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Research Article

Assessment of factors implicated in bone fusion after percutaneous endoscopic lumbar intervertebral fusion

Zheng Huang[1]*, Xialin Li[1]*, Weihong Yi[1], Junfeng Gong[2], Yue Zhou[2]#, Yu Tang[2]

#[1]*Department of Orthopedics, Huazhong University of Science and Technology Union Shenzhen Hospital, Shenzhen, Guangdong, China*
[2]*Department of Orthopedics, Xinqiao Hospital affiliated to Army Military Medical University, Chongqing, China*
**These authors have made equal contributions to this study*

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ORCID iDs of the authors:
Z.H. 0000-0002-8857-3166;
X.L. 0000-0003-3313-9263;
W.Y. 0009-0001-4628-3312;
J.G. 0009-0002-8663-1956;
Y.Z. 0009-0005-3951-6148;
Y.T. 0009-0000-7790-9851.

#**Corresponding author:**
Yue Zhou
yankehuang52@163.com

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ABSTRACT:

Objective: Lumbar spinal fusion is a common procedure for treating spinal degenerative diseases. Percutaneous endoscopic lumbar interbody fusion (PELIF) is a minimally invasive technique that has gained popularity. However, the factors influencing fusion success rates after PELIF have not been well-studied.

Methods: This single-center retrospective study reviewed the medical records of 96 patients who underwent single-level PELIF for degenerative pathologies between 2018 and 2020. Fusion was evaluated using thin-slice computed tomography scans at 12 months by 2 independent radiologists and defined as no detectable lucency between bone and graft. Patients were categorized into fusion and non-fusion groups. Data on age, operative time, blood loss, drainage, hospital stay, surgical level, osteoporosis, endplateitis, body mass index, lumbar curvature, and bone morphogenetic protein (BMP) use were collected. Univariate tests (chi-square, Student's *t*-test, and analysis of variance) were employed to compare factors between groups. Significant factors were included in a multivariate logistic regression model with fusion as the dependent variable.

Results: The overall fusion success rate was 85.6% (86 fusion and 10 non-fusion). Univariate analysis revealed significant differences in age, osteoporosis, hypertension, diabetes, endplateitis, and BMP use between groups. Multivariate analysis identified osteoporosis (odds ratio (OR)=5.44, 95% CI, $P < .05$) and end-plate osteochondritis (OR=10.449, 95% CI, $P < .05$) as independent risk factors for non-fusion.

Conclusion: The use of BMP and endplateitis are significant factors that affect bone fusion outcomes after the PELIF procedure. These factors should be taken into account in order to improve postoperative bone fusion.

Level of Evidence: Level IV, Therapeutic Study.

Introduction

Spinal degenerative diseases, such as intervertebral disc herniation, spinal stenosis, and spondylolisthesis, are prevalent disorders in middle-aged and elderly patients.[1] Among these, degeneration of the lumbar intervertebral disc is the most common condition.[2] Lumbar spinal fusion is a common procedure used to treat spinal degenerative diseases.[3,4] In recent years, an increasing number of spine surgeons have started utilizing minimally invasive surgery (MIS) techniques for lumbar interbody fusions, which were first reported in 2002.[5] Minimally invasive surgery reduces tissue injuries, blood loss, and postoperative pain, and allows for faster recovery.[6-9] One example of MIS is percutaneous endoscopic lumbar interbody fusion (PELIF). The approach involves making a small incision of approximately 2.50 cm in length, located 2-3 cm next to the midline of the affected vertebral body segment. The paraspinalparaspinal muscles are then separated using a dilator, and the working channel of the METRxX-Tube minimally invasive surgery system is connected. Decompression, intervertebral disc removal, and intervertebral fusion are performed within the working channel.[10] However, compared to open surgery, minimally invasive fusion surgery has a smaller range for endplate processing and utilizes less autogenous bone graft. The factors that impact the success rate of fusion in full-endoscopic transforaminal lumbar interbody fusion have not been reported.

In this single-center study, we investigated patients who underwent lumbar spine fusion surgery for degenerative pathologies to identify the technical and patient-related factors that influence the success rate of fusion after PELIF. Our findings provide insights into the influencing factors which can be taken into account by surgeons to improve bone fusion after PELIF.

Material and methods

Patient recruitment

In the current study, we retrospectively reviewed the medical records of orthopedic patients who underwent single-level PELIF from 2018 to 2020 in a single medical institute. The study was approved byXinqiao Hospital affiliated to Army Military Medical University Xinqiao Hospital affiliated to Army military medical university (approval no: 20220617 date: 2022.6.17), and written informed consent was obtained from all individual participants. Inclusion

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criteria: (1) patients above the age of 45; (2) patients diagnosed with degenerative pathologies such as spondylolisthesis, stenosis, and intervertebral disk degeneration; and (3) patients who underwent single-level PELIF for degenerative pathologies. Exclusion criteria: (1) patients who underwent previous surgery in the same area; (2) fusion of the entire lumbosacral levels (L1–S1 fusion); (3) less than 6-month follow-up data available; or (4) nonexplorative spinal pathologies such as tumors, infections, or wounds.

Surgical procedure, diagnosis, and patient data collection

The single-level PELIF was conducted as previously described.[10] The surgical procedures involve the following steps: (1) Anesthesia: the patient was placed under general anesthesia to ensure comfort and unconsciousness during the procedure. The patient was positioned lying face down on a special operating table that allows access to the spine. (2) Incisions: one or more small incisions, typically less than an inch in length, were made on the patient's back over the affected lumbar spine region, serving as entry points for the specialized PELIF instruments. (3) Dilators and guide wires: a series of dilators and guide wires were inserted through the incisions. The dilators gradually enlarged the pathway to the spine, while the guide wires functioned to guide the subsequent instruments. (4) Endoscope insertion: once the access pathway was prepared, an endoscope—a thin, flexible tube with a camera and light source—was inserted through the dilated opening, providing visual guidance and magnified views of the spinal structures. (5) Discectomy and decompression: using specialized endoscopic instruments, any herniated disc material that may have been pressing on nearby nerves was removed. Additionally, a decompression procedure was conducted to relieve pressure on the spinal cord or nerve roots. (6) Interbody fusion: after completing the discectomy and decompression, the remaining disc material was removed to implant interbody in the prepared disc space between the adjacent vertebral bodies. FORGE® Cervical Allograft Spacer was utilized for the fusion (a corticocancellous interbody spacer, Globus Medical, Audubon, PA, USA), with pedicle screws being used for fixation. (7) Closure: once the interbody implants were in place, the endoscope and other instruments were removed, and the incisions were closed with sutures or surgical glue. Sterile dressings or adhesive bandages were applied to protect the incision sites. After PELIF, patients followed a standardized rehabilitation protocol. This involved using a lumbosacral orthosis for 6-8 weeks and avoiding bending, twisting, and lifting over 5 pounds. Physical therapy focused on core strengthening and flexibility exercises.

The diagnosis of degenerative spine was conducted by computed tomography (CT) scanning, and the fusion after PELIF was evaluated using thin-slice CT scanning by 2 experienced radiologists. The success of fusion was defined as no detectable cracks or lucency between lumbar intervertebral bones and graft (grade I and grade II fusion according to the Bridwell interbody fusion grading system).

HIGHLIGHTS

- This study analyzed factors influencing fusion success in 96 patients who underwent single-level PELIF for degenerative spinal pathologies, using thin-slice CT scans at 12 months to assess fusion and identify risk factors for non-fusion.
- The results showed an overall fusion success rate of 85.6%. Moreover, age, osteoporosis, hypertension, diabetes, endplateitis, and bone morphogenetic protein (BMP) use were associated with fusion status
- The results indicate that while BMP usage improve bone fusion after PELIF, osteoporosis and endplateitis may be factors negatively impacting post-PELIF bone fusion.

Endplateitis was diagnosed through magnetic resonance imaging (MRI) scanning by 2 independent radiologists to detect endplate cartilage inflammation and defects.

We collected information on patients' sex, age, operation time, intraoperative bleeding, postoperative drainage, length of hospitalization, surgical section, past medical history of osteoporosis and endplateitis (endplate osteochondritis), body mass index (BMI), lumbar curvature, and use of bone morphogenetic proteins (BMPs). Based on the data 12 months post-surgery, patients were categorized into either the non-fusion group or the fusion group.[3,4]

Statistical analysis

The aforementioned factors were assessed for normality, and a nonparametric test was conducted for single-factor analysis. Univariate and multivariate analyses were conducted to identify the independent factors influencing non-fusion in patients. Factors that showed significant differences between the groups were included in the multivariate analysis, with fusion as the dependent variable. A binary logistic regression model was employed to identify the independent factors causing non-fusion. Dichotomous variables were analyzed using chi-square examination. Uninterrupted variables were analyzed using Student's *t* examination and analysis of variance. Multivariate logistic regression was performed using a clinically derived model, which included confounding factors and excluded collinear factors after adjustment.

Results

The current study analyzed data from 96 patients who underwent single-level PELIF surgery for degenerative spinal conditions between 2018 and 2020. The cohort consisted of 37 males (38.5%) and 59 females (61.5%), with ages ranging from 45 to 77 years and a median age of 55 years. An overall fusion success rate of 85.6% was observed in this patient population. Out of the 96 patients, 86 were categorized into the fusion group, while the remaining 10 patients were assigned to the non-fusion group based on CT scanning results at 12 months post-surgery.

Initial normality testing revealed that variables such as age, operation time, intraoperative blood loss, postoperative drainage, and length of hospital stay did not follow a normal distribution in the dataset (Table 1). Single-factor analysis demonstrated significant differences between the fusion and non-fusion groups for the following factors: age, presence of osteoporosis, hypertension, diabetes, endplateitis, and use of BMPs. Notably, BMPs were only utilized in patients diagnosed with osteoporosis (Table 2).

Table 1. Single factor analysis by normality test

		Shapiro–Wilk		
	Fusion	**Statistics**	***df***	**Significance**
Age	Non-fusion	0.872	10	0.105
	Fusion	0.957	86	0.006
Operation time	Non-fusion	0.682	10	0.001
	Fusion	0.893	86	<0.001
Intraoperative bleeding	Non-fusion	0.781	10	0.008
	Fusion	0.646	86	<0.001
Postoperative drainage	Non-fusion	0.778	10	0.008
	Fusion	0.886	86	<0.001
Hospitalization time	Non-fusion	0.731	10	0.002
	Fusion	0.88	86	<0.001

Table 2. Single factor analysis of factors for fusion success

		Non-Fusion	Fusion	Z/c^2	*P*
Age		71 (62.5-75)	54 (49-63)	−3.619	<.001
Operation time		133.5 (129.25-146.25)	129.5 (115-145.25)	−0.943	.346
Intraoperative bleeding		50 (37.5-62.5)	50 (40-60)	−0.269	.788
Postoperative drainage		40 (30-42.5)	40 (30-50)	−0.044	.965
Hospital stay		3 (3-4)	3.5 (3-4)	−0.146	.884
Sex	Male	1 (10%)	36 (41.9%)	–	.083△
	Female	9 (90%)	50 (58.1%)		
Diagnosis	Spondylolisthesis	5 (50%)	42 (48.8%)	–	1△
	Non-spondylolisthesis	5 (50%)	44 (51.2%)		
Segments	L3/4	0 (0%)	6 (7%)	1.331△	.799△
	L4/5	8 (80%)	67 (77.9%)		
	L5/S1	1 (10%)	9 (10.5%)		
	L3/4, L4/5	1 (10%)	4 (4.7%)		
Osteoporosis	Normal	1 (10%)	65 (75.6%)	−4.951	<.001
	Osteopenia[a]	3 (30%)	19 (22.1%)		
	Osteoporosis[b]	6 (60%)	2 (2.3%)		
BMI	Normal	3 (30%)	38 (44.2%)	−1.465	.143
	Overweight	3 (30%)	37 (43%)		
	T1DM	4 (40%)	8 (9.3%)		
	T2DM	0 (0%)	3 (3.5%)		
Smoking	No	10 (100%)	79 (91.9%)	–	1△
	Yes	0 (0%)	7 (8.1%)		
High blood pressure	No	7 (70%)	80 (93%)	–	.049△
	Yes	3 (30%)	6 (7%)		
Diabetes	No	6 (60%)	84 (97.7%)	–	.001△
	Yes	4 (40%)	2 (2.3%)		
Physiological curvature of lumbar spine	Abnormal	1 (10%)	24 (27.9%)	–	.446△
	Normal	9 (90%)	62 (72.1%)		
Endplateitis	No	5 (50%)	83 (96.5%)	–	<.001△
	Yes	5(50%)	3 (3.5%)		
BMP*	Without BMP	2(20%)	68 (79.1%)	–	<.001△
	With BMP	8(80%)	18 (20.9%)		

△, Fisher's exact test; *P*, *P* value; Z/c^2, chi-square.
[a]Osteopenia: Bone mass density is measured using a dual-energy X-ray absorptiometry (DXA) scan. Bone mass density is 1 and 2.5 standard deviations (SDs) below the average peak young adult. This translates to a *T*-score between −1 and −2.5.
[b]Osteoporesis: diagnosed when bone mass density is 2.5 standard deviations (SDs) below the average of young adults, referred to as a *T*-score of −2.5 or lower.
*BMP was only used for patients with osteoporosis.

Multivariate logistic regression analysis identified osteoporosis and endplateitis as independent risk factors significantly associated with non-fusion after PELIF surgery (Table 3). The regression coefficient for osteoporosis (B = 1.694) indicated that with each increase in osteoporosis severity, the likelihood of non-fusion increased by a factor of 4.44 (odds ratio (OR)=5.44, $P < .05$). Similarly, patients with endplateitis had a significantly higher probability of non-fusion, with an odds ratio of 10.449 (B = 2.438, $P < .05$) compared to those without endplateitis (Figure 1). Other factors such as age, hypertension, diabetes, and BMP use did not demonstrate a statistically significant association with fusion success rates.

Discussion

The success of spinal surgery relies on achieving both immediate and long-term spinal stability. However, PELIF surgery has certain limitations that result in a reduced availability of autogenous bone for interbody fusion. Therefore, it is crucial to investigate the factors that influence interbody fusion. Currently, the success rate of

Table 3. Multi-factor analysis

							95% CI	
		B	Standard Error	Wald	Significant Difference	OR	Lower Limit	Upper Limit
Age		0.06	0.082	0.54	0.462	1.062	0.905	1.246
Osteoporosis		1.694	0.82	4.268	**0.039**	5.44	1.091	27.135
High blood pressure	With	-0.911	1.627	0.313	0.576	0.402	0.017	9.757
	Without	0				1		
diabetes	With	1.008	1.452	0.482	0.487	2.741	0.159	47.237
	Without	0				1		
Endplateitis	With	2.438	1.133	4.627	**0.031**	11.449	1.242	105.567
	Without	0				1		
BMP	With	1.357	1.29	1.106	0.293	3.883	0.31	48.649
	Without	0				1		

Values in bold indicate statistical significance.
B, regression coefficient; OR, odds ratio.

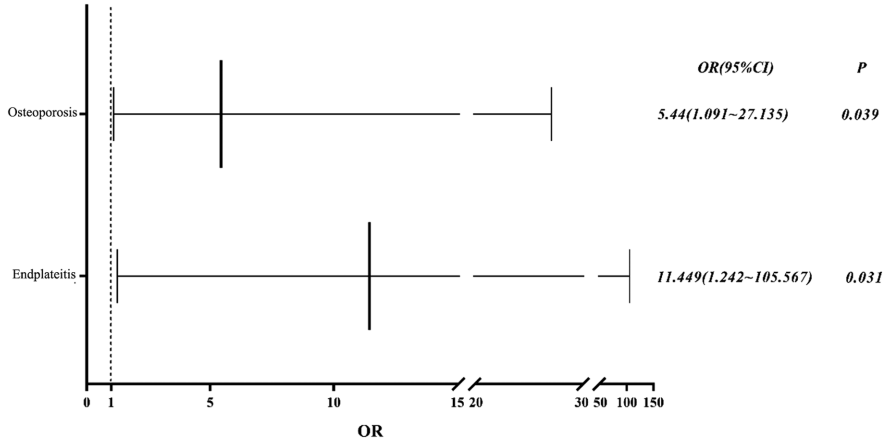

Figure 1. Forest map showing the analysis of independent factors.

lumbar fusion surgery ranges from 85% to 95%[11] In our study, we also showed an overall fusion success rate of 85.6%.

Osteoporosis is a significant public health issue worldwide, particularly due to the aging population and changing lifestyles. In their study, Liu et al. established an experimental model and found that approximately 6.6% of elderly Chinese patients suffer from osteoporosis. This proportion is expected to rise to 8.2% by 2010 and a staggering 13.6% by 2050.[12] Notably, osteoporosis has been shown to affect spinal fusion, as demonstrated in animal experiments.[13] Our findings indicate that the severity of osteoporosis is directly related to the likelihood of non-fusion. Osteoporosis reduces vascular distribution, bone marrow quality, and osteoblast function after lumbar fusion surgery.[14] Furthermore, the development of osteoporosis significantly decreases endochondral ossification after lumbar fusion, negatively impacting bone maturation and formation.[6] Additionally, osteoporosis is associated with various complications such as kyphosis,[15-17] screw loosening,[18-19] and hardware subsidence,[20] all of which increase the risk of spinal non-fusion. To improve the success rate of spinal fusion in individuals with osteoporosis, it is crucial to enhance bone constitution in the early stages after fusion operation.

Since the initiation of market-oriented economic reform in 1978, China has implemented reforms in various sectors, including the privatization of industry and agriculture.[21] These reforms have had an adverse impact on the public medical insurance system and medical service system, making it challenging for some individuals to afford basic curative services.[22] As the current medical insurance policy does not offer reimbursement, none of the patients in this study received treatment for osteoporosis prior to surgery. However, providing early treatment for osteoporosis could potentially enhance bone condition and facilitate fusion.

In this study, a total of 5 cases of non-fusion were observed in patients with endplateitis, accounting for 50% of all non-fusion cases. This indicates that endplateitis has a significant impact on fusion. Endplateitis, also known as endplate osteochondritis, is often caused by intervertebral disc degeneration.[23,24] There are various risk factors associated with vertebral endplate inflammation, such as age, old trauma, aseptic inflammation, and long-term hormone use. Clinical manifestations include lower back pain and local fluid accumulation, which can cause intervertebral disc inflammation, yellow ligament atrophy, and peripheral tissue inflammation. Patients with endplateitis are more likely to experience non-fusion compared to those without it. This association is supported by changes in signal intensity in the bone marrow of the vertebral body adjacent to the degenerative disc and endplate, as observed in MRI scans. These changes in vertebral bone marrow can be classified into 3 types.[23,24] While there have been numerous studies on endplate degeneration and its symptoms, only a few have investigated the correlation between model change (MC) and spinal fusion. Kwon et al. demonstrated that the fusion success rate for non-degenerative patients was 97%, whereas for MC patients it was 83%.[25] Modic degenerative lesions result in edema of the vertebral endplate and subchondral bone, subsequently leading to microfractures in cancellous bone and cracks in the endplate. This is accompanied by an increase in vascular density, as well as the number of nerve endings and the levels of pro-inflammatory chemical mediators. Inflammatory cytokines contribute to the differentiation and activity of osteoclasts and facilitate their recruitment to the bone surface.[26-28] Studies have shown that RANKL, high levels of IGF-1, and MCP-1 can diffuse into the subchondral bone, leading to osteoclastogenesis and bone loss.[29-31] Additionally, inflammatory factors can also promote osteogenesis, which contributes to the development of MC type III endplate sclerosis. Thicker endplate sclerosis poses challenges in creating a suitable fusion bed.[32] Therefore, we hypothesize that the inflammatory factors secreted by degenerative endplates and intervertebral discs worsen vertebral body erosion and play a significant role in fusion failure.

This study also demonstrated that the use of BMP does have a significant impact on fusion. Bone morphogenetic protein can stimulate the conversion of mesenchymal stem cells into osteoblasts and promote osteoblast formation.[33,34] Recombinant BMP-2 (rhBMP-2) administered through systemic injection has been shown to enhance bone formation in animal models and patients with type I and type II osteoporosis.[35] However, there are urgent issues related to the use of growth factors that need to be addressed, such as short-term bioavailability, the requirement for biological carriers, and the regulation of growth factor release over time.[36] While BMP offers numerous advantages, it does not improve the mechanical stiffness and strength despite increasing the volume of the fusion block after spinal surgery.[37,38] The efficacy of BMP is also influenced by the dosage and delivery method.[39,40] The original rhBMP-2, an Food and Drug Administration-approved commercially available analog of BMP, has been used in clinical practice since 2002. Nevertheless, the biological activities of its analogues are comparatively lower in vivo. Therefore, in clinical practice, it is recommended to use rhBMP-2 with a high level of biological activity.

There are several other limitations in our study. First of all, due to the limited sample size and the usage of BMP only in patients with osteoporosis, we could not draw the conclusion that the usage of BMP is beneficial in non-osteoporotic patients. Moreover, the usage of different types of allografts may also differentially affect bone fusion, which requires a more detailed study using a large cohort of patients. Importantly, future studies should compare the performance of PELIF and other surgical interventions on the bone fusion, as well as the associated complications.

Based on our research, the fusion success rate in our study was 85.6% in patients with lumbar degenerative pathology who had been subjected to PELIF. Notably, cases that utilized allograft bone and BMP demonstrated a higher fusion success rate of 80%, and the use of BMP and the presence of endplateitis were significant factors influencing postoperative fusion after PELIF. Therefore, surgeons should take these factors into account these factors for achieving successful postoperative fusion.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Xinqiao Hospital affiliated to Army military medical University (Approval no.20220617: Date: 2022.6.17).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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