

Percutaneous transforaminal endoscopic discectomy in the treatment of senior patients with lumbar degenerative disc disease

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Abstract. The aim of the current study was to analyze the efficacy of percutaneous transforaminal endoscopic discectomy (PTED) in the treatment of lumbar degenerative disc disease for senior patients. The clinical and follow-up data of senior patients were retrospectively reviewed. Patients were divided into a PTED group and an open surgery group. Parameters were analyzed, including surgery time, intraoperative fluoroscopy time, intraoperative blood loss, postoperative complications, visual analog scale (VAS) and Japan Orthopedic Association (JOA) scores. Compared with the open surgery group, the surgery time and intraoperative blood loss were decreased, while the intraoperative fluoroscopy time was increased, in the PTED group ($P<0.001$). Significant improvements in VAS and JOA scores were identified within both groups from preoperative to 12 months following surgery ($P<0.001$). VAS and JOA scores were significantly improved in the PTED group compared with the open surgery group at 1 week after surgery ($P<0.001$), but there was no significant difference between groups prior to and at 12 months following surgery. The incidence of venous thrombosis of the lower extremities in the PTED group was decreased compared with the open surgery group ($P<0.05$). In the open surgery group, patients suffered from multiple postoperative complications, including constipation, urinary system infection, wound infection, gastrointestinal hemorrhagic stress ulcer, pneumonia, pulmonary embolism, mortality following myocardial infarction, mortality following cerebral infarction, and hemiplegia following cerebral hemorrhage. By contrast, patients in the

PTED group did not experience any of these complications. In conclusion, PTED resulted in reduced trauma and a lower incidence of severe complications compared with open surgery, which suggests that PTED is a safe and effective minimally invasive surgery for senior patients with lumbar degenerative disc disease.

Introduction

Lumbar degenerative disc disease is a common disease that occurs in older people and develops with age. In the past, the standard treatment for this disease has been internal fixation surgery (1-3). However, traditional open surgery results in considerable trauma in senior patients. It has been reported that age is an independent factor in the severity of lumbar degenerative disc disease; the disease becomes more severe and complex with age (4). At the same time, due to physiological decline, senior patients are often affected by a variety of systemic chronic diseases, with significant increases in surgical risk (5). Li *et al* (6) demonstrated that the incidence and mortality rate of patients undergoing traditional open surgery increased with age; in patients aged over 65 years the incidence was 11.6% and the mortality rate was 0.15%, leading to difficulties in the treatment of senior patients.

Currently, a variety of spinal minimally invasive technologies offer novel strategies that may avoid the aforementioned problems. Percutaneous transforaminal endoscopic discectomy (PTED) has quickly gained attention because it has numerous notable advantages, including small incision, short hospitalization time, small economic burden and fewer surgical complications (7-10). However, the limited scope of decompression and reduced capacity to recover the stability of the spine have made the indications and contraindications of the surgery the focus of academic debate (11). Kim *et al* (12) proposed that the application of PTED should be carefully considered in patients aged over 57 years as these patients have a higher reoperation risk.

In the current study, the records of senior patients aged over 70 years with lumbar degenerative disc disease were reviewed, and efficacy of PTED in the treatment of lumbar degenerative disc disease for senior patients was evaluated. The current

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study provides support for the clinical application of PTED in treating elderly lumbar degenerative disc disease.

Materials and methods

Subjects. This retrospective study was approved by the Ethics Committee of The Third Hospital of Hebei Medical University (Shijiazhuang, China). All patients provided written informed consent for their inclusion in the study. A total of 318 patients aged >70 years with lumbar degenerative disc disease were selected in the Department of Spine Surgery in The Third Hospital of Hebei Medical University from June 2012 to June 2015. The patients were allocated to two groups according to their choice of treatment: A PTED group and an open surgery group. In the PTED group, there were 41 patients, including 17 males and 24 females, aged from 70 to 83 years, with a mean age of 74 years. All patients in this group underwent PTED. In the open surgery group, there were 277 patients, including 102 males and 175 females, aged from 70 to 79 years with a mean age of 73 years. The patients underwent traditional open reduction and internal fixation. Among the 277 patients, 75 underwent transforaminal lumbar interbody fusion (TLIF) and 202 underwent posterior lumbar interbody fusion (PLIF).

The inclusion criteria were as follows: Lumbar degenerative disc disease patients aged >70 years with single or bilateral lower extremity numbness, pain and intermittent claudication as the clinical manifestations; patients whose imaging findings were consistent with the symptoms and signs of degenerative manifestations, such as intervertebral disc protrusion and spinal stenosis; patients with ineffective conservative treatment for >6 months; patients undergoing single segment TLIF, PLIF or PTED.

The exclusion criteria were as follows: Patients <70 years old; patients with Grade II or above lumbar spondylolisthesis; patients with elevated infection indicators, including erythrocyte sedimentation rate and C-reactive protein; patients with lumbar trauma, cancer, severe osteoporosis or congenital malformations; patients with rheumatoid arthritis disease or other serious systemic diseases, or metal allergy; patients with incomplete data or who were lost to follow-up.

Surgery. In the PTED group, nucleus removal was conducted using the transforaminal endoscopic surgical system technique (13). In the open surgery group, PLIF (14) and TLIF (15) were used for decompression of laminectomy, nucleus removal, and cage and pedicle screw implantation. The surgeries of the patients in the two groups were completed by the same surgical team.

Postoperative management. Patients in the PTED group were given grade II nursing with the same diet as pre-operation (16), and they did moderate exercise out of bed following rest for 12 h. Blood glucose was monitored for the preoperative underlying disease, and the preoperative drugs were continually used for the treatment of underlying disease.

Patients in the open surgery group were given grade I nursing with oxygen inhalation. Vital signs were monitored for 24 h and patients were prohibited from eating or drinking for 6 h, then given liquid food for 1 day. Once defecation was normal, the preoperative diet was restored. After routine rehydration and

anti-infective treatment, the patients received anticoagulant therapy with the subcutaneous injection of low molecular weight heparin 24 h after surgery. Patients rested in bed and were prohibited from all strenuous exercise. Limbs were passively exercised, and the dressing was regularly replaced on the wound. Biochemical indicators were closely monitored. Common postoperative symptoms, including fever, anemia, electrolyte imbalance and coagulation dysfunction, were promptly treated with supportive treatments, including antipyresis, blood transfusion and fluid infusion. Once the condition had been stable for 7 days following surgery, without the formation of deep venous thrombosis of the lower limbs, moderate activity out of bed was allowed. The suture was removed 12-14 days following surgery, depending on the condition of wound.

Follow-up and indices. All patients were followed up for 12-48 months (mean follow-up, 21.6 months). Surgery time was regarded as the time from skin incision to the incision being completely sutured. Intraoperative fluoroscopy time was regarded as the time of intraoperative fluoroscopy exposure using C-arm X-ray. The average exposure time was 1 sec for each fluoroscopy. Japan Orthopedic Association (JOA) evaluation and treatment scores (17) were used to evaluate nerve function prior to surgery, 1 week following surgery and during the 12-month follow-up. Visual analog scale (VAS) scores (18) were used to evaluate the severity of pain prior to surgery, 1 week following surgery and during the 12-month follow-up. The Charlson Comorbidity Index (CCI) was used to evaluate the degree of severity of preoperative underlying disease (Table I).

Statistical analysis. SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. Measurement data were expressed as the mean \pm standard deviation. Kolmogorov-Smirnov test was used to determine the distribution of the data. The paired sample t-test was used to analyze paired data. Comparisons between groups in terms of age, surgery time, intraoperative fluoroscopy time, intraoperative blood loss, VAS and JOA scores prior to surgery, 1 week following surgery and 12 months following surgery, and preoperative CCI score were analyzed by independent sample t-test. Comparisons within groups in terms of VAS and JOA scores prior to surgery and at 12 months following surgery were analyzed by paired sample t-test. The incidence of deep venous thrombosis was compared between groups by Pearson's chi-squared test. The incidence of postoperative cerebrospinal fluid leakage was compared by Fisher's exact probability test (test level, $\alpha=0.05$). $P<0.05$ was considered to indicate a statistically significant difference.

Results

Comparison of observation indices between the PTED group and the open surgery group. As indicated in Table II, there were significant differences in surgery time, intraoperative fluoroscopy time, and intraoperative blood loss between the PTED group and the open surgery group ($P<0.001$), whereas there was no significant difference in age. The surgery time in the PTED group was significantly reduced compared with the open surgery group (74.5 ± 19.72 vs. 169.8 ± 24.5 min). The intraoperative fluoroscopy time in the PTED group was significantly longer compared with that in the open surgery

Table I. Charlson Comorbidity Index.

Disease	Score
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic lung disease	1
Connective tissue disease	1
Ulcer	1
Mild liver disease	1
Diabetes	1
Hemiplegia	2
Moderate/severe kidney disease	2
Diabetes combined with organ damage	2
Tumor	2
Leukemia	2
Lymphoma	2
Moderate/severe liver disease	2
Metastatic tumors	2
Acquired immunodeficiency syndrome	2

group (23.7 ± 6.08 vs. 4.9 ± 1.8 sec). Intraoperative blood loss in the PTED group was significantly reduced when compared with the open surgery group (13.5 ± 4.6 vs. 668.0 ± 260.4 ml).

Comparison of pain and neurological function between the PTED group and the open surgery group. There were significant differences in VAS score and JOA score at 1 week after surgery between the PTED group and the open surgery group ($P < 0.001$), whereas no significant differences were identified in preoperative VAS score, preoperative JOA score, VAS score at 12 months after surgery or JOA score at 12 months after surgery between the two groups (Table II). Furthermore, there were significant differences in the VAS and JOA scores prior to surgery and at 12 months after surgery within each group ($P < 0.001$; Table III). Preoperative CCI in the PTED group was significantly higher compared with the open surgery group (4.44 ± 1.62 vs. 2.78 ± 0.92 ; $P < 0.001$; Table II). In summary, these results indicated that lumbar and leg pain was significantly alleviated, and neurological function was significantly improved in the two groups at 12 months after surgery.

Benefits of PTED surgery. Two senior patients had underlying diseases, including L2-3 disc herniation and left nerve root compression (Figs. 1 and 2). The intervertebral disc decompression following a PTED on senior patients with underlying disease was good as the VAS score was reduced and JOA score improved (data not shown). Another senior patient had a L3-4 disc herniation, stenosis of left nerve root canal and an intervertebral foramen (Fig. 3). Following the PTED surgery under local anesthesia, the compression of the nerve root and the pain experienced by the senior patient were largely relieved (data not shown). After removal of nucleus pulposus following a PTED (Fig. 4), the VAS score was reduced and the JOA score was

improved, suggesting the recovery of nerve function (Table III). The last senior patient had multi-segment lumbar disc herniation and spinal stenosis with degenerative scoliosis prior to surgery (Fig. 5A); there was a remarkable decompression effect of spinal canal following PTED surgery (Fig. 5B).

Postoperative complications. The incidence of postoperative deep venous thrombosis of lower limbs in the PTED group was significantly lower compared with the open surgery group (12.1 vs. 28.2% ; $P < 0.05$), whereas no significant difference in the incidence of postoperative cerebrospinal fluid leakage was identified between the two groups (Table II).

In the open surgery group, the incidence of constipation, urinary system infection and wound infection following surgery was 56.7 , 19.5 and 9.4% , respectively. Patients undergoing intraoperative and postoperative transfusion therapy accounted for 44.8% . There were 12 cases of gastrointestinal hemorrhagic stress ulcer, 3 of pneumonia, 2 of pulmonary embolism, 1 of mortality following myocardial infarction, 1 of mortality following cerebral infarction and 1 of hemiplegia following cerebral hemorrhage. Patients in the PTED group did not experience any complications.

Discussion

Lumbar degenerative disc disease is a pathophysiological progress that develops with lumbar tissue aging, including lumbar disc herniation, lumbar spinal stenosis, lumbar spondylolisthesis and lumbar instability (15). Therefore, instability of the spine is an important part of lumbar degeneration. Studies have hypothesized that the first cause of the instability of the spine is loss of intervertebral height, followed by dehydration of intervertebral disc or nucleus pulposus (16,19,20). In addition, instability of the spine contributes to lumbar segments exceeding the normal range and exhibiting abnormal activities, thus causing a range of clinical symptoms, including continuous low back pain with or without radiation pain in the buttocks and the posterolateral lower extremities (17,18). For patients in good physical condition and with strong surgical tolerance, traditional open surgeries, including lumbar decompression, intervertebral discectomy and interbody fusion, are commonly used. These methods have numerous advantages, including complete decompression, instantly restored spinal stability and stable surgical efficacy. Currently, PLIF and TLIF are the standard procedures in the treatment of lumbar degenerative disc disease (21-24). PTED is a technically demanding procedure with a steep learning curve, and therefore requires an experienced surgeon (25). Therefore, it is difficult to apply in primary hospitals. For patients with severe lumbar degenerative disc disease, intraspinal vascular hyperplasia often occurs, resulting in a large volume of bleeding during PTED surgery, which will cover the surgical field. Currently, PTED cannot achieve fixation of instability segments of the spine; therefore, degenerative clinical symptoms, mainly caused by instability of the lumbar spine, are not yet suitable for PTED treatment.

However, traditional open surgery also has many drawbacks, including a large surgical incision, considerable intraoperative blood loss, slow recovery after surgery, and a wide range of complications (26). It has been demonstrated that lumbar degenerative disc disease is likely to become

Table II. Comparison of observation indices between the two groups.

Index	PTED group	Open surgery group	P-value
Age (year)	74.30±3.13	73.40±2.48	0.13
Surgery time (min)	74.50±19.72	169.80±24.50	<0.001
Intraoperative fluoroscopy time (sec)	23.70±6.08	4.90±1.80	<0.001
Intraoperative blood loss (ml)	13.50±4.60	668.00±260.40	<0.001
Preoperative VAS score	6.20±1.24	6.10±1.40	0.67
Preoperative JOA score	11.90±4.09	11.50±3.88	0.32
VAS score 1 week after surgery	2.60±0.85	3.10±0.79	<0.001
JOA score 1 week after surgery	23.60±2.28	19.40±1.79	<0.001
VAS score 12 months after surgery	2.00±0.97	2.09±0.90	0.56
JOA score 12 months after surgery	23.40±2.14	23.60±2.29	0.64
Preoperative CCI score	4.44±1.62	2.78±0.92	<0.001
Incidence rate of postoperative deep venous thrombosis of lower limbs (%)	12.10	28.20	0.03
Incidence rate of postoperative cerebrospinal fluid leakage (%)	4.90	7.60	0.75

PTED, percutaneous transforaminal endoscopic discectomy; VAS, visual analog score; JOA, Japan Orthopedic Association; CCI, Charlson Comorbidity Index.

Table III. Comparison of pain and neurological function between the two groups before and after surgery.

Time	PTED group		Open surgery group	
	VAS	JOA	VAS	JOA
Preoperative	6.20±1.24	11.90±4.09	6.10±1.40	11.50±3.88
12 months after surgery	2.00±0.97	23.40±2.14	2.09±0.90	23.60±2.29
P-value	<0.001	<0.001	<0.001	<0.001

PTED, percutaneous transforaminal endoscopic discectomy; VAS, visual analog score; JOA, Japan Orthopedic Association.

more severe and complex with age (4). At the same time, the incidence and severity of underlying diseases in other systems also increases with age. Therefore, during surgery on senior patients with lumbar degenerative disc disease, surgeons are likely to face many problems, including long surgery times and large surgical trauma.

In recent decades, the concept of minimally invasive surgery has been widely accepted, and a variety of spinal minimally invasive techniques have emerged (7,27-32). The technique of intervertebral foramen nucleus removal can achieve decompression of the spinal canal and can be performed with local anesthesia and a small incision, which has been widely studied and developed (7-10). PTED addressed many of the aforementioned problems in senior patients and some studies indicated it was an ideal surgery option for senior patients (33). However, PTED is not able to achieve intervertebral fusion, internal fixation or reconstruction of spine stability. It has been indicated that the recurrence rate is higher in patients older than 57 years treated with PTED when compared with patients treated with open surgery at 3-4 years after surgery (12). Therefore, the use of PTED in senior patients requires further investigation.

Compared with traditional open surgery, PTED is a minimally invasive surgery that offers direct access to the lesion. It avoids the destruction of the paravertebral muscles, vertebral lamina, spinous process and posterior spinal muscular ligamentous complex, so it has a minimal effect on the stability of the spine and involves minimal intraoperative bleeding. Patients are able to regain function quickly following surgery, and the time of hospitalization is greatly shortened, which reduces the economic burden for patients. One of the major advantages of PTED is the protection of the stability of the spine. In the current study, postoperative recurrence or instability were not observed during the follow-up period, which may be associated with the relatively stable state of spine in the elderly patients and the absorption of degenerated nucleus pulposus. These results were consistent with previous reports (18,24).

In the current study, perioperative indices and short-term results of senior patients with lumbar degenerative disc disease were compared following treatment with PTED and traditional open surgery. There was no significant difference in age between the two groups, but the preoperative CCI in the PTED group was significantly higher compared with the open surgery

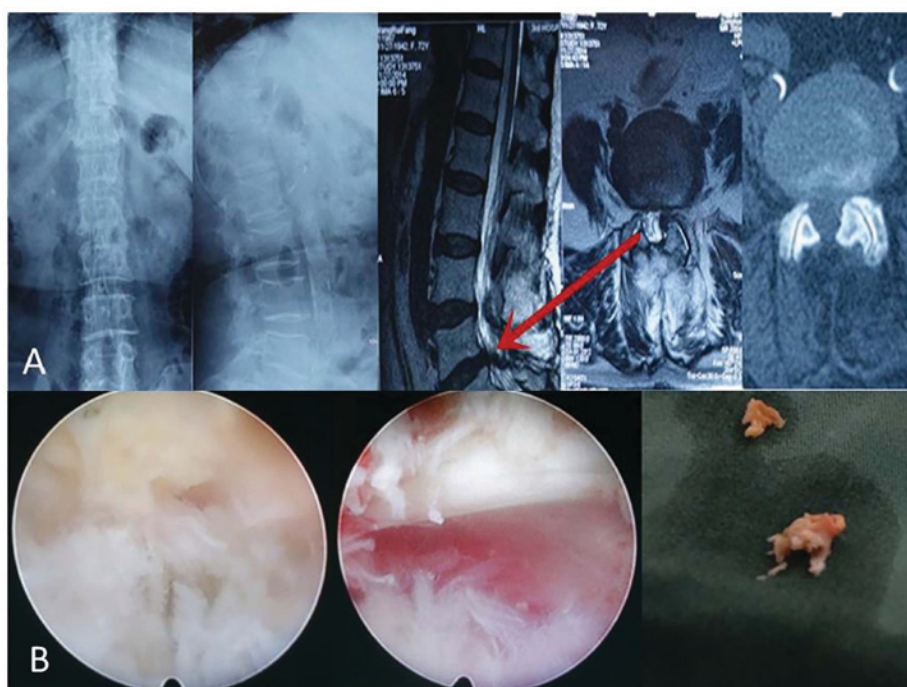


Figure 1. A 72-year-old female with numbness and pain in both lower limbs for 10 years and with aggravated pain in the right lower limb for 6 months. The patient had a history of lumbar surgery for 20 years with ineffective conservative treatment. Underlying diseases included hypertension, diabetes, nephropathy and bronchial asthma. The preoperative CCI, VAS and JOA scores were 5, 8 and 10, respectively. VAS and JOA scores 12 months after surgery were 2 and 21, respectively. (A) Preoperative imaging examination showed L4-5 disc herniation, adhesion of spinal scar tissue and spinal stenosis (red arrow). (B) Intervertebral disc decompression performed by percutaneous transforaminal endoscopic discectomy. Intraoperative image (left) and the removal of intervertebral disc tissue (right).

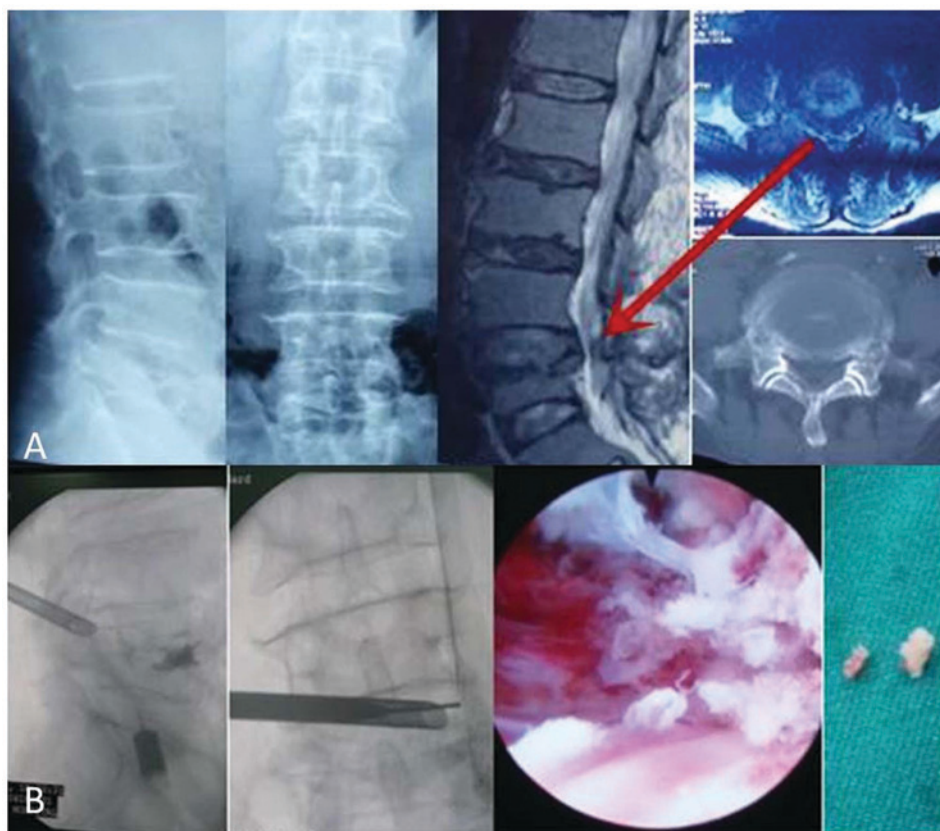


Figure 2. A 72-year-old male with lumbar sprain pain combined with lower extremity pain for 2 weeks with ineffective conservative treatment. The patient had a history of several surgeries. Underlying diseases included hypertension, diabetes, leukemia and coronary heart disease. The preoperative CCI, VAS, and JOA scores were 5, 8 and 9, respectively. VAS and JOA scores 12 months after surgery were 2 and 19, respectively. (A) Preoperative imaging examination showed L4-5 disc herniation and spinal stenosis (red arrow). (B) Intraoperative images of the percutaneous transforaminal endoscopic discectomy and the removal of intervertebral disc tissue.

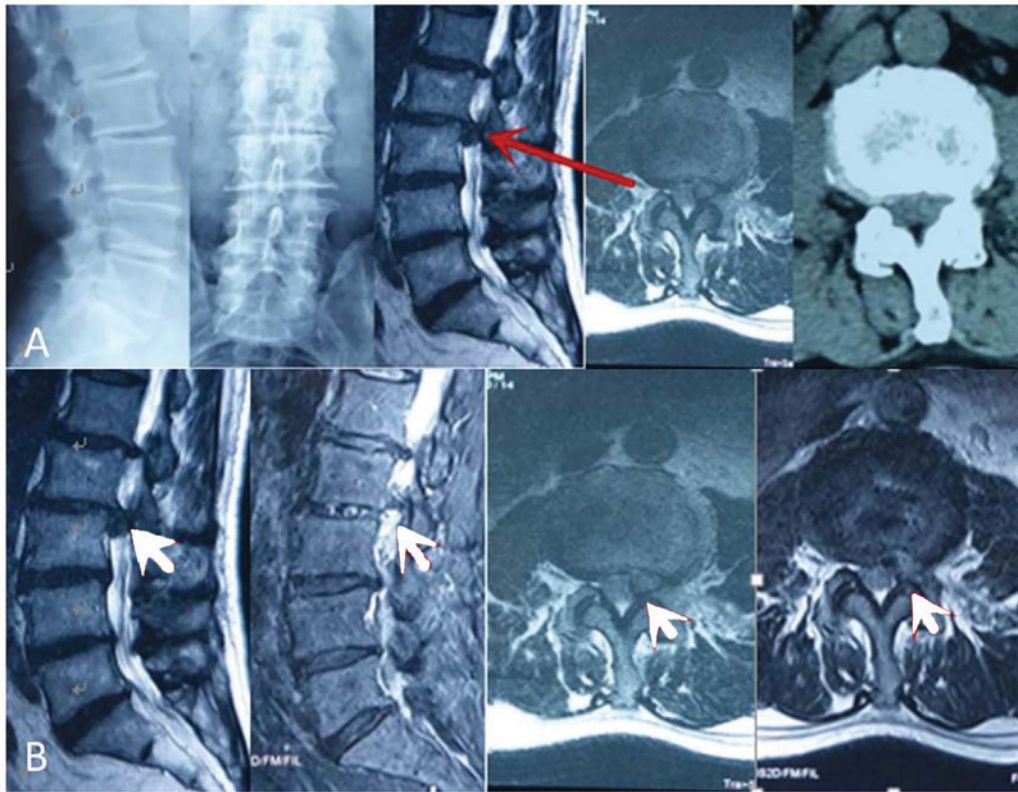


Figure 3. A 74-year-old male with lumbar pain combined with left lower limb pain for 2 months with ineffective conservative treatment. Underlying diseases included hypertension, diabetes, coronary heart disease and pulmonary infection. The preoperative CCI, VAS and JOA scores were 4, 8 and 14, respectively. VAS and JOA scores 12 months after surgery were 1 and 23, respectively. (A) Preoperative imaging examination showed L2-3 disc herniation and compressed left nerve root (red arrow). (B) Preoperative and postoperative decompression effects for percutaneous transforaminal endoscopic discectomy (white arrow heads).

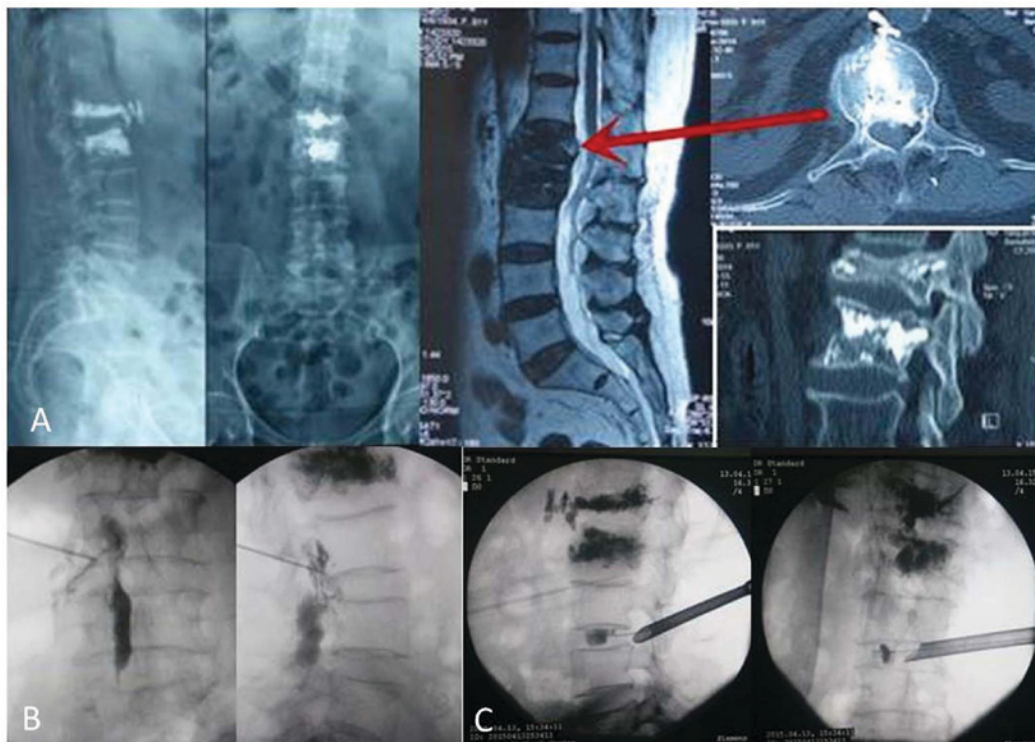


Figure 4. A 81 year-old female with lumbar pain combined with left lower limb pain for 6 months. The patient had a history of several surgeries for lumbar compression fractures. The underlying diseases included hypertension, diabetes and cerebrovascular disease. The preoperative CCI, VAS and JOA scores were 3, 7 and 12, respectively. VAS and JOA scores 12 months after surgery were 2 and 20, respectively. (A) There was no nerve compression in preoperative imaging examination. The arrow is pointing to L3-4 disc herniation. (B) Nerve root angiography showed L3-4 disc herniation, stenosis of left nerve root canal and intervertebral foramen. (C) Removal of nucleus pulposus by transforaminal endoscopic spine surgery.



Figure 5. A 75 year-old female with lumbar pain combined with right lower limb pain for 2 years and aggravated for 2 months. The patient had a history of lumbar degenerative scoliosis for 5 years. The underlying diseases included hypertension, diabetes, cerebrovascular disease and chronic bronchitis. The preoperative CCI, VAS and JOA scores were 4, 6 and 13, respectively. VAS and JOA scores 12 months after surgery were 2 and 24, respectively. (A) Preoperative imaging examination demonstrated multi-segment lumbar disc herniation, spinal stenosis with degenerative scoliosis (red arrow). (B) PTED surgery had remarkable decompression effect of spinal canal (red arrow).

group, indicating that the severity of preoperative underlying disease was greater in the PTED group. Open internal fixation surgery was a more established treatment option and was still the preferred surgery for patients. For patients in poor physical condition that could not undergo open internal fixation surgery, PTED was preferred, possibly resulting in the higher levels of preoperative CCI in the PTED group. Compared with traditional open fixation surgery, PTED surgery has advantages in terms of surgery time and intraoperative blood loss, but the intraoperative radiation exposure time was significantly higher when compared with open surgery, which was inconsistent with previous reports (8,34). The comparison of pain and neurological scores of patients in the two groups prior to and 12 months after surgery indicated that both surgeries could significantly alleviate pain and improve nerve function of the lower limbs, and there was no significant difference in short-term effects between the two surgeries. However, the pain scores were lower and neurological scores were higher among patients in the PTED group compared with the open surgery group at 1 week after surgery. These findings may be associated with the small incision and minimal injury to surrounding tissues during PTED surgery. Patients undergoing PTED surgery recovered faster, got out of bed earlier and suffered less perioperative pain, which was beneficial for the fast recovery of postoperative neurological function.

Patients in the open surgery group suffered from multiple postoperative complications, while patients in PTED group did not experience these complications. Patients with moderate levels of activity 12 h after PTED surgery protect the circulation of lower extremities (35), which is likely to lead to non-occurrence of postoperative complications. In addition, the use of low molecular weight heparin in the open surgery group could cause complications, particularly for the senior patients with distinct deterioration of cardiovascular function and poor stability of coagulation.

Four advantages of PTED were indicated in the treatment of lumbar degenerative disc disease for senior patients. First, in minimally invasive surgery under local anesthesia, there is a reduced requirement for high surgical tolerance. The surgery was suitable for patients with underlying diseases. Second, there was no constraint with regards to general anesthesia contraindications. After PTED surgery under local anesthesia, the compression of the nerve root and pain in patients was relieved, and neurological function was well recovered. Third,

PTED surgery was predicted to be effective in repairing lumbar disc herniation and multi-segment disc degeneration in patients with degenerative scoliosis. Lastly, the surgery was associated with fast recovery and fewer complications caused by long-term bed rest. Therefore, PTED surgery can achieve bilateral decompression, markedly shortened surgery time and improved prognosis for patients with neurological symptoms of both lower extremities.

Several points regarding PTED surgery are worth noting. First, due to the deformity of local anatomical structure of the spine, favorable images were of vital importance for patients with degenerative scoliosis. Surgery should be performed after adjusting the standard post-anterior position images of the responsible segments to avoid neurovascular injury. Second, for patients with distinct spinal stenosis, surgeons should pay attention to the decompression of lateral recess and removal of hypertrophic yellow ligament when removing the nucleus pulposus. Lastly, patients with severe degeneration were often accompanied by intravascular vascular hyperplasia with bleeding in PTED surgery, which obscured the surgical field. For older patients, their ability to coagulate was dysfunctional and the hemostatic drugs were not effective, to combat this complication surgeons can rotate the angle of channel or close the outlet using water pressure to stop bleeding. If the bleeding still cannot be effectively stopped, surgeons can fill the channel with hemostatic material.

Treatment selection should not be guided only by patient age. Surgeons should note the underlying diseases and physical tolerance of patients, and clinical treatment should be guided by functional examination of main organs. There was no recurrence in the PTED group during the follow-up period, which may be associated with relatively stable lumbar vertebrae. However, in the current study, the sample size of the PTED group was limited with a short follow-up time, leading to the ineffective evaluation of the postoperative recurrence of lumbar degenerative disc disease, which requires further study.

In conclusion, PTED resulted in reduced trauma and lower incidence of severe complications in the treatment of senior patients with lumbar degenerative disc disease compared with open surgery. Therefore, PTED is a safe and effective minimally invasive method for senior patients with lumbar degenerative disc disease, particularly those with underlying diseases and high anesthesia risk.

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Availability of data and materials

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

Authors' contributions

JYB and WZ designed the study, recruited the patients, analyzed the data and drafted the manuscript. XZL, JHC and XZW analyzed the data and revised the manuscript, WYD and YS collected and analyzed the pre-, intra- and postoperative data. All authors reviewed and approved the final manuscript.

Ethics approval and consent to participate

All experiments were approved by the Ethics Committee of The Third Hospital of Hebei Medical University (Shijiazhuang, China).

Patient consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

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