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Surgical Outcomes of Full-Endoscopic Degenerative Lumbar Lateral Recess Stenosis Decompression Through an Interlaminar Approach

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ABSTRACT

Objective: The conventional open decompression surgery for degenerative lumbar lateral recess stenosis (DLLRS) yields definitive therapeutic outcomes; however, it confronts numerous challenges, including extensive surgical trauma and iatrogenic spinal instability. The purpose of this study is to investigate the surgical outcomes of full-endoscopic DLLRS decompression by an interlaminar approach.

Methods: A consecutive cohort of 275 patients, including 148 males and 127 females, with an average age of 64.62 (55–82) years, with DLLRS between July 2021 and December 2022, was reviewed in this retrospective study. The involved segments were L4/5 in 126 patients and L5/S1 in 149 patients. The computed tomography (CT) and magnetic resonance imaging (MRI) of the lumbar were examined before and after surgery to evaluate the degree of decompression. The VAS score of back and leg pain and the ODI scale were recorded preoperatively, 1 day, 1, 3, 6, and 12 months after surgery, and at the last follow-up. The modified Macnab score was determined at the last follow-up. One-way analysis of variance (ANOVA) was used to compare the VAS and ODI scores of back/leg pain at various time points before and after surgery.

Results: All of the patients underwent surgery successfully. The average duration of surgery was 84.90 min, the average blood loss was 47.33 mL, and the length of hospitalization was 3–4 (3.31 ± 0.46) days, with no nerve injury, infections, or other complications. One-way ANOVA results showed significantly improved VAS and ODI scores for back/leg pain at each time point after surgery compared to those preoperatively ($p < 0.05$). The mean follow-up was 23.6 ± 2.3 (range, 15–32) months; at the last follow-up, the modified Macnab was excellent in 143 patients, good in 102 patients, fair in 18 patients, and poor in 12 patients.

Chengqian Huang, Yingying Qin and Yizhu Huang have contributed equally to this work and should be regarded as co-first authors.

Conclusion: Full-endoscopic lumbar lateral recess decompression through an interlaminar approach is a safe and effective approach for DLLRS.

1 | Introduction

Lumbar spinal stenosis (LSS) is a common degenerative spine disease in the elderly. Anatomically, stenosis can occur in the central and lateral recess and foraminal spinal canal, with degenerative lumbar lateral recess stenosis (DLLRS) as the most common condition in clinical practice [1, 2]. The compression of the spinal canal stenosis on the spinal cord and nerve roots causes lower back and leg pain and decreases lower limb muscle strength, thereby affecting the quality of life in patients [2, 3]. Patients with LSS who fail to respond to conservative treatment require surgical intervention. Although conventional open lumbar decompression and fusion techniques are effective, they are often accompanied by considerable surgical trauma and extended recovery periods. Therefore, it is meaningful to seek a minimally invasive surgical approach to treat DLLRS.

Endoscopic lumbar lateral recess stenosis decompression through the percutaneous transforaminal approach has gradually become one of the preferred alternative surgical methods for some elderly patients with prolonged disease and poor overall condition but cannot tolerate open surgery [4, 5]. Nonetheless, the percutaneous transforaminal approach has a narrow pathway to decompress the lateral recess at the foramen level effectively but cannot decompress the lateral recess area at the pedicle level [3]. The interlaminar approach involves accessing the working channel through the intermuscular space directly to the surface of the lamina or ligamentum flavum, allowing for spinal canal decompression. This approach is particularly effective for patients with lateral recess stenosis, as it enables direct visualization and partial resection of hypertrophic facet joints, thickened ligamentum flavum, herniated disc material, and calcified structures causing spinal canal narrowing. Noncompressive bony and ligamentous structures are preserved during the procedure. The purposes of this study are (i) to investigate the safety and efficiency of full-endoscopic DLLRS decompression by the interlaminar approach and (ii) to provide clinicians with a minimally invasive procedure to treat DLLRS.

2 | Materials and Methods

2.1 | Patients

A retrospective analysis of clinical data of 275 patients (148 males and 127 females, average age 64.62 years) with DLLRS, who visited the First Affiliated Hospital of Guangxi Medical University from July 2021 to December 2022, was conducted. All patients were diagnosed based on their medical history, physical signs, and imaging examination. Approval for this study was obtained from the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (2024-E730-01). As this was a retrospective analysis devoid of personal privacy concerns, individual informed consent was not deemed necessary.

2.2 | Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) Magnetic resonance imaging (MRI) or computed tomography (CT) shows single-segment DLLRS, with or without disc herniation at the same segment; (2) clinically, the main manifestation of DLLRS is intermittent neurogenic claudication, which may be accompanied by radiating pain in the lower limb, and the signs and symptoms are consistent with the affected nerve roots; (3) the effect of a 3-month stringent and standardized conservative treatment was not satisfactory; and (4) complete clinical data are available. Patients with the following conditions were excluded from the study: (1) Lumbar instability, spondylolisthesis, and coronal scoliosis; (2) Multiple segments of LSS or adjacent segments of intervertebral disc herniation requiring decompression or discectomy of multiple segments or any one of these conditions; (3) history of lumbar spine surgery and trauma; and (4) imaging reveals comorbidity, such as infection, ankylosing spondylitis, tumors, and other lumbar spine diseases.

2.3 | Surgical Procedures

The patients were laid in a prone position, with hip flexion and knee flexion, on an arched frame to undergo tracheal intubation under general anesthesia. C-arm x-ray fluoroscopically located and marked the intervertebral space of the affected segment. After routine disinfection and draping, a 7 mm longitudinal surgical incision was made at the skin positioning marker point, the percutaneous puncture intervertebral disc surgical instrument package was opened, and a soft tissue expander was inserted to reach the surface of ligamentum flavum and expanded step-by-step. The entry position was confirmed by fluoroscopy before inserting the expander into the working sleeve with a tongue-shaped incision; then, an endoscope was placed after removing the expander. Finally, the soft tissue behind the ligamentum flavum is removed to expose the dorsal side of the ligamentum flavum and the medial edge of the articular process. Any bleeding is staunched promptly using radiofrequency electrodes. In patients with narrow intervertebral space, the bone at the lower edge of the upper vertebral plate and the inner edge of the lower articular process was polished using a microdrill to expose the inner side of the lower lumbar upper articular process. This joint, along with the upper edge of the lower vertebral plate, was thinned with a grinding drill, and the remaining bone was removed using a miniature vertebral plate rongeur to reach the inner lower edge of the lower lumbar pedicle. The outer and lower edges of the ligamentum flavum were freed and removed, the dural sac and the nerve root were exposed, and the calcified intervertebral disc protrusions and osteophytes were excised using miniature vertebral plate rongeurs. This approach facilitated the endoscopic exploration and complete decompression of nerve roots, hemostasis with a radiofrequency scalpel, and the removal of the cannula (Figure 1).

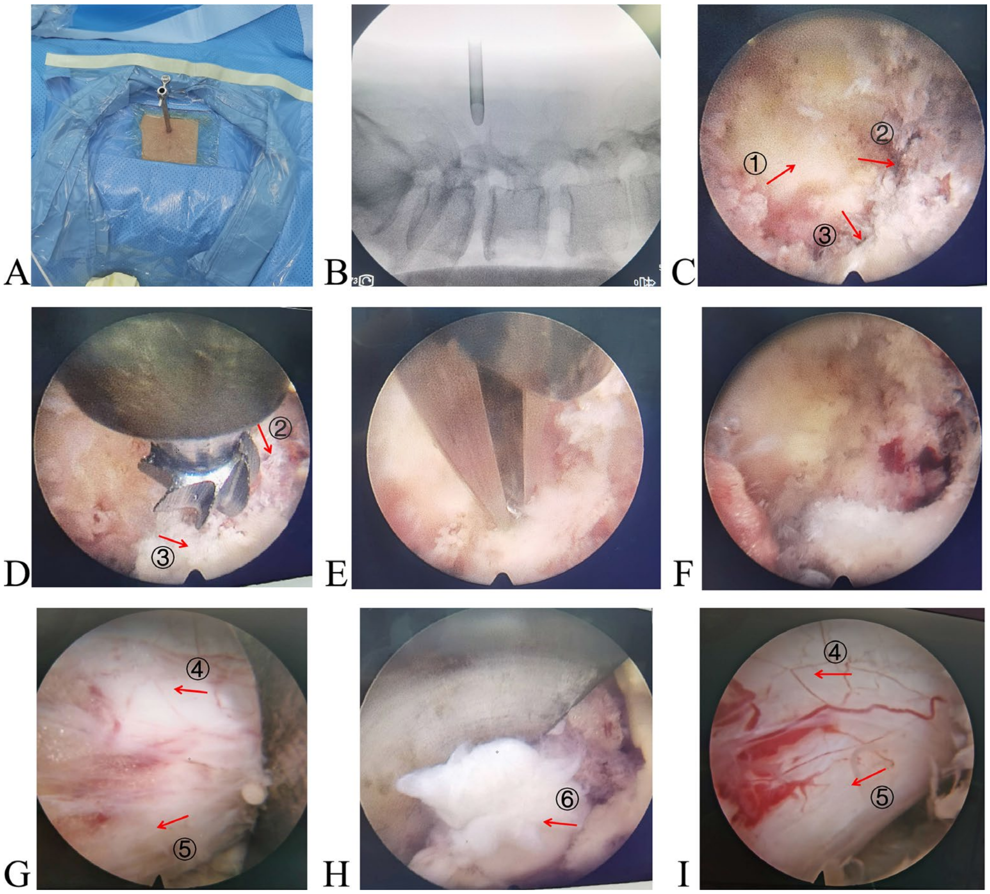

FIGURE 1 | Surgical procedure images. Image annotations: (A, B) Insertion of the working cannula with C-arm fluoroscopy, confirming the correct surgical segment. (C) Under endoscopic visualization, removal of posterior soft tissues from the ligamentum flavum, exposing the dorsal surface of the ligamentum flavum, the inferior edge of the lamina, and the medial edge of the facet joint. (D, E) Using a microdrill to thin the inferior edge of the superior lamina and the medial edges of the superior and inferior facets, followed by the removal of the remaining bone with a Kerrison rongeur. (F, G) Lateral and inferior margins of the ligamentum flavum are freed and excised, exposing the dural sac and traversing nerve root. (H, I) Herniated disc material, calcified tissue, and osteophytes are removed using disc forceps and a Kerrison rongeur, with endoscopic inspection ensuring thorough decompression of the traversing nerve root. Arrow annotations: ① Ligamentum flavum; ② inferior edge of the lamina; ③ medial edge of the facet joint; ④ dural sac; ⑤ traversing nerve root; and ⑥ herniated disc material.

2.4 | Postoperative Management

After surgery, neurotrophic drugs were administered, and symptomatic treatment was provided for dehydration, swelling, and pain. In addition, bed rest was mandatory for a minimum of 6 h postsurgery, and after 24 h, a waist circumference was worn for movement. Follow-up CT and MRI were performed after surgery to evaluate the decompression of DLLRS. In addition, the patients are guided to wear a waist circumference for getting out-of-bed activities and back and waist muscle function recovery exercises within 6 weeks to avoid bending, weight-bearing, and vigorous physical activities.

2.5 | Clinical Assessment

The visual analog scale (VAS) and the Oswestry disability index (ODI) scores of back/leg pains were recorded before and 1 day, 1, 3, 6, 12 months after surgery, and the last follow-up. A questionnaire survey was conducted on patients to evaluate the surgical efficacy using modified Macnab evaluation [1, 6]. The questionnaire was assessed once by an orthopedic physician and recalculated by another to resolve the objections.

2.6 | Statistical Analysis

ANOVA was used to compare the VAS and ODI scores of back/leg pain at various time points before and after surgery. The data were statistically analyzed using Statistical Package for Social Sciences (SPSS, version 26, IBM, Armonk, NY, USA), and $p < 0.05$ indicated a statistically significant difference.

3 | Results

3.1 | Basic Information

The operation was successful in all 275 patients. The baseline demographic characteristics of patients (age, gender, body mass index [BMI], hypertension, diabetes, duration of symptoms, surgical segment, and duration of surgery) are listed in

TABLE 1 | The basic demographic characteristics of patients.

Characteristics	Total ($n = 275$)
Age (years)	64.62 ± 7.08
BMI	23.01 ± 2.92
Gender, *n* (%)	
Male	148 (53.82)
Female	127 (46.18)
Smoke, *n* (%)	
No	273 (99.27)
Yes	2 (0.73)
Hypertension, *n* (%)	
No	202 (73.45)
Yes	73 (26.55)
Diabetes, *n* (%)	
No	248 (90.18)
Yes	27 (9.82)
Surgical segment, *n* (%)	
L4/5	126 (45.82)
L5/S1	149 (54.18)
Course of disease (month)	45.59 ± 65.79
Duration of surgery (min)	84.90 ± 15.94
Intraoperative bleeding (mL)	47.33 ± 12.45
Total length of hospital stay (day)	3.31 ± 0.46

Table 1. Importantly, none of the patients has to be switched to open surgery midway during the procedure. The average surgical duration for the patients was 84.90 ± 15.94 min, the average blood loss was 47.33 ± 12.45 mL, and the average hospitalization time was 3.31 ± 0.46 days. On the day after surgery, 226 patients experienced significant relief or disappearance of lower back and leg pain, reduced numbness and fatigue, and improved intermittent claudication. Subsequently, 39 patients experienced gradual relief from limb pain and numbness within 1 month after surgery. On the other hand, nine patients experienced aggravated lower limb pain and numbness on the affected side after surgery and were treated with oral anti-inflammatory and nutritional nerve drugs outside the hospital; their symptoms improved gradually after 2 weeks of treatment. The remaining patients did not experience complications, such as dural sac and nerve root injury or surgical segment intervertebral space infection. The follow-up CT and MRI scans 1 day after surgery revealed sufficient decompression of the spinal canal at the surgical segment, effective treatment of calcification at the posterior edge of the vertebral body, articular process hyperplasia and cohesion, hypertrophy of the posterior longitudinal ligament, and intervertebral disc herniation (Figure 2). No instability or slippage of the surgical segment was detected during postoperative follow-up. According to the modified Macnab evaluation in the last follow-up, 143 cases were excellent, 102 cases were good, 18 cases were fair, and 12 cases were poor, with a fineness rate of 89.09% (Figures 3 and 4).

3.2 | Pain Indicators

The VAS and ODI scores for back/leg pain preoperatively and 1 day, 1, 3, 6, 12 months after surgery, and the last follow-up are shown in Table 2 (Table S1). The VAS back pain score decreased from 4.46 ± 1.27 preoperatively to 2.85 ± 0.78, 1.69 ± 0.58, 1.23 ± 0.53, 0.48 ± 0.59, 0.19 ± 0.39, and 0.23 ± 0.45 at 1 day, 1, 3, 6, 12 months after surgery, and the last follow-up, respectively. The VAS leg pain score decreased from 8.09 ± 0.96 preoperatively to 3.53 ± 1.66, 2.54 ± 1.76, 2.01 ± 2.05, 1.35 ± 1.67, 0.89 ± 1.33, and 0.66 ± 0.98 at 1 day, 1, 3, 6, 12 months after surgery, and the last follow-up, respectively. The ODI score decreased from 39.07 ± 4.66 preoperatively to 23.59 ± 3.30, 17.12 ± 2.18, 10.51 ± 2.06, 8.04 ± 2.06, 6.47 ± 2.27, and 4.73 ± 2.29 at 1 day, 1, 3, 6, 12 after surgery, and the last follow-up. One-way ANOVA results showed significantly improved VAS and ODI scores for back/leg pain at each time point after surgery compared to those preoperatively ($p < 0.05$).

4 | Discussion

4.1 | Main Findings

In this study, the surgery was successful in 275 patients with no conversions to open surgery. Average surgical duration was 84.90 ± 15.94 min, blood loss was 47.33 ± 12.45 mL, and hospitalization time was 3.31 ± 0.46 days. Most patients experienced pain relief postsurgery. Nine patients had aggravated symptoms but improved after treatment. Follow-up scans showed effective decompression. No instability or slippage was detected. Modified Macnab evaluation showed an 89.09% fineness rate. VAS and ODI scores significantly decreased from preoperative levels to the last follow-up. Compared to traditional open decompression procedures, our surgical approach is less invasive, offering advantages in terms of reduced surgical time, lower intraoperative blood loss, shorter hospitalization, and faster postoperative recovery.

4.2 | Background of Research

The conventional surgical method for lumbar lateral recess stenosis includes laminoplasty or total laminectomy, and that for decompression is articular process resection. Although the decompression is sufficient and the short-term effect is relatively positive, surgery causes inevitable damage to the muscles, supraspinous and interspinous ligaments, and normal bone structures, leading to iatrogenic lumbar instability [4, 7–9]. Guha et al. [4] analyzed 2496 patients in a meta-analysis and found that up to 12% of patients who underwent conventional open surgery experienced postoperative instability of the surgical segment, and 4.1% underwent a reoperation. Some patients often require supplementary lumbar fusion and internal fixation surgery due to the impact on spinal stability [9, 10]. These additional procedures result in prolonged surgical duration, increased surgical

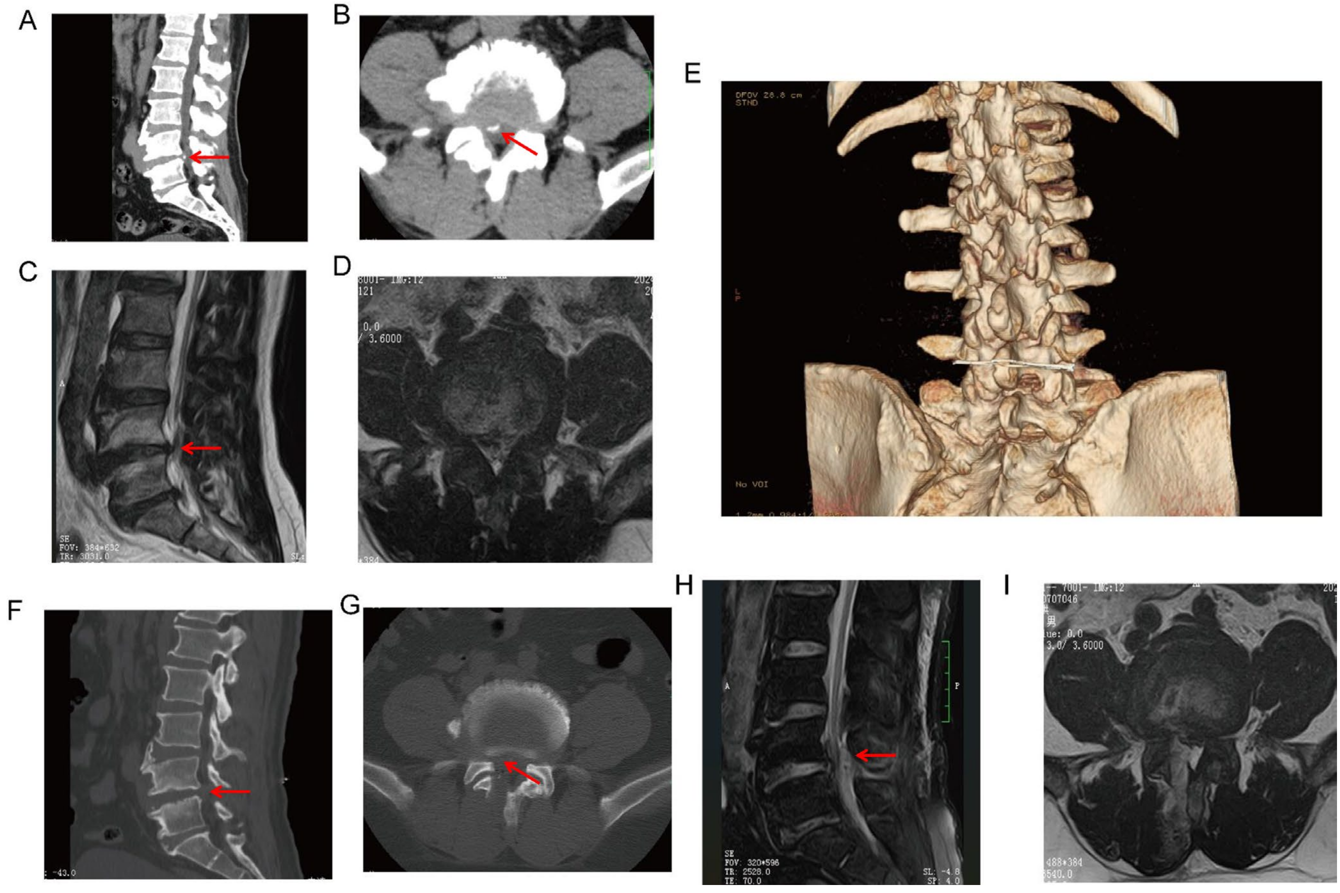

FIGURE 2 | A 66-year-old male patient with L4-5 lateral recess stenosis (symptomatic on the right side only) underwent percutaneous right-sided interlaminar approach L4-5 laminoplasty for endoscopic lateral recess decompression. (A–D) Preoperative CT and MRI scans showed bilateral facet joint degeneration and hypertrophy, laminar thickening, ligamentum flavum thickening, accompanied by calcification of the posterior longitudinal ligament and disc tissue, more pronounced on the right side. This resulted in significant right-sided bony lateral spinal canal stenosis, with compression of the dural sac and the right L5 nerve root. (E) Postoperative three-dimensional CT demonstrated the window created by the removal of the right lamina. (F–I) Postoperative CT and MRI revealed the resection of 1–3 mm of the lower edge of the L4 lamina, the inferior articular process, and the inner edge of the superior articular process of L5, as well as the upper edge of the lamina. The right-sided lateral recess stenosis was resolved, and the calcified posterior longitudinal ligament and disc tissue were completely removed. The red arrows indicate the changes in important anatomical parts before and after the operation.

trauma and risk, and increased surgical costs. The risk of adjacent segment degeneration after fusion surgery is also markedly raised [11, 12]. Ren et al. [13] found that up to 16% of elderly patients undergoing lumbar fusion surgery underwent reoperation 2 years postoperatively.

Compared to conventional open surgery, endoscopic decompression for lumbar lateral recess stenosis reduces the postoperative complications [4, 14, 15]. Percutaneous transforaminal endoscopic decompression for lumbar lateral recess stenosis is one of the most commonly used surgical methods [5]. Yin et al. [16] performed endoscopic decompression through a transforaminal approach on 47 elderly patients with lumbar lateral recession stenosis; the curative effect rate of modified Macnab after surgery was 89.36%, with no permanent nerve injury, infection, or other operation-related complications. However, whether the percutaneous transforaminal approach can effectively and thoroughly decompress the lateral recess at the pedicle level is yet to be elucidated. The outer side of the lateral recess is the inner wall of the pedicle, followed by the anterior wall of the superior articular process, the outer part of the ligamentum flavum, and the corresponding upper edge of the vertebral plate. The anterior side is the outer part of the posterior edge of the vertebral body and the corresponding intervertebral disc. This specific anatomical structure indicates that the lateral recess at the pedicle level is the relative "blind spot" of the intervertebral foramen approach [17]. Moreover, factors such as high iliac bone, transverse process hypertrophy, and osteophyte hyperplasia significantly increase the surgical difficulty of decompression through the transforaminal approach [17–19]. Furthermore, choosing a suitable approach is crucial to achieving optimal results and avoiding surgical complications in patients [20, 21].

4.3 | Selection of Interlaminar Approach

In this study, the indication for full-endoscopic decompression surgery for DLLRS using the interlaminar approach included patients with single-segment DLLRS, with or without disc herniation, who presented severe symptoms, had poor outcomes from standardized conservative treatment, and required surgical intervention. This approach was especially suitable for

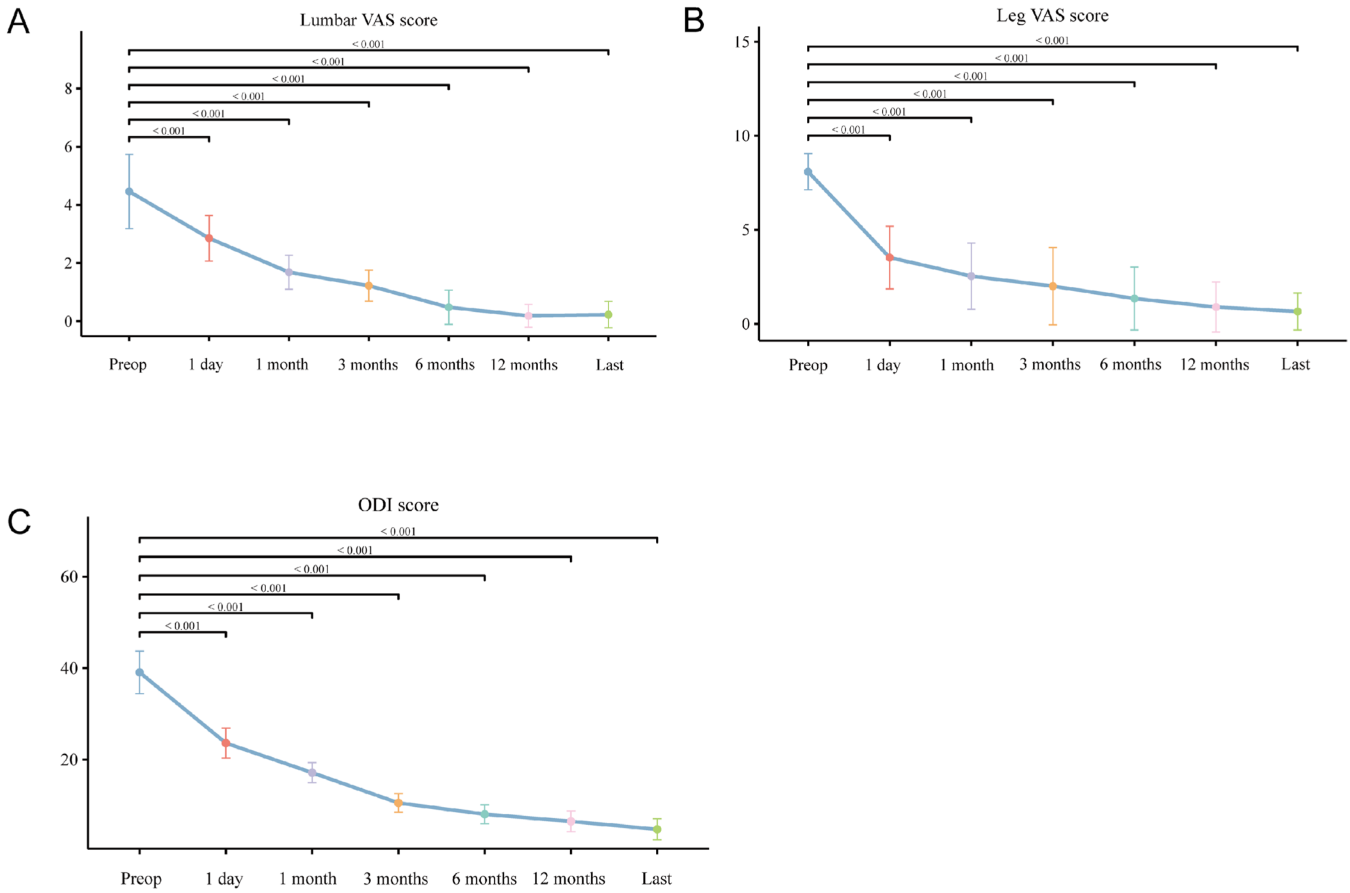

FIGURE 3 | ODI and VAS scores for lumbar and leg at various time points before and after surgery. (A) Lumbar VAS score; (B) leg VAS score; and (C) ODI score.

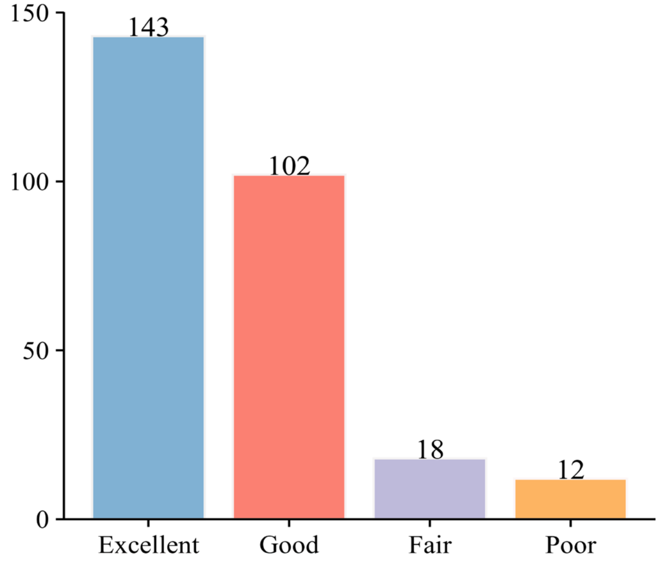

FIGURE 4 | Modified Macnab criteria.

older patients or those with multiple underlying conditions who may not tolerate prolonged surgery. Research has demonstrated that the interlaminar approach is effective for decompressing central stenosis, with or without lateral recess stenosis [6, 21]. This technique aligns with standard spinal surgical practices, enabling direct endoscopic visualization for decompression of the dorsal spinal canal. During the surgery, a microdrill was used to polish the bone at the lower edge of the upper vertebral plate and the inner edge of the lower articular process, exposing the inner side of the upper articular process of the lower lumbar vertebrae. Then, the inner part of the upper articular process and the upper edge of the lower vertebral plate were thinned using the drill, and the remaining bone was removed using a micro vertebral plate rongeur until it reached the inner lower edge of the lower pedicle, thereby reaching the lateral recess space and reducing the risk of damage to the outlet nerve root and dural sac [22]. Several studies have attempted modified techniques to improve surgical safety and effectiveness [23, 24]. Krzok et al. [20] achieved optimal results of lateral recess decompression through a narrow contralateral intervertebral space approach; however, this technique risks damage to the interspinous ligament. In contrast, the interlaminar approach used in our study reaches the surface of the lamina or ligamentum flavum through the muscle gap for spinal canal decompression, causing minimal damage to the posterior ligamentous complex. Intraoperatively, only the marginal lamina and medially hypertrophic facet osteophytes are trimmed, typically removing just 1–3 mm, and not exceeding one-third of the facet joint, which has minimal impact on lumbar stability. Moreover, spine surgeons are familiar with this approach, as it shares the same anatomical landmarks as conventional posterior spinal open surgery, and the magnified imaging system facilitates the learning and mastery of this technique. Compared to open

TABLE 2 | ODI and VAS scores for lumbar and leg at various time points before and after surgery.

	Preop	1 day	1 month	3 months	6 months	12 months	Last	*p*
Lumbar VAS score	8.09 ± 0.96	3.53 ± 1.66	2.54 ± 1.76	2.01 ± 2.05	1.35 ± 1.67	0.89 ± 1.33	0.66 ± 0.98	< 0.001
Leg VAS score	4.46 ± 1.27	2.85 ± 0.78	1.69 ± 0.58	1.23 ± 0.53	0.48 ± 0.59	0.19 ± 0.39	0.23 ± 0.45	< 0.001
ODI score	39.07 ± 4.66	23.59 ± 3.30	17.12 ± 2.18	10.51 ± 2.06	8.04 ± 2.06	6.47 ± 2.27	4.73 ± 2.29	< 0.001

surgery, endoscopic lumbar discectomy and decompression significantly reduce intraoperative blood loss and operative time, and substantially shorten postoperative recovery for patients [8, 25]. However, there are also relative contraindications for full-endoscopic decompression surgery through the interlaminar approach, such as stenosis in the foraminal or extraforaminal area, previous lumbar open surgery, lumbar responsible segment instability, lumbar spondylolisthesis of degree II and above, lumbar spondylolysis, severe deformities, spinal infections, lesions, and spinal tumors.

4.4 | Analysis of Related Results and Complications

The VAS and ODI scores for back/leg pain in this group of patients improved significantly after the surgery and at the last follow-up. According to the modified Macnab evaluation, 143 cases were evaluated as excellent, 102 as good, and 12 as poor, with a fineness rate of 89.09% (Figure 4). These values were in the upper range of the reported excellent and good rates in previous studies. In a meta-analysis, Lee et al. [26] found that a complete endoscopic decompression through the interlaminar approach for LLS improves the VAS leg and back pain scores by 5.95 and 4.22 points, respectively, and ODI scores by 41.71 points. This finding is consistent with the results of our study. These values may be related to direct and sufficient decompression through the interlaminar approach. Additionally, in this group, nine patients experienced increased numbness and pain in the lower limb postsurgery, likely due to the following reasons. First, inserting the working cannula hastily before adequate decompression of the spinal canal may cause traction and compression on the dura mater or nerve roots, leading to temporary, intensified numbness and pain in the lower limbs. Imaging examinations now provide significant assistance in the assessment of our diseases. Previous studies have utilized thin-slice CT to evaluate fine anatomical structures. Therefore, it is crucial for us to carefully review thin-slice CT images both preoperatively and postoperatively to minimize the risk of misdiagnosis [27–29]. Second, postoperative hematoma at the surgical site may compress the nerve roots, resulting in similar symptoms. To address the first issue, the surgical procedure should be performed in a gradual, meticulous manner. Sufficient decompression of the dorsal side of the spinal canal should be achieved first, followed by decompression of the lateral, anterior, and central regions, ensuring complete relief of the compressed nerve roots before inserting the working cannula. Regarding the second issue, hematoma absorption typically takes 3–4 weeks. Symptomatic treatment, including anti-inflammatory, pain relief, and neurotrophic therapies, may alleviate symptoms as the hematoma resolves.

4.5 | Limitations and Prospect

Nevertheless, the present study has several limitations. First, this is a single-center study with a small sample size, which may lead to selection and subjective bias. The limited sample size could restrict the statistical power of the findings and may not adequately represent a broader population, thereby limiting the generalizability of the results. Therefore, future research should be conducted in a multicenter setting and involve a larger number of participants to enhance the representativeness of the sample and the external validity of the results. Second, the retrospective design of this study did not include a randomized control group, which is essential for establishing a clear causal relationship. In the absence of a control group, it is challenging to determine whether the observed outcomes can be directly attributed to the intervention or are influenced by other confounding factors. To address this limitation, subsequent studies should adopt a prospective design with a randomized control group to strengthen the credibility of the findings. Additionally, there is a potential for selection bias, as participants may not have been randomly selected and could differ systematically from those who did not participate. This may affect the validity of our results and their applicability to other patient populations. Future research should implement more stringent inclusion criteria and consider using random sampling methods to mitigate the impact of selection bias. Finally, while this study focused on specific lumbar spine pathologies, the findings may not be generalizable to other types of spinal disorders. To enhance the generalizability of the research findings, future studies should investigate the efficacy of interventions across different types of lumbar pathologies and validate the results in diverse populations. Furthermore, increasing comparative studies on various pathological types would contribute to a more comprehensive understanding of the differences in treatment effects.

5 | Conclusion

The interlaminar approach of endoscopic DLLRS is a safe and effective treatment. It can thoroughly decompress the lateral recess and protect the integrity of the posterior structure of the spine. These characteristics make it an optimal choice for patients with lumbar lateral recess stenosis, especially those who cannot tolerate open surgery.

Author Contributions

C.H., Y.Q., Y.H., and X.Z. designed the study. X.W., J.Z., C.L., S.W., and J.C. analyzed the data. J.C.Z., T.C., B.Z., S.F., C.Z., and J.X. processed the digital visualization. C.H. wrote and revised the manuscript. Y.Q., Y.H., and X.Z. revised the manuscript. All authors read and approved the final manuscript. All co-authors participated in the laboratory operation. All authors read and approved the final manuscript.

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Ethics Statement

Due to the retrospective nature of the study, informed consent was waived. This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (2024-E730-01).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data of this study were derived from degenerative lumbar lateral recess stenosis patients who underwent full-endoscopic decompression by the interlaminar approach in the First Affiliated Hospital of Guangxi Medical University from July 2021 to December 2022.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.