

## Systematic Review

# Prevalence of Recurrent Herniation Following Percutaneous Endoscopic Lumbar Discectomy: A Meta-Analysis

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**Background:** Percutaneous endoscopic lumbar discectomy (PELD) is a minimally invasive surgery for the treatment of lumbar disc herniation (LDH) with a smaller incision, decreased damage to soft tissues, faster recovery, and fewer postoperative complications. However, the exactly epidemiological prevalence of recurrent herniation after PELD remains unclear.

**Objectives:** To investigate the epidemiological prevalence of recurrent herniation in patients following PELD and to analyze the potentially related risk factors.

**Study Design:** Meta-analysis and systematic review of prospective and retrospective studies.

**Methods:** We conducted a comprehensive search in MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials that mentioned the incidence of recurrent herniation after PELD. The overall prevalence estimate was calculated by an appropriate meta-analysis. Subgroup analysis, sensitivity analysis, and publication bias assessment were also performed in our study, respectively.

**Results:** Our results showed the overall prevalence of recurrent herniation after PELD was 3.6% (95% CI 3.0-4.3%). The prevalence estimates after percutaneous endoscopic interlaminar discectomy (PEID) and percutaneous endoscopic transforaminal discectomy (PETD) were 4.2% and 3.4%, respectively. Individuals with older age ( $\geq 50$  years) and higher BMI ( $\geq 25$ ) had increased recurrence rates after PELD than those with younger age (4.3% vs. 2.7%) and normal body mass index (BMI) (4.8% vs. 1.5%). The prevalence was significantly higher at upper discs (5.4%) than that at L4-5 (2.7%) and L5-S1 (3.1%) level. The incidence of recurrent herniation at lateral disc was 4.7%, and the recurrence rate of migrated herniation was 3.8%. In most cases, the recurrent herniation occurred within 6 months postoperatively (accounting for 61.7%).

**Limitations:** A majority of the included articles were relatively low quality retrospective studies with significant heterogeneity among them. Furthermore, owing to the paucity of data focused on recurrence, many potentially predictive factors related to subgroup analyses could not be conducted, which might have influenced the accuracy and comprehensiveness of our meta-analysis.

**Conclusions:** PELD is associated with a certain rate of recurrence (3.6%), which usually occurred within 6 months postoperatively. Older age ( $\geq 50$  years), obesity (BMI  $\geq 25$ ), upper lumbar disc and central disc herniation might be independent risk factors for recurrence after PELD; however, different surgical approaches (PETD or PEID), lateral discs, migrated discs and foraminoplasty did not affect the incidence. These factors could be useful in preoperative evaluation, appropriate patient selection and informed consent before PELD.

**Key words:** Percutaneous endoscopic lumbar discectomy, prevalence, recurrent herniation, meta-analysis

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**P**ercutaneous endoscopic lumbar discectomy (PELD) is a minimally invasive surgery for the treatment of lumbar disc herniation (LDH) and has been increasingly used for more than 20 years. Numerous clinical studies have confirmed that PELD has similar effectiveness to conventional surgery and has obvious advantages such as smaller incisions, decreased damage to soft tissues, faster recovery, and fewer postoperative complications (1-2). However, along with the widespread use of the procedure, the recurrent herniation after PELD has become an issue of concern for researchers and surgeons (3). The recurrence rate after successful PELD is reported at 0 to 12.5%, showing a significant range, with many studies focused on the risk factors causing recurrent herniated lumbar disc (4-5). Some of the most often mentioned risk factors for recurrence are age at the time of surgery, gender, obesity, herniation type, location of herniation, surgical approach, and learning curve of the surgeon (6-7).

Up to now, there has been a lack of a recognized uniform understanding about etiology, pathomechanism and even epidemiological assessment of the recurrent herniation after successful PELD. To the best of our knowledge, no studies have been conducted by meta-analysis regarding the epidemiological prevalence of recurrent herniation after PELD. Therefore, the purpose of the present study is to review the related literature referring to the recurrent herniation after PELD and to investigate its prevalence and related risk factors, in attempt to provide available detailed evidence-based data for preoperative evaluation, appropriate patient selection and informed consent.

## **METHODS**

### **Search Strategy and Eligibility Criteria**

Through an electronic search and independent, manual searches by 2 clinical librarians (SY and WY), we identified all qualified articles that referred to the incidence of recurrent herniation after PELD in all languages up to August 2017. The sources of electronic searching include MEDLINE, EMBASE, and The Cochrane Central Register of Controlled Trials. The following key terms were included in our searches: "percutaneous endoscopic lumbar discectomy," "percutaneous endoscopic transforaminal discectomy," "percutaneous endoscopic interlaminar discectomy," "transforaminal lumbar discectomy," "transforaminal full-endoscopic lumbar discectomy," "recurrent herniation," "recurrence," and "recurrent rate." Additionally,

bibliographies of all selected full text articles were reviewed to identify more articles. Two reviewers (SY and WY) independently checked the titles and abstracts of all articles identified from the database. The full texts of all potentially relevant studies were also assessed by 2 reviewers if necessary. If no agreement could be reached, a third reviewer (HT) made the final decision.

The eligibility criteria of the included articles were: 1) those that mentioned the incidence of recurrent herniation after primary PELD for the treatment of LDH; 2) a retrospective study, prospective study, cohort study, regardless of sample size; 3) sufficient reported data for extraction and calculation of a recurrence rate with 95% confidential interval (CI); 4) patients were followed up for at least 6 months; 5) in the case of duplicate publication, the most recent or largest study was selected; 6) publications were excluded if the patients underwent PELD as revision procedures, and publications were also excluded if they were review articles, comments, case reports, letters, animal trials, or cadaver studies; 7) No restriction related to the languages was defined.

### **Data Extraction**

Two reviewers (SY and CF) independently extracted the data of included studies and reached consensus on each item. Data included: 1) authors' names and nationality, language, publication time, study design, recruitment period, follow-up time, and journal title of each included study; 2) sample size and patient's demographic characteristics including age, gender, body mass index (BMI); 3) recurrence case number, recurrence time and other details; 4) the location, type and level of herniated disc; 5) proportion of surgical type including percutaneous endoscopic transforaminal discectomy (PETD), percutaneous endoscopic interlaminar discectomy (PEID), with or without additional procedures such as foraminoplasty, annular sealing, etc. Recurrence was defined as disc herniation on the same side and level as the primary operative site after successful initial removal of the protruding disc and a pain-free interval after operation, which was revealed on an immediate postoperative MRI (6). In addition, recurrence was classified according to time period, with early recurrence at less than 6 months and late recurrence at > 6 months postsurgical intervention (8).

### **Assessment of Heterogeneity and Publication Bias**

The heterogeneity was assessed by using Cochran's Chi square-based Q statistic and I<sup>2</sup> test (I<sup>2</sup> = 0–25 %

represents no heterogeneity;  $I^2 = 25-50\%$  represents moderate heterogeneity;  $I^2 = 50-75\%$  represents large heterogeneity;  $I^2 = 75-100\%$  represents extreme heterogeneity (9-10). The value of  $I^2$  greater than 50% would be considered substantial heterogeneity. A sensitivity analysis was performed for the measured effects by omitting the studies which may largely influence the clinical results (11). In addition, potential publication bias was assessed using funnel plot and Egger's regression test for all included studies and each subgroup analysis (12).

### Statistical Analysis

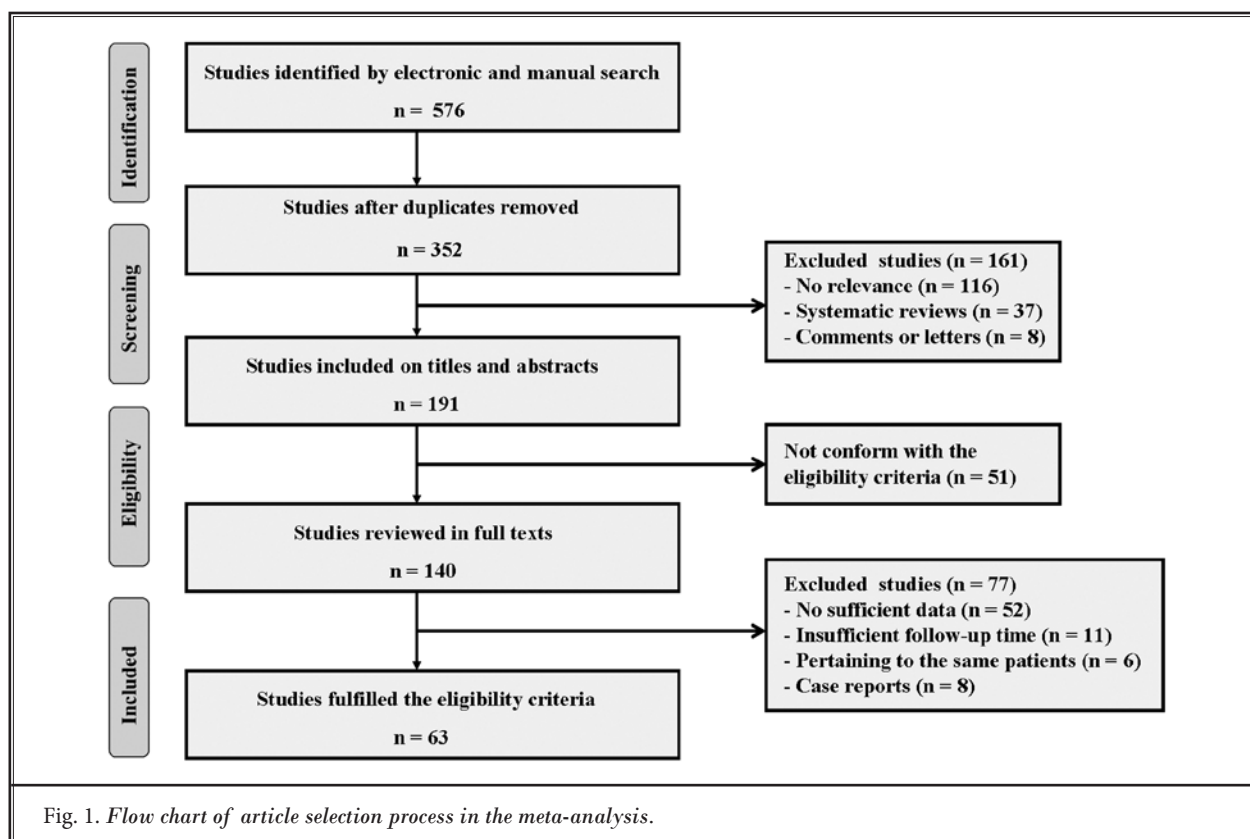
We conducted a meta-analysis using STATA package version 12.0 program (StataCorp, College Station, TX, USA) for all extracted data. When a significant Q test ( $P < 0.10$ ) or  $I^2 > 50\%$  indicated heterogeneity across studies, the Dersimonian and Laird method random effects model was used for meta-analysis, otherwise the Mantel-Haenszel method fixed effects model was used. Based on this, we calculated the point prevalence of recurrent herniation after PELD with its 95% CI for each individual study, and then a pooled prevalence estimate

and 95% CI were generated. We also performed subgroup analysis based on surgical procedure (PETD and PEID), age ( $< 50$  and  $\geq 50$  years), BMI ( $< 25$  and  $\geq 25$ ), level of herniated disc (upper discs, L4-5 and L5-S1), location of herniated disc (central, paramedian and lateral), type of herniated disc (migrated and non-migrated), recurrence time ( $< 6$  months and  $> 6$  months), and with or without additional procedures such as foraminoplasty. Sensitivity analysis was conducted to evaluate the influence of excluding prospective studies, excluding studies with total patients  $< 50$  and  $< 500$ , and excluding studies with period of follow-up less than 12 months, respectively. All statistic tests performed in this study were 2-tailed, and  $P < 0.05$  was taken as being statistically significant.

### RESULTS

#### Characteristics of Included Studies

After applying the search strings, we identified 576 potentially eligible articles. Of the 576 articles, 224 were duplicates (Fig. 1). One hundred and sixty-one articles were excluded based on their titles and abstracts



with apparent lack of relevance. Using the eligibility criteria, another 51 of the left 191 manuscripts were excluded after the full texts were reviewed. Furthermore, 77 articles were excluded for no sufficient data, insufficient follow-up time, and pertaining to the same patients, or only clinical case reports. The exclusions left 63 studies (2,4-6,8,13-70) for the current review and meta-analysis, involving a total of 23,930 patients.

We recorded the characteristics and details of the clinical outcomes of the 63 included papers (Appendix 1). Fifteen studies were prospective (including 2 randomized controlled trials), and the remainder were retrospective. The sample size ranged from 16 to 10,228 with a median of 80. The follow-up of all included studies ranged from 6 to 60 months. The mean age of patients at surgery ranged from 16.5 to 62.3 years. Most of the included articles were published in English except 2 manuscripts written in Chinese. Among all included studies, 34 articles were focused on recurrent herniations following PETD, while 12 articles focused on PEID. Partial studies mentioned the incidence of recurrent herniation after PELD in terms of age, BMI, recurrence time, the location, and type and level of herniated disc. All relevant information listed and other general characteristics of the included articles were recorded.

### **Overall Prevalence of Recurrent Herniation after PELD**

Sixty-three studies of a total of 23,930 patients, including 470 patients with recurrent herniation after PELD, were included for the current study. The meta-analysis showed that the pooled prevalence of recurrent herniation by random effects model was 3.6% (95% CI 3.0-4.3%), with substantial heterogeneity among included trials (Fig. 2). The recurrence rate among the studies varied between 0 and 12.5%.

### **Subgroup Meta-Analysis**

#### ***Surgical Approach Related Recurrence***

Table 1 summarizes the stratified meta-analysis based on different surgical procedures including PETD and PEID. There was no significant difference between the pooled prevalence estimates of recurrent herniation after PEID (4.2%, 95% CI 2.6-5.7%) and PETD (3.4%, 95% CI 2.6-4.2%).

#### ***Age and Obesity Related Recurrence***

The results shown in Table 1 revealed that the pooled recurrence rate after PELD in older patients ( $\geq$

50 years) was significantly higher than those who were younger ( $< 50$  years) (4.3% vs. 2.7%), and the lowest incidence of recurrence in older patients was almost the same as the peak incidence of recurrence in younger patients. Our meta-analysis also showed that the obese patient (BMI  $\geq 25$ ) had an obviously higher (more than triple) prevalence estimate than those with normal BMI (4.8% vs. 1.5%), and the pooled highest recurrence rate was 5.7% and 2.2%, respectively.

#### ***Herniated Disc Level Related Recurrence***

The levels of lumbar discs were divided into 3 categories that were upper disc (includes L1-2, L2-3, and L3-4), L4-5, and L5-S1, respectively. The results in Table 1 show that the prevalence of recurrent herniation at upper discs was significantly higher than that at L4-5 and L5-S1, with a highest incidence of 14.8%, 5.0% and 4.6%, respectively. The pooled estimates of recurrence at L4-5 and L5-S1 were 2.7% (95% CI 0.3-5.0%) and 3.1% (95% CI 1.6-4.6%), with no significant differences detected.

#### ***Herniated Disc Location and Type Related Recurrence***

Since there were too little data for recurrence focused on central and paramedian herniated disc, only prevalence of recurrent herniation at the lateral disc (including foraminal and extraforaminal disc) was pooled in our meta-analysis. The estimated recurrence rate at the lateral disc was slightly higher than the overall incidence of recurrence (4.7% vs. 3.6%), but with no significant difference. The subgroup analysis also revealed that the recurrence rate of migrated herniation was 3.8% (95% CI 2.9-4.6%), which was comparable to the overall prevalence.

#### ***Recurrence Time Related Incidence***

The pooled results showed that the early ( $\leq 6$  months) recurrence rate after PELD was significantly higher than the later ( $> 6$  months) recurrence rate (2.1% vs. 1.2%), with a highest incidence of 2.9% and 1.9%, respectively. Meanwhile, the early recurrence accounted for 61.7% of total recurrent herniations in included studies.

#### ***Recurrence Rate With or Without Additional Procedure***

The results summarized in Table 1 suggested that the prevalence of recurrent herniation after PELD with foraminoplasty was 3.4%, with a highest incidence of

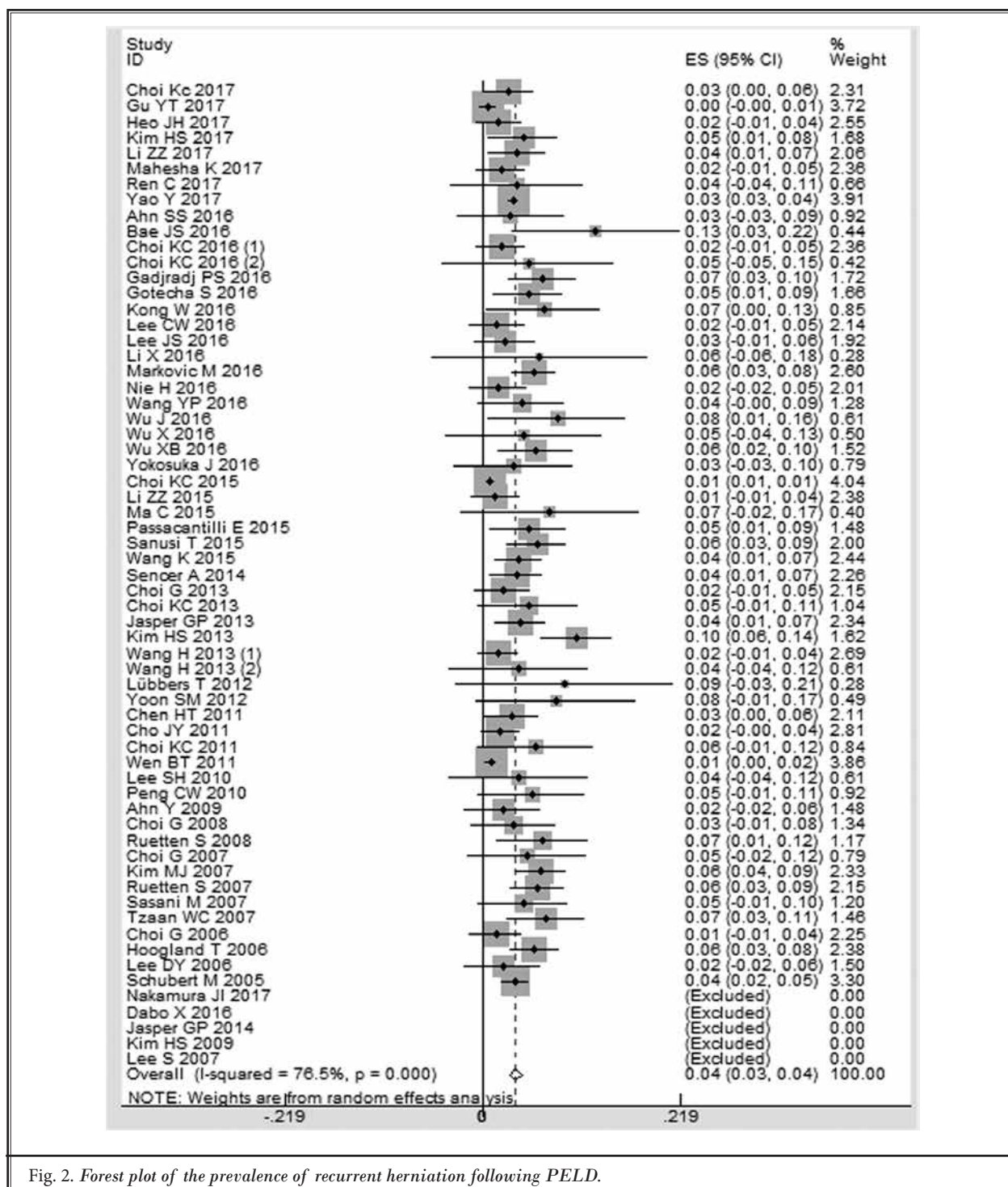


Fig. 2. Forest plot of the prevalence of recurrent herniation following PELD.

4.5%, which was comparable to the overall prevalence. For annular sealing, only one study reported a recurrence rate of 5.5%, which was significantly lower than those without annular sealing (13.5%).

### Sensitivity Analysis

Sensitivity analysis was conducted to confirm the stability and liability of the meta-analysis by omitting the studies which may largely influence the clinical



Table 1. Stratified meta-analysis of recurrence rate following PELD.

Subgroups	No. of trials	No. of total patients	No. of recurrence	Pooled recurrence rate (%)	95% CI	Heterogeneity	
						I <sup>2</sup> (%)	Q test P value
Surgical procedure							
PETD	34	17591	354	3.4	2.6-4.2	78.1	< 0.001
PEID	12	1260	68	4.2	2.6-5.7	45.6	0.043
Age (years)							
< 50	5	2076	57	2.7	2.0-3.4	0	0.996
≥ 50	2	1612	70	4.3	3.3-5.3	0	0.756
BMI							
< 25	2	1395	23	1.5	0.9-2.2	60.2	0.113
≥ 25	3	2100	102	4.8	3.9-5.7	0	0.452
Level of herniated disc							
Upper disc	3	102	5	5.4	0-14.8	0	0.680
L4-5	4	624	14	2.7	0.3-5.0	47.8	0.125
L5-S1	13	1179	49	3.1	1.6-4.6	55.5	0.008
Special types							
Foraminal/extraforaminal	4	158	8	4.7	1.4-8.0	0	0.879
Migrated	4	1946	73	3.8	2.9-4.6	0	0.974
Recurrence time							
Early (≤ 6 months)	18	1538	45	2.1	1.2-2.9	22.7	0.185
Late (> 6 months)	10	955	19	1.2	0.5-1.9	0	0.530
With foraminoplasty	6	1012	36	3.4	2.3-4.5	0	0.885
Total	63	20390	470	3.6	3.0-4.3	76.5	< 0.001

Abbreviation: No = number, CI = confidential interval, PETD = percutaneous endoscopic transforaminal discectomy, PEID = percutaneous endoscopic interlaminar discectomy, BMI = body mass index

results. We performed a series of sensitivity analysis by excluding 15 prospective studies, by excluding 21 studies with total patients < 50 or > 500, and by excluding 9 studies with period of follow-up less than 12 months, respectively. The pooled results showed that no single one had a remarkable influence on the overall prevalence. All the findings indicate the robustness of the results of our meta-analysis.

### Publication Bias

According to the funnel plot (Fig. 3) and the result of Egger's regression test ( $P = 0.485$ ), no obviously statistical evidence of publication bias was detected among the included studies. Likewise, the results of Egger's regression test for subgroup analysis revealed no significant publication bias in included studies (Table 3).

### Discussion

To our knowledge, this is the most comprehensive

and detailed meta-analysis focused on the prevalence estimates of recurrent herniation after PELD. The current meta-analysis involved a total of 20,390 patients and 63 studies from 13 countries and territories and the result showed that the overall prevalence of recurrent herniation after PELD was 3.6%. No statistical evidence of publication bias was detected, and sensitivity analyses confirmed the robustness of the results of our meta-analysis (Table 2). Our review differs from previously published reviews (71-72) because it assesses the updated and full range of relevant trials with no or fewer restrictions related to the study design, language, and follow-up periods. Our pooled overall recurrence rate was slightly higher than that of 3.33% reported by Li X et al (71), who reviewed only 7 related articles dating up to September 2015. In the last 2 years, 27 reports referring to the recurrence after PELD have been published, so it is very necessary to update statistical data for obtaining accurate information.

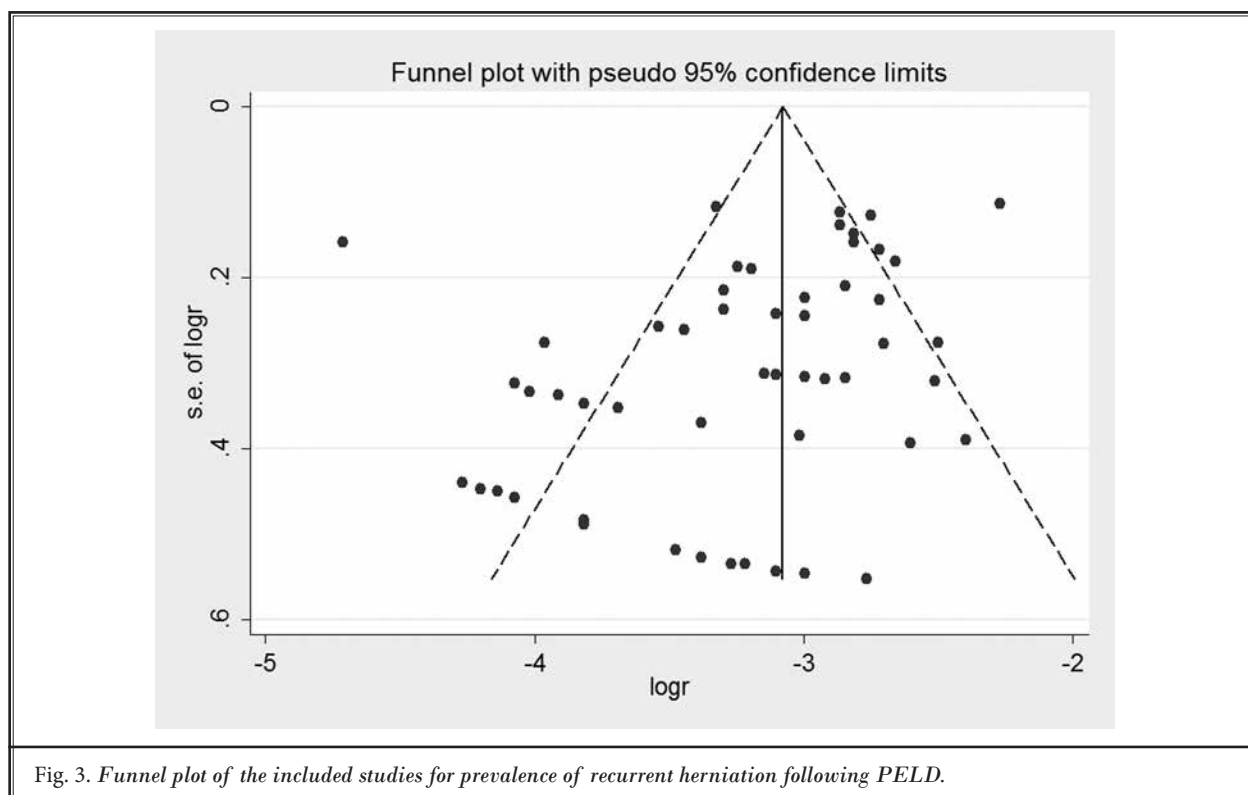


Fig. 3. Funnel plot of the included studies for prevalence of recurrent herniation following PELD.

Table 2. Sensitivity analysis of the rate of recurrence rate following PELD.

Sensitivity analysis	Remained studies	Pooled recurrence rate (%)	95% CI	Heterogeneity	
				I <sup>2</sup> (%)	Q test P value
1. Excluded studies that were prospective	48	3.1	2.4-3.8	76.2	< 0.001
2. Excluded studies with No. of total patients <50 and >500	42	3.8	3.0-4.6	57.3	< 0.001
3. Excluded studies with period of follow-up < 12 months	54	3.5	2.8-4.2	77.1	< 0.001

Abbreviation: CI = confidential interval, No = number

Another highlight of the present study is the subgroup analyses based on surgical procedure, age, BMI, recurrence time, the location, type and level of herniated disc, and additional procedures to investigate the prevalence of recurrence and confirm potential risk factors. Subgroup analysis by surgical procedure shows that the pooled recurrence rates following PETD and PEID were approximately equal. Although previous studies have not reached a consensus, most studies' conclusions were consistent with our result (43,45,60).

It is generally accepted that old age and obesity are potential risk factors for recurrence after PELD (5-6,31,41). The finding of our meta-analysis reconfirmed that the prevalence of recurrent herniation after PELD

was significantly higher in older ( $\geq 50$  years) and obese (BMI  $\geq 25$ ) patients. The conclusion is reasonable given that the older discs are often degenerative, and the remaining fragment of the nucleus pulposus is more susceptible to prolapse in response to mechanical overload, which was caused by annular incision during surgery (73). Likewise, excess weight with the cyclical increase of the intradiscal pressure could lead to higher shear strains in the posterolateral part of the annulus fibrosus, which would result in disc herniation (74-75).

Consistent with observations from previous studies (32,57), the result of our meta-analysis suggests that the prevalence of recurrent herniation at upper disc is obviously higher than that at L4-5 and L5-S1. The

Table 3. Publication bias analysis of the included studies for subgroup analysis.

Subgroup analysis	Egger's test	
	P value	
Surgical procedure		
PETD	0.969	
PEID	0.064	
Age (years)		
< 50	0.221	
≥ 50	0.317	
BMI		
< 25	0.317	
≥ 25	0.551	
Herniation level		
Upper discs	0.208	
L4-5	0.089	
L5-S1	0.080	
Special types		
Foraminal/extraforaminal	0.225	
Migrated	0.980	
Recurrence time		
Early (≤ 6 months)	0.105	
Late (> 6 months)	0.120	
With foraminoplasty	0.700	
Total	0.485	

Abbreviation: PETD = percutaneous endoscopic transforaminal discectomy, PEID = percutaneous endoscopic interlaminar discectomy, BMI = body mass index

definite reason remains unclear; however, it can be speculated that the unique anatomical environment of the upper lumbar level such as a smaller spinal canal, a larger dural sac, and conus medullaris in the dural sac, and the inherent technical difficulty might be the main reason for the high incidence of recurrence (76). On the other hand, the prevalence of recurrent herniation at L4-5 was comparable to that at L5-S1 level.

Owing to the paucity of pooled data, the subgroup analysis by the location and type of herniated disc was only conducted for the prevalence estimate of the recurrent herniation at the lateral disc and migrated disc. Neither of the estimated recurrence rates showed significant difference compared with the overall incidence of recurrence. However, only one large sample-based study by Yao Y et al (6) reported a recurrence rate of 4.7% for the central disc herniation, which was significantly higher than that of paramedian herniation (2.7%,  $P = 0.008$ ). One possible reason is that, for the

treatment of central herniation with PETD approach, the working channel is placed inside the nucleus pulposus with a very steep trajectory angle. As a result, the ruptured intervertebral disc is not easily accessible, and the choice of working channel position may be the main cause of the high incidence of recurrence (36). Therefore, for central herniation, especially at the L5-S1 level, the PEID approach might be the best option. Previous studies demonstrated that migrated herniation was a risk factor responsible for recurrence after PELD (7,33,59), given that the view of endoscopic surgery is limited, and it is difficult to remove the hidden fragments beyond the operation area (6). However, in this current study there was no significant increase in recurrence of migrated disc herniation compared with the overall estimate. This might indicate the patients benefited from the progress made in the endoscopic technique, especially in the last 10 years. The incomplete removal of the herniated fragment caused by the migrated herniations has been reduced.

According to the result of our meta-analysis, the incidence of early recurrence was nearly double the late recurrence rate, and patients with early recurrence account for the majority of patients with recurrent herniations. In other words, recurrence after PELD usually occurred within 6 months, which was consistent with observations from previous studies (8,77). For additional procedures, the pooled result of subgroup analysis showed that there was no obvious difference between the recurrence rates after PELD with or without foraminoplasty. Kim et al (8) proposed a new technique of annular sealing after fragmentectomy to minimize the annular defects during PEID. The circumference of the annular fissure was coagulated by more than 10 times, using bipolar radiofrequency toward the annular defect. Radiofrequency was adjusted to 15 watts and coagulation duration was timed to less than one second per coagulation. After constriction, tightening and reduction of the annular fissure were observed. They reported that the PEID with annular sealing resulted in lower recurrence rate than without annular sealing (5.5% vs. 2.7%,  $P = 0.026$ ).

Other probable predictive factors include gender, smoking, degenerated disc, the Modic changes, and learning curve of the surgeon, disputes remain. However, Kim et al (7) reported that the old age, higher BMI, the presence of the Modic changes and the protrusion increased the recurrence rates after successful PELD. Yao et al (6) also suggested that the older age, obesity, learning curve of the surgeon, treatment period, and



central location of herniation were independently significant risk factors for recurrence after PELD. Likewise, Cinotti et al. (78) reported that those male patients with markedly degenerated discs could be risk factors for recurrent herniation after microdiscectomy. On the other hand, it was reported by Swartz that age, gender, smoking status, level of herniation and duration of symptoms were not associated with a higher rate of recurrence after partial laminectomy and discectomy (79).

Based on the results of our meta-analysis, some advice could be provided for the appropriate patient selection and surgical indication of PELD. Surgeons need to be more aware of the older, obese patients, and patients with upper lumbar disc herniation or central disc herniation when using the PELD procedure. However, with the PELD technique, experience can also affect the success of the surgery, and experienced surgeons and medical centers who are experienced with PELD, can expand the indications of PELD.

Readers should be aware of limitations in the literature and with our study, in particular. First, significant heterogeneity among studies was observed. As it is generally recognized that heterogeneity often exists in such meta-analyses of overall prevalence (80-81), we conducted subgroup analysis to explore the probable source of prevalence heterogeneity; however, none of them could sufficiently explain the heterogeneity. Sec-

ondly, a majority of included articles were retrospective studies with relatively low quality of evidence. Furthermore, not all of the included studies were designed for the prevalence study. Not all of them provided detailed characteristics of patients with recurrent herniation; this may have led to the impreciseness of the pooled data. Thirdly, owing to the paucity of data focused on recurrence from included studies, many potentially predictive factors related subgroup analyses could not be conducted, which may have influenced the accuracy and comprehensiveness of our meta-analysis.

### **CONCLUSION**

Our meta-analysis revealed that the overall pooled prevalence of recurrent herniation after PELD was 3.6%, and recurrence usually occurred within 6 months postoperatively. Older age ( $\geq 50$  years), obesity (BMI  $\geq 25$ ), upper lumbar disc and central disc herniation may be independent risk factors for recurrence after PELD; however, different surgical approach (PETD or PEID), lateral disc, migrated disc and foraminoplasty did not affect the incidence of recurrent herniation. Considering the limitations mentioned above, future studies of high quality and large populations are needed to better evaluate the prevalence of recurrent herniation and related risk factors after PELD.

Appendix 1. Characteristics of the included studies.

Study	Recurrent rate	No. of total patients	No. of recurrence	Age (years)	Study design	Country	Language	Recruitment period	Follow-up (months)
Choi KC 2017	2.9%	136	4	42.8	Retrospective Study	Korea	English	Dec 2014 to Dec 2015	12.7
Gu YT 2017	0.5%	209	1	46.4	Retrospective Study	China	English	Jan 2012 to Jun 2013	26.3
Heo JH 2017	1.8%	109	2	37.4	Retrospective Study	Korea	English	Aug 2014 to May 2016	7.2
Kim HS 2017	4.5%	111	5	53.3	Retrospective Study	Korea	English	Jan 2016 to Oct 2016	6.4
Li ZZ 2017	3.7%	134	5	41.4	Prospective Study	China	English	Apr 2007 to Apr 2009	60.0
Mahesha K 2017	2.0%	100	2	40.3	Retrospective Study	India	English	May 2012 to Jan 2014	24.0
Nakamura JI 2017	0%	50	0	40.3	Retrospective Study	Japan	English	Since Apr 2014	15.0
Ren C 2017	3.8%	26	1	41.2	Retrospective Study	China	English	Jun 2014 to Oct 2015	19.3
Yao Y 2017	3.4%	3378	116	47.5	Retrospective Study	China	English	Mar 2005 to Mar 2016	24.0
Ahn SS 2016	3.1%	32	1	22.4	Retrospective Study	Korea	English	May 2012 to Jan 2014	13.7
Bae JS 2016	12.5%	48	6	38.0	Retrospective Study	Korea	English	Jan 2011 to Dec 2011	29.9
Choi KC 2016 (1)	2.0%	100	2	36.5	Retrospective Study	Korea	English	Jul 2011 to Dec 2013	24.0
Choi KC 2016 (2)	5.0%	20	1	33.9	Retrospective Study	Korea	English	Jul 2011 to Jun 2012	27.5
Dabo X 2016	0.0%	60	0	36.0	Retrospective Study	China	English	Mar 2011 to May 2013	12.0
Gadjradj PS 2016	6.6%	166	11	43.5	Prospective Study	Netherlands	English	Jan 2009 to Dec 2012	13.0
Gotecha S 2016	5.0%	120	6	31-40	Prospective Study	India	English	Aug 2012 to Dec 2014	6.0
Kong W 2016	6.7%	60	4	51.6	Retrospective Study	China	English	Aug 2012 to Mar 2014	12.0
Lee CW 2016	1.6%	64	1	52.7	Retrospective Study	Korea	English	Aug 2012 to Apr 2014	12.2
Lee JS 2016	2.5%	80	2	40.0	Retrospective Study	Korea	English	Jan 2011 to Jun 2013	13.0
Li X 2016	6.3%	16	1	45.1	Retrospective Study	China	English	NR	26.2
Markovic M 2016	5.7%	350	20	NR	Prospective Study	Serbia	English	NR	36.0
Nie H 2016	1.7%	60	1	37.4	RCT	China	English	Jan 2010 to Jun 2010	27.6
Wang YP 2016	4.3%	69	3	34	Prospective Study	China	English	Mar 2011 to Dec 2015	11.8
Wu J 2016	8.2%	49	4	58.7	Retrospective Study	China	English	Dec 2008 to Oct 2014	29.9
Wu X 2016	4.5%	22	1	41.1	Retrospective Study	China	English	Jun 2012 to Feb 2014	18.1
Wu XB 2016	5.8%	120	7	40.3	Retrospective Study	China	English	Jun 2011 to Aug 2013	15.9
Yokosuka J 2016	3.4%	29	1	56.8	Retrospective Study	Japan	English	Jan 2014 to Apr 2016	12.0
Choi KC 2015	0.8%	10228	78	39.9	Retrospective Study	Korea	English	Jan 2001 to Dec 2012	21
Li ZZ 2015	1.4%	72	1	40.5	Retrospective Study	China	English	Apr 2011 to Dec 2011	12.0
Ma C 2015	7.4%	27	2	47.8	Retrospective Study	China	Chinese	Jan 2012 to Jan 2014	12.0
Passacantilli E 2015	5.0%	100	5	51.0	Prospective Study	Italy	English	2009 to 2011	24.0
Sanusi T 2015	6.0%	201	12	41.0	Retrospective Study	UK	English	Oct 2011 to Dec 2013	6.0

Recurrence Following PELD

Appendix 1. Characteristics of the included studies.

Study	Recurrent rate	No. of total patients	No. of recurrence	Age (years)	Study design	Country	Language	Recruitment period	Follow-up (months)
Wang K 2015	3.9%	207	8	45.7	Retrospective Study	China	English	Jan 2013 to Sep 2014	12.0
Jasper GP 2014	0.0%	41	0	46.0	Retrospective Study	USA	English	2007 to 2012	12.0
Sencer A 2014	3.7%	163	6	47.0	Retrospective Study	Turkey	English	Aug 2009 to Jan 2012	12.0
Choi G 2013	2.2%	89	2	46.6	Retrospective Study	Korea	English	NR	24.0
Choi KC 2013	5.0%	60	3	35.4	Retrospective Study	Korea	English	Jan 2010 to Dec 2010	27.0
Jasper GP 2013	4.1%	195	8	62.3	Retrospective Study	USA	English	2007 to 2011	6.0
Kim HS 2013	10.3%	224	23	41.5	Retrospective Study	Korea	English	Jan 2008 to Feb 2010	19.5
Wang H 2013 (1)	1.7%	120	2	45.1	Retrospective Study	China	English	Sep 2005 to May 2011	23.0
Wang H 2013 (2)	4.0%	25	1	17.9	Retrospective Study	China	English	Jan 2001 to May 2011	12.0
Lübberts T 2012	9.1%	22	2	53.8	Retrospective Study	Germany	English	Sep 2004 to Apr 2010	43.2
Yoon SM 2012	8.1%	37	3	45.9	Prospective Study	Korea	English	2007 to 2011	20.0
Chen HT 2011	3.2%	123	4	39.1	Prospective study	China	English	Oct 2006 to Jun 2009	12.0
Cho JY 2011	1.9%	154	3	45.0	Retrospective Study	Korea	English	Jan 2006 to Dec 2008	8.0
Choi KC 2011	5.8%	52	3	36.2	Prospective Study	Korea	English	Aug 2007 to Jan 2008	24.0
Wen BT 2011	0.9%	689	6	39.8	Retrospective Study	China	Chinese	Jul 2002 to Oct 2010	33.0
Lee SH 2010	4.0%	25	1	39.2	Retrospective Study	Korea	English	Mar 2003 to May 2004	32.5
Peng CW 2010	5.4%	55	3	35.6	Prospective study	Singapore	English	2002 to 2006	36.0
Ahn Y 2009	2.2%	45	1	NR	Retrospective Study	Korea	English	Jan 2001 to Mar 2003	38.8
Kim HS 2009	0.0%	53	0	NR	Retrospective Study	Korea	English	May 2006 to Mar 2008	9.8
Choi G 2008	3.4%	59	2	50.0	Retrospective Study	Korea	English	Jan 2002 to Jun 2006	25.4
Ruetten S 2008	6.6%	91	6	43.0	RCT	Germany	English	Jan 2004 to Dec 2004	24.0
Choi G 2007	4.9%	41	2	58.7	Retrospective Study	Korea	English	May 2001 to Jun 2004	34.1
Kim MJ 2007	6.4%	295	19	34.9	Retrospective Study	Korea	English	Jul 2003 to Dec 2004	18.0
Lee S 2007	0.0%	116	0	35.5	Retrospective Study	Korea	English	NR	14.5
Ruetten S 2007	6.0%	232	14	41.0	Prospective Study	Germany	English	Jan 2004 to June 2004	24.0
Sasani M 2007	4.5%	66	3	52.0	Prospective Study	Turkey	English	Jun 1998 to Jul 2005	12.0
Tzaan WC 2007	0.7%	134	1	38.0	Retrospective Study	Taiwan, China	English	Sep 2001 to Jul 2005	8.0
Choi G 2006	1.5%	67	1	44.0	Retrospective Study	Korea	English	Mar 2002 to Nov 2002	18.0
Hoogland T 2006	5.7%	280	16	40.6	Prospective Randomized Study	Germany	English	Jan 1996 to Jan 1998	24.0
Lee DY 2006	2.2%	46	1	16.5	Retrospective Study	Korea	English	Jun 2000 to May 2002	37.2
Schubert M 2005	3.6%	558	20	43.8	Retrospective Study	Germany	English & German	Jan 1999 to Jan 2002	24.0

Abbreviation: No = number, RCT = randomized controlled trial, NR = not reported

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