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Development of Modic Changes After Percutaneous Endoscopic Transforaminal Lumbar Discectomy: From Risk Analysis to Prediction Modeling

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Objective: This study examines the occurrence of Modic changes (MC) within the first year following percutaneous endoscopic transforaminal lumbar discectomy (PETD) and investigates associated risk factors.

Methods: This study adopted a retrospective cohort design. Between January 2019 and June 2023, 538 patients diagnosed with single-level lumbar disc herniation and treated with PETD were included. The patients were divided into a training set and a validation set based on their surgery dates. Preoperative radiographic parameters and perioperative indicators were evaluated. Univariate analysis examined risk factors for postoperative MC. Gender-specific subgroups were analyzed. Binary logistic regression developed a predictive model for postoperative MC, assessed using ROC, calibration, and decision curves.

Results: The incidence of MC at one year after PETD was 24.8%. Logistic regression identified 8 significant risk factors for MC after PELD: longer symptom duration, proximity of herniated segment to sacrum, severe disc degeneration, reduced disc height, greater vertebral endplate concavity angle, segmental instability, and lumbar-sacral fusion. Menopause and herniation type were identified as female-specific risk factors. In males, total cholesterol levels were additionally found to be a risk factor for postoperative MC. The male and female subgroup models exhibited satisfactory performance across ROC analysis, calibration plots, and decision curve analysis. Specifically, for male patients, the area under the curve (AUC) was 0.831 for the training set and 0.820 for the validation set; for female patients, the AUC was 0.911 for the training set and 0.868 for the validation set. A nomogram was developed to visualize the model.

Conclusion: This study explored the relevant risk factors of MC after PETD and visualized the prediction model by nomogram, which is beneficial to optimize the surgical scheme of PETD to improve the clinical efficacy.

Keywords: Modic changes, percutaneous endoscopic transforaminal discectomy, lumbar disc disease, risk analysis

Introduction

Lumbar disc herniation (LDH) is a prevalent cause of back and leg pain, significantly impairing quality of life. Conservative treatments like medication, rest, or physical therapy can partially alleviate symptoms. Surgical interventions, especially percutaneous endoscopic transforaminal lumbar discectomy (PETD), are the optimal choice for patients unresponsive to conservative treatments.[1] It causes minimal damage to adjacent structures, reduces soft tissue injury, leads to fewer complications, and requires shorter operation time.[2,3] This procedure directly targets nerve root compression, alleviating pain in lower limbs. However, 5–20% of the patients may experience unsatisfactory outcomes following PETD surgery,[1] enduring residual back pain that significantly disrupts daily activities.[4] Studies suggest that PETD surgery may exacerbate Modic changes at the surgical site.[5,6] Barzouhi et al found that 50.6% (85/168 cases) of the

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patients developed new Modic changes within the first year following lumbar discectomy, predominantly transitioning from no Modic changes to Modic Type 1.[7] Modic changes, especially Type 1, are linked with chronic back pain. Patients showing new Modic changes after PETD surgery often experience delayed relief of back pain.[8] Therefore, postoperative Modic changes may influence the clinical prognosis of LDH patients who had undergone PETD to some extent. Identifying risk factors of post-PETD Modic changes to predict and improve adverse outcomes of LDH patients is crucial for enhancing clinical decision-making and patient satisfaction.

However, the additional risk factors contributing to post-PETD Modic changes remain unclear. In this paper, we conducted a cohort study aiming to: a) investigate the incidence rate of post-PETD Modic changes; b) thoroughly analyze related risk factors and construct a predictive model to assist with preoperative assessment; and c) explore interventions to improve the outcomes of the patients who had undergone PETD.

Methods

Patient Population

This retrospective cohort study was conducted at a single center and included a total of 538 patients who underwent PETD treatment at our institution between January 2019 and June 2023. The participants were divided into two independent cohorts based on their recruitment dates: a training set and an external validation set. Inclusion criteria were as follows: 1) LDH patients who failed to respond to the conservative treatment and had radicular pain for at least 6 weeks; 2) patients showing no spinal instability on functional X-rays; 3) patients who were followed up for at least 1 year after disc excision surgery and had complete preoperative and postoperative imaging data; and 4) Patients without Modic changes at the surgical segment preoperatively, but who developed Modic changes within one year after PETD. Exclusion criteria included spinal stenosis, lumbar segment instability, cauda equina syndrome, spinal infection, and history of lumbar spine surgery.

Surgical Procedure

Surgeries were performed by the same surgical team, which possesses extensive clinical experience and proficiency in PETD techniques. During the procedure, the surgeons utilized microsurgical instruments under endoscopic guidance to excise all extradural and subdural tissues that were compressing the intervertebral disc, including protruding or degenerated disc material. Additionally, they removed the loose portions of the disc to alleviate pressure on the nerve roots. After exploring the dural sac and performing nerve root decompression, bipolar radiofrequency coagulation was employed for hemostasis, followed by the closure of the incision.

During the procedure, we successfully achieved a complete decompression endpoint. By employing precise endoscopic techniques, we meticulously identified and effectively removed the pathological tissue and bony structures that were compressing the nerve roots. The high-definition endoscopic view enabled the surgeon to monitor the status of the neural structures in real time, ensuring adequate decompression while maximizing the preservation of surrounding healthy tissues. This was further validated by the observation of nerve relaxation following the alleviation of compression.

Postoperative evaluations demonstrated a significant improvement in the patient's clinical symptoms, with a marked reduction in pain scores and a satisfactory recovery of functional mobility. Additionally, postoperative imaging studies confirmed the normal position and morphology of the nerve roots and spinal cord, revealing no signs of residual compression.

Clinical Evaluation

All patients underwent preoperative magnetic resonance imaging (MRI) of the lumbar spine, three-dimensional computed tomography (CT) scanning, and X-ray examinations. Clinical follow-ups were conducted at 1 month, 3 months, 6 months, and 1 year postoperatively, along with MRI examinations at each time point. Each MRI image was assessed to determine whether there were lumbar Modic changes and the types. To eliminate bias, all radiological parameters were analyzed and confirmed by one spine surgeon and one radiologist. Any discrepancies in scoring were discussed until a consensus was reached.

The sagittal T1-weighted images were reviewed at first and then their correlations with sagittal and axial T2-weighted images were analyzed. Modic MRI classification included: low signal areas extending from the vertebral endplate on T1-weighted images and high signal areas on T2-weighted images (Type 1), high signal areas on both T1- and T2-weighted images (Type 2), and low signal areas on both T1- and T2-weighted images (Type 3). To differentiate Modic changes from signal variations caused by other vertebral bone marrow abnormalities, only vertebral marrow signal changes extending from the endplate and involving two or more adjacent sagittal slices were classified as Modic changes. Postoperative Modic changes were defined as the absence of Modic changes before surgery and the appearance of Modic changes (of any type) within 1 year after surgery (Supplementary Figure 1). Data on perioperative factors that might affect the development of postoperative Modic changes were collected, including: (1) demographic characteristics (ie, age, gender, menopausal status, BMI, comorbidities such as hypertension, diabetes, rheumatoid arthritis); (2) preoperative radiological parameters (ie, Pfirrmann grade, disc height index (DHI), lumbar lordosis angle, endplate concavity angles, segmental instability, lumbar-sacral fusion,[9] posterior ring apophyseal fracture (PRAF),[10] disc calcification or presence of gas, disc protrusion type and side, and scoliosis); (3) surgical factors (ie, duration of symptoms, operation time, surgical approach, surgical segment, and blood loss); and (4) blood parameters (ie, triglycerides and total cholesterol).

We analyzed the T2-weighted sagittal sequences and used the classification system proposed by Pfirrmann et al to assess the degree of disc degeneration. According to the Fardon classification, disc herniations were categorized into three types, including protrusion, extrusion, and sequestration.[11] Endplate concave angle (ECA), defined as the angle of endplate concavity, was measured separately for the upper and lower endplates. On the sagittal reconstruction of three-dimensional CT, the endplates of the vertebral body are curved. A line is drawn from the top/bottom of the curve to the endpoints, and the angle between these two lines.[12] DHI was evaluated according to the measurement method proposed by Kim.[13] The disc height is measured at different points (anterior and posterior sections) and then normalized against the vertebral body height. Lumbar lordosis angle is measured by drawing lines along the superior endplate of L1 and the superior endplate of S1 on a lateral X-ray. Measurements of flexion IVA, extension IVA, and sROM in the flexion and extension positions were taken. IVA is defined as the angle between the upper and lower endplates, and sROM refers to the difference between extension and flexion IVA values[14](Supplementary Figure 2). Flexion-extension radiographs are used to assess the range of motion and detect any abnormal vertebral movements or excessive motion, which helps to quantify instability.

Statistical Analysis

We performed statistical analysis of the data using SPSS 22.0 statistical software and Python 3.7. Non-normally distributed continuous data were represented as median (Q1, Q2) and compared between groups using the Mann–Whitney *U*-test. Normally distributed continuous data were indicated by mean ± standard deviation, and between-group comparisons were conducted using independent sample *t*-tests. Categorical data were expressed as frequencies and percentages, and between-group comparisons were performed using the chi-square test or Fisher's exact test. Variables with a P-value of < 0.2 in between-group comparisons were further included in the multivariable logistic regression analysis. A P-value of < 0.05 was considered statistically significant. The subgroup analysis was performed based on gender. A multivariable stepwise logistic regression analysis was used to develop the predictive model. The model was externally validated and its performance was evaluated in terms of discrimination, calibration, and clinical utility. Discrimination was assessed using the receiver operating characteristic (ROC) curve, while calibration was evaluated through the Hosmer-Lemeshow goodness-of-fit test and calibration plots. Clinical utility was assessed using decision curve analysis (DCA). Based on the cutoff levels generated from the ROC analysis, participants were classified into low-risk and high-risk groups. Finally, a nomogram was created to visualize the model using the "rms" package.

Results

Population Characteristics and Imaging Data

A total of 538 patients with LDH who underwent PETD treatment were included in this study (male-to-female ratio = 276:243). Based on the surgical date (with January 1, 2023, as the cutoff) and ensuring that the sample size of the validation set was no less than 20% of the training set, the participants were divided into a training set of 419 patients (male-to-female ratio = 226:193) and a validation set of 119 patients (male-to-female ratio = 50:69). No statistically significant differences were found in the baseline characteristics between the training set and the validation set, suggesting that the validation set meets the criteria for external validation and is well-matched with the training set (Table 1). The incidence rate of post-PETD Modic changes among the patients was 24.8%. The patients in the training set were divided into two groups: those with new Modic changes (n = 148) and those without new Modic changes (n = 367). There were no statistically significant differences in age (p=0.414) or BMI (p=0.515) between the two groups. However, a significant difference in gender was observed between the two groups (p=0.01). Table 1 summarizes the differences in demographic characteristics and relevant risk factors between the two groups at baseline. It was found that there were statistically significant differences between the two groups in terms of symptom duration (p=0.000), surgical segment (p=0.014), calcification and the presence of gas in the surgical segment (both p=0.001), intervertebral space height (p=0.000), degree of disc degeneration (p=0.000), angles of upper and lower endplate concavities (both p=0.000), postoperative segmental instability (p=0.000), and lumbar-sacral fusion (p=0.001) (Table 2). Subsequently, variables with a p value of < 0.10 were selected for the multivariate logistic regression analysis. Further analysis revealed that longer symptom duration (OR: 1.031, 95% CI: 1.018–1.044), surgical segment proximity to the sacrum (OR: 2.492, 95% CI: 1.538–4.037), disc degeneration (OR: 2.856, 95% CI: 1.951–4.179), greater angle of upper (OR: 0.982, 95% CI: 0.961–1.004) or lower (OR: 0.923, 95% CI: 0.878–0.970) endplate concavity, postoperative segmental instability (OR: 2.151, 95% CI: 1.119–4.136), and lumbar-sacral fusion (OR: 4.429, 95% CI: 1.125–17.432) were significant risk factors for the development of postoperative new Modic changes (all P < 0.05) (Figure 1). A predictive model was constructed based on the risk factors selected, demonstrating good discrimination with an area under the curve (AUC) of 0.836 (95% CI: 0.790–0.881). The equation for predicting the probability of developing new Modic changes in individual patients after PETD surgery is as follows:

Probability of developing new Modic changes after PETD surgery = 0.031 * symptom duration + 0.913 * surgical segment + 1.049 * disc degeneration grade + 0.766 * postoperative segmental instability + 1.488 * lumbar-sacral fusion - 0.076 * intervertebral space height - 0.018 * angle of upper endplate concavity - 0.080 * angle of lower endplate concavity + 10.726.

Subgroup Analysis - Post-PETD Modic Changes in Females

Considering the influence of gender on the progression of postoperative Modic changes, we further investigated the risk factors for the development of new MODIC changes separately in male and female patients.

In the subgroup analysis of female patients showing new Modic changes after surgery, the patients were divided into two groups, namely, those showing new Modic changes (n=62) and those showing no new Modic changes (n=131). Significant differences were observed between the two groups in menopause (p=0.000), duration of symptoms (p=0.000), side of protrusion (p=0.007), surgical segment (p=0.008), calcification or the presence of gas in the surgical segment (both p=0.001), disc height (p=0.000), degree of disc degeneration (P=0.000), angles of upper and lower endplate concavities (both p=0.000), segmental instability (p=0.000), and lumbar-sacral fusion (p=0.023) (Table 3). Subsequently, fourteen indicators with a P value of < 0.10 were selected for the multivariate logistic regression analysis. The results

Table 1 Baseline Characteristics of Training and Validation Sets

Items	Male Group			Female Group		
	Training Set	Validation Set	p	Training Set	Validation Set	p
Age (years)	47.64 ± 16.97	49.70 ± 17.05	0.515	54.58 ± 15.60	54.16 ± 14.14	0.823
BMI (kg/m²)	26.01 ± 3.81	26.27 ± 3.5	0.558	24.87 ± 3.50	25.36 ± 3.73	0.335
HTN, n (%)	0.22	0.20	0.790	0.30	0.30	0.888
DM, n (%)	0.05	0.02	0.320	0.13	0.12	0.770
RA, n (%)	0.01	0.04	0.200	0.02	0.02	0.694

Abbreviations: HTN, hypertension; DM, Diabetes Mellitus; RA, rheumatoid arthritis.

Table 2 Characteristics of Total Patients

Items	Post-PETD Modic Changes Group (n=419)		
	EG	**CG**	**p**
Female, n (%)	62 (59.6%)	42 (40.4%)	**0.010**
Menopause, n (%)	29 (46.8%)	70 (53.4%)	0.387
Age (years)	52.4 (41.0,62.8)	50.3±17.5	0.414
BMI (kg/m²)	25.7 ± 3.4	25.4±3.8	0.511
TG (mmol/L)	1.8 ± 3.8	1.7 ± 1.4	0.085
TC (mmol/L)	5.4 ± 1.2	5.2 ± 1.2	0.103
DM, n (%)	6 (5.8%)	31 (9.8%)	0.204
HTN, n (%)	23 (22.1%)	83 (26.3%)	0.389
RA, n (%)	2 (1.9%)	5 (1.6%)	0.817
Preoperative duration (month)	6.3 (2.5,29.8)	2.5 (1.0,6.1)	**0.000**
Surgical duration (min)	107.3 ± 32.5	101.8±32.9	0.141
Intraoperative bleeding (mL)	5:58:41	44:181:90	**0.014**
Surgical segment (L3/4: L4/5: L5/S1)	10.4 ± 3.5	10.8±7.5	0.507
Herniation type (protrusion: extrusion: sequestration)	2:39:63	3:132:180	0.563
DHC,n (%)	45 (43.3%)	84 (26.7%)	**0.001**
Gas, n (%)	24 (23.1%)	32 (10.2%)	**0.001**
SCS,n (%)	17 (16.3%)	53 (16.8%)	0.910
Pfirrmann grade (2: 3: 4)	8:46:50	133:102:80	**0.000**
DH (mm)	10.5 (8.8,13.2)	12.4 (10.2,15.6)	**0.000**
sROM (deg)	3.3 (2.0,5.7)	3.9 (1.7,6.2)	0.611
LL (deg)	32.4 ± 12.2	33.6 ± 14.3	0.469
Sacral slope angle (deg)	22. 5 ± 8.6	23.7 ± 9.9	0.215
Superior ECA (deg)	167.7 (162.8,173.1)	173.2 (167.7,176.8)	**0.000**
Inferior ECA (deg)	172.2 (167.6,176.8)	175.5 (171.6,177.9)	**0.000**
Slippage, n (%)	32 (30.8%)	45 (14.3%)	**0.000**
LSTV,n (%)	9 (8.7%)	5 (1.6%)	**0.001**

Notes: Bold font when p<0.05; n (%): the number of positive individuals in each group and their proportion in that group.
Abbreviations: EG, Experimental group; CG, Control group; TG, triglycerides; TC, total cholesterol; DM, Diabetes Mellitus; HTN, hypertension; RA, rheumatoid arthritis; DHC, Disk Herniation Calcification; SCS, Spinal Curvature Scoliosis; DH, intervertebral disc height; sROM, sagittal range of motion; LL, Lumbar lordosis angle; ECA, endplate concave angle; LSTV, lumbosacral transitional vertebrae.

showed that menopause, longer duration of symptoms, surgical segment proximity to the sacrum, disc degeneration, decreased disc height, increased angle of upper endplate concavity, segmental instability, and protruded type of disc herniation were significant risk factors for the development of new Modic changes in female patients (P<0.05) (Figure 1). Based on the risk factors selected, a predictive model was established (Figure 2), with an AUC of 0.911 (95% CI: 0.868–0.954). The equation for calculating the probability of post-PETD Modic changes in female patients is as follows:

Probability of post-PETD Modic changes in female patients = 0.952 menopause + 0.047 duration of symptoms (months) + 1.186surgical segment + 1.338 disc degeneration grade + 1.067 segmental instability - 0.230 disc height - 0.112*angle of upper endplate concavity in the surgical segment + 0.154.

Subgroup Analysis - Post-PETD Modic Changes in Males

In the subgroup analysis of male patients who developed postoperative new Modic changes, the patients were classified into two groups, ie, the group with new Modic changes (n=61) and the group without new Modic changes (n=202). Significant differences were observed between the two groups in terms of total cholesterol (p=0.025), duration of symptoms (p=0.000), disc height (p=0.048), degree of disc degeneration (P=0.000), angles of upper and lower endplate concavities (p=0.000 and p=0.016, respectively), and lumbar-sacral fusion (p=0.016) (Table 3). Nine indicators with a P value of < 0.10 were selected for the subsequent multivariate logistic regression analysis (Figure 1). The study revealed that longer duration of symptoms, severe disc degeneration, decreased disc height, and increased angle of upper endplate

Predictor	β	OR (95%CI)	p
Subgroup A: Postoperative new-onset VS non-onset MC			
Preoperative duration	0.031	1.031 (1.018,1.044)	0.000
Surgical segment	0.913	2.492 (1.538,4.037)	0.000
Pfirrmann grade	1.049	2.856 (1.951,4.179)	0.000
Surgical segmental slippage	0.766	2.151 (1.119,4.136)	0.022
Lumbosacral transitional vertebrae	1.488	4.429 (1.125,17.432)	0.033
Disc height	-0.076	0.926 (0.86,0.998)	0.044
Superior ECA	-0.018	0.982 (0.961,1.004)	0.106
Inferior ECA	-0.08	0.923 (0.878,0.97)	0.002
Subgroup B: Postoperative new-onset VS non-onset MC in females			
Preoperative duration	0.047	1.048 (1.02,1.077)	0.001
Surgical segment	1.186	3.275 (1.453,7.381)	0.004
Pfirrmann grade	1.338	3.813 (1.88,7.735)	0.000
Surgical segmental slippage	1.067	2.907 (1.033,8.182)	0.043
Herniation type	1.154	3.171 (1.322,7.607)	0.010
Menopause	0.952	2.591 (0.987,6.803)	0.053
Disc height	-0.23	0.794 (0.687,0.918)	0.002
Superior ECA	-0.112	0.894 (0.833,0.96)	0.002
Subgroup C: Postoperative new-onset VS non-onset MC in males			
Preoperative duration	0.03	1.031 (1.014,1.047)	0.000
Pfirrmann grade	0.781	2.185(1.316,3.628)	0.003
Total cholesterol	0.405	1.499(1.094,2.054)	0.012
Superior ECA	-0.127	0.881(0.829,0.936)	0.000

Figure 1 Logistic regression analysis for patients in each subgroup.
Abbreviation: ECA, endplate concave angle.

concavity were significant risk factors for the development of new Modic changes in male patients (P<0.05). Based on the risk factors selected, a predictive model was established (Figure 2), with an AUC of 0.831 (95% CI: 0.765, 0.897). The equation for predicting the probability of post-PETD Modic changes in male patients is as follows:

Probability of post-PETD Modic changes in male patients = 0.405 total cholesterol + 0.030 duration of symptoms (months) + 0.781 degree of disc degeneration grade - 0.127 angle of upper endplate concavity in the surgical segment + 15.041.

Evaluation of the Predictive Model

Logistic regression models for predicting postoperative new Modic changes in the overall population and subgroups of men and women were established. The AUCs of the models for men and women were 0.777 (95% CI: 0.701, 0.854) and 0.877

Table 3 Characteristics of Patients in the Male and Female Subgroups of Post-PETD Modic Changes

	Male Subgroup			Female Subgroup		
	EG	**CG**	**p**	**EG**	**CG**	**p**
Age (years)	49.81±12.88	47(32.0, 61.0)	0.308	54.8 ± 16.2	58.0 (42.0,67.0)	0.509
Menopause, n (%)				44 (57.0%)	57 (43.5%)	**0.000**
BMI (kg/m²)	26.4 ± 2.9	25.7 (22.6,28.4)	0.322	25.0 (22.4,27.0)	24.7 ± 3.5	0.647
TG (mmol/L)	1.24 (0.91,2.04)	1.4 (0.91,2.04)	0.973	1.0 (0.8,1.5)	1.3 (0.8,1.9)	0.085
TC (mmol/L)	5.42 (4.83,6.12)	5.04 (4.28,5.76)	**0.025**	5.3 ± 1.1	5.3 ± 1.3	0.960
DM, n (%)	0	12 (6.5%)	0.089	6 (9.7%)	19 (14.5%)	0.351
HTN, n (%)	8 (19%)	41 (22.3%)	0.646	15 (24.2%)	42 (32.1%)	0.263
RA, n (%)	0 (0.00%)	3 (1.6%)	0.405	2 (3.2%)	2 (1.5%)	0.439
Preoperative duration (month)	5.63 (1.25,18.7)	2.25 (0.5,6.0)	**0.000**	7.5 (2.5,41.7)	2.5 (1.0,8.3)	**0.000**
Surgical duration (min)	105 (78.75,120)	95 (75,125)	0.516	108.2 ± 32.9	101.1 ± 30.8	0.145
Intraoperative bleeding (mL)	9.88 ± 3.4	11.03 ± 9.14	0.196	10.8 ± 3.5	10.5 ± 4.2	**0.008**
Surgical segment (L3/4: L4/5: L5/S1)	2:23:17	28:91:65	0.937	3:35:24	16:90:25	0.254
Herniation type (protrusion: extrusion: sequestration)	1:18:23	2:66:116	0.532	1:21:40	1:66:64	0.093
DHC,n (%)	14 (33.3%)	50 (27.2%)	0.424	31 (50.0%)	34 (26.0%)	**0.001**
Gas, n (%)	6 (14.3%)	19 (10.3%)	0.460	18 (29.0%)	13 (9.9%)	**0.001**
SCS,n (%)	5 (11.9%)	29 (15.8%)	0.069	50 (80.6%)	24 (18.3%)	0.863
Pfirrmann grade (2: 3: 4)	5:22:15	89:48:47	**0.000**	3:24:35	44:54:33	**0.000**
DH (mm)	11.1 (9.1,15.1)	12.6 (10.6,15.9)	**0.048**	10.3 (8.1,12.5)	12.1 (9.9,14.9)	**0.000**
sROM (deg)	3.3 (2.1,6.7)	4 (1.8,6.4)	0.848	3.2 (1.4,5.4)	3.7 (1.6,6.0)	0.643
LL (deg)	34.2 ± 13.03	34.1 (22.9,41.9)	0.587	31.2 ± 11.6	34.7 ± 14.1	0.091
Sacral slope angle (deg)	23.5 ± 7.8	23.6 ± 10.2	0.96	21.9 ± 9.1	23.5 (17.2,29.7)	0.277
Superior ECA (deg)	167.7 (161.1,172.5)	172.9 (167.43,176.4)	**0.000**	168.7 (163.0,173.4)	174 (168.5,177.7)	**0.000**
Inferior ECA (deg)	171.9 (169.6,177.6)	175.5 (171.4,177.7)	**0.016**	172.8 (167.1,176.2)	175.7 (172.2,178.0)	**0.000**
Slippage, n (%)	8 (19%)	24 (13%)	0.314	24 (38.7%)	19 (14.5%)	**0.000**
LSTV,n (%)	3 (7.1%)	2 (1.1%)	**0.016**	6 (9.7%)	3 (2.3%)	**0.023**

Notes: Bold font when p<0.05; n (%): the number of positive individuals in each group and their proportion in that group.
Abbreviations: EG, Experimental group; CG, Control group; TG, triglycerides; TC, total cholesterol; DM, Diabetes Mellitus; HTN, hypertension; RA, rheumatoid arthritis; DHC, Disk Herniation Calcification; SCS, Spinal Curvature Scoliosis; DH, intervertebral disc height; sROM, sagittal range of motion; LL, Lumbar lordosis angle; ECA, endplate concave angle; LSTV, lumbosacral transitional vertebrae.

(95% CI: 0.823, 0.931), respectively. The predictive models for subgroups of men and women were superior to that for the overall population, indicating the rationality of subgroup analyses for the patients showing postoperative new Modic changes. The cutoff thresholds of 0.218 and 0.570 were set for predicting the probabilities of developing postoperative new Modic changes in men and women, respectively. Based on the cutoff thresholds, both male and female patients were divided into low-risk and high-risk groups. Less than 21.8% of males were at low-risk and ≥21.8% at high-risk. There were <57.0% of female patients at low risk and ≥57.0% at high-risk. Calibration plots showed that the probabilities predicted by the models for men and women subgroups fitted well with the actual recurrence rates (p=0.295 and p=0.693, respectively). DCAs demonstrated that the models adjusted by subgroup analyses had good net benefits. The logistic regression analysis results were visualized using R software and nomograms were constructed. Nomograms showed the characteristics of each individual included and were used to predict the probability of developing new Modic changes after PETD surgery. The risk of postoperative new Modic changes in patients was thus assessed (Figures 3). Additionally, the subgroup model demonstrated good predictive consistency in both the training and validation sets, confirming the model's accuracy and predictive capability. The acceptable performance on the DCA curve indicates that the model offers substantial clinical benefit.

Discussion

The study found that the incidence of post-PETD Modic changes was 24.8% among patients. By analyzing baseline demographics, surgical factors, imaging indicators, and lab tests, the study aimed to identify risk factors for post-PETD Modic changes. Regression analysis revealed eight associated factors: symptom duration, surgical segment, disc degeneration grade, disc height, angles of upper and lower endplate concavities, segmental instability, and lumbosacral

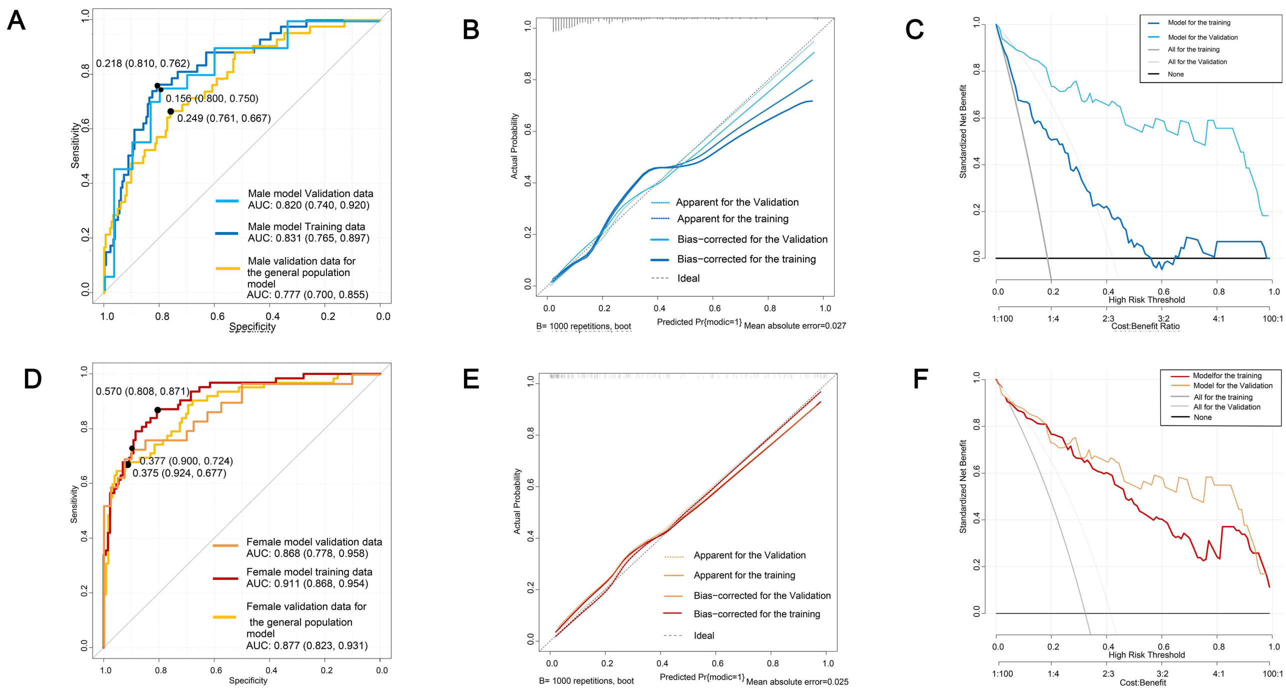

Figure 2 ROC Curves, Calibration Curves, and Decision Curves for Male (ABC) and Female (DEF) Subgroups. This figure presents the ROC curves (**A** and **D**), calibration curves (**B** and **E**), and decision curves (**C** and **F**) for the male (**A**–**C**) and female (**D**–**F**) subgroups. ROC analysis shows AUCs of 0.831 for males and 0.911 for females, indicating good predictive performance. Calibration curves reveal strong agreement between predicted probabilities and observed outcomes for both subgroups. Decision curves demonstrate net clinical benefits at various threshold probabilities, supporting the models' applicability in clinical decision-making. All results were validated externally.

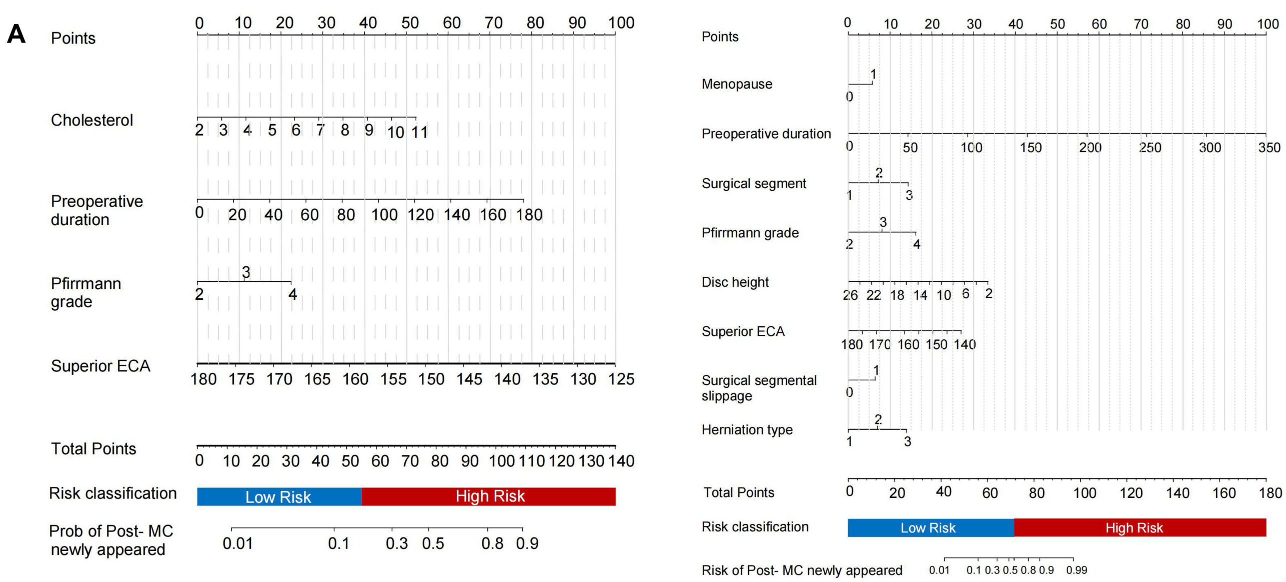

Figure 3 Nomogram for predicting added risk of post-PETD Modic changes in male (**A**) and female patients (**B**). Display model variables, transcription scores, and corresponding nomogram points. The risk of Modic changes after PETD can be predicted based on the total score.

fusion. Since PETD surgery aims for optimal outcomes with minimal trauma, preventing new Modic changes is crucial. Logistic regression was used to identify risk factors and establish predictive models for new Modic changes in both males and females after PETD, enhancing the accuracy of treatment outcome evaluations and patient management strategies.

Biomechanical Basis

Intervertebral Disc Degeneration

Local vertebral disc diseases, including degeneration, protrusion, and herniation, influence the development of new Modic changes after surgery, as confirmed in this study. Disc degeneration affects the progression of Modic changes across all subgroups by altering the internal structure of intervertebral discs. Mediators from damaged disc cells can trigger inflammation and tissue degradation in the discs and adjacent bone marrow. Previous reports indicate that these structural changes lead to peak forces rather than uniformly distributed ones, potentially causing endplate fractures. Such fractures can lead to edema, observable as Modic changes on MRI. Additionally, glycosaminoglycans and type II collagen in cartilaginous endplates enhance hydration, stress absorption, and impact buffering.[15] They are essential to the biomechanics of the lumbar spine, and their concentration indicates the degeneration of cartilaginous endplates. As intervertebral discs degenerate, the water and type II collagen content in the nucleus pulposus decreases. This can cause part of the nucleus pulposus to protrude into the vertebral canal, reducing the disc's ability to absorb axial stress and cushion impact. Consequently, biomechanical changes occur in the lumbar spine, leading to increased pressure on the vertebrae and eventual damage to the endplates.[16]

Disc Height Index

DHI is linked to disc degeneration and lumbar spine stability, influencing postoperative Modic changes. Previous studies showed that decreased height of a single disc correlates with Modic Type 2 changes in adjacent vertebrae and overall lumbar disc height. This study supports that more new Modic changes occur after PETD surgery. Microfractures in the endplate are key biomechanical factors for Modic changes, and lower disc height raises the risk of endplate damage from surgical instruments.[17–19] Potential trauma to intervertebral discs during lumbar spine surgery results in the release of inflammatory factors and metabolites from microfractures in the endplate.[20] These substances directly penetrate the endplate and vertebral body, triggering inflammatory reactions and leading to postoperative Modic changes.

Sagittal Endplate Concavity Angle of the Operating Segment

Vertebral endplates consist of trabecular bone layers that supply nutrients to intervertebral discs and withstand pressure from above. Several studies have shown a correlation between morphological changes in endplates and degeneration of lumbar intervertebral discs.[21,22] As disc degeneration worsens, the axial stress on vertebral endplates gradually shifts from the central region to the periphery.[21] The peripheral endplates have to absorb the stress and are remodeled. As a result, the endplates become flattened and the axial stress is dispersed. Thus, the angle of endplate concavity significantly affects the axial stress applied to intervertebral discs. Endplate flattening may serve as a self-protective mechanism and partially reflect the degree of disc degeneration sensitivity. In this study, the sagittal endplate concavity angle (SECA) of the operating segment was identified as a risk factor for the development of postoperative new Modic changes.

Segmental Instability

Spinal slippage is a common degenerative change defined as translation relative to the adjacent lower vertebra in the sagittal plane, with an incidence of 17% in middle-aged populations. It can negatively impact the biomechanics of intervertebral discs and potentially lead to lumbar instability. This instability can worsen after PETD, increasing the risk of postoperative Modic changes. Despite advancements in equipment and techniques allowing for nearly complete decompression during PETD, the lack of corresponding segment fixation inevitably affects the stability of local biomechanical structures.[14] The present study found that segmental instability significantly affects postoperative Modic changes. Spinal slippage can cause compensatory joint hypertrophy and spinal canal stenosis, requiring the resection of the upper facet joint for complete decompression, which may lead to iatrogenic instability. Thus, surgeons should develop personalized surgical plans to minimize damage to facet joints and bony structures, thereby reducing instability.

Physiological Basis

Menopause

Menopause is a unique risk factor for the development of postoperative new Modic changes in females. In the present study, it was inferred that the rapid decline in estrogen levels following menopause resulted in a much faster decrease in bone density in postmenopausal women, compared with that in age-matched men.[16] The study by Margulies et al suggested that the reduction in the bone mineral density of the lumbar spine led to a decrease in the number of trabeculae in the vertebral body, an increase in bone fragility, and finally microfractures beneath the vertebral endplate. The association between Modic changes and age, particularly menopause, suggests the degenerative nature of Modic changes and the crucial role of aging or related factors in the pathogenesis of Modic changes.

Total Cholesterol

In individuals aged 50 and above, a negative correlation was observed between total cholesterol and total bone mineral density of the lumbar spine in previous studies. In the present study, higher cholesterol levels in male patients were identified as a risk factor for the development of postoperative Modic changes. Additionally, it has been established that hypercholesterolemia inhibits bone formation by secreting factors such as PPAR-γ adipogenic differentiation factor and adiponectin.[23] High-cholesterol diets hinder the expression of osteogenic genes, such as alkaline phosphatase, type I collagen, bone morphogenetic protein, and runt-related transcription factor 2, thus preventing osteoblast differentiation and maturation. In this study, male patients with postoperative Modic changes had a total cholesterol level of 5.53 ± 1.18, higher than the control group's 5.15 ± 1.15. Although these slightly elevated cholesterol levels have chronic effects on bone density, their immediate impact on the development of postoperative Modic changes is limited. Further research is needed to investigate the specific effects of cholesterol on these changes in males.

Disease-Specific Factors

Duration of Symptoms

Research shows that Modic changes are linked to morphological abnormalities of intervertebral discs, particularly lumbar disc protrusion. Degenerative changes in these discs are risk factors for vertebral degeneration, and abnormalities in the sagittal plane accelerate this degeneration, increasing susceptibility to Modic changes. PETD also heightens this susceptibility and accelerates disc degeneration. This study found that in highly susceptible patients, a longer duration of symptoms correlates with a higher likelihood of new postoperative Modic changes. Thus, early surgery, when conservative treatments fail, can help prevent the occurrence and progression of postoperative Modic changes by minimizing chronic degeneration stimuli.

Protrusion Segment

Postoperative Modic changes mainly occur at the L4/5 and L5/S1 segments. This finding is consistent with that of previous studies on preoperative Modic changes.[6] Postoperative Modic changes are more frequently observed at L5/S1 than at L4/5.[24] Previous studies have shown that preoperative Modic changes are closely related to lumbar curvature. Patients with Modic changes have smaller LL and SS angles, and the straightening of physiological curvatures will inevitably increase the stress load on vertebral endplates, leading to the occurrence of Modic changes.[25] However, in the present study, no significant differences were found in lumbar curvature-related indices before surgery. The reason may be that the decrease in lumbar curvature and the increase in mechanical load on the lower lumbar spine may induce Modic changes, although the effect is slow.[26] These changes accelerate lumbar degeneration in patients with lumbar disc protrusion after external interventions such as surgery.

Type of Protrusion

A study by Barth et al reported a higher incidence of Modic changes in patients undergoing lumbar disc excision surgery and a potential association between disc excision and Modic changes. This effect is exacerbated by a prolapse type of disc herniation leading to the removal of larger volumes of the nucleus pulposus during surgery. The reduced intradiscal pressure caused by the loss of nuclear material and subsequent changes in pressure load distribution on the disc may partly explain this hypothesis.[27,28] Additionally, during PETD, protruding and degenerated intervertebral discs are removed to minimize the risk of postoperative recurrence, which further reduces intervertebral disc volume and inevitably weakens cushioning and redistributing loads on adjacent vertebrae, resulting in postoperative Modic changes in the short term.

Posterior Ring Apophyseal Fracture and Calcified Intervertebral Discs

Posterior Ring Apophyseal Fracture (PRAF) is a spinal injury commonly observed in adolescents and young adults, especially in cases of LDH.[29] This fracture involves the posterior ring apophyseal, a bony structure around the intervertebral endplate, and is typically caused by excessive mechanical stress or acute trauma. During rapid growth, the apophysis is not fully ossified, making it particularly vulnerable to stress-induced injuries. Studies show that Modic changes are more likely to occur in areas previously under stress or where degeneration has begun, as in PRAF cases, where the posterior ring fracture may predispose the surrounding vertebral structures to degeneration.[30] This relationship suggests that PRAF, by altering spinal stability and leading to adjacent disc degeneration, may set the stage for the development of Modic changes in the postoperative period.

Calcified intervertebral discs may increase the risk of Modic changes after PETD. Calcification reduces disc elasticity, resulting in greater mechanical stress on the endplate post-surgery, making it more prone to microdamage that can lead to Modic Type I changes, characterized by bone marrow edema and inflammation.[31] Additionally, calcified discs may impair healing and nutrient supply to the endplate, increasing the likelihood of endplate degeneration and promoting Modic Type II changes associated with fatty degeneration.[32] These pathological changes can lead to postoperative back pain and negatively impact recovery and long-term outcomes.

In this study, no significant differences in preoperative PRAF and disc calcification were found between male and female patients. Possible reasons include: PRAF indicates endplate damage that may have led to preexisting Modic changes, which were excluded from analysis; most enrolled patients were middle-aged or elderly, where PRAF incidence is lower; and the limited follow-up period of at least one year may have resulted in fewer patients with preoperative PRAF and calcified discs, leading to the lack of statistically significant differences. Therefore, further research is needed to explore the relationship between PRAF, calcified intervertebral discs, and Modic changes following PETD.

Clinical Value

The multifactorial results of all subgroups in the present study indicated that physiological factors that caused bone destruction and biomechanical changes in the lumbar spine increased patients' susceptibility to postoperative Modic changes. Lumbar disc protrusion leads to postoperative Modic changes. It is advised that surgeons should take targeted treatment measures according to controllable factors. The measures include: a) supplementing calcium and vitamin D to control total cholesterol and improve bone quality in patients; b) taking early surgical intervention to reduce the impact of lumbar disc protrusion on Modic changes; c) designing more precise surgical instrument channels for patients with preoperative lumbar mechanical-related risk factors to minimize damage to facet joints while ensuring surgical efficacy, thus reducing instability of the operating segments to the greatest extent; and d) adopting precise surgical techniques to avoid endplate damage in highly susceptible populations. Additionally, modeling is recommended as it can help predict the progression of postoperative new Modic changes before surgery, improve the efficacy of surgery to a certain extent, assist with clinical decision-making in determining the most suitable time for surgery, and provide cutoff values for the estimation of the best surgical timing.

Limitations

This study is a retrospective analysis, which presents inherent limitations in establishing causal relationships. Consequently, future prospective studies are essential to examine the impact of PETD surgery on the development of Modic changes in patients with lumbar disc herniation. Furthermore, our research only provided a qualitative assessment of postoperative Modic changes; thus, additional investigations are warranted to quantitatively evaluate these alterations. Lastly, the sample size in this study is relatively small, with most postoperative follow-up durations averaging around one year. An increased patient population and extended follow-up periods would significantly enhance the model's accuracy. Therefore, larger cohorts with longer follow-up durations are necessary to further explore, refine, and validate the predictive model.

Conclusion

This study is the first to explore factors associated with Modic changes following PETD. Using regression analysis, predictive models for postoperative Modic changes were developed separately for male and female patients. The models demonstrated good performance, as indicated by the AUC and calibration curves. A line chart was used to visualize the models, which can be used to estimate the risk of developing new Modic changes after surgery. The findings of this study provide new insights into factors potentially associated with residual back pain after PETD and offer a reference for developing individualized and improved treatment strategies for patients with lumbar disc herniation.

Ethics Approval

The research was approved by the Ethics Committee of Affiliated Hospital of Qingdao University (QYFY WZLL 28600) and was carried out in compliance with the Declaration of Helsinki. All participants in the study gave their informed consent.

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Disclosure

The authors have nothing to disclose.

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