# Associations of recurrent lumbar disc herniation after percutaneous endoscopic lumbar discectomy with age, body mass index, modic change, disc degeneration and sacral slope: A quantitative review

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**Abstract.** Recurrent lumbar disc herniation (rLDH) seriously affects the quality of life of patients and increases the medical burden. The purpose of the present study was to determine the risk factors for rLDH after percutaneous endoscopic lumbar discectomy (PELD). The PubMed, Cochrane Library and Embase databases were searched for studies on the factors associated with rLDH after PELD. The databases were searched from inception to March 30, 2023. The combined effects of categorical variables and continuous variables were measured using odds ratios (ORs) and weighted mean differences (WMDs), respectively, and their corresponding 95% confidence intervals (CIs) were calculated. RevMan 5.3 software was used for data analysis. A total of 9 case-control studies were included in this meta-analysis, comprising 5,446 patients. This study explored a total of 18 potential risk factors for rLDH after PELD; ultimately, 5 factors were associated with the risk of rLDH. Meta-analysis showed that older age (WMD=6.49, 95% CI: 2.52 to 10.46), greater body mass index (WMD=1.16, 95% CI: 0.69 to 1.62), modic change (OR=2.48, 95% CI: 1.54 to 3.99), Pfirrmann grade ≥4 (OR=2.84, 95% CI: 1.3 to 6.16) and greater sacral slope angle (WMD=3.48, 95% CI: 0.53 to 6.42) were risk factors for rLDH after PELD. The risk factors identified in the present study may enable clinicians to identify high-risk populations early and to select appropriate surgical procedures to reduce the risk of rLDH. Perioperative interventions targeting the modifiable factors identified in this study may be beneficial for reducing the risk of rLDH.

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*Abbreviations:* BMI, body mass index; CI, confidence interval; DHI, disc height index; DM, diabetes mellitus; IV, inverse variance; M-H, Mantel-Haenszel test; NOS, Newcastle-Ottawa scale; NR, not reported; OR, odds ratio; PELD, percutaneous endoscopic lumbar discectomy; rLDH, recurrent lumbar disc herniation; sROM, sagittal range of motion

*Key words:* risk factors, recurrent lumbar disc herniation, percutaneous endoscopic lumbar discectomy, meta-analysis

## Introduction

Lumbar disc herniation (LDH) refers to a series of syndromes characterized by low back pain and lower limb radiation pain induced by the stimulation or compression of nerves due to degeneration or injury of the lumbar intervertebral disc, leading to rupture of the fibrous ring and protrusion of the nucleus pulposus (1,2). LDH mainly occurs at L4-5 and L5-S1 and is mainly observed in middle-aged and elderly individuals, with a male predominance (3). LDH can limit mobility and the ability to perform physical activities, and cause disability (4), thereby reducing the quality of life of patients and increasing medical costs. Although conservative treatment is the first choice for treating LDH, surgery is necessary for severe LDH to achieve good clinical outcomes (5,6).

With the continuous development of minimally invasive spinal technology, percutaneous endoscopic lumbar discectomy (PELD) is the main method of surgical treatment for LDH (7). PELD has numerous advantages, such as minimal trauma,

less bleeding, a clear surgical field, relatively low surgical costs and high patient satisfaction (8). In addition, PELD can be performed under local anaesthesia, which may lead to the acquisition of knowledge regarding a patient's neurological and vascular injuries during surgery (9). Whether from a medical or patient perspective, the use of PELD to treat LDH has numerous technical advantages. However, the widespread application of endoscopic technology has led to post-PELD complications, including recurrent LDH (rLDH), receiving increased attention (10). According to the literature, 2-25% of patients who undergo PELD experience rLDH after surgery (10-12). Surgical intervention is necessary for patients with rLDH who have been clearly diagnosed and have not yet achieved remission after conservative treatment. However, scar tissue after the initial surgery increases the difficulty of repeated discectomy and increases the risk of dural tears or nerve damage (13,14). In addition, removing the posterior structure during reoperation may increase the risk of lumbar segmental instability (15,16). There is no doubt that both reoperation and the clinical symptoms associated with rLDH have a significant negative impact on the psychological burden and economic pressure of patients.

PELD is a common surgical method for the treatment of LDH, and rLDH is a possible serious complication. In this context, identifying the risk factors for rLDH after PELD has important clinical value for formulating appropriate surgical protocols and evaluating postoperative efficacy. However, there is a lack of high-level evidence regarding the risk factors for rLDH after PELD. To fill this gap, a meta-analysis was performed to evaluate and identify the risk factors for rLDH after PELD. The conclusions of this study are intended to provide a theoretical basis for the clinical prevention and reduction of postoperative rLDH after PELD.

## Materials and methods

*Data sources and retrieval strategies*. The design and implementation of the present study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (17). Three databases, including PubMed (www.pubmed.ncbi.nlm.nih.gov), Cochrane Library (www.cochranelibrary.com) and Embase (www.embase.com), were searched to identify studies that examined risk factors for rLDH after PELD. The databases were searched from inception to March 30th, 2023. Furthermore, the reference lists of the included studies were manually searched to obtain additional eligible studies. The search strategy included a combination of MeSH terms and free words. The key words included 'recurrent lumbar disc herniation', 'rLDH', 'reoperation', 'repeat discectomy', 'PELD', 'percutaneous endoscopic lumbar discectomy', 'percutaneous transforaminal endoscopic discectomy', and 'Yeung endoscopic spine system'. The details of the search strategies for each database are provided in Appendix S1.

*Inclusion and exclusion criteria*. The inclusion criteria were as follows: i) Study participants of any age, sex, ethnicity or region, including patients in need to be diagnosed with LDH and treated with PLED; ii) the research topic was risk factors for rLDH and complete data on grouping comparison of rLDH and non-rLDH were available in the literature; iii) due to the fact that the present study is a secondary literature analysis, the study type was limited to cohort and case-control studies based on the existing literature. Ostensibly, rLDH typically occurs after surgery. Due to ethical considerations and implementation difficulties, randomized controlled trials may not be the most appropriate method for studying risk factors, and thus, the present quantitative review only included cohort studies and case-control studies; iv) the included literature was required to contain reports of at least one risk factor; v) the outcome measurement data were required to be expressed as the frequency (%) or mean ± standard deviation in order to help reduce statistical heterogeneity. There were no restrictions regarding the language of the publications.

The exclusion criteria were as follows: i) Duplicate literature, case reports and animal experiments; ii) obvious statistical errors in the literature; iii) repeated publications of the same study population; and iv) the full text cannot be obtained.

*Data extraction*. Two researchers (GL, BS) independently extracted data from the included literature and cross-checked them. Disagreements were resolved through discussion or consultation with the corresponding author. The process of literature selection included selecting the literature that met the research purpose by reading the titles and abstracts, then reading the full texts of the literature according to the inclusion and exclusion criteria, and finally selecting the literature that met the research purpose. The following data were extracted: First author, publication time, research design type, sample size, follow-up time and risk factors.

*Literature quality evaluation*. The quality of the included studies was evaluated by two researchers using the Newcastle-Ottawa scale (NOS) (18). The NOS consists of three components, including study subject selection (4 points), intergroup comparability (2 points) and outcome or exposure factor evaluation (3 points), with a total score of 9 points. Scores of 0 to 3, 4 to 6 and 7 to 9 were considered to indicate low-, moderate- and high-quality research, respectively.

*Data analysis*. RevMan 5.3 software (The Cochrane Collaboration) was used for data analysis. For categorical and continuous variables, odds ratios (ORs) and weighted mean differences (WMDs) were used as effect size measures, respectively, and point estimates and 95% confidence intervals (CIs) for each effect size measure were calculated. The random-effects model was used for all meta-analyses. The test level for meta-analysis was set to $\alpha$=0.05. Sensitivity analysis was performed by comparing the result consistency between the fixedeffects and randomeffects models and eliminating studies with greater impact. And the method exclusion of one study at a time and re-performing the meta-analysis was also performed. A funnel plot was constructed to assess whether there was evidence of publication bias. In addition, each outcome was required to be examined by at least 3 studies to be considered for pooled data analysis.

## Results

*Literature search results*. Based on the search strategy of the present study, a total of 391 relevant documents were retrieved. After removing duplicate publications and reading the titles

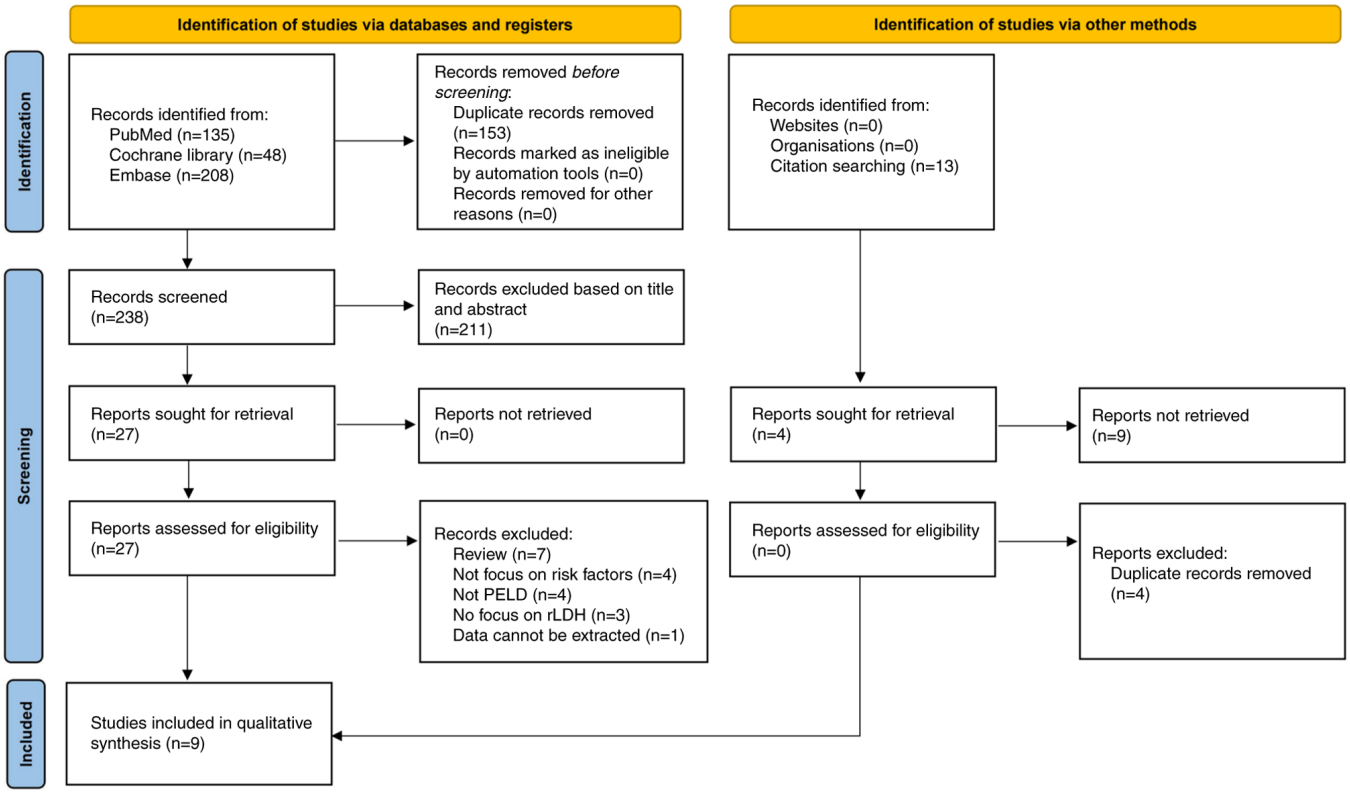


Figure 1. Flow diagram of systematic literature search. PELD, percutaneous endoscopic lumbar discectomy; rLDH, recurrent lumbar disc herniation.

and abstracts of the studies, 27 articles remained for full-text screening. Referring to the inclusion criteria of the present study and after reading the full texts, 9 case-control studies were ultimately included in the present meta-analysis (19-27). The specific details of the study selection process are presented in Fig. 1.

*Basic characteristics of the included studies*. A total of 9 case-control studies were included in the present study and they were published between 2020 and 2023, indicating that research on rLDH after PELD has received extensive attention from researchers in recent years. A total of 5,446 patients who underwent PELD were included in this meta-analysis, with 560 rLDH patients (343 males and 217 females) and 4,886 non-rLDH patients (2,811 males and 2,075 females). The weighted mean age was 50.75 in the rLDH group and 44.53 in the non-rLDH group. The follow-up period ranged from 6-48 months. The operative segments of LDH were mainly L4/5 and L5/S1. The basic characteristics of the nine included studies are presented in Table I.

*Results of the literature quality evaluation*. The NOS scores of the nine included studies (19-27) are shown in Table II. The NOS scores ranged from 7-8, which indicates that the methodological quality of all studies included in the present study is high.

*Meta-analysis*

*Sociodemographic and anthropometry factors*. A total of 9 related factors were analysed (Table III) and the corresponding forest maps of sociodemographic and anthropometry factors are shown in Figs. S1-S9. The meta-analysis found that age and body mass index (BMI) are both significant risk factors for rLDH. Sex, symptom duration, smoking, drinking, DM and hypertension were not risk factors for rLDH (all P>0.05). A total of 8 studies (19,21-27) reported an association between age and rLDH, and there was heterogeneity among the studies ($I^2$=93%). The random-effects model was used to perform meta-analysis and the results showed that higher patient age was associated with a greater risk of rLDH after PELD (WMD=6.49, 95% CI: 2.52 to 10.46, P=0.001).

A total of 8 studies (19,21-27) reported the association between BMI and rLDH. There was heterogeneity among the eight studies, and thus, a random-effects model was used for meta-analysis. It was found that a higher BMI significantly increased the risk of rLDH (WMD=1.16, 95% CI: 0.69 to 1.62, P<0.001).

*Clinical and imaging factors*. Similarly, this study also analysed the association of 9 clinical and imaging factors with rLDH (Table III) the corresponding forest maps are provided in Figs. S10-S18. A total of 7 studies (19,20,22-25,27) reported the effect of modic change on rLDH, and there was heterogeneity among these studies ($I^2$=73%). The meta-analysis results showed that there was an association between modic change and the risk of rLDH after PELD (OR=2.48, 95% CI: 1.54 to 3.99, P=0.0002).

A total of 3 studies (19,25,27) reported the association of the Pfirrmann grade with rLDH. The meta-analysis results showed that a Pfirrmann grade ≥4 was a risk factor for rLDH after PELD (OR=2.84, 95% CI: 1.30 to 6.16) and this association was statistically significant (P=0.008).

Table I. Characteristics of the included studies.

| First author, year | Design | Sample size (M/F), n | | Mean age,years | | Level of herniated disk, n (L2/L3,L3/L4,L4/5,L5/S1) | | Type of herniation, n (central/paracentral/ lateral or extreme lateral) | | Follow-up (months) | (Refs.) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | RLDH | Non-RLDH | RLDH | Non-RLDH | RLDH | Non-RLDH | RLDH | Non-RLDH | | |
| He *et al*, 2023 | Case-control study | 63 (45/18) | 627 (410/217) | 51.49 | 42.87 | 0/0/37/26 | 0/0/370/257 | NR | NR | 24 | (19) |
| Jia *et al*, 2021 | Case-control study | 32 (18/14) | 320 (212/108) | NR | NR | 0/2/18/12 | 0/12/165/143 | 1/31/0 | 3/177/140 | 6 | (20) |
| Kong *et al*, 2020 | Case-control study | 46 (22/24) | 608 (333/275) | 54.4 | 44.9 | NR | NR | 31/13/20 | 165/212/231 | 28 | (21) |
| Li *et al*, 2023 | Case-control study | 56 (30/26) | 589 (296/293) | 51.82 | 48.32 | 4/6/29/17 | 6/22/412/149 | 4/26/11 | 50/360/179 | 24 | (22) |
| Ren *et al*, 2023 | Case-control study | 130 (80/50) | 1059 (640/419) | 46.62 | 44.2 | NR | NR | NR | NR | 38 | (23) |
| Shi *et al*, 2021 | Case-control study | 68 (47/21) | 136 (94/42) | 46.21 | 47.36 | 0/0/41/27 | 0/0/82/54 | NR | NR | 24 | (24) |
| Wang *et al*, 2022 | Case-control study | 57 (39/18) | 885 (462/423) | 56.7 | 41.2 | 0/0/30/27 | 3/18/405/459 | 6/42/9 | 69/732/84 | 24 | (25) |
| Yu *et al*, 2020 | Case-control study | 46 (25/21) | 438 (229/209) | 52.98 | 47.74 | NR | NR | 13/27/6 | 100/237/101 | 12 to 48 | (26) |
| Zhao *et al*, 2021 | Case-control study | 62 (37/25) | 224 (135/89) | 52.1 | 44.9 | NR | NR | NR | NR | 24 | (27) |

rLDH, recurrent lumbar disc herniation; M, male; F, female; NR, not reported.

Table II. Newcastle-Ottawa scale for risk of bias assessment of studies included in the meta-analysis.

| First author, year | Selection | | | Outcome not present at start | Comparability | Outcome | | | Overall | (Refs.) |
|---|---|---|---|---|---|---|---|---|---|---|
| | Representativeness of exposed cohort | Selection of nonexposed | Ascertainment of exposure | | | Assessment of outcome | Adequate follow-up length | Adequacy of follow-up | | |
| He *et al*, 2023 | - | * | * | * | ** | * | * | * | 8 | (19) |
| Jia *et al*, 2021 | - | * | * | * | ** | * | * | - | 7 | (20) |
| Kong *et al*, 2020 | - | * | * | * | ** | - | * | * | 7 | (21) |
| Li *et al*, 2023 | - | * | * | * | ** | * | * | * | 8 | (22) |
| Ren *et al*, 2023 | - | * | * | * | ** | - | * | * | 7 | (23) |
| Shi *et al*, 2021 | - | * | * | * | ** | * | * | * | 7 | (24) |
| Wang *et al*, 2022 | - | * | * | * | ** | * | * | * | 8 | (25) |
| Yu *et al*, 2020 | - | * | * | * | ** | * | * | * | 8 | (26) |
| Zhao *et al*, 2021 | - | * | * | * | ** | - | * | * | 7 | (27) |

*, score of 1; **, score of 2; -, score of 0.

Table III. Meta-analysis of the risk factors.

A, Sociodemographic and anthropometry factors

| Factor | Studies, n | OR or WMD | 95% CI | P-value | $I^2$,% | Analysis model |
|---|---|---|---|---|---|---|
| Age, years | 8 | 6.49 | 2.52-10.46 | 0.001 | 93 | IV, random |
| Male sex | 9 | 1.08 | 0.90-1.30 | 0.410 | 2 | M-H, random |
| Female sex | 9 | 0.92 | 0.77-1.11 | 0.410 | 2 | M-H, random |
| BMI, kg/m$^2$ | 8 | 1.16 | 0.69-1.62 | <0.001 | 69 | IV, random |
| Symptom duration, months | 4 | 1.71 | -0.18-3.59 | 0.080 | 97 | IV, random |
| Smoking (yes vs. no) | 8 | 1.43 | 0.95-2.14 | 0.090 | 69 | M-H, random |
| Drinking (yes vs. no) | 5 | 1.13 | 0.83-1.53 | 0.450 | 0 | M-H, random |
| DM (yes vs. no) | 7 | 1.22 | 0.85-1.74 | 0.280 | 5 | M-H, random |
| Hypertension (yes vs. no) | 4 | 1.00 | 0.69-1.47 | 0.990 | 1 | M-H, random |

B, Clinical and imaging factors

| Factor | Studies, n | OR or WMD | 95% CI | P-value | $I^2$,% | Analysis model |
|---|---|---|---|---|---|---|
| Operation time, min | 3 | -0.19 | -5.54-5.15 | 0.940 | 59 | IV, random |
| Modic change (yes vs. no) | 7 | 2.48 | 1.54-3.99 | <0.001 | 73 | M-H, random |
| Pfirrmann grade ≥4 | 3 | 2.84 | 1.30-6.16 | 0.008 | 81 | M-H, random |
| DHI | 5 | -0.01 | -0.04-0.02 | 0.640 | 92 | IV, random |
| sROM, ° | 5 | 1.50 | -0.59-3.58 | 0.160 | 96 | IV, random |
| Facet orientation, ° | 3 | -1.82 | -3.72-0.07 | 0.060 | 76 | IV, random |
| Facet tropism, ° | 3 | -0.36 | -0.80-0.08 | 0.110 | 10 | IV, random |
| Lumbar lordosis angle, ° | 4 | -1.18 | -6.43-4.07 | 0.660 | 95 | IV, random |
| Sacral slope angle, ° | 3 | 3.48 | 0.53-6.42 | 0.020 | 86 | IV, random |

The forest maps of all risk factors are shown in Figs. S1-S18. BMI, body mass index; DM, diabetes mellitus; DHI, disc height index; sROM, sagittal range of motion; OR, odds ratio; WMD, weighted mean difference; M-H, Mantel Haenszel test; IV, inverse variance; random, random-effects model.

A total of 3 studies (23,26,27) reported the association between sacral slope angle and rLDH, and there was heterogeneity among these three studies ($I^2$=86%). Meta-analysis showed that a larger sacral slope angle was a risk factor for rLDH after PELD (WMD=3.48, 95% CI: 0.53 to 6.42), with a statistically significant difference (P=0.02).

*Publication bias*. Four funnel plots (age, male, female, BMI) were constructed to evaluate publication bias (Fig. 2). The scattered points in the funnel diagram are basically symmetrical, suggesting that there is no evidence of publication bias in the evaluation of age, male, female and BMI.

## Discussion

Due to population ageing and changes in modern lifestyles, the occurrence of LDH exhibits a trend of growth (28). Epidemiological studies have shown that the overall incidence rate of LDH ranges from 2-3%, but the incidence rates among men and women aged >35 years are 4.8 and 2.5%, respectively (28). PELD is often used to treat LDH that is not effectively managed by conservative treatment (6). Identifying the risk factors for rLDH after PELD surgery and formulating the best treatment strategy or informing patients of the risks before surgery is an important task. In the past 20 years, there have been 2 systematic reviews evaluating the risk factors for rLDH (29,30), but these two studies have certain limitations that may prevent us from applying their conclusions to the identification of rLDH after PELD. The two systematic evaluations (29,30) comprised patients who underwent surgery, including microdiscectomy, laminotomy, PELD, decompression, lumbar fusion and open discectomy, indicating significant clinical heterogeneity among the included studies. In addition, both systematic evaluations are concerned with a small number of potential risk factors, providing less evidence for clinical application. Since PELD is the most commonly used surgical method, only the risk factors for rLDH after PELD were examined; the present results may allow clinicians to evaluate risk of rLDH following PELD. In addition, there were 18 potential risk factors observed in the present meta-analysis, but only 5 factors were significant, which provide more comprehensive information. The present study found that higher age, greater BMI, modic change, Pfirrmann grade ≥4 and greater sacral slope angle are all significant risk

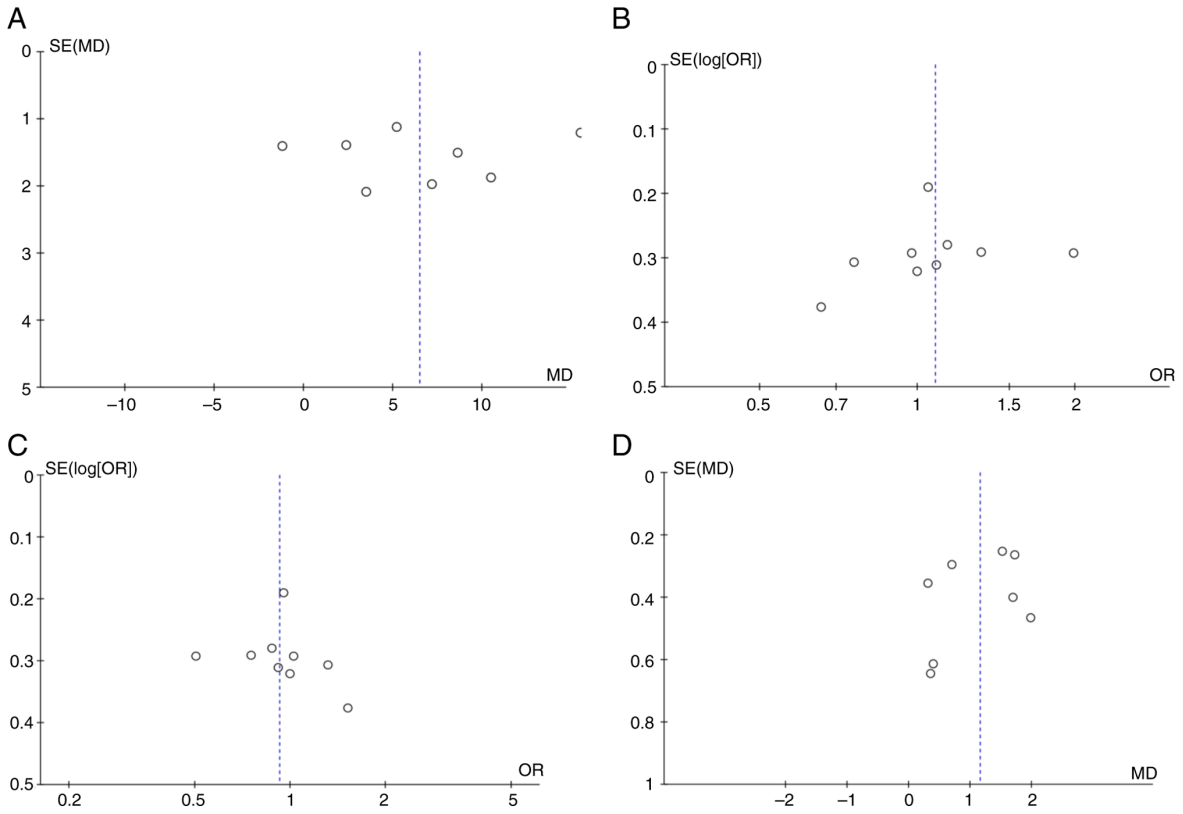


Figure 2. Funnel plots of (A) age, (B) male, (C) female, and (D) BMI. BMI, body mass index.

factors for rLDH after PELD. Therefore, PELD may not be the best option at the stage of developing medical strategies for patients with one or more of the above risk factors. The findings of the present study will help spine surgeons develop appropriate surgical protocols and better inform patients of surgical risks.

Regarding sociodemographic and anthropometry factors, consistent with previously published research findings (31-33), the present study also found a significant association between higher age and the occurrence of rLDH. A retrospective cohort study showed that the reoperation rate of patients aged ≥57 years who underwent PELD was higher than that of patients aged <57 years (34), and this study found that rLDH after PELD was the main reason for reoperation. As ageing progresses, the degradation of spinal tissue becomes increasingly severe. Ehrendorfer *et al* (35) found that the severity of preoperative disc degeneration in patients with rLDH is significantly higher than that in non-rLDH patients. A study indicated that obese patients are more prone to LDH (36) and are prone to adverse clinical outcomes after surgery. A Cox regression analysis showed that a BMI ≥25 kg/m$^2$ is an important risk factor for rLDH after PELD (37). The study by Yaman *et al* (38) indicated that the reoperation rate of overweight or obese patients after PELD is significantly higher than that of patients with LDH with a normal BMI, which may be related to increased load on the intervertebral disc. Therefore, it may be indicated that both older age and a greater BMI are highly associated with the risk of rLDH.

Clinical and imaging factors were also examined in the present meta-analysis. Modic changes typically include reactive vertebral changes associated with inflammation, an unstable microenvironment or degenerative disc disease (39,40). As the intervertebral disc itself does not contain vascular tissue, the micropores in the endplate are exchange channels for nutrients, water and other metabolic products. When the endplate changes, its nutritional effect on the intervertebral disc decreases (39,40). Therefore, it is not difficult to understand that modic changes are associated with a higher risk of rLDH. The present study found that a Pfirrmann grade ≥4 is associated with a higher risk of rLDH, which is consistent with the findings of Kim *et al* (41). This latter study concluded that a higher degree of intervertebral disc degeneration is associated with a higher risk of rLDH (41). During the process of intervertebral disc degeneration, type I collagen increases, while type II collagen decreases, and the content of proteoglycans and elastin decreases (42), which causes the nucleus pulposus to lose elasticity and the annulus fibrosus to appear cracked. Therefore, more severe degeneration of the intervertebral disc is associated with poorer self-repairing ability of the fibrous ring, ultimately leading to the protrusion of the nucleus pulposus (42). The present study found that the sacral slope angle is associated with the risk of rLDH after PELD. Studies have shown that a large sacral slope angle can lead to L5-S1 vertebral body slippage and its mechanism is increased stress in the L5-S1 vertebral body (43-45), which may indicate a potential association between the susceptibility to rLDH after PELD. A biomechanical study found that a larger sacral slope angle can lead to lumbar lordosis (45) and increase stress in the lumbar intervertebral disc. Therefore, correcting the sacral slope angle can reduce the risk of rLDH after PELD. A larger sacral slope angle can be considered a risk factor for rLDH.

The present study has several limitations, and resolving these limitations will further increase the reliability of its findings. Due to these limitations, readers need to consider not only the conclusions of this study but also real clinical scenarios to interpret them. First, the present meta-analysis involved only association analyses, so the determination of causal relationships requires further prospective cohort studies or Mendelian randomization studies in the future. Furthermore, although strict inclusion and exclusion criteria were established to ensure comparability among studies, unclear definitions of rLDH, inconsistent sample sizes and differences in follow-up time between certain studies may reduce the reliability of the conclusions of the present study. Finally, there was high statistical heterogeneity for most risk factors in the present study, but our attempt to find the source of heterogeneity was not successful. Therefore, the application of the conclusions of the present study requires clinical workers to consider their clinical experiences.

In conclusion, as significant risk factors for rLDH after PELD surgery, older age, higher BMI, modic change, intervertebral disc degeneration and larger sacral slope angle were identified in the present study. These findings will enable medical workers to identify high-risk populations early and to choose appropriate surgical procedures to reduce the risk of rLDH. Future research should further validate the modifiable risk factors identified in the present study to improve outcomes for patients with rLDH.

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**Availability of data and materials**

The data generated in the present study may be requested from the corresponding author.

**Authors' contributions**

JZ, JL and YZ conceived the study and are responsible for the overall content. Literature screening and data processing were performed by GL and BS. SZ, LZ, GL, BS, HF, WY and JZ analyzed and interpreted the data. JZ, LZ and GL prepared the manuscript. JL and LZ edited the manuscript. JZ, LZ and SZ contributed equally to this work. JL and YZ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable.

**Patient consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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