<u>META-ANALYSIS</u>

Influencing Factors of Recurrence of Lumbar Disc Herniation After Percutaneous Transforaminal Endoscopic Discectomy: A Meta-Analysis

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ABSTRACT

Background • Lumbar disc herniation (LDH) remains one of the extremely common diseases in the elderly population, and despite the fact that percutaneous transforaminal endoscopic discectomy (PTED) can be an effective treatment for LDH, prognostic recurrence of the patients is still a clinical problem that needs to be addressed.

Objective • To perform a meta-analysis of the influencing factors of disease recurrence after PTED for LDH to provide evidence for clinical practice.

Methods • By screening the PubMed, EMbase, and Cochrane Library databases for relevant studies on disease recurrence after PTED for LDH, we extracted the authors, publication time, outcome measures, and other indicators were extracted for meta-analyses using RevMan 5.3 software.

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INTRODUCTION

Clinically, lumbar disc herniation (LDH) is one of the most common degenerative diseases of the spine, mainly caused by the protrusion of the nucleus pulposus (NP) and other contents due to annulus fibrosus rupture.1 LDH can compress the dural sac and nerve roots, causing a series of typical symptoms such as numbness, pain and fatigue in the lower back and lower extremities.² According to statistics, people aged 20-50, especially those with long-term bending-over labor or sedentary habits, are predisposed to LDH.3 LDH afflicted approximately 2 million people worldwide in the year 2021 and shows an ever-higher incidence year by year.⁴ Clinically, surgery has been shown to be effective in treating LDH. Of various surgical modalities, percutaneous transforaminal endoscopic discectomy (PTED) can treat LDH through the posterolateral transforaminal approach, which works by removing NP through the transforaminal approach to release and relieve intraspinal spinal

Results • The online retrieval and rigorous screening returned 8 valid articles for analysis, all with high reference value, as their Newcastle Ottawa Scale (NOS) scores were above 6. According to meta-analyses, there were no differences in gender and LDH type and location among patients with LDH recurrence after PTED treatment (P > .05); however, statistical significance was present in Pfirrmann grading, incomplete nucleus pulposus removal during surgery, and Modic changes (P < .05), indicating that these indexes were the influencing factors of LDH recurrence.

Conclusions • Pfirrmann grading, incomplete nucleus pulposus removal during surgery, and Modic changes are related factors affecting LDH recurrence after PTED. (*Altern Ther Health Med.* 2024;30(7):174-178).

cord and nerve root compression.⁵ PTED, as a minimally invasive procedure, offers several advantages, including reduced paravertebral tissue injury, shorter preoperative preparation time, local anesthesia, minimal invasiveness, lower risk of complications, and faster recovery.⁶

Meanwhile, the diseased NP tissue is directly removed during the operation without the need to strip the muscle tissue, which causes minor collateral damage, contributing to minor pain, short hospital stay, rapid postoperative symptom relief, faster recovery, and high patient comfort.⁷ Related research has demonstrated that PTED has a higher success rate and a lower incidence of complications than other current mainstream surgical modalities.^{8,9} However, with the popularization and development of PTED, postoperative recurrence of patients has also been reported from time to time, which has become a major factor affecting the prognosis and health of LDH patients.¹⁰ Despite the success of PTED, postoperative recurrence in LDH patients remains a challenge, and the underlying causes are still a subject of debate. Addressing this knowledge gap is essential for improving long-term patient outcomes.

Therefore, this paper aimed to evaluate the factors affecting postoperative disease recurrence through metaanalysis of the literature on factors related to postoperative recurrence in LDH patients treated by PTED, with a view to providing a valuable reference for clinical prevention and reduction of LDH recurrence and improvement of long-term efficacy through effective intervention.

MATERIALS AND METHODS

Literature retrieval strategy

Through computer retrieval of PubMed, EMbase, Cochrane Library databases with the keywords set as "lumbar disc herniation or LDH", "percutaneous transforaminal endoscopic discectomy or PTED", "percutaneous endoscopic lumbar discectomy or PELD", and "recurrence", we screened literature related to LDH treatment by PTED or PELD. The retrieval time of the literature in the above database was from January 2000 to May 2020. Taking PubMed as an example, the retrieval formula is as follows:

- #1 lumbar disc herniation [Title/Abstract]
- #2 LDH [Title/Abstract]
- #3 Recurrent lumbar disc herniation[Title/Abstract]
- #4 RLDH [Title/Abstract]
- #5 #1 0R #2 OR #3 OR #4
- #6 percutaneous transforaminal endoscopicdiscectomy [Title/Abstract]
- #7 percutaneous endoscopic lumbar discectomylTitle/ Abstract]
- #8 PTED [Title/Abstract]
- #9 PELD [Title/Abstract]
- #10 #6 OR #7 OR #8 OR #9
- #11 recurrence [Title/Abstract]
- #12 postoperative recurrence [Title/Abstract]
- #13 recrudescence [Title/Abstract]
- #14 relapse [Title/Abstract]

Literature inclusion and exclusion criteria

Inclusion of relevant studies on recurrent relapse after PTED for LDH. Literature was excluded based on the following criteria: review, systematic review, duplicate literature, case report, experience summary, animal experiments, etc., because these experiments are not relevant to our research goals; papers with obvious errors, such as statistical errors; articles with incomplete data or data that cannot be extracted; literature with defective or uncountable data in relapsed and non-relapsed groups; papers of non-PTED subjects; literature on treatment of recurrent LDH; literature with a Newcastle-Ottawa Scale (NOS) score $\leq 5.$ ¹¹

Literature screening and data extraction

Two evaluators independently complete literature retrieval, screening, and data extraction. Specifically, by reading the titles and abstracts, they first selected the documents that met the research purpose and then conducted full-text retrieval and evaluation on those meeting the inclusion and exclusion criteria. In case of disagreement, consultation and discussion were carried out, or consulting experts made the decision. The extracted data mainly included elements such as author(s), published years, included research participants, and outcome measures.

Literature quality evaluation

The NOS, a literature quality evaluation scale recommended by the Cochrane Collaboration, was used to evaluate the risk of literature bias, including 9 items such as selection, comparability, and outcome assessment. On a nine-point scale, a score of \geq 7, 6, and \leq 5 indicated high-, medium-, and low-quality, respectively.

Outcome measures

The primary outcome measures were gender, LDH type and location, intervertebral disc degeneration grade, NP removal during surgery and Modic changes.

Statistical analysis

For specific meta-analysis, RevMan 5.3 (Cochrane Collaboration), a data processing software provided by the Cochrane Collaboration, was used for statistical analysis. The odds ratio (OR) was used as the combined effect size for counting data, while the results of continuous variables or measuring data were represented by mean difference (MD). Both OR and MD were expressed by the effect size and its 95% confidence interval (95%CI). Chi-square tests were performed to evaluate the heterogeneity among the combined effect sizes. Heterogeneity was present among the included studies if P > .1 and $I^2 < 50\%$, in which case, a fixed-effects model (FEM) was selected for analysis; otherwise, there was significant heterogeneity among studies, for the analysis of which a random-effects model (REM) was selected. The Mantel-Haenszel (M-H) test was used for comparisons. The results of the meta-analysis were represented as forest plots, and funnel plots determined the risk of publication bias.

RESULTS

Literature screening results

The online database retrieval returned 84 articles, 46 of which were obtained by importing them into the Endnote software to eliminate duplicates. Through cursory reading of the titles and abstracts, 20 articles were initially screened, 8¹²⁻¹⁹ of which were finally included after further reading of the article content and screening according to the inclusion and exclusion criteria (Figure 1).

Data extraction and quality evaluation of the included literature

The quality of the included papers was assessed by two independent evaluators according to the NOS scoring criteria, with five papers being of high quality and three of medium quality. The basic information of the articles can be found in Table 1.

META-ANALYSIS RESULTS

Effect of gender on recurrence

Eight articles¹²⁻¹⁹ reported the influence of gender on LDH recurrence after PTED, involving 218 patients. Given the absence of heterogeneity among these articles, a FEM was used for analysis (I^2 = 38%). The meta-analysis results showed



no statistical difference between male and female patients with post-PTED LDH recurrence (P = .19) (Figure 2).

Influence of LDH types on recurrence

Six articles¹³⁻¹⁸ reported on the impact of LDH types on disease recurrence, involving 144 patients. The literature classified LDH into protrusion and extrusion (including the sequestration type) types s ($I^2 = 34\%$). Through the FEM analysis, it can be seen that there was no significant difference in LDH types in recurrent patients (P = .49) (Figure 3).

Influence of LDH locations on recurrence

Five articles^{12-14,16,17} reported on the influence of the location of herniated disc NP on disease recurrence, involving 148 patients. The literature divided LDH locations into central and bilateral types, with obvious heterogeneity among articles ($I^2 = 75\%$). The analysis identified no marked difference in LDH location in relapsed patients (P = .80) (Figure 4).

Effect of Pfirrmann grading of intervertebral disc on disease recurrence

Eight articles,¹²⁻¹⁹ involving 218 patients, reported on the influence of Pfirrmann grading of intervertebral disc on disease recurrence. The literature divided patients into Pfirrmann I-II and Pfirrmann III-IV ($I^2 = 48\%$). By comparison, it was found that the number of relapsed patients with Pfirrmann III-IV was significantly higher than that of relapsed patients with Pfirrmann I-II (P < .05). It can be seen that the higher the Pfirrmann grade, the greater the possibility of LDH recurrence (Figure 5).

Tabe 1. The basic characteristics of the literature

Author / Published	n	Follow up time	NOS Score	Observed indicators
				Gender, LDH location, intervertebral disc
Kim HS 201912	28	3 months	6	degeneration grade, NP removal during surgery
Kim JM 200713	42	2	0	Gender, LDH type, LDH location, intervertebral
Kim JM 2007.5	42	2 years	8	disc degeneration grade, NP removal during surgery
Kong M 202014	46	2 100250	7	Gender, LDH type, LDH location, intervertebral
Kong M 2020	40	3 years	· /	disc degeneration grade, Modic changes
Li ZP 202215	19	6 months	8	Gender, LDH type, intervertebral disc
	19	omonuis	0	degeneration grade, Modic changes
Shin EH 201816	21	3 years	6	Gender, LDH type, LDH location, intervertebral
51111 2018	21	5 years	0	disc degeneration grade, Modic changes
		6 months	7	Gender, LDH type, LDH location, intervertebral
Tacconi L 202017	11			disc degeneration grade, NP removal during
				surgery, Modic changes
Wang A 202018	5	1 year	7	Gender, LDH type, intervertebral disc degeneration
mang ri 2020		i year	L '	grade, NP removal during surgery, Modic changes
Yu C 202019	46	4 years	6	Gender, intervertebral disc degeneration grade, NP removal during surgery, Modic changes

Figure 2. Effect of gender on recurrence, the results of the fixed-effects model analysis showed no significant effect of gender on LDH recurrence.

	Mal	е	Fema	le		Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI	
Kim HS 2019	16	28	12	28	10.5%	1.78 [0.62, 5.12]			
Kim JM 2007	22	42	20	42	19.4%	1.21 [0.51, 2.85]			
Kong M 2020	30	46	16	46	11.3%	3.52 [1.49, 8.29]			
Li ZP 2022	7	19	12	19	15.4%	0.34 [0.09, 1.27]			
Shin EH 2018	10	21	11	21	11.7%	0.83 [0.25, 2.77]			
Tacconi L 2020	6	11	5	11	4.6%	1.44 [0.27, 7.71]			
Wang A 2020	3	5	2	5	1.6%	2.25 [0.18, 28.25]			-
Yu C 2020	22	46	24	46	25.5%	0.84 [0.37, 1.90]			
Total (95% CI)		218		218	100.0%	1.28 [0.89, 1.86]		•	
Total events	116		102						
Heterogeneity: Chi#=	11.32, df	= 7 (P	= 0.13); P	= 38%			0.02	0.1 1 10	50
Test for overall effect	Z=1.32	(P = 0.1	9)				0.02	Favours [Male] Favours (Female)	50

Figure 3. Influence of LDH types on recurrence, the results of the fixed-effects model analysis showed no significant effect of LDH type on LDH recurrence.

	Protrus	sion	Extrus	ion		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Kim JM 2007	16	42	26	42	40.2%	0.38 [0.16, 0.91]	
Kong M 2020	22	46	24	46	31.3%	0.84 [0.37, 1.90]	
Li ZP 2022	12	19	7	19	6.4%	2.94 [0.79, 10.98]	
Shin EH 2018	10	21	11	21	14.4%	0.83 [0.25, 2.77]	
Tacconi L 2020	6	11	5	11	5.7%	1.44 [0.27, 7.71]	
Wang A 2020	3	5	2	5	2.0%	2.25 [0.18, 28.25]	
Total (95% CI)		144		144	100.0%	0.85 [0.54, 1.34]	+
Total events	69		75				
Heterogeneity: Chi#=	7.59, df=	5 (P=	0.18); [*=	34%			0.02 0.1 1 10 50
Test for overall effect	Z=0.70	(P = 0.4	19)				0.02 0.1 1 10 5 Favours [Protrusion] Favours [Extrusion]

Figure 4. Influence of LDH locations on recurrence, the results of the fixed-effects model analysis showed no significant effect of LDH locations on LDH recurrence.

	Centr	al	Bilate	ral		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl
Kim HS 2019	10	28	18	28	20.6%	-0.29 [-0.54, -0.03]	
Kim JM 2007	24	42	18	42	22.2%	0.14 [-0.07, 0.35]	
Kong M 2020	20	46	26	46	22.5%	-0.13 [-0.33, 0.07]	
Shin EH 2018	8	21	13	21	18.8%	-0.24 [-0.53, 0.06]	
Tacconi L 2020	8	11	3	11	15.8%	0.45 [0.08, 0.83]	
Total (95% CI)		148		148	100.0%	-0.03 [-0.26, 0.20]	-
Total events	70		78				
Heterogeneity: Tau* :	: 0.05; Ch	P= 15.	82, df = 4	(P = 0)	003); I*=	75%	-1 -0.5 0 0.5
Test for overall effect	Z = 0.25	(P = 0.8	30)				Favours [Central] Favours [Bilateral]

Figure 5. Effect of Pfirrmann grading of intervertebral disc on disease recurrence, fixed-effects model analysis showed that the higher the disc Pfirrmann classification, the greater the risk of LDH recurrence.

	1-11		III-IV	1		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Kim HS 2019	14	28	14	28	8.5%	1.00 [0.35, 2.85]	
Kim JM 2007	15	42	27	42	21.0%	0.31 [0.13, 0.75]	
Kong M 2020	22	46	24	46	15.1%	0.84 [0.37, 1.90]	
Li ZP 2022	8	19	11	19	7.7%	0.53 [0.15, 1.92]	
Shin EH 2018	7	21	14	21	11.3%	0.25 [0.07, 0.90]	
Tacconi L 2020	5	11	6	11	4.0%	0.69 [0.13, 3.72]	
Wang A 2020	2	5	3	5	2.2%	0.44 [0.04, 5.58]	
Yu C 2020	12	46	34	46	30.4%	0.12 [0.05, 0.32]	
Total (95% CI)		218		218	100.0%	0.42 [0.29, 0.61]	•
Total events	85		133				
Heterogeneity: Chi ² =	13.50, df	= 7 (P :	= 0.06); P	= 48%			0.01 0.1 1 10 100
Test for overall effect	Z= 4.49	(P < 0.0	00001)				0.01 0.1 1 10 100 Favours (I-II) Favours (III-IV)

Figure 6. Effect of NP removal during surgery on disease recurrence, the results of the fixed-effects model analysis showed the greater the risk of LDH recurrence in patients who had their NP removed during surgery.

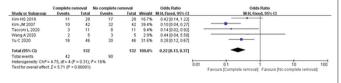


Figure 7. Effect of Modic change on disease recurrence, the results of the fixed-effects model analysis showed the greater the risk of LDH recurrence in patients with Modic alterations.

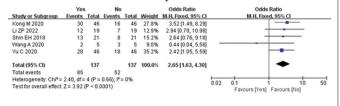
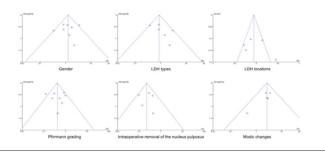


Figure 8. Publication bias analysis, all funnel plots were essentially symmetric with no publication bias.



Effect of NP removal during surgery on disease recurrence

Meta-analysis^{12,13,17-19} showed that the number of patients with recurrence who had complete intraoperative NP removal was less than the number who did not, and the difference was statistically significant ($I^2 = 16\%$, P < .05) (Figure 6).

Effect of Modic change on disease recurrence

The effect of Modic change on recurrence was reported in 5 papers^{14-16,18,19} with a total of 137 patients. There was no significant heterogeneity in the differences between the literatures ($I^2 = 0\%$), and after analysis, it was seen that the number of patients with Modic change was significantly higher in recurrence, with statistically significant differences (P < .05) (Figure 7).

Publication bias analysis

Finally, a publication bias analysis was carried out for the 8 papers included. After drawing the funnel plot, it can be seen that the indicators of each effect size were based on the vertical line as the center line, and the left and right sides were evenly distributed, forming a pyramid-like dashed line range without obvious separation or obvious bias (Figure 8), confirming small publication bias of the above literature, which is worthy of clinical reference.

DISCUSSION

The number of LDH patients is increasing year by year, which is the result of the intensification of population aging and changes in people's lifestyles brought about by social progress.20 Patients have widely accepted PTED because of its advantages of less trauma, relatively complete bone structure preservation, and faster postoperative recovery.²¹ However, the issue of postoperative recurrence cannot be ignored. At present, there are many influencing factors for LDH recurrence after PTED, and the specific causes are also diverse. There is no definitive conclusion as to whether this is due to the patient's disease progression, surgical/non-surgical factors, or a combination of factors. However, due to differences in individual conditions, access criteria, research methods, surgical techniques, follow-up time, and sample size in relevant literature reports, the results regarding the related factors affecting patient postoperative recurrence are not completely consistent and controversial. Therefore, this meta-analysis of factors associated with LDH recurrence after PTED can effectively summarize the factors of LDH recurrence that are currently controversial at this stage and provide a reference for better clinical diagnosis and treatment of LDH in the future.

In this study, we finally screened 8 articles with high quality, as indicated by literature quality evaluation results (NOS score ≥ 6) for meta-analysis. Through meta-analyses, we found no differences in gender, LDH type, and location among patients with post-PTED LDH recurrence, confirming that the above factors had no significant influence on LDH recurrence. However, some researchers in previous studies have suggested otherwise. For example, Li X et al. believe that the recurrence possibility of extruded LDH is higher,²² but the specific mechanism is not clear, which, in our view, may be related to demographic differences or improper surgical procedures. Significant differences were identified in Pfirrmann grading and Modic changes, indicating that these indicators have an important impact on LDH recurrence. The effect of complete NP removal and the integrity of the annulus fibrosus has been recognized in several studies as being closely associated with postoperative recurrence,^{23,24} which is consistent with the results of this analysis. However, excessive NP removal is a double-edged sword. The more the NP removal, the less the residue and the lower the recurrence, but too much NP removal will result in faster degeneration of the remaining intervertebral disc tissue and the more likely it is to cause adjacent lesion.²⁵ Therefore, clinicians are required to conduct specific analyses on a case-by-case basis.

Furthermore, many potential factors influence LDH recurrence, such as untreated narrow lateral recess in PTED, length of disease course, and height of intervertebral disc collapse.²⁶⁻²⁸ However, we cannot conduct meta-analyses on such indicators due to the lack of relevant literature on them. Second, as a degenerative disease, aging has always been considered one of the key factors affecting the progression and recurrence of LDH.^{29,30} However this was also not analyzed in this study. The reason is that the age of patients was recorded as (mean±standard deviation) in some articles

but as [median (lowest value, highest value)] in some others, making it impossible for us to obtain uniform data results for analysis. On the other hand, if analyzed independently according to the type of data, the number of studies is too small, which may skew the results. Therefore, we have not discussed the influence of age on LDF recurrence, which will be supplemented in the future.

Moreover, there are various outcome measures and a lack of uniformity, which may also bias the results. In addition, all of the included studies were retrospective, without randomized controlled trials or prospective studies, with low credibility. Meanwhile, different surgical evaluation schemes and unequal follow-up time will also impact the final conclusions. In order to obtain more credible results, more high-quality, large sample, prospective, randomized controlled clinical trials are needed to further confirm or correct the conclusions.

CONCLUSION

By meta-analysis, it can be seen that gender and LDH type and location have no obvious correlation with post-PTED LDH recurrence in patients. In contrast, the Pfirrmann grade of the affected intervertebral disc, complete NP removal during surgery, and Modic changes are the relevant factors for LDH recurrence after PTED treatment, suggesting that attention should be paid to the specific situation of these indicators in patients in future clinical treatment of LDH.

CONFLICTS OF INTEREST

The authors report no conflict of interest

AVAILABILITY OF DATA AND MATERIALS

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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Not applicable

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