Systematic Review

Comparison of Different Operative Approaches for Lumbar Disc Herniation: A Network Meta-Analysis and Systematic Review

Fei-Long Wei, MD¹, Cheng-Pei Zhou, MD¹, Kai-Long Zhu, MD¹, Ming-Rui Du, MD^{1,2}, Ya Liu, BN³, Wei Heng, MD¹, Huan Wang, MD¹, Xiao-Dong Yan, MD¹, Li-Li Sun, BN⁴, and Ji-Xian Qian, MD¹

From: ¹Department of Orthopedics, Tangdu Hospital, Fourth Military Medical University, Xi'an, China; ²School of Basic Medicine, Fourth Military Medical University, Xi'an, China; ³Department of Outpatient, Xijing Hospital, Fourth Military Medical University, Xi'an, China; ⁴Department of Neurology, Xijing Hospital, Fourth Military Medical University, Xi'an, China

Address Correspondence: Ji-Xian Qian, PhD Department of Orthopaedics, Tangdu Hospital, Fourth Military Medical University 569 Xinsi Road Xi'an, 710038, China E-mail: pasmis2012@163.com

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Free full manuscript: www.painphysicianjournal.com **Background:** New approaches and technologies can be beneficial for patients but also bring corresponding complications. Traditional pairwise meta-analyses cannot be used to comprehensively rank all surgical approaches.

Objectives: The purpose of this systematic review and network meta-analysis (NMA) was to compare the outcomes of different surgical approaches for lumbar disc herniation (LDH).

Study Design: NMA of randomized controlled trials (RCTs) for multiple treatment comparisons of LDH.

Methods: The PubMed, Embase, MEDLINE, Ovid, and Cochrane Library databases were searched for RCTs comparing different surgical approaches for patients with LDH from inception to February 10, 2020. The Markov chain Monte Carlo methods were used to perform a hierarchical Bayesian NMA in WinBUGS version 1.4.3 using a random effects consistency model. The primary outcomes were disability and pain intensity. The secondary outcomes were complications and reoperation. The PROSPERO number was CRD42020179406.

Results: A total of 22 trials including 2529 patients and all 5 different approaches (open discectomy or microdiscectomy [OD/MD], microendoscopic discectomy [MED], percutaneous endoscopic discectomy [PED], percutaneous discectomy [PD], and tubular discectomy [TD]) were retrospectively retrieved. PED had the best efficacy in improving patients' dysfunction with no statistical significance (probability = 50%). PD was significantly worse than OD/MD, MED, and PED in relieving patients' pain (standardized mean differences: 0.87 [0.03, 1.76], 0.94 [0.06, 1.88], and 1.02 [0.13, 1.94], respectively). There was no statistically significant difference between any 2 surgical approaches in dural tear; intraoperative, postoperative, and overall complications; or reoperation rate. PED had the lowest dural tear rate and the lowest intraoperative and overall complication rates (probability = 51%, 67%, and 33%, respectively). TD had the lowest postoperative complication and reoperation rates (probability = 35% and 39%, respectively).

Limitations: The limitations of this NMA include the inconsistent follow-up times, the criteria for complications, and the reasons for reoperation.

Conclusions: Compared with other approaches used to treat LDH, PED had the best safety and efficacy in general, and TD had the lowest reoperation rate. Finally, we recommended PED for LDH.

Key words: Lumbar disc herniation, network meta-analysis, minimally invasive surgery, surgical approaches, efficacy, safety

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umbar disc herniation (LDH) usually manifests as sciatica with low back pain (LBP), which is one of the health problems that affect quality of life, and the medical burden is heavy (1-3). The incidence of LDH is 1% to 3%, which is the main complaint requiring spinal surgery (4). This poses a great challenge to the health systems of both developed and developing countries. When systematic conservative treatment fails, surgical intervention should be considered (5,6). However, surgical intervention is considered to be more effective in providing rapid pain relief for patients with indications for surgery (7,8). This is supported by the results of the Spine Patient Outcomes Research Trial (SPORT). The results revealed that surgical intervention is associated with greater reduction in pain, improvement in function, and higher satisfaction in patients with LDH than those who were managed nonoperatively (9-12). The surgical interventions for LDH include open discectomy or microdiscectomy (OD/MD), microendoscopic (MED), percutaneous discectomy endoscopic discectomy (PED), percutaneous discectomy (PD), and tubular discectomy (TD) according to the surgical approaches (13,14).

In 1934, Mixter and Barr (15) described the first successful OD. With the wide application of surgical microscopy, MD performed under a microscope was introduced (16,17). OD/MD is the standard procedure for patients with LDH (18). Since Smith and Foley first proposed MED in 1997, this classic operation has achieved stable and satisfactory clinical results (19-21). However, it is inevitable that this approach destroys the spine tension band, which may lead to postoperative lumbar instability and LBP. The development of endoscope technology makes it possible to perform discectomy under direct vision and local anesthesia, which has gained more interest. PED causes minimal damage to muscles and soft tissues and has good visualization (22,23). PD is the use of laser energy to vaporize the nucleus pulposus through the percutaneous route (23,24). TD allows surgeons to work with 2 hands through a small diameter; this approach was proposed in 1997 (25).

New approaches and technologies can be beneficial for patients, but also bring corresponding complications. Some studies currently compared the efficacies and safeties of the 2 approaches, but there is no comprehensive study on the efficacies and safeties of all approaches (13,16,26-31). Although there has been a previous study comparing different surgical approaches (13), the traditional pairwise meta-analysis failed to comprehensively rank all surgical approaches. Therefore we conducted this hierarchical Bayesian multitreatment network meta-analysis (NMA) to compare the surgical efficacy and complications of different approaches to aid treatment decisions. These results will be helpful in selecting the most suitable surgery for patients.

METHODS

Search Strategy and Selection Criteria

The PubMed, Embase, MEDLINE, Ovid, and Cochrane Library electronic databases and major scientific websites were searched in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, the PRISMA NMA extension statement, and the Cochrane Collaboration recommendations to identify all relevant studies published prior to February 10, 2020 (32-35). The search terms and combinations used in the search strategy included lumbar disc herniation (LDH), intervertebral disc, discectomy, and randomized controlled trial (RCT). No language was restricted. The search details are shown in Supplementary Table S1. After preliminarily screening titles or abstracts, 2 independent reviewers evaluated the full texts and reference lists of relevant publications for final inclusion. The PROSPERO number was CRD42020179406.

Inclusion Criteria

Inclusion criteria included (1) study design: RCT; (2) patients with LDH who have indications for surgery; (3) interventions and comparisons: therapy that included 2 of the 5 approaches; and (4) outcomes: primary outcomes including disability (Oswestry Disability Index [ODI] scores) and pain intensity (Visual Analog Scale), second outcomes including complication and reoperation.

Exclusion Criteria

Exclusion criteria included (1) letters, case series, review, retrospective study, and single-arm prospective cohorts; and (2) patient with unexplained LBP.

Study Selection

All the titles and abstracts in the initial online search were reviewed independently by 2 authors, and studies that were not related to the subject were excluded. In the study selection process, differences between reviewers were resolved by consensus or with the help of a third-party reviewer.

Data Extraction and Assessment for Risk of Bias

Two reviewers used standardized forms for data extraction to report the most relevant details. The accuracy of the extracted data was checked by a third reviewer. We contacted corresponding authors to obtain missing data. The extracted data included study time, study design, number of patients, inclusion and exclusion criteria, mean follow-up time, age, gender, interventions, and outcomes (disability, pain, number of complications, and reoperations). The risk of bias of individual studies was assessed independently by the same reviewers with the Cochrane risk of bias method (36).

Data Syntheses and Statistical Analysis

Odds ratios (ORs)were estimated for dichotomous outcomes, and standardized mean differences (SMD) were estimated for continuous outcomes. Because of the heterogeneity between studies, a random effects model was used for NMA. First, pairwise meta-analyses were performed by synthesizing studies that compared the same surgery with a random effects model to assess the effects of different approaches (37,38). Review Manager version 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used to conduct this analysis. Forest plots and the I2 statistic were used to investigate heterogeneity. Heterogeneity between different studies were evaluated by χ^2 and I², and P < 0.10 was considered statistically significant. I² values of < 25%, 25% to 75%, and > 75% represented mild, moderate, and severe heterogeneity, respectively (39).

The network geometry of NMA was performed using statistical analysis software Stata version 14.0 (StataCorp LLC, College Station, TX). The Markov chain Monte Carlo methods were used to perform a hierarchical Bayesian NMA in WinBUGS version 1.4.3 (MRC Biostatistics Unit, Cambridge, United Kingdom) using a random effects consistency model (40-42). The estimated result of each relative treatment effect was a combination of direct evidence between the 2 treatments and indirect evidence from an NMA. We assumed that they were consistent. When there was no direct connection between the 2 treatments, the effect estimate could only come from indirect evidence (41,43). We used the noninformative prior distribution and the overdispersed initial value (with a scaling of 5) in the models of the 2 chains to fit the model, yielding 100,000 iterations (including 50,000 tuning iterations), and the refinement interval of each chain was 10 times. According to ORs and posterior probabilities, we ranked the probability of each treatment being the safest, followed by the second, third, and so forth.

Inconsistency was evaluated by comparing statistics for the deviance information criteria in fitted consistency and inconsistency models and by node-split; P < 0.05suggested significant inconsistency (41,44). In addition, pairwise meta-analysis was conducted in a frequentist framework by using Review Manager to provide direct estimates (ORs, SMD, and 95% confidence intervals) (39). The random effects model was used if significant heterogeneity existed, and otherwise, we used the fixed effects model. We compared NMA results (indirect results) with pairwise meta-analysis results (direct results) to explore the causes of inconsistencies.

Patient and Public Involvement

Patients were not involved in the study design or implementation plans. There are no plans to disseminate the results of the research to study patients or the relevant patient groups. There was no assessment of whether the studies included in this review included any patients.

RESULTS

Systematic Review and Qualitative Assessment

The flow chart of the study screening process and the main reasons for elimination are shown in Fig. 1. A total of 22 trials (n = 2,529) and 5 approaches (OD/MD, MED, PED, and TD) were included (Fig. 2) (45-66). Two (9.1%) of the 22 trials were conducted in North and South America, 7 (31.8%) were conducted in Asia, 11 (50%) were conducted in Europe, and 2 (9.1%) were conducted in Africa. The baseline characteristics of the 22 studies are shown in Supplementary Table S2.

The risk of selection bias for each study was described according to the Cochrane Back and Neck Group guidelines (36). Supplementary Fig. S1 shows a summary of the risk of bias assessment. Five studies were evaluated as having a high risk of selection bias (49,54,55,59,60). Regarding blinding methods, 8 studies were considered high risk (54,55,57-60,65,66). No study had been evaluated as having a high risk of reporting bias. One study was assessed as having a high risk of outcome detection bias (63). In addition, no studies had been evaluated as





Fig. 2. Network plots of comparison-based NMA. Each circular node represents a type of intervention. The circle size is proportional to the total number of patients. The width of lines is proportional to the number of studies performing head-to-head comparisons in the same study.

having a high risk of selective reports and other potential biases. All included studies have been published with a low risk of bias (Supplementary Figs. S1 and S2).

ODI

Fourteen studies (63.63%) with 1,805 patients (71.37%) presented usable results for ODI (5 approaches). In the consistency model, the difference in the mean change of ODI between any 2 different approaches was not statistically significant (Fig. 3A). The results obtained in the consistency model were in good agreement with those obtained in the inconsistency model; node-splitting analysis showed no significant inconsistency (all P > 0.05; Supplementary Table S3). The direct and indirect results of different approaches are shown in Fig. 4A. The NMA results were consistent with the corresponding pairwise meta-analysis results in significance and trend. These results indicate that the efficacy profile of each approach was the same.

The ODI change ranking from high to low was as follows: PED (probability = 50%), TD (22%), PD (15%), MED (12%), and OD/MD (2%) (Fig. 3B). The probabilities are detailed in Supplementary Table S4.

Pain

Seventeen studies (77.27%) with 1,979 patients (78.25%) presented usable results for pain (5 approaches). In the consistency model, PD was significantly worse than OD/MD, MED, and PED in relieving patients' pain (SMD: 0.87 [0.03, 1.76], 0.94 [0.06, 1.88], and 1.02 [0.13, 1.94], respectively). The results obtained in the consistency model were in good agreement with those obtained in the inconsistency model; node-splitting analysis showed no significant inconsistency (all P > 0.05; Supplementary Table S5). The direct and indirect results of different approaches are shown in Fig. 4B. The NMA results were consistent with the corresponding pairwise meta-analysis results in significance and trend. These results indicate that the efficacy profile of each approach, except for PD, was the same.

Pain change ranking from high to low was TD (probability = 56%), PED (27%), MED (15%), OD/MD (2%), and PD (1%) (Fig. 3B). The probabilities are detailed in Supplementary Table S6.

Complications

Twenty studies (90.91%) with 2,198 patients (86.91%) presented usable results for complications (5 approaches). Nonsignificant differences in the ORs of dural tears, intraoperative complications, postoperative complications, and overall complications were observed between any 2 surgical approaches in the consistency model (Fig. 5A and 5B). The results obtained in the consistency model were in good agreement with those obtained in the inconsistency model; node-splitting analysis showed no significant inconsistency (all P > 0.05;Supplementary Table S7). The direct and indirect results of different approaches are shown in Fig. 6. The NMA results were consistent with the corresponding pairwise meta-analysis

ODI	Co	mparison	Pain	
OD /MD	-0.07 (-0.38, 0.23)	-0.14 (-0.44, 0.18)	0.87 (0.03, 1.76)	-0.23 (-0.60, 0.20)
0.35 (-2.34, 2.73)	MED	-0.08 (-0.46, 0.33)	0.94 (0.06, 1.88)	-0.16 (-0.62, 0.37)
1.49 (-1.18, 4.01)	1.14 (-2.13, 4.48)	PED	1.02 (0.13, 1.94)	-1.09 (-2.06, -0.17)
-1.00 (-6.81, 4.73)	-1,33 (-7.55, 4.98)	-2,50 (-8.75, 3.88)	PD	-0.08 (-0.53, 0.38)
0.70	0.34 (-3.38, 4.29)	-0.80 (-4.34, 2.85)	1.71 (-4.74, 8.09)	Tubular Diskectom



Fig. 3. (A) Disability (ODI) and pain (Visual Analog Scale) profile. (B) Rank possibility of disability and pain-based NMA in the consistency model. Each cell of the profile contains the pooled mean difference and 95% credibility intervals for disability and pain change; significant results are in bold.

results in significance and trend. These results indicate that the safety profile of each treatment was the same.

Dural tears ranked from low to high were PED (probability = 51%), OD/MD (20%), TD (17%), and MED (12%). Intraoperative complications ranked from low to high were PED (probability = 67%), TD (20%), MED (7%), and OD/MD (5%). Postoperative complications ranked from low to high were TD (35%), PD (33%), PED (24%), MED (5%), and OD/MD (2%) (Fig. 5C). In addition, the overall complication ranking from low to high was PED (33%), TD (31%), PD (30%), MED (4%), and OD/MD (1%) (Fig. 5C). The probabilities are detailed in Supplementary Table S8.

Reoperation

Twenty-one studies (95.45%) with 2,398 patients (94.82%) presented usable results for reoperation (5 approaches). Nonsignificant differences in the ORs of reoperation were observed between any 2 surgical approaches in the consistency model (Fig. 7A). The results obtained in the consistency model were in good agreement with those obtained in the consistency model; node-splitting analysis showed no significant inconsistency (all P > 0.05; Supplementary Table S9). The direct and indirect results of different approaches are shown in Fig. 7B. The NMA results were consistent with the corresponding pairwise meta-analysis results in significance and trend.



MED therapy as control

Direct Network meta-

TD

-0.23 (-060 to 0.20) -4/577 0 1 -1 0.20 (-0.18 to 0.58) 0.31 NA PED 1/153 -0.08(-0.46 to 0.33) --2 -1 4 2

results analysis results --0-Pain

Fig. 4. Forest plots depicting the direct and indirect results of head-to-head comparisons. NA = not applicable. *Values in brackets are 95% CrIs.

NA

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R e o p eration ranking from low to high was TD (probability = 39%), MED (32%), PED (17%), OD/MD (9%), and PD (3%) (Fig. 7C). The probabilities are detailed in Supplementary Table S10.

DISCUSSION

With the extensive application of endoscopic techniques in surgery, an increasing number of surgiapproaches cal are available for patients with LDH. Given that a comprehensive efficacy and safety profile for different surgical approaches still remains to be clearly defined, we conducted this NMA including 22 RCTs. The NMA results were consistent with the corresponding pairwise metaanalysis results in significance and trend.

This NMA consistently suggested that PED had the best

OD /MD	1.05	0.58	1.02	
0.84	(0.49, 2.29) MED	(0.20, 1.78) 0.55 (0.17, 1.84)	(0.27, 3.27) 0.97 (0.19, 3.84)	
1.23 (0.33, 4.37)	1.40 (0.36, 5.96)	PED	(0.19, 5.04) 1.77 (0.29, 8.35)	
0.80 (0.31, 2.48)	0.99 (0.25, 3.64)	0,67 (0.14, 3.61)	Tubular Diskectomy	
Post-c	omplication	Comparis	on	All-complication
OD /MD	1.02 (0.49, 2.15)	0.65 (0.26, 1.62)	0.85 (0.11, 7.05)	0.69 (0.19, 2.08)
0.93 (0.50, 1.84)	MED	0.64 (0.22, 1.84)	0.84 (0.09, 7.79)	0.68 (0.15, 2.51)
1.18 (0.54, 2.67)	1.31 (0.49, 3.30)	PED	1.32 (0.13, 12.99)	1.07 (0.21, 4.35)
1.09 (0.23, 5.65)	1,17 (0.22, 6.87)	0.99 (0.16, 5.69)	PD	0.81 (0.07, 7.96)
1.28 (0.51, 3.65)	1,40 (0.44, 4.58)	1.08 (0.31, 3.99)	1.15 (0.18, 7.92)	Tubular Diskectomy
0.6 Dural tea 0.6 Intra-com Post-ope All compl 41004 0.2	plication ration	*******	it is	

Fig. 5. (A) Dural tear, intraoperative, postoperative, and overall complications profile. (B) Rank possibility of dural tear, intraoperative, postoperative, and overall complications-based NMA in the consistency model. Each cell of the profile contains the pooled mean difference and 95% credibility intervals for disability and pain change; significant results are in bold.

2 3

Tubular Diskectom

efficacy in improving patients' dysfunction. However, Alvi et al (13) found that TD was associated with significantly higher ODI scores at the last follow-up. This

0.6

0.2

0.0

PD

difference may be due to fewer studies being included, thus producing conflicting results. Our result was consistent with most previous meta-analyses (16,28-30,67).

Groups	No of studies	Odd Ratio	Odd Ratio	p value	Hetero	geneity
	/patients	(95%CI)	(95%CI)	,	l² (%)	p (χ ²)
MED vs OD/MD	(as control)					
Dural tear	7/745		1.16 (0.61, 2.22)	0.65	0	0.77
			1.19 (0.54, 2.55)	-	-	-
Intra-operation	8/804		1.12 (0.66, 1.90)	0.68	34	0.15
			1.05 (0.49, 2.29)		-	-
Post-operation	6/644		1.12 (0.69, 1.80)	0.65	12	0.34
			1.08 (0.54, 2.02)		-	
All complication	8/804		1.13 (0.78, 1.64)	0.52	55	0.03
			1.02 (0.49, 2.15)		-	
PED vs OD/MD	(as control)		•			
Dural tear	5/49.4		0.27 (0.03, 2.47)	0.25	0	0.89
Durai tear	5/404		0.81 (0.23, 2.99)	-	-	-
			0.37 (0.15, 0.94)	0.04	5	0.37
Intra-operation	4/484		0.58 (0.20, 1.78)	-		
Beet en en tier			0.80 (0.42, 1.54)	0.51	40	0.14
Post-operation	6/604		0.85 (0.37, 1.86)		-	
	e		0.67 (0.38, 1.17)	0.16	51	0.07
All complication	6/604		0.65 (0.26, 1.62)		-	
PD vs OD/MD (a	s control)					
Post-operation	4/442		0.87 (0.27, 2.79)	0.82	NA	NA
roat-operation	0/112		0.85 (0.37, 1.86)			
All complication	4/442		0.87 (0.27, 2.79)	0.82	NA	NA
All complication	0112		0.65 (0.26, 1.62)	-	-	-
TD vs OD/MD (a	s control)	i i i i				
Dural tear	3/485		1.28 (0.60, 2.72)	0.52	34	0.22
			1.25 (0.40, 3.22)			-
Intra-operation	3/485		1.18 (0.62, 2.25)	0.61	17	0.30
			1.02 (0.27, 3.27)		-	-
Post-operation	3/485		0.95 (0.52, 1.75)	88.0	30	0.24
			0.78 (0.27, 1.96)	-	-	-
All complication	3/485		0.69 (0.19, 2.08)	0.00	-	0.00
			0.00 (0.10, 2.00)			
PED vs MED (as	control)					
Dural tear	1/152		0.91 (0.06, 14.84)	0.95	NA	NA
Durai tear	1/155		0.71 (0.17, 2.75)		-	
			0.79 (0.29, 2.17)	0.65	NA	NA
Intra-operation	1/153		0.55 (0.17, 1.84)	-	-	-
Post operation			0.91 (0.18, 4.65)	0.91	NA	NA
Post-operation	1/153		0.77 (0.30, 2.03)		-	-
All compliantia	1/153		0.81 (0.33, 1.97)	0.64	NA	NA
All complication	1/153		0.64 (0.22, 1.84)		-	
Direct Network	meta-					
results analysis r	esults					
• •	Complica	ation				
Fig. 6. Forest plo not applicable. *	ts depicting th Values in bro	he direct and indirect ackets are 95% CrIs.	t results of head-	to-head com	ıparison	s. NA =

PD was significantly worse than OD/MD, MED, and PED in relieving patients' pain. The result was consistent with a previous pairwise meta-analysis (13,69). Nonsignificant differences in the ORs of dural tears, intraoperative complications, postoperative complications, and overall complications were observed between any 2 surgical interventions. MED had a higher incidence of dural tears, and OD/MD had a higher incidence of overall complications. Alvi et al (13) found that TD was associated with a significantly higher rate of overall complications and dural tears. They came to this conclusion because retrospective results were included (46), and only RCTs were included in ours. The NMA results were consistent with the corresponding pairwise meta-analysis results in significance and trend. In addition, the difference in reoperation between any 2 different approaches was not statistically significant. A previous study suggested that the reoperation rate of OD/MD was lower than that of minimally invasive surgery (13). The reason for this difference was that we included the latest RCT (50), and the data we extracted from the literature were different (13,53). The complication and reoperation rates of these NMA results were consistent with most previous studies (13, 16, 26, 27, 29-31, 67, 69-71).

Limitations

Although high-quality RCTs were included in our study to evaluate different surgical approaches, there were limitations to this study. First, studies with varied follow-up were included, which affected the consistency of the results. Second, in previous RCTs, it remains an unresolved issue whether the reoperation was because of the recurrence of the surgical segment or the other segments. Therefore we cannot conclude that the varied reoperation rate was caused by surgical interventions. In addition, the sample size of many trials was small (48,56,62), leading to an unconvincing conclusion. The criteria for complications were different, which led to heterogeneity. Therefore there is an urgent need to formulate clinical trial standards so that different studies will not have heterogeneity when synthesized.

CONCLUSIONS

As a new mature surgical approach, PED has excellent safety and efficacy, therefore we recommend this surgery for LDH when conditions permit.

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Fig. 7. (A) Reoperation profile. (B) Forest plots depicting the direct and indirect results of head-to-head comparisons. (C) Rank possibility of reoperation-based NMA in the consistency model. Each cell of the profile contains the pooled mean difference and 95% credibility intervals for disability and pain change; significant results are in bold. NA = not applicable. *Values in brackets are 95% CrIs.

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				Num-			Follow	No	. of Compli	cations	No. of
Number	Studies	Study Country	Surgery Type	ber of Partici- pants	Age (Mean±SD)	Gender (M/F)	up (m)	dural tear	intra- operation	post- operation	Reoper- ations
1	Bhavuk Garg	RCT	MED	55	37 ±8	39/19	12	5	5	7	1
1	2011[7]	India	OD/MD	57	38 ±6	44/13	12	5	5	10	0
	Evgenii	DOT	OD/MD	48	39.5 (37-49)	27/21		NA	NA	NA	NA
2	Belykh	Russia	TD	39	39 (36-48)	27/12	12	NA	NA	NA	NA
	2016[2]		PELD	44	41 (32-49)	28/16		NA	NA	NA	NA
3	Frank U. Hermantin	RCT	OD/MD	30	40 (18-67)	17/17	31	1	1	1	1
5	1999[9]	USA	PELD	30	39 (15-66)	22/8	32	0	0	0	0
4	Mayer H. M.	RCT	PELD	20	39.8 ±10.4	12/8	24	0	NA	NA	3
4	1993[14]	Germany	OD/MD	20	42.7 ±10	14/6	24	0	NA	NA	0
5	Jörg Franke	RCT	OD/MD	48	44 (21-72)	30/20	12	3	3	5	5
5	2009[6]	Germany	TD	52	44 (21-72)	30/21	12	2	2	2	2
	J. N. Alaistair	RCT	PELD	70	42 ±9	30/40	24	NA	2	4	5
6	Gibson 2017[8]	UK	OD/MD	70	39 ±9	40/30	24	NA	0	1	2
7	Lei Pan	RCT	PELD	10	NA	NA	6	NA	NA	1	0
<i>`</i>	2014[13]	China	OD/MD	10	NA	NA	6	NA	NA	0	0
	Marco Teli	PCT	MED	70	39 ± 12	45/25	26 ± 2	6	8	11	8
8	2010[21]	RCT Italy	MD	72	40 ± 12	48/24	26 ± 3	2	2	8	4
			OD	70	39 ± 12	46/24	26 ± 2	2	2	5	3
0	Mark P. Arts	RCT the Noth	TD	166	41.6 ± 9.8	84/82	24	14	20	19	23
9	2011[1]	erlands	OD/MD	159	41.3 ± 11.7	88/71	24	7	13	14	14
	Mohamed	RCT	MED	95	30.2	58/42	104.2	6	6	13	6
10	Hussein 2014[12]	Egypt	OD/MD	90	31.5	54/46	101.3	5	5	8	9
	Mohamed	RCT	MED	37	30.5	20/17	25.5	1	1	3	3
11	Hussein 2016[11]	Egypt	OD/MD	36	31.9	21/15	26.2	0	2	7	7
	Orlando	RCT	OD/MD	19	46.0 ±12.4	13/6	24	0	0	1	1
12	Righesso 2007[15]	Brazil	MED	21	42.0 ± 10.7	10/11	24	1	1	2	1
	Patrick A	RCT	PLDD	55	43,2 ± 11,8	35/19	24	NA	NA	6	29
13	Brouwer 2017[3]	the Neth- erlands	MD/OD	57	43,7 ± 9,7	42/24	24	NA	NA	7	12
	Saeid	RCT	PLDD	100	39.7 ± 9.2	82/18	12	NA	NA	NA	7
14	Abrishamkar 2015[20]	Iran	OD/MD	100	40.2 ± 8.8	78/22	12	NA	NA	NA	8
	Sebastian	RCT	PELD	91	NA	NA	24	0	3	6	6
15	Ruetten 2008[17]	Germany	OD/MD	87	NA	NA	24	0	12	5	5
	Sebastian	RCT	MED	50	39 (23-59)		24	1	3	NA	5
16	Ruetten 2009[18]	Germany	OD/MD	50	39 (23-60)	56/44	24	3	10	NA	5
	Tycho	RCT	MED	30	40 (17-59)	18/12	12	NA	3	NA	1
17	Tullberg 1993[22]	Sweden	OD/MD	30	38 (18-64)	21/9	12	NA	1	NA	1

Supplementary Table S2. Basic data.

				Num-			Follow-	No	. of Compli	cations	No. of
Number	Studies	Study Country	Surgery Type	ber of Partici- pants	Age (Mean±SD)	Gender (M/F)	Gender (M/F) up (m)		intra- operation	post- operation	Reoper- ations
	Tsung-Jen	RCT	MED	10	39.2 ± 10.8	6/4	18.9	1	1	0	0
18	Huang 2005[10]	China	OD/MD	12	39.8 ± 11.0	9/3	18.9	0	0	1	0
Yu-Mi Ryang	RCT	OD/MD	30	39.1 ±11.3	19/11	26	2	2	4	4	
19	2008[19]	Germany	TD	30	38.2 ± 9.3	13/17	26	0	0	2	2
20	Zhimin Pan	RCT	PELD	48	39.5 (22-58)	26/22	16.7	0	0	3	0
20	2016[16]	China	OD/MD	58	42.8 (27-61)	31/27	17.3	2	2	10	0
21	Zihao Chen	RCT	PELD	80	40.2 ± 11.4	52/28	12	1	8	3	5
21 2018[4]	China	MED	73	40.7 ± 11.1	37/36	12	1	9	3	3	
Zhen-mei	RCT	PELD	50	41.32 ±11.53	30/20	12	0	NA	1	0	
22	Ding 2017[5]	China	OD/MD	50	43.90 ±11.8	27/23	12	0	NA	3	0

Supplementary Table S2. Basic data (continued).

Supplementary Table S3. Node-splitting analyses of disability.

Comparison	Direct Effect	Indirect Effect	Overall	P-Value
OD/MD , MED	0.09 (-2.53, 3.04)	-2.61 (-9.14, 3.98)	-0.35 (-2.73, 2.34)	0.41
OD/MD, PED	-1.85 (-4.81, 1.15)	0.81 (-5.59, 7.37)	-1.49 (-4.01, 1.18)	0.41
MED, PED	0.72 (-5.21, 6.54)	-2.02 (-6.19, 1.87)	-1.14 (-4.48, 2.13)	0.40
PED, Tubular Diskectomy	2.83 (-3.03, 8.90)	0.41 (-4.26, 5.18)	0.80 (-2.85, 4.34)	0.48

Supp	lementary	7 Table S4.	Rank	possibility o	of	disability	y.

Intervention	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5
OD/MD	0.14	0.41	0.32	0.11	0.02
MED	0.15	0.24	0.25	0.24	0.12
PD	0.57	0.10	0.09	0.09	0.15
PED	0.03	0.06	0.13	0.29	0.50
Tubular Diskectomy	0.11	0.18	0.22	0.28	0.22

Supplementary Table S5. No	ode-splitting	analyses of	f pain.
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Comparison	Direct Effect	Indirect Effect	Overall	<i>P</i> -Value
OD/MD, MED	-0.02 (-0.35, 0.30)	-0.39 (-1.22, 0.45)	-0.07 (-0.38, 0.23)	0.39
OD/MD, PED	-0.22 (-0.55, 0.16)	0.18 (-0.71, 1.07)	-0.14 (-0.44, 0.18)	0.39
MED, PED	0.20 (-0.56, 0.98)	-0.17 (-0.62, 0.31)	-0.08 (-0.46, 0.33)	0.39
PED, Tubular Diskectomy	0.04 (-0.65, 0.77)	0.12 (-0.49, 0.72)	-0.08 (-0.53, 0.38)	0.86

Supplementary Table S6. Rank possibility of pain.

Intervention	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5
OD/MD	0.01	0.52	0.35	0.10	0.02
MED	0.01	0.26	0.34	0.25	0.15
PD	0.97	0.01	0.01	0.01	0.01
PED	0.00	0.11	0.20	0.41	0.27
Tubular Diskectomy	0.01	0.09	0.11	0.23	0.56

Dural Tear				
Comparison	Direct Effect	Indirect Effect	Overall	P Value
OD/MD, MED	0.21 (-0.58, 0.99)	-0.03 (-4.23, 3.79)	0.17 (-0.62, 0.94)	0.85
OD/MD, PED	-0.13 (-1.48, 1.11)	0.09 (-3.65, 3.53)	-0.21 (-1.48, 1.09)	0.89
MED, PED	-0.11 (-4.01, 3.46)	-0.35 (-2.00, 1.23)	-0.34 (-1.78, 1.01)	0.87

Supplementary Table S7. Node-splitting analyses of complication.

Post-complication							
Comparison	Direct Effect	Indirect Effect	Overall	P Value			
OD/MD, MED	0.12 (-0.66, 0.82)	-0.17 (-2.44, 2.17)	0.07 (-0.61, 0.70)	0.82			
OD/MD, PED	-0.19 (-1.10, 0.70)	0.01 (-2.25, 2.25)	-0.17 (-0.98, 0.62)	0.86			
MED, PED	-0.10 (-2.17, 2.03)	-0.31 (-1.42, 0.86)	-0.27 (-1.19, 0.71)	0.88			

Intra-Complication							
Comparison	Direct Indirect Effect Effect		Overall	P Value			
OD/MD, MED	0.12 (-0.72, 0.97)	-0.48 (-2.80, 1.97)	0.05 (-0.70, 0.83)	0.61			
OD/MD, PED	-0.72 (-2.04, 0.69)	-0.13 (-2.24, 1.99)	-0.55 (-1.62, 0.57)	0.61			
MED, PED	-0.25 (-2.18, 1.66)	-0.86 (-2.38, 0.80)	-0.60 (-1.75, 0.61)	0.58			

Overall complication							
Comparison	Direct Effect	Direct Indirect Effect Effect		P Value			
OD/MD, MED	0.05 (-0.78, 0.87)	-0.28 (-2.58, 2.06)	0.02 (-0.71, 0.76)	0.77			
OD/MD, PED	-0.50 (-1.56, 0.57)	-0.15 (-2.38, 2.07)	-0.43 (-1.33, 0.48)	0.76			
MED, PED	-0.21 (-2.29, 1.85)	-0.54 (-1.88, 0.81)	-0.45 (-1.53, 0.61)	0.76			

Supplementary Table S8. Rank possibility of complication.

Dural tear							
Intervention Rank 1 Rank 2 Rank 3 Rank							
OD/MD	0.07	0.31	0.42	0.20			
MED	0.36	0.32	0.21	0.12			
PED	0.16	0.17	0.15	0.51			
Tubular Diskectomy	0.42	0.20	0.21	0.17			

Post-complication						
Intervention	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	
OD/MD	0.10	0.34	0.38	0.15	0.02	
MED	0.29	0.28	0.19	0.18	0.05	
PED	0.15	0.14	0.17	0.29	0.24	
PD	0.31	0.10	0.12	0.14	0.33	
Tubular Diskectomy	0.14	0.14	0.14	0.23	0.35	

Intra-Complication							
Intervention Rank 1 Rank 2 Rank 3 Rank							
OD/MD	0.19	0.45	0.31	0.05			
MED	0.35	0.30	0.28	0.07			
PED	0.07	0.08	0.18	0.67			
Tubular Diskectomy	0.39	0.17	0.23	0.20			

Overall complication						
Intervention	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5	
OD/MD	0.18	0.40	0.31	0.10	0.01	
MED	0.28	0.29	0.23	0.15	0.04	
PED	0.06	0.09	0.18	0.33	0.33	
PD	0.36	0.09	0.10	0.15	0.30	
Tubular Diskectomy	0.12	0.13	0.17	0.27	0.31	

Comparison Direct Effect Indirect Effect Overall P Value OD/MD, MED -0.09 (-0.89, 0.69) -0.50 (-2.84, 1.76) -0.11 (-0.85, 0.63) 0.73 OD/MD, PELD 0.02 (-0.93, 1.00) 0.42 (-1.73, 2.72) 0.09 (-0.77, 0.97) 0.73 MED, PELD 0.53 (-1.51, 2.62) 0.08 (-1.17, 1.34) 0.20 (-0.80, 1.27) 0.72

Supplementary Table S9. Node-splitting analyses of reoperation.

Supplementary Table S10. Rank possibility of reoperation.

Intervention	Rank 1	Rank 2	Rank 3	Rank 4	Rank 5
OD/MD	0.02	0.18	0.39	0.32	0.09
MED	0.04	0.16	0.21	0.27	0.32
PED	0.13	0.32	0.19	0.19	0.17
PD	0.75	0.13	0.05	0.04	0.03
Tubular Diskectomy	0.07	0.21	0.16	0.18	0.39