



## OPEN Comparison of the efficacy of microendoscopic discectomy and percutaneous endoscopic lumbar discectomy for treating adolescent lumbar disc herniation

Lu Mao<sup>1</sup>, Zicong Shen<sup>1</sup>✉, Weiye Zhu<sup>1</sup>, Kun Wang<sup>1</sup>, Pan Fan<sup>1</sup>, Xiaotao Wu<sup>1</sup>, Lijun Li<sup>2</sup>✉ & Guanyi Liu<sup>3</sup>✉

Microendoscopic discectomy (MED) has long been employed as the standard operation for adolescent lumbar disc herniation (ALDH). However, due to iatrogenic injury, it has been suspected to cause adverse effects. Alternatively, percutaneous endoscopic lumbar discectomy (PELD) is considered as effective as MED. Few studies have compared MED and PELD in the treatment of ALDH. The purpose of this study was to compare the possible differences in young patients who underwent MED or PELD. From January 2011 to January 2021, 49 consecutive patients were treated with MED (17 patients) or PELD (32 patients) at the authors institution. Numeric Rating Scales (NRS) scores, Oswestry Disability Index (ODI) and modified MacNab criteria demonstrated significant improvement in both early and late follow-up evaluations ( $P < 0.01$ ). PELD group resulted in shorter operative times and lower re-operation and complication rate. The PELD group exhibited shorter incision length, length of hospital stay and less intraoperative blood loss than the MED group. Both PELD and MED have demonstrated great efficacy in managing symptomatic ALDH. PELD appears to offer superior control over surgical trauma and promotes rapid recovery compared to MED.

**Keywords** Lumbar, Disc herniation, Endoscopic, Discectomy, Adolescent

Conflicting evidence and practice variation are present in the surgical treatment of adolescent lumbar disc herniation (ALDH)<sup>1,2</sup>. Microendoscopic discectomy (MED) or percutaneous endoscopic lumbar discectomy (PELD) has long been considered the important surgical options for adolescent lumbar disc herniation owing to their positive outcomes. However, a comparison of the surgical results of MED and PELD in adolescents remains unclear<sup>3</sup>.

Lumbar disc herniation (LDH) in adolescents is a relatively uncommon condition that can significantly impact quality of life, accounting for only 0.8–2.8% of all LDH surgeries<sup>1–4</sup>. But for those in whom conservative management fail to improve symptoms or when compressive spinal emergencies are present, surgical intervention becomes warranted<sup>4,5</sup>. While the clinical outcomes of MED or PELD surgery for lumbar disc herniation have been previously reported<sup>6–8</sup>, there is a lack of comparative studies examining the outcomes of MED and PELD during adolescence. Furthermore, most of these reports are from single institutions or surgeons, indicating a need to establish the superiority of PELD compared to the existing standard procedure, MED, in the management of ALDH. Younger patients typically have higher activity levels, different expectations, and longer life expectancy. Another concern with surgery in adolescents is the likelihood of revision surgery due to growth and a continuously changing skeletal structure.

Our team has previously described the MED technique for lumbar disc herniation in 2006<sup>2,8,9</sup> and presented a case series of 16 patients employing one-stage PELD for symptomatic double-level contiguous lumbar disc herniation in 2021<sup>10</sup>. Subsequently, in 2022, we expanded research by reporting 44 adolescents with lumbar disc herniation who underwent PELD involving the high iliac crest<sup>11</sup>. Recently, we focusing on the clinical

<sup>1</sup>Department of Spine Surgery, Medical College, Zhongda Hospital, Southeast University, No. 87, Dingjiaqiao Road, Nanjing, Jiangsu, China. <sup>2</sup>Department of Orthopedics, Shanxi Provincial People's Hospital, Taiyuan, Shanxi, China. <sup>3</sup>Department of Spine Surgery, Ningbo No.6 Hospital, Ningbo, China. ✉email: 827672895@qq.com; llj\_11070715@sina.com; 18906628697@163.com

characteristics and outcomes of the repeat surgical interventions for patients aged < 21 years who had undergone primary PELD<sup>12,13</sup>. Building on our previous studies<sup>2,8–13</sup>, we conducted a comprehensive comparative analysis of MED and PELD.

Comparative analyses of MED and PELD for LDH management have been extensively documented in adult populations. However, systematic analysis of existing literature reveals a paucity of rigorous investigations focusing on adolescent patients with LDH—a clinically distinct subgroup characterized by unique spinal developmental considerations. The present study specifically investigates this underrepresented clinical population through comprehensive evaluation of perioperative outcomes and long-term functional recovery metrics. The resultant data provide evidence-based insights to optimize surgical decision-making for this specialized patient demographic.

At present, there is a lack of corroborative evidence evaluating the safety and efficacy of MED or PELD in adolescent populations. Therefore, a comparison of the outcomes that are associated with each of these surgical methods is warranted. This study aimed to evaluate and compare the efficacy of both MED and PELD in the treatment of adolescent lumbar disc herniation.

## Materials and methods

### Patient population

This study was a retrospective comparative analysis of MED and PELD in the treatment of symptomatic lumbar disc herniation in adolescents. Ethical approval was granted by the Medical Ethical Committee (No.2020ZDSYLL080-P01). Adolescents who had undergone primary MED or PELD surgery for lumbar disc herniation below 21 years of age between January 2011 to January 2021 were identified.

Primary reasons for surgery were mainly uncontrolled back and radiating leg pain. The detailed inclusion criteria were as follows: (1) age at the time of primary surgery under 21 years old; (2) sciatic pain and signs consistent with the imaging findings; (3) failure of conservative treatment for at least 4–6 weeks. Patients with spinal instability, previous surgery involving the spine, inadequate medical or imaging records, or loss of follow-up were excluded.

Consequently, we enrolled 49 patients who underwent surgical treatment and completed follow-up. The study population was divided into two groups based on the surgical procedure performed: the MED group and the PELD group. The final surgical plan was established through collaborative discussions between the physician and the patient. The patients underwent an outpatient clinical study by an independent observer (Zicong Shen and Weiye Zhu), who was not involved in the primary surgical treatment of the patients. A senior doctor (Xiaotao Wu) would give objective advises when any inconsistencies exist. All patients were followed up using a patient-based outcome questionnaire, either at an outpatient clinic or through a telephone assessment and WeChat. The baseline characteristics of included subjects are shown in Table 1.

### Operative procedures of PELD and MED

All operations were performed by or under the supervision of the senior author, Xiaotao Wu, and were based on methods previously reported<sup>9–12</sup>. In this study, both PELD and MED were inpatient procedures and were performed under local anesthesia, epidural anesthesia, or general anesthesia.

Parameter	MED	PELD	P value
Number	17	32	
Age	18.29 ± 2.76	18.75 ± 2.02	0.68
Sex			0.75
Male	12	24	
Female	5	8	
History of trauma	3/17	10/32	0.32
Smoking rate	2/17	4/32	0.96
Symptoms			0.24
Low back pain	15	31	
Leg pain	17	32	
Signs			0.73
Lasegue test (+)	13	26	
Enhanced Lasegue test (+)	16	30	
Surgery segment			0.65
L4/L5	8	16	
L5/S1	7	15	
L4/L5 and L5/S1	2	1	

**Table 1.** Comparison of demographic and baseline characteristics between the two cohorts. *MED* microendoscopic discectomy, *PELD* percutaneous endoscopic lumbar discectomy.

## MED

Our team described the MED technique for lumbar disc herniation<sup>2,9</sup>. The patient was placed in the prone position with the abdomen free. After confirming the target segment using fluoroscopy, a 2.5 cm longitudinal incision was made from 1.5 to 2.0 cm of the posterior midline. Next, the rigid endoscope was inserted into the tubular retractor. Then, flavectomy, laminotomy, nerve root retraction, and discectomy were performed until the nerve root was decompressed completely. Following the loose and protruded disc tissue was removed, the intervertebral space and the wound were irrigated with saline solution with higher pressure. Finally, the muscle, subcutaneous, and dermal tissues were sutured.

## PELD

PELD procedures were performed as we described previously<sup>8,10–12</sup>. The patients were positioned in a modified knee-chest position. After routine disinfection and infiltrating with 35–45 ml of 0.5–0.8% lidocaine, a long 18-gauge spinal needle was inserted from the entry point toward the mid-line under intermittent fluoroscopic guidance. Individualized targeted foraminoplasty was performed using a 7.5-mm diameter trephine. An endoscopic rongeur was used to remove the protruded disc tissue. The decompression was performed during constant irrigation and concluded when the spinal nerves were visibly decompressed. The surgical sheath was removed, and the wound was closed.

## Clinical outcome measurements

The primary outcomes were clinical outcomes evaluated by the modified Macnab criteria, Oswestry Disability Index (ODI), and the Numeric Rating Scales (NRS) scores. Secondary outcomes included incision length, length of hospital stay, intraoperative blood loss volume, the rates of complications and reoperations between the MED group and the PELD group.

## Statistical analysis

All statistical analyses were performed using R (version 4.3.1 <https://www.R-project.org/>). Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were compared using the Mann–Whitney U test. A *p*-value of less than 0.05 was considered statistically significant. Data normality was assessed using the Shapiro–Wilk test. Given the non-normal distribution of some continuous variables, we used the Mann–Whitney U test to compare differences between the two groups.

## Ethics approval and consent to participate

The study approval (No. 2020ZDSYLL080-P011) was given by the ethics committee of Zhongda Hospital, Southeast University, which waived the requirement for informed consent due to the retrospective design of the study and the anonymized nature of the data used. All methods were performed in accordance with the relevant guidelines and regulations.

## Results

There were no significant differences between the MED and PELD groups in terms of baseline demographics or clinical characteristics, which are summarized in Table 1. Forty-nine individuals participated in this study (17 with MED and 32 with PELD). The mean age at surgery was  $18.6 \pm 2.3$  years, with a range from 11 to 21 years. The mean follow-up duration was  $7.98 \pm 3.03$  years, ranging from 2.2 to 11.8 years. Among these patients, there were 36 males and 13 females, 24 cases affected the L4–L5 level, 22 cases affected the L5–S1 level and 3 affected both.

## Clinical outcomes

### *The numeric rating scale (NRS) scores*

The NRS scores improved postoperatively and were maintained thereafter in both the MED group and the PELD group ( $P < 0.01$ ). Before surgery, the NRS scores for back and leg pain were  $4.97 \pm 2.36$  and  $7.31 \pm 1.26$  in the PELD group,  $5.00 \pm 2.96$  and  $6.71 \pm 1.79$  in the MED group respectively. The day after surgery, the NRS scores for back pain and leg pain were respectively  $1.13 \pm 1.36$  and  $0.94 \pm 0.76$  in the PELD group,  $1.82 \pm 1.13$  and  $0.82 \pm 1.19$  in the MED group. Three months after surgery, the NRS scores for back and leg pain were,  $0.94 \pm 0.84$  and  $0.56 \pm 0.62$  in the PELD group,  $1.65 \pm 1.17$  and  $0.65 \pm 0.70$  in the MED group respectively. At final follow-up, the NRS scores for back and leg pain were  $2.03 \pm 1.47$  and  $1.91 \pm 1.35$  in the PELD group,  $2.00 \pm 1.41$  and  $2.00 \pm 1.32$  in the MED group, respectively. Difference significant ( $P < 0.01$ ) before and after operation NRS back / leg and ODI scores at each time point. No significant difference existed after operation at every follow-up (Table 2).

### *Oswestry disability index (ODI)*

The ODI scores decreased significantly following surgery in both groups and continued to decline throughout the follow-up period ( $P < 0.05$ ). Before surgery, the ODI scores were  $44.06 \pm 12.66$  in the PELD group and  $40.71 \pm 12.53$  in the MED group respectively. The day after surgery, the ODI scores were  $7.81 \pm 5.55$  in the PELD group and  $10.12 \pm 4.66$  in the MED group respectively. Three months after surgery, the ODI scores were  $4.63 \pm 3.95$  in the PELD group and  $6.94 \pm 4.25$  in the MED group respectively. At the final follow-up, the ODI scores were  $7.63 \pm 7.14$  in the PELD group and  $6.47 \pm 5.64$  in the MED group respectively (Table 2).

## The modified Macnab criteria

For the modified Macnab criteria at the final follow-up, the excellent or good outcome rate was 28/32 (87.5%) in the PELD group and 14/17 (82.35%) in the MED group, respectively. Overall clinical comparison outcomes are summarized in Table 2.

Parameter	MED (N=17)	PELD (N=32)	P value
NRS back			
Preoperative	5.00 ± 2.96	4.97 ± 2.36	0.899
1 day	1.82 ± 1.13 <sup>a</sup>	1.13 ± 1.36 <sup>a</sup>	0.033
3 months	1.65 ± 1.17 <sup>a</sup>	0.94 ± 0.84 <sup>a</sup>	0.027
Final follow-up	2.00 ± 1.41 <sup>a,b</sup>	2.03 ± 1.47 <sup>a,b</sup>	0.013
Mean postoperative	1.82 ± 1.24 <sup>a,b</sup>	1.37 ± 1.22 <sup>a,b</sup>	0.002
NRS leg			
Preoperative	6.71 ± 1.79	7.31 ± 1.26	0.190
1 day	0.82 ± 1.19 <sup>a</sup>	0.94 ± 0.76 <sup>a</sup>	0.008
3 months	0.65 ± 0.70 <sup>a</sup>	0.56 ± 0.62 <sup>a</sup>	0.034
Final follow-up	2.00 ± 1.32 <sup>a,b</sup>	1.91 ± 1.35 <sup>a,b</sup>	0.042
Mean postoperative	1.16 ± 1.07 <sup>a,b</sup>	1.14 ± 0.91 <sup>a,b</sup>	0.031
ODI			
Preoperative	40.71 ± 12.53	44.06 ± 12.66	0.297
1 day	10.12 ± 4.66 <sup>a</sup>	7.81 ± 5.55 <sup>a</sup>	0.023
3 months	6.94 ± 4.25 <sup>a</sup>	4.63 ± 3.95 <sup>a</sup>	0.049
Final follow-up	6.47 ± 5.64 <sup>a,b</sup>	7.63 ± 7.14 <sup>a,b</sup>	0.021
Mean postoperative	7.84 ± 4.85 <sup>a,b</sup>	6.69 ± 5.55 <sup>a,b</sup>	0.024
MacNab evaluation			
Excellence	8	10	
Good	6	18	
Fair	2	3	
Poor	1	1	
Excellence/ good rate	14/17 (82.35%)	28/32 (87.5%)	

**Table 2.** Comparison of change of mean values for patients. *NRS* the numeric rating scales, *ODI* Oswestry disability index, *MED* microendoscopic discectomy, *PELD* percutaneous endoscopic lumbar discectomy. <sup>a</sup>Compared with pre-op  $P < 0.05$ ; <sup>b</sup>compared with 1d post-op, 3 m post-op and final follow-up  $P > 0.05$ .

Parameter	MED (N=17)	PELD (N=32)	P value
Operation time (min)	57.35 ± 25.41	77.94 ± 27.52	0.026 *
The postoperative bed rest duration (day)	15.82 ± 2.97	6.22 ± 2.51	0.035*
Hospital length of stay (day)	6.53 ± 3.18	3.97 ± 1.80	0.001*
Intraoperative blood loss volume (ml)	55.14 ± 4.59	19.14 ± 2.68	0.001*
Incision length (cm)	3.52 ± 1.35	0.72 ± 1.02	0.002*
Rate of conversion to open surgery	0	0	–
Mode of incision exposure	Expansion by diameter of 18 mm tubular retractor	Expansion by diameter of 7.5 mm beveled working cannula	–
The anesthetic method	General anesthesia/epidural anesthesia	Local anaesthesia/Monitored anesthesia care	–

**Table 3.** Comparison of surgical information between the two groups. *MED* microdiscectomy, *PELD* percutaneous endoscopic lumbar discectomy. \*Statistically significant ( $P < 0.05$ ).

#### Secondary outcomes

The mean hospital length of stay was significantly shorter in the PELD group (3.97 ± 1.80 days) than in the MED group (6.53 ± 3.18 days;  $P = 0.001$ ). The postoperative bed rest duration was significantly shorter in the PELD group (6.22 ± 2.51 days) than in the MED group (15.82 ± 2.97;  $P = 0.035$ ). The mean intraoperative blood loss volume was significantly less in the PELD group (19.14 ± 2.68 ml) than in the MED group (55.14 ± 4.59 ml;  $P = 0.001$ ). The incision length was 0.72 ± 1.02 cm in the PELD group and 3.52 ± 1.35 cm in the MED group ( $P = 0.002$ ) (Table 3).

#### Complications and treatments

New disc herniation of adjacent level occurred in 2 patients in the MED group, homo-lateral re-herniation at the same level occurred in 4 patients in the PELD group (4/32, 12.5%) and 2 patients in the MED group (2/17, 11.76%). A third revision operation was required in 3 patients in the MED group (3/17, 17.64%) and 1 patient in the PELD group (1/32, 3.12%). The rate of third re-operation was 3.12% in the PELD group compared with 17.6% in the MED group at the final follow-up. Revision surgeries and their cause are also summarized in Tables 4 and 5.

Parameter	MED (N=17)	PELD (N=32)	P value
Total complications	4 (23.52%)	4 (12.5%)	0.001*
Intraoperative nerve root injury	0	0	–
Dural tear	0	0	–
New disc herniation of adjacent level	2	0	0.001*
Homo-lateral re-herniation at the same level	2	4	0.06
A third operation is required	3/17 (17.64%)	1/32 (3.12%)	0.002*
Residual leg pain or numbness	3/17 (17.64%)	5/32 (15.62%)	0.02*

**Table 4.** Complications between the two groups. *MED* microendoscopic discectomy, *PELD* percutaneous endoscopic lumbar discectomy. \*Statistically significant ( $P < 0.05$ ).

Patients	Sex	Age (year)	First operation mode	Second operation mode	The reason for re-operation	Third surgery mode	The reason for re-operation
1	Female	13	MED (L4-5, R)	MED (L4-5, R)	Homo-lateral re-herniation at the same level	PELD (L4-5, R)	Re-herniation
2	Male	18	MED (L4-5 + L5-S1, L)	MED (L4-5, L)	Homo-lateral re-herniation at the same level	MED (L4-5 + L5-S1, L)	Re-herniation
3	Female	18	PELD (L4-5, L)	PELD (L4-5, R)	Hetero-lateral re-herniation at the same level	TLIF (L3-5)	Re-herniation
4	Female	19	MED (L5-S1, L)	PELD (L4-5, L)	New disc herniation at adjacent level	PELD (L5-S1, L)	Re-herniation

**Table 5.** Comparison of the incidence of tertiary surgical interventions between the two groups. *MED* microendoscopic discectomy, *PELD* percutaneous endoscopic lumbar discectomy.

## Discussion

This study compared MED to PELD for lumbar disc herniation in adolescents, aiming to compare the surgical results and identify which procedure yields better functional outcomes. Symptomatic disc herniation requiring operative treatment in the young patient population is rare. Although the results after disc excision in young people are usually favorable. Whether PELD can achieve comparable clinical outcomes to MED has always been a concern of spine surgeons.

Children experience significant growth and a continuously changing skeletal structure, highlighting the importance of age-appropriate strategies that address the unique needs of adolescents. Theoretically, epiphyseal fusion is a significant event in skeletal development, which indicates that the skeletal growth is largely complete. For the lumbar spine, the closure of the vertebral epiphyseal cartilage with the vertebral body is generally completed at around 21 years. So, the age of 21 years being defined as the upper age limit for adolescent lumbar disc herniation. Adolescents are in a period of growth; their spinal structures are not fully matured and are often more physically active.

Spinal surgery at a young age sparks concern regarding the future prognosis of these patients over several decades. Clinically, conservative management is often the first line of treatment for adolescents with lumbar disc herniation. However, conservative management is not as effective in adolescent populations as in adults, leading to an increased period of disability and delay in returning to normal activities. Adolescent patients who are refractory to conservative treatment for LDH, MED or PELD appear plausible as a therapeutic intervention. When surgery is necessary, the techniques used may differ to minimize impact on the growth spine and to avoid major surgery such as wide laminectomy and fusion surgery.

Previously, our team described the MED technique for lumbar disc herniation in 2006<sup>2,9</sup>. Subsequently, we clinical investigations focused on the application of PELD for the management of lumbar disc herniation in the adolescent population in 2021, 2022, and 2024<sup>8,10–13</sup>. To deepen understanding of the surgical results of MED and PELD in adolescents, we compared the outcomes in patients who underwent either MED or PELD and aimed to identify which procedure yielded better functional outcomes.

To date, limited studies have compared the clinical outcomes of PELD and MED for adolescents. MED was employed as the standard operation for ALDH for a long time<sup>6,7,15</sup>. However, due to iatrogenic injury for soft tissue and bony structures, this option may result in clinically adverse effects. Furthermore, the re-operation rate must be included, the reasonable doubt arising<sup>15</sup>. The incidence of surgery for ALDH in Sweden is estimated to be 1.4% of all spine surgeries, with an approximately 11% risk of re-surgery in adolescence<sup>12–15</sup>. These statistics underscore the importance of longer follow-up periods to delineate the relationships between disc degeneration, symptoms, and the need for additional spine surgery.

Notably, the first documented case of lumbar disc herniation in a teenager was reported by Wahren in 1945, highlighting a rare occurrence of herniated nucleus pulposus in skeletally immature adolescent patients<sup>16</sup>. Furthermore, the first microendoscopic discectomy, a significant advancement in spinal surgery, was performed by Yasargil in 1977<sup>13–17</sup>. Alternatively, more minimally invasive approaches have been introduced as alternatives for symptomatic ALDH. Endoscopic techniques have been widely used for lumbar disc herniation since the first introduction by Ruetten et al.<sup>18</sup>. PELD offers the unique advantage of reducing surgical invasiveness, which is particularly beneficial for the adolescent population still undergoing growth and development. Numerous studies have demonstrated the efficacy of PELD in relieving patient symptoms<sup>10–17</sup>.

However, limited studies have compared the clinical outcomes of PELD and MED for symptomatic ALDH. In our study, we conducted a retrospective evaluation of the outcomes of patients who underwent MED and PELD, with the average follow-up time after surgery being  $7.98 \pm 3.03$  years.

For the modified Macnab criteria at the final follow-up, the excellent or good outcome rate was 28/32 (87.5%) in the PELD group and 14/17 (82.35%) in the MED group, which are comparable with these respective rates in other studies<sup>13–17</sup>. Our results indicated that no significant differences were found between treatment groups in terms of functional disability, back pain, leg pain, and quality of life at the final follow-up. Furthermore, our study indicates that both MED and PELD yielded similarly favorable outcomes for symptomatic ALDH. The NRS and ODI scores improved postoperatively and were sustained over time. The significant improvements in NRS and ODI scores observed in both groups indicate substantial pain relief and functional recovery, which are crucial for enhancing the quality of life in adolescent patients. Additionally, the excellent or good outcome rate according to the modified Macnab criteria was similar between the PELD and MED groups, which is consistent with findings from other studies<sup>15–19</sup>.

Our results indicate that PELD may lead to faster recovery compared to MED, as evidenced by shorter length of hospital stay and postoperative restrictions. The advantages of PELD, such as reduced surgical invasiveness, decreased intraoperative blood loss, and rapid pain relief, facilitate a quicker recovery and an earlier return to daily activities. These factors are particularly significant, especially for younger patients who wish to return to work more promptly.

Considering published literature and our study<sup>10–15</sup>, we suggest that PELD, with its ability to be performed under local anesthesia with minimal sedation, facilitates faster recovery and has the potential to replace MED as the standard of care for lumbar disc disease management.

Therefore, the PELD technique was superior to MED and preferentially recommended for ALDH.

At the final follow-up, 8 out of 49 patients experienced recurrence and required subsequent surgical intervention, resulting in a total recurrence rate of 19.45%. Notably, the rate of re-interventions and tertiary surgical procedures was higher in the MED cohort (4/17, 23.52%) compared to the PELD group (4/32, 12.50%) respectively, studies with longer follow-up are needed to verify this conclusion<sup>19–22</sup>. The higher reoperation rate in the MED group compared to the PELD group may be attributed to the more invasive nature of MED, which could lead to greater tissue damage and higher risk of recurrence. Future studies should focus on identifying risk factors for reoperation and developing strategies to minimize these risks<sup>23</sup>. The investigation of factors leading to the necessity of a third surgical intervention in adolescents with lumbar disc herniation will be discussed in another study we did. We know of no prior studies that have documented this specific finding<sup>24</sup>.

### Limitations

Several limitations have to be acknowledged. Firstly, the sample size is relatively small with a retrospective design, we cannot rule out the risk of selection bias. Secondly, different types of disc herniation were not compared due to the lower incidence of foraminal and sequestered herniation in adolescents. Thirdly, variations in surgical timing and the experience of the surgeon and assistants may have influenced clinical outcomes. Additionally, single-center medical records may have resulted in incomplete or missing questionnaire data and recall bias was also an issue limiting the generalizability of our findings. Moreover, the absence of a healthy control group complicates distinguishing the effects of the intervention from the natural progression of lumbar disc disease or the impact of surgery. Lastly, the variety of conservative treatments before surgery could not be accounted for, which may have influenced the reported postoperative and follow-up outcomes. Also, the study did not account for technique-related biases between MED and PELD, future studies should consider these biases to provide more accurate comparisons. To address these limitations, future multi-center clinical studies and randomized controlled trials are warranted.

### Conclusion

Both PELD and MED have demonstrated efficacy in managing symptomatic ALDH. PELD appears to offer superior control over surgical trauma and promotes rapid recovery compared to MED.

### Data availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## Author contributions

L.M. and Z.C.S. conceived the study and analyzed the data. W.Y.Zh., K.W., P.F., discussed the results. L.J.L., G.Y.L. and X.T. W. contributed data collection and result interpretation. L.M. and Z.C.S. wrote the initial draft. G.Y.L. revised the manuscript. All authors reviewed the manuscript.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Ethical approval

The study approval (No. 2020ZDSYLL080-P011) was given by the institutional review board of Zhongda Hospital, Southeast University.

## Additional information

**Correspondence** and requests for materials should be addressed to Z.S., L.L. or G.L.

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