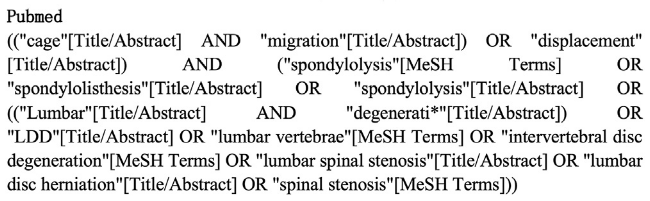

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(("cage"[Title/Abstract] AND "migration"[Title/Abstract]) OR "displacement"[Title/Abstract]) AND ("spondylolysis"[MeSH Terms] OR "spondylolisthesis"[Title/Abstract] OR "spondylolysis"[Title/Abstract] OR (("Lumbar"[Title/Abstract] AND "degenerati*"[Title/Abstract]) OR "LDD"[Title/Abstract] OR "lumbar vertebrae"[MeSH Terms] OR "intervertebral disc degeneration"[MeSH Terms] OR "lumbar spinal stenosis"[Title/Abstract] OR "lumbar disc herniation"[Title/Abstract] OR "spinal stenosis"[MeSH Terms]))

Fig. 1. The PubMed's retrieval strategy for risk factors influencing cage migration due to lumbar degenerative diseases postoperatively.

3) The original data should provide OR value and 95% confidence interval (95%CI) or the OR value and 95%CI can be calculated from the data; 4) cage migration should be clearly defined as the movement of the posterior margin of the cage beyond the posterior margin of either adjacent vertebral body[9,10]; 5) The summary results can be expressed by corresponding statistical indicators.

2.2. Exclusion criteria

Literatures meeting one of the following conditions were excluded: (1)animal studies; (2) meta-analysis and reviews; (3) duplicate studies; (4) case reports; (5) articles without available data; (6) unrelated studies.

2.3. Methodological quality evaluation

The Newcastle–Ottawa Scale (NOS) scoring system was used to evaluate the methodological quality of the included studies. The quantitative principle of the star system was adopted, and the full score was 9 stars.

2.4. Statistical analysis

Stata version 16.0 (Stata Corp LP, College Station, Texas) was used to synthesize, summarize, and evaluate the data. The collected data were tested for heterogeneity and the combined OR value and 95%CI were calculated. To determine heterogeneity across the studies, the I^2 Higgins (0–100%) was adopted. The fixed-effect model was used for meta-analysis when the heterogeneity statistic I^2 is less than 50%. In the meanwhile, the random-effect model was applied when the heterogeneity statistic I^2 is greater than or equal to 50%. Funnel plot was used to analyze potential publication bias when the number of articles included was more than 5. Sensitivity analysis was used to test the stability of meta-analysis results: (1) comparison of results between random effect model and fixed effect model; (2) When the number of included literatures is more than 5, the points with significant deviation from 95%CI in the funnel chart are excluded for meta-analysis, and the results are compared with those when all the literatures are included. The *p* value for statistical significance was set at <0.05.

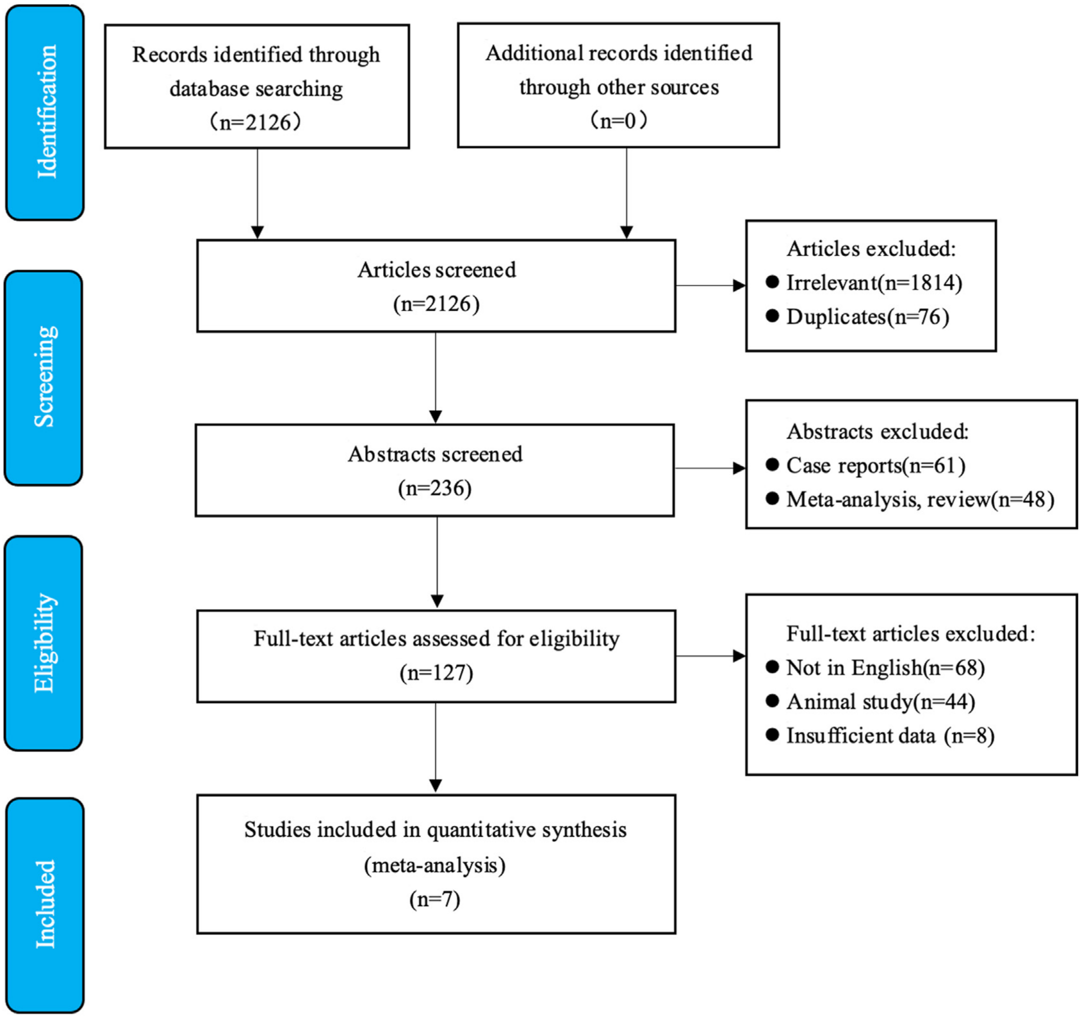


Fig. 2. Flow chart of the searched, identified and included studies for meta-analysis.

3. Results

3.1. *Study selection*

According to the search terms of the literature, a total of 2126 relevant articles were initially identified. Of those articles, 76 were duplicated in databases, and 1814 were not relevant to the objectives of this study. After screening the remaining articles using titles and abstracts, most of the studies were excluded because they were case reports (61) or meta-analysis and reviews (48). After reading the full text of the remaining 127 articles, a total of 120 were excluded due to the non-English writing (68), animal experiments (44) and insufficient data (8). Finally, 7 articles were included in this study for data extraction and meta-analysis (Fig. 2).

3.2. *Study characteristics*

The eligible studies included 6 retrospective studies and 1 case–control study.[9,11–16] The NOS scores of all articles were 7 (Table 1). A total of 5737 patients were included in the study, with an average age of 61.73 years, and 40.61% of them were male. The basic characteristics and NOS scores of the included studies are shown in Table 1.

3.3. *Meta-analysis*

According to the research contents of the included literature and the number of references for each factor, four risk factors including bony endplate injury, pear-shaped disc, posterior cage positioning (depth ratio) and screw loosening were selected for meta-analysis.

3.4. *Bony endplate injury*

A total of four studies have reported the relationship between bony endplate injury and cage migration.[13–16] Taking bony endplate injury as an independent factor, the results of meta-analysis using a random effect model showed that there was significant correlation between the cage migration and bony endplate injury after lumbar fusion surgery [combined OR values = 7.170, 95%CI (3.015, 17.051), $P < 0.01$, Fig. 3]. There was moderate heterogeneity among these studies ($I^2 = 59.2\%$, $P = 0.062$), therefore the random effect model was used to statistically analyze the data.

3.5. *Pear-shaped disc*

Three studies reported the relationship between pear-shaped disc and cage migration.[9,15,16] There was no heterogeneity among these studies ($I^2 = 0.0\%$, $P = 0.964$) and the fixed effect model was used to perform the meta-analysis. The statistical results demonstrated the significant correlation between the pear-shaped disc and cage migration after lumbar fusion surgery [combined OR values = 8.056, 95%CI (4.050, 16.023), $P < 0.01$, Fig. 4].

3.6. *Depth ratio*

Meta-analysis of the two included studies using random effect model showed that depth ratio had no significant effect on the cage migration after lumbar decompression surgery [OR = 0.058, 95%CI (0.000, 180.489), $P = 0.488$, Fig. 5].[11,16] In addition, strong heterogeneity occurred between the two studies ($I^2 = 99.5\%$, $P < 0.01$).

3.7. *Screw loosening*

Two studies have demonstrated that screw loosening could significantly increase incidence of cage migration.[9,14] Meta-analysis of the two studies using random effect model indicated that screw loosening is an independent influencing factor of cage migration [OR = 12.840, 95%CI (3.570, 46.177), $P < 0.01$, Fig. 6]. A random-effects model was used for statistical analysis of the data due to the moderate heterogeneity between the two studies ($I^2 = 67.8\%\%$, $P = 0.078$).

3.8. *Publication bias analysis*

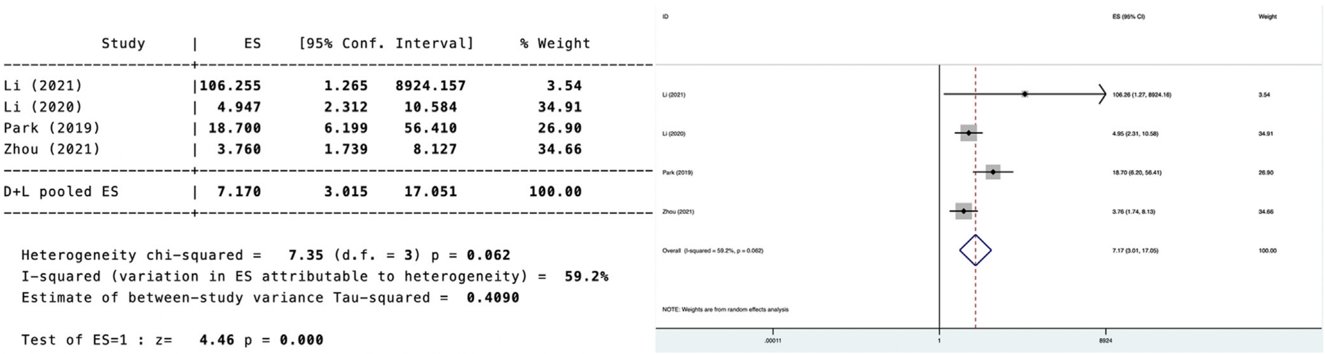
The scatter points in the funnel plots of bony endplate injury and pear-shaped disc were symmetrically distributed, suggesting that there was no publication bias. Using bony endplate injury and pear-shaped disc as indicators to detect publication bias, the Egger's and Begg's test results are as follows: 1) bony endplate injury (0.276, 0.734); 2) pear-shaped disc (0.161, 0.296). The above test results are all $P > 0.05$, indicating that there is little possibility of publication bias in the current meta-analysis.

Table 1

Characteristics and quality evaluation of the included studies.

Author, year	Study design	Date of data collection	Sample(N)	Mean age (years)	Male (N)	Definition of cage migration	Prognostic factors	Statistical method	NOS scores
Hu, 2019	retrospective study	2014–2015	953	62.65	314	migrated posteriorly >2 mm	1. Depth ratio 2. Height variance	Multivariate logistic regression	7
Lee, 2018	retrospective study	2006–2016	744	68.3	307	beyond the posterior margin	1. Low body mass index 2. Screw loosening 3. Pear-shaped disc	Multivariate logistic regression	7
Li, 2017	retrospective study	2011–2015	286	45.2	130	beyond the posterior margin	1. Surgeon's experience (less than 3 y) 2. Small cage size 3. Spondylolisthesis	Multivariate logistic regression	7
Li, 2021	retrospective study	2016–2020	335	65.2	122	migrated posteriorly>3 mm	1. Bony endplate injury 2. Greater preoperative range of motion	Multivariate logistic regression	7
Li, 2020	retrospective study	2015–2017	1662	68.7	692	beyond the posterior margin	1. Screw loosening 2. Endplate injury	Multivariate logistic regression	7
Park, 2019	prospective study	2011–2015	784	63.63	302	beyond the posterior margin	1. Osteoporosis 2. Pear-shaped disc 3. Endplate injury	Multivariate logistic regression	7
Zhou, 2021	retrospective study	2010–2016	973	58.4	463	beyond the posterior margin	1. Pear-shaped disc 2. Depth ratio 3. Endplate injury	Multivariate logistic regression	7

Abbreviations: NOS, The Newcastle–Ottawa Scale; PLIF, Posterior lumbar interbody fusion; TLIF, Transforaminal lumbar interbody fusion; LDDs, Lumbar degenerative diseases.



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           Study     |     ES    [95% Conf. Interval]     % Weight
---------------------+---------------------------------------------------
Li (2021)            |106.255      1.265   8924.157         3.54
Li (2020)            |  4.947      2.312     10.584        34.91
Park (2019)          | 18.700      6.199     56.410        26.90
Zhou (2021)          |  3.760      1.739      8.127        34.66
---------------------+---------------------------------------------------
D+L pooled ES        |  7.170      3.015     17.051       100.00
---------------------+---------------------------------------------------

  Heterogeneity chi-squared =   7.35 (d.f. = 3) p = 0.062
  I-squared (variation in ES attributable to heterogeneity) =  59.2%
  Estimate of between-study variance Tau-squared =  0.4090

  Test of ES=1 : z=   4.46 p = 0.000
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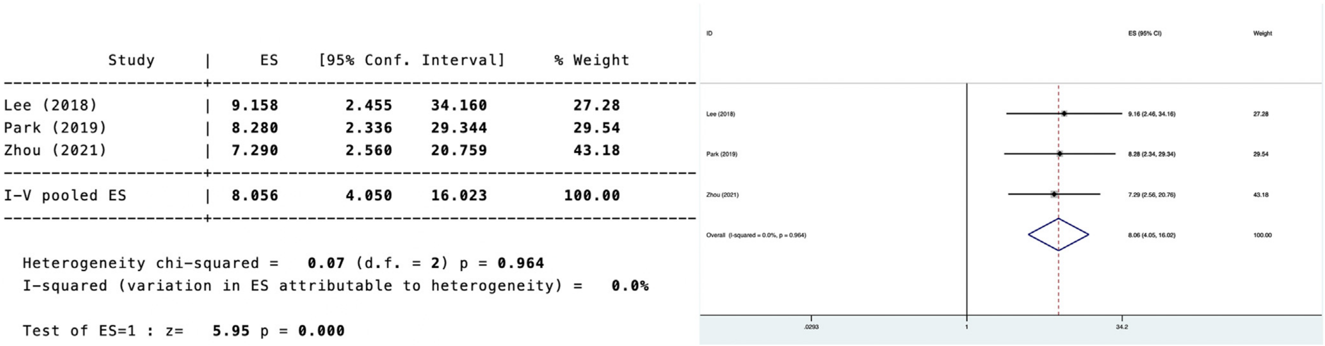
Fig. 3. Multivariate analysis of endplate injury in a forest map.



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           Study     |     ES    [95% Conf. Interval]     % Weight
---------------------+---------------------------------------------------
Lee (2018)           |  9.158      2.455     34.160        27.28
Park (2019)          |  8.280      2.336     29.344        29.54
Zhou (2021)          |  7.290      2.560     20.759        43.18
---------------------+---------------------------------------------------
I-V pooled ES        |  8.056      4.050     16.023       100.00
---------------------+---------------------------------------------------

  Heterogeneity chi-squared =   0.07 (d.f. = 2) p = 0.964
  I-squared (variation in ES attributable to heterogeneity) =   0.0%

  Test of ES=1 : z=   5.95 p = 0.000
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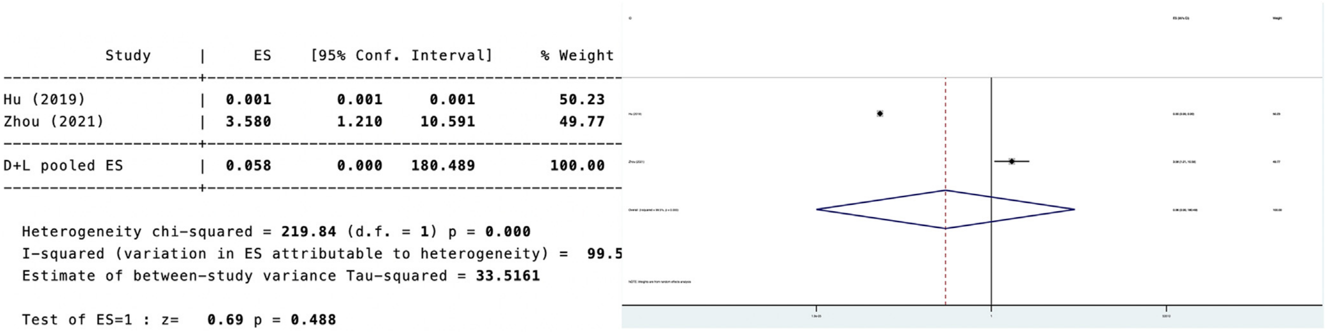
Fig. 4. Multivariate analysis of pear-shaped disc in a forest map.



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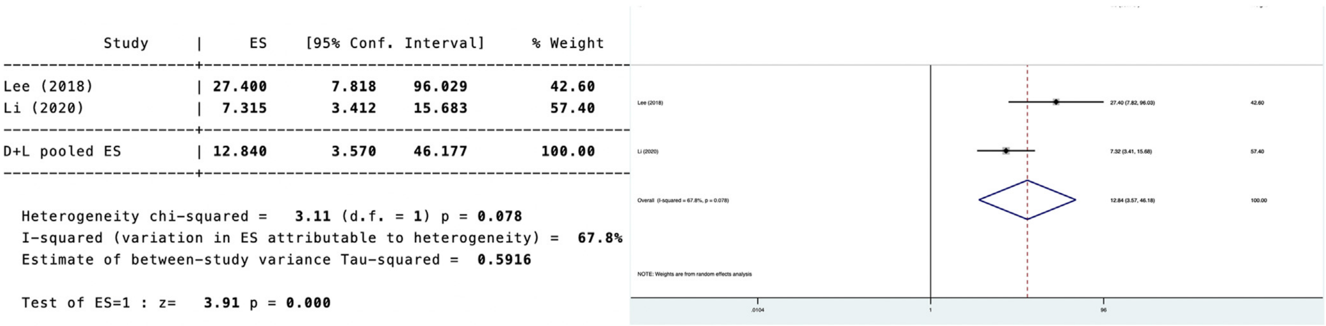
           Study     |     ES    [95% Conf. Interval]     % Weight
---------------------+---------------------------------------------------
Hu (2019)            |  0.001      0.001      0.001        50.23
Zhou (2021)          |  3.580      1.210     10.591        49.77
---------------------+---------------------------------------------------
D+L pooled ES        |  0.058      0.000    180.489       100.00
---------------------+---------------------------------------------------

  Heterogeneity chi-squared = 219.84 (d.f. = 1) p = 0.000
  I-squared (variation in ES attributable to heterogeneity) =  99.5
  Estimate of between-study variance Tau-squared = 33.5161

  Test of ES=1 : z=   0.69 p = 0.488
```

Fig. 5. Multivariate analysis of depth ratio in a forest map.



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           Study     |     ES    [95% Conf. Interval]     % Weight
---------------------+---------------------------------------------------
Lee (2018)           | 27.400      7.818     96.029        42.60
Li (2020)            |  7.315      3.412     15.683        57.40
---------------------+---------------------------------------------------
D+L pooled ES        | 12.840      3.570     46.177       100.00
---------------------+---------------------------------------------------

  Heterogeneity chi-squared =   3.11 (d.f. = 1) p = 0.078
  I-squared (variation in ES attributable to heterogeneity) =  67.8%
  Estimate of between-study variance Tau-squared =  0.5916

  Test of ES=1 : z=   3.91 p = 0.000
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Fig. 6. Multivariate analysis of screw loosening in a forest map.

4. Discussion

This study systematically collected the relevant studies on risk factors of cage migration after lumbar fusion surgery. A total of 7 literatures were included, which clearly specified the inclusion and exclusion criteria. The quality of all eligible literatures was evaluated using NOS (Newcastle–Ottawa scale) scores (all = 7 stars). The meta-analysis results showed that bony endplate injury and pear-shaped disc were closely related to cage migration after lumbar fusion surgery. In addition, the depth ratio is not an independent risk factor causing cage migration after surgery.

Previous studies have emphasized the importance of maintaining the integrity of the bony endplate to prevent the cage subsidence or migration.[8,17,18] Park et al[15] reported that if endplate injury occurs during interbody fusion surgery, the intervertebral space lacks sufficient strength to support the stability of the cage. The presence of cortical or cancellous bone fragments in the contents of the endplate during curettage indicates possible injury to the endplate. Currently, the best choice is to transfer to the opposite side for cage insertion, rather than continue on the same side. The influence of endplate injury on cage migration can be explained as follows. First, endplate injury reduces the contact area and associated friction between the cage and the endplate.[19] Second, it may lead to improper cage placement, thus reducing the axial pressure distributed on the cage and creating less friction to resist posterior cage migration.[11] Third, injury to the cranial endplate on the posterior region provides a broad pathway for cage migration after surgery.[16]

Several studies have shown that pear-shaped discs may be an independent influencing factor of cage migration.[9,15,16] Meta-analysis showed that patients with pear-shaped discs had higher incidence of cage migration after lumbar fusion surgery. Because the pear-shaped disc does not tend to contact all four corners of the cage at the sagittal level, instability between the endplate and the cage may occur.[9] Therefore, when surgeons prepare endplates in patients with pear-shaped discs, careful endplate decortications are required to avoid cage migration. In addition, adequate cage size and axial compression are required to achieve firm interbody fusion.

Depth ration has been reported to reflect the relative position of cage in the intervertebral space without being affected by the length and width of the endplate.[11] Lower depth ratio indicates that cage is more forward in the intervertebral space, so it is possible to bear more pressure as gravity transmits and generates greater friction to resist posterior migration.[11] Hu et al[15] and Zhou et al[16] have reported that cases with lower depth ration had significantly higher incidence of cage migration. Therefore, they advocated that the cage should be placed as anteriorly as possible in the disc space to reduce the incidence of cage migration. However, several biomechanical studies have shown that the posterolateral endplate exhibits the most biomechanical strength, which can effectively reduce the incidence of cage subsidence.[20,21] Therefore, there is no unified standard on the ideal placement of cage during lumbar interbody fusion. The current meta-analysis did not demonstrate a significant correlation between depth ratio and cage migration. We consider that this is related to the strong heterogeneity of the two studies. Differences in measurement methods, errors, and cage shapes between studies may cause strong heterogeneity. Therefore, more studies are required to further confirm the influence of cage position on postoperative cage migration in the future.

Studies have shown the importance of additional posterior instrumentation to prevent cage migration. Applying posterior instrumentation and significantly increasing axial compression stiffness can reduce posterior bending forces, especially flexion and extension torques.[22,23] Lee et al[9] and Li et al[14] have shown that segmental instability due to early screw failure can lead to cage migration. The results of meta-analysis showed that screw loosening was an independent factor influencing cage migration. Therefore, strong posterior internal fixation is essential to prevent cage migration, which can lead to mechanical spinal failure.

The meta-analysis conducted by Liu et al[5] indicated that the pear-shaped disc and straight cage are significant risk factors for cage migration. However, there are two main problems in this study: 1) only a few of risk factors that may affect cage migration are included; 2) some literatures do not meet the inclusion criteria of the study. Therefore, the conclusions of the study have certain limitations in clinical application. The limitation of the current meta-analysis is that some potential risk factors such as height variance, osteoporosis, and BMI, etc were not analyzed due to lack of raw data.

5. Conclusion

The current meta-analysis demonstrated that bony endplate injury, pear-shaped disc, and screw loosening are significantly correlated with cage migration. However, there is not enough research evidence to support lower depth ratio as a risk factor for cage migration. Although the number of included studies was limited, this study can still provide an important reference for the prevention of cage migration after lumbar interbody fusion. In the meanwhile, more studies are required to investigate risk factors for cage migration in the future.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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