The Value of Perioperative Serum Indexes in Predicting the Risk of Intercostal Neuralgia After PVP in Postmenopausal Patients With Osteoporotic Vertebral Compression Fractures

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AIM: Intercostal neuralgia is a clinically relevant complication after percutaneous vertebroplasty (PVP) in postmenopausal patients with osteoporotic vertebral compression fracture (OVCF), and its risk remains difficult to predict using conventional approaches. Perioperative serum markers are generally used as indicators of metabolic and nutritional status; however, their systematic association with the risk of post-PVP intercostal neuralgia has not been well established. This study aims to evaluate the predictive value of perioperative serological indicators and clinical factors for intercostal neuralgia after PVP in postmenopausal OVCF patients, to provide a reference for clinical risk stratification and individualized intervention.

METHODS: A total of 122 postmenopausal OVCF patients who underwent PVP from December 2023 to June 2025 were enrolled in this single-center retrospective cohort study. According to the occurrence of postoperative intercostal neuralgia, patients were divided into the intercostal neuralgia group (52 cases) and the non-intercostal neuralgia group (70 cases). Serum indexes were collected preoperatively and on postoperative day 1. Preoperative indicators included 25-hydroxyvitamin D (25(OH)D), alkaline phosphatase (ALP), serum calcium (Ca), and serum phosphorus (P). Postoperative indicators collected on postoperative day 1 included albumin (Alb) and fasting blood glucose (Glu). Univariate and multivariate logistic regression analyses were performed to identify independent predictors, and a combined predictive model was constructed. Model discrimination was assessed using the receiver operating characteristic (ROC) curve, while calibration was evaluated using a bootstrap method for assessing the model's predictive consistency.

RESULTS: Multivariate logistic regression analysis showed that elevated postoperative Glu (odds ratio [OR] = 2.25, 95% confidence interval [CI]: 1.22–4.15) was an independent risk factor for postoperative intercostal neuralgia, while higher levels of postoperative albumin (OR = 0.90, 95% CI: 0.84–0.96), preoperative 25(OH)D (OR = 0.91, 95% CI: 0.85–0.98), and bone mineral density (BMD) T-score (OR = 0.18, 95% CI: 0.05–0.59) were protective factors. Fracture location (lower thoracic) was also independently associated with neuralgia risk (OR = 0.28, 95% CI: 0.11–0.73). The area under the receiver operating characteristic curve (AUC) of the combined predictive model constructed with these five indicators was 0.82 (95% CI: 0.75–0.89). The calibration curve demonstrated good agreement between predicted and observed risk (mean absolute error = 0.048), indicating satisfactory model discrimination and calibration.

CONCLUSIONS: BMD T-score, fracture location, postoperative Glu, postoperative Alb, and 25(OH)D can be used as independent predictors to predict intercostal neuralgia after PVP in postmenopausal OVCF patients. The combined model integrating BMD T-score, fracture location, postoperative Glu, postoperative Alb, and preoperative 25(OH)D demonstrates good predictive performance and may facilitate early risk stratification and individualized perioperative management of postoperative neuralgia.

Keywords: osteoporotic vertebral compression fractures; percutaneous vertebroplasty; intercostal neuralgia; serological markers; menopause

Introduction

Osteoporotic vertebral compression fracture (OVCF) is one of the primary causes of pain and disability. Generally, the incidence of OVCF is much higher in postmenopausal women due to estrogen decline after menopause [1]. In addition to severe low back pain near the level of the fractured vertebra, some patients experience intercostal neuralgia symptoms such as chest or upper abdominal costal pain. OVCF-related pain is a form of neuropathic pain [2], yet it remains widely neglected by patients, which may delay timely treatment. Intense intercostal neuralgia greatly impairs the quality of life and independent living ability of patients [3].

Percutaneous vertebroplasty (PVP), a minimally invasive interventional technique first introduced by Galibert *et al.* [4], is widely used in the treatment of osteoporotic vertebral compression fractures. This procedure provides rapid pain relief and significantly improves patients' quality of life [5]. Although PVP improves vertebral stability and relieves pain, some patients still develop new or significantly

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worsened intercostal neuralgia compared with the preoperative baseline level. At present, the exact pathophysiological mechanism underlying post-PVP intercostal neuralgia remains unclear. Clinically, the prediction of this complication mainly relies on the operator's experience in judgment and preoperative imaging evaluation of vertebral fracture morphology, spinal canal, and intervertebral foramen [6]. However, objective, quantitative, and universally applicable biological early warning indicators are lacking. Therefore, identifying markers that can effectively predict the risk of intercostal neuralgia is of great clinical significance for improving surgical strategies and guiding targeted perioperative management.

Although PVP can effectively relieve the axial pain associated with fractures, certain patients would still develop new or aggravated radiation-induced pain along the intercostal nerve after surgery. The characteristics of this pain (e.g., burning or pinprick sensation) are suggestive of neuropathic pain, which is significantly different from postoperative incisional pain or residual axial bone pain. However, the literature on intercostal neuralgia after PVP is relatively limited, and the clinical understanding and standardized diagnostic criteria of intercostal neuralgia as an independent complication remain poorly established. Attributed to surgical trauma, this condition is often overlooked, despite its adverse impacts on early postoperative rehabilitation and quality of life. Therefore, clarifying the clinical characteristics of intercostal neuralgia after PVP and identifying associated risk factors is of great clinical significance for improving surgical outcome evaluation and guiding individualized perioperative management. Based on this, this study aims to systematically investigate, using strict diagnostic criteria, the association between perioperative serological indicators and the risk of intercostal neuralgia after PVP in postmenopausal OVCF patients.

As indicators reflecting systemic stress, metabolic status, and nutritional condition, serological biomarkers are increasingly recognized for their potential value in predicting neuropathic pain [7]. The occurrence and development of pain result from the complex multisystem interplay, with inflammatory markers, metabolic, and nutritional factors all related to pain development [8,9]. A number of studies have shown the correlation between serological indicators and neuralgia. 25-hydroxyvitamin D (25(OH)D) deficiency is inversely correlated with postherpetic neuralgia. Some inflammatory mediators, such as interleukin-6 (IL-6), can directly activate nociceptors and participate in pain production [10,11]. In addition, poor glycemic control may affect nerve repair and aggravate pain [9], and Micheo *et al*. [12] showed that axonal regeneration and functional recovery are significantly lower in diabetic patients than in healthy people. Collectively, this growing body of evidence highlights the potential value of serological biomarkers in predicting neuropathic pain.

Given the limited research on the association between serological biomarkers and the risk of post-PVP intercostal neuralgia in postmenopausal OVCF patients, the present study aimed to systematically evaluate their relationship using a retrospective cohort design. Univariate and multivariate logistic regression analyses were performed to identify independent risk factors in a cohort of postmenopausal OVCF patients undergoing PVP, and the predictive performance of the model was assessed using receiver operating characteristic (ROC) curve analysis. The novelty of this study lies in the systematic integration of perioperative serological biomarkers reflecting inflammatory status and nutritional metabolism in a high-risk postmenopausal OVCF population, with specific focus on post-PVP intercostal neuralgia. These findings may help improve the surgical experience and overall prognosis of patients, as well as promote the precision and safety of PVP treatment.

Methods

Study Participants

This was a single-center retrospective cohort study. Consecutive patients with OVCF admitted to Wenzhou TCM Hospital of Zhejiang Chinese Medical University from December 2023 to June 2025 were enrolled. Patients were classified into an intercostal neuralgia group and a non-intercostal neuralgia group. This study adhered to the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of Wenzhou TCM Hospital of Zhejiang Chinese Medical University (approval number: WZY2026-LW-001-01). All data used for research analysis were collected from the electronic health record system under the premise of protecting patient privacy. Inclusion criteria of this study included: (1) postmenopausal women; (2) patients with OVCF; (3) patients with osteoporosis diagnosed by imaging examination; (4) patients receiving single-level or multi-level PVP; (5) patients with complete data of serological biomarkers; (6) patients with complete key demographic and clinical data. Exclusion criteria included: (1) presence of other pathological fractures (such as tumor, infection); (2) presence of malignant tumor, acute infection, or severe systemic disease; and (3) incomplete clinical data. Patients with intercostal neuralgia typically present with diffuse pain radiating from the back to the chest or upper abdomen along the intercostal nerves, often triggered by lying down or positional changes. The pain is usually sharp or tingling, sometimes accompanied by numbness. The pain may last for minutes or hours. Postoperative intercostal neuralgia was defined as new-onset intercostal neuralgia or a significant worsening of pre-existing symptoms compared with the preoperative baseline following PVP. Patients meeting the diagnostic criteria for postoperative intercostal neuralgia outlined in Section of "Definition and Evaluation of Outcome Indicators" were assigned to the intercostal neuralgia group,

while the remaining patients were classified into the non-intercostal neuralgia group.

Definition and Evaluation of Outcome Indicators

The primary outcome measure of the study was new or worsening intercostal neuralgia after PVP, with postoperative pain assessment completed by clinicians within 48 to 72 hours after surgery. The diagnosis of intercostal neuralgia was based on the following criteria: (1) pain located in the area of the back radiating along the intercostal nerve to the chest wall or upper abdomen, and manifested as burning, pinprick, or electric shock pain; and (2) a score $\geq$4 in the Douleur Neuropathique 4 (DN4) questionnaire, which is indicative of neuropathic pain. Pain intensity was also assessed using the visual analogue scale; by using this instrument, patients were required to indicate the score that best represented their worst pain at rest during the previous 24 hours. Postoperative intercostal neuralgia was defined as a DN4 score $\geq$4 combined with an intercostal Visual Analogue Scale (VAS) score $\geq$4 (moderate to severe pain). Pain attributable to incisional injury, pulmonary infection, rib fracture, or cardiovascular emergency was excluded.

Surgical Procedure and Perioperative Management

Local infiltration anesthesia was administered, and the patient was placed in a prone position with soft pillows supporting the chest and iliac regions, allowing the abdomen to hang freely. Under C-arm fluoroscopic guidance, the pedicle of the injured vertebra was identified and marked. After skin disinfection and sterile draping, 2% lidocaine hydrochloride was injected into the skin and muscle around the pedicle on the puncture site. Following successful anesthesia, the lateral superior part of the pedicle of the injured vertebra was selected as the puncture point, and the bilateral puncture needles were inserted into the vertebral body, the needle tip of the fluoroscopy needle reached the posterior edge of the vertebral body, and the needle tip of the fluoroscopy needle was located at the medial wall of the pedicle in the anteroposterior view to make sure that the puncture needle did not enter the spinal canal. Again, anteroposterior fluoroscopy confirmed that the puncture needle tip was located between the medial side of the pedicle and the spinous process. The needle core was pulled out, and the bone cement was prepared to a viscous, gel-like consistency. The high-viscosity bone cement was slowly injected bilaterally at the same time. Injection was discontinued immediately when satisfactory filling of the vertebral fissure was achieved, and bone cement had reached the anterior and posterior edges of the vertebral body and the upper and lower endplates. The C-arm fluoroscopy was used again to observe the dispersion of bone cement. When the observed distribution of the bone cement was satisfactory, the needle was removed, the wound was covered with sterile dressing, and the patients were sent back to the ward after the bone cement had fully polymerized. During the operation, vital signs of the patients were continuously monitored, and their lower limb sensation and motor function were assessed during puncture and bone cement injection to ensure the absence of spinal cord injury and compression. Routine preoperative assessments, such as blood tests, coagulation function, and electrocardiography, were performed to evaluate surgical tolerance. None of the patients received prophylactic antibiotics before surgery. Postoperative anti-osteoporotic therapy was routinely administered.

Collection of Biological Data

Preoperative and postoperative serological biomarkers were collected in accordance with the standardized procedures. Preoperative samples were obtained within 24 hours before surgery, including alkaline phosphatase (ALP), serum calcium, serum phosphorus, and 25(OH)D, which were measured using the continuous monitoring method, arsenazo III method, direct ultraviolet method, and chemiluminescence immunoassay, respectively. Postoperative samples were collected on the morning of the first postoperative day, including albumin (Alb) and fasting blood glucose (Glu), which were measured using the bromocresol green and glucose oxidase methods, respectively. These early postoperative measurements were used to assess the patient's acute inflammatory response and metabolic status immediately after surgery, serving as potential early indicators of subsequent neuralgia development. Bone mineral density (BMD) T-scores were assessed using dual-energy X-ray absorptiometry shortly before admission (within one month prior to surgery). The standard measurement sites were the posterior-anterior lumbar spine (L1–L4) and the left femoral neck. According to the World Health Organization diagnostic criteria, a T-score $\leq$–2.5 at either site was defined as osteoporosis, and patients meeting this criterion were included in this study. All assays were performed in adherence to standardized laboratory quality control procedures.

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria) was used for supplementary analyses. First, the Shapiro–Wilk test was performed to assess the normal distribution of continuous data. Normally distributed data were expressed as mean $\pm$ standard deviation, and the differences between groups were compared using an independent samples *t*-test. Variables not conforming to normal distribution were presented as median and interquartile range, and the between-group differences were analyzed using the Mann–Whitney *U* test. Categorical variables were expressed as counts and percentages, and the chi-square test was used for analysis. As part of the process of identifying related factors of intercostal neuralgia in postmenopausal OVCF patients after undergoing PVP, univariate logistic regression analysis was

Table 1. Baseline characteristics of patients.

Variables	Total (n = 122)	Non-intercostal neuralgia group (n = 70)	Intercostal neuralgia group (n = 52)	Statistic	p
Age (years), mean ± SD	71.28 ± 7.74	71.34 ± 7.70	71.19 ± 7.85	t = 0.11	0.92
Years since menopause, mean ± SD	17.62 ± 5.24	17.31 ± 5.14	18.04 ± 5.39	t = –0.75	0.45
BMD T-score, mean ± SD	–3.33 ± 0.41	–3.26 ± 0.42	–3.42 ± 0.39	t = 2.10	0.04
BMI (kg/m^2), mean ± SD	21.90 ± 3.67	21.75 ± 3.45	22.11 ± 3.97	t = –0.53	0.59
Bone cement volume (mL), M (Q_1, Q_3)	5.15 (4.32, 6.30)	5.10 (4.23, 6.07)	5.40 (4.47, 6.43)	Z = –0.67	0.51
Duration of surgery (min), M (Q_1, Q_3)	65.00 (58.00, 72.00)	64.00 (58.00, 71.00)	68.00 (60.75, 73.25)	Z = –1.64	0.10
Location, n (%)				χ^2 = 5.82	0.02
Middle thoracic vertebrae	55 (45.08)	25 (35.71)	30 (57.69)		
Lower thoracic vertebrae	67 (54.92)	45 (64.29)	22 (42.31)		
Hypertension, n (%)				χ^2 = 0.02	0.88
No	53 (43.44)	30 (42.86)	23 (44.23)		
Yes	69 (56.56)	40 (57.14)	29 (55.77)		
Diabetes, n (%)				χ^2 = 0.60	0.44
No	100 (81.97)	59 (84.29)	41 (78.85)		
Yes	22 (18.03)	11 (15.71)	11 (21.15)		
Postoperative albumin (g/L), mean ± SD	39.25 ± 7.53	41.36 ± 8.06	36.41 ± 5.67	t = 3.98	<0.01
Postoperative Glu (mmol/L), mean ± SD	5.95 ± 0.80	5.80 ± 0.70	6.15 ± 0.89	t = –2.36	0.02
Preoperative ALP (U/L), mean ± SD	99.75 ± 16.06	98.81 ± 15.79	101.00 ± 16.49	t = –0.74	0.46
Preoperative 25(OH)D (ng/mL), mean ± SD	32.89 ± 6.42	34.70 ± 5.85	30.44 ± 6.40	t = 3.82	<0.01
Preoperative calcium (mmol/L), M (Q_1, Q_3)	2.17 (1.99, 2.39)	2.17 (2.01, 2.39)	2.15 (1.87, 2.39)	Z = –0.81	0.42
Preoperative phosphorus (mmol/L), M (Q_1, Q_3)	1.31 (1.14, 1.44)	1.32 (1.17, 1.47)	1.26 (1.11, 1.36)	Z = –1.36	0.17

Abbreviations: 25(OH)D, 25-hydroxyvitamin D; ALP, alkaline phosphatase; BMI, body mass index; BMD, bone mineral density; Glu, fasting blood glucose; SD, standard deviation.

first performed. Variables with $p < 0.05$ in the univariate analysis were entered into the multivariate logistic regression model using the enter method. The results were reported as odds ratios (ORs) and 95% confidence intervals (CIs), and a predictive model was subsequently constructed. To assess the potential risk of model overfitting, the events-per-variable (EPV) ratio was calculated. In this study, 52 outcome events and five predictors were included in the final multivariate model, yielding an EPV of 10.4, which exceeds the commonly recommended minimum threshold of 10, indicating a low risk of overfitting. The ROC curve was generated based on the predicted probabilities obtained from the final multivariate logistic regression model to evaluate its discriminative ability, and the area under the curve was calculated. Bootstrap resampling with 1000 iterations was performed for internal validation to generate the calibration curve and obtain optimism-corrected estimates of model performance. Model calibration was assessed using the mean absolute error, defined as the average absolute difference between predicted and observed probabilities. A mean absolute error value closer to 0 indicates better calibration. Additionally, the Hosmer–Lemeshow goodness-of-fit test was performed to further assess model calibration, with $p > 0.05$ indicating no significant deviation between predicted and observed probabilities. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.

Results

Baseline Characteristics of Patients

A total of 122 patients were included in this study. According to whether intercostal neuralgia occurred after the operation, they were divided into the non-intercostal neuralgia group and the intercostal neuralgia group. There were 70 patients (57.38%) without intercostal neuralgia and 52 patients (42.62%) with intercostal neuralgia. There were no significant differences in age, menopausal years, body mass index (BMI), bone cement volume, duration of surgery, hypertension, diabetes, preoperative ALP, preoperative calcium, or preoperative phosphorus between the two groups ($p > 0.05$). However, the postoperative Glu levels in the intercostal neuralgia group were significantly higher than those in the non-intercostal neuralgia group ($p < 0.05$), and the BMD T-score, postoperative albumin, and preoperative 25(OH)D levels in the intercostal neuralgia group were significantly lower than those in the non-intercostal neuralgia group ($p < 0.05$). Fracture location was also significantly associated with intercostal neuralgia ($p < 0.05$). Detailed characteristics are shown in Table 1.

Univariate and Multivariate Logistic Regression Analyses

Univariate logistic regression analysis showed that lower thoracic vertebrae, postoperative Glu, BMD T-score, postoperative albumin, and preoperative 25(OH)D were significantly correlated with intercostal neuralgia after PVP in

Table 2. Results of univariate and multivariate logistic regression analyses.

Variables	Univariate					Multivariate				
	β	S.E	Z	p	OR (95% CI)	β	S.E	Z	p	OR (95% CI)
Age (years)	–0.00	0.02	–0.11	0.91	1.00 (0.95–1.05)					
Years since menopause	0.03	0.04	0.76	0.45	1.03 (0.96–1.10)					
BMD T-score	–0.95	0.46	–2.05	0.04	0.39 (0.16–0.96)	–1.73	0.62	–2.80	0.005	0.18 (0.05–0.59)
BMI (kg/m^2)	0.03	0.05	0.54	0.59	1.03 (0.93–1.13)					
Bone cement volume (mL)	0.04	0.12	0.37	0.71	1.05 (0.83–1.32)					
Duration of surgery (min)	0.03	0.02	1.43	0.15	1.03 (0.99–1.07)					
Location										
Middle thoracic vertebrae					1.00 (Reference)					
Lower thoracic vertebrae	–0.90	0.38	–2.39	0.02	0.41 (0.20–0.85)	–1.27	0.49	–2.59	0.009	0.28 (0.11–0.73)
Hypertension										
No					1.00 (Reference)					
Yes	–0.06	0.37	–0.15	0.88	0.95 (0.46–1.95)					
Diabetes										
No					1.00 (Reference)					
Yes	0.36	0.47	0.77	0.44	1.44 (0.57–3.63)					
Postoperative albumin (g/L)	–0.10	0.03	–3.42	<0.01	0.90 (0.85–0.96)	–0.11	0.03	–3.24	0.001	0.90 (0.84–0.96)
Postoperative Glu (mmol/L)	0.58	0.25	2.35	0.02	1.78 (1.10–2.89)	0.81	0.31	2.61	0.009	2.25 (1.22–4.15)
Preoperative ALP (U/L)	0.01	0.01	0.75	0.46	1.01 (0.99–1.03)					
Preoperative calcium (mmol/L)	–0.58	0.63	–0.92	0.36	0.56 (0.16–1.93)					
Preoperative 25(OH)D (ng/mL)	–0.12	0.03	–3.47	<0.01	0.89 (0.83–0.95)	–0.09	0.04	–2.43	0.015	0.91 (0.85–0.98)
Preoperative phosphorus (mmol/L)	–0.60	0.75	–0.80	0.43	0.55 (0.13–2.40)					

OR, odds ratio; CI, confidence interval; S.E, standard error.

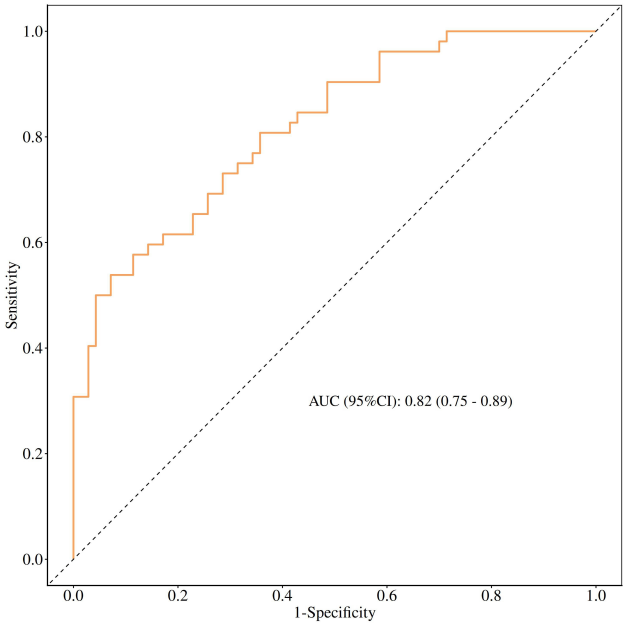

Fig. 1. Receiver operating characteristic (ROC) curve analysis of the predictive model. AUC, area under the receiver operating characteristic curve; CI, confidence interval.

postmenopausal patients with OVCF. Variables with $p < 0.05$ in univariate analysis were included in the multivariate logistic regression model for correction. The results showed that higher levels of postoperative Glu were associated with an increased risk of intercostal neuralgia, while lower thoracic vertebrae and higher levels of BMD T-score, postoperative Alb and preoperative 25(OH)D were associated with a decreased risk of intercostal neuralgia. The detailed results are shown in Table 2.

Evaluation of the Model's Diagnostic Performance

Based on the independent predictors identified in the multivariate logistic regression analysis, we constructed a model for predicting the risk of intercostal neuralgia after PVP in postmenopausal OVCF patients. The model equation is as follows: Logit(P) = 4.87 – 1.73 × (BMD T-score) – 1.27 × (fracture location) + 0.81 × (postoperative Glu) – 0.11 × (postoperative albumin) – 0.09 × (preoperative 25(OH)D), where P is the probability of postoperative intercostal neuralgia. Fracture segments were classified as binary variables (the middle thoracic vertebra was assigned 0, the lower thoracic vertebra was assigned 1). Postoperative Glu unit was mmol/L, postoperative albumin unit was g/L, and preoperative 25(OH)D unit was ng/mL. The area under the receiver operating characteristic curve (AUC) of the model for predicting postoperative intercostal neuralgia was 0.82 (95% CI: 0.75–0.89), indicating good discriminative ability of the model (Fig. 1). The best predictive cut-off value determined by the Youden index was 0.634, which had a sensitivity of 54.0% (95% CI: 40.0%–67.0%), a specificity of 93.0% (95% CI: 87.0%–99.0%), and a positive predictive value of 85.0% (95% CI: 73.0%–97.0%). The negative

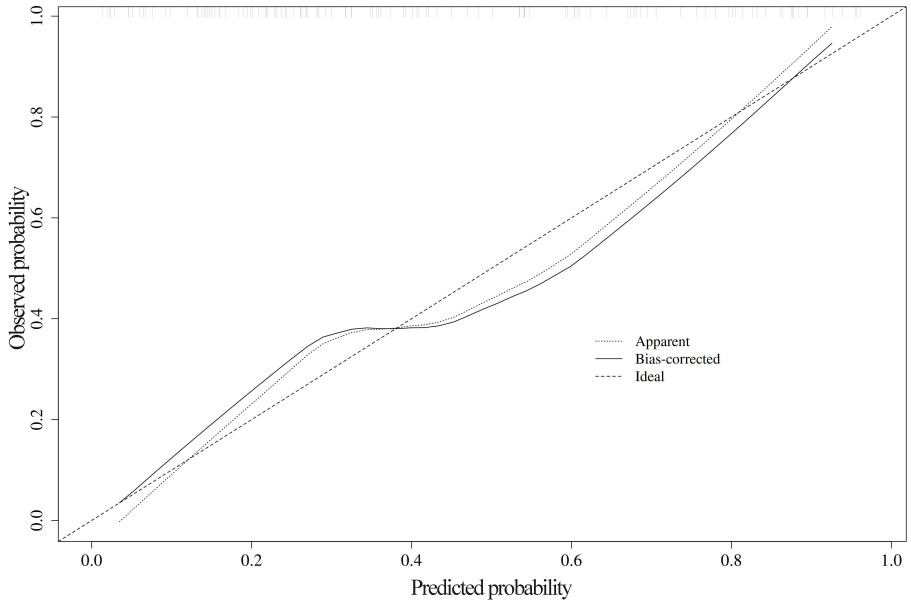

Fig. 2. Calibration curve of the predictive model.

predictive value was 73.0% (95% CI: 64.0%–82.0%), and the overall accuracy was 76.0% (95% CI: 68.0%–83.0%).

Model Calibration Assessment

Bootstrap resampling with 1000 iterations was used for internal validation to obtain optimism-corrected estimates of model discrimination and to assess model calibration. The optimism-corrected area under the receiver operating characteristic curve (AUC) was 0.79 (95% CI: 0.72–0.87), with an optimism of 0.05, indicating stable discriminative performance. The calibration curve was generated to evaluate the agreement between the predicted probability of the model and the observed risk. As shown in Fig. 2, the calibration curve after bias correction was very close to the ideal diagonal (45° line), indicating that the model had good calibration performance at different risk levels. The quantitative measure of calibration is the mean absolute error, which is calculated as the average of the absolute difference between the predicted probability and the observed probability. The mean absolute error of the model was 0.048, indicating the average deviation between the predicted risk and the observed risk was only 4.8%, which further supported good agreement between the predicted risk and the actual risk. In addition, the Hosmer–Lemeshow goodness-of-fit test showed that there was no significant difference between the predicted probability and the observed probability ($\chi^2 = 5.76$, df = 8, $p = 0.67$), which again confirmed the good calibration performance of the model.

Discussion

Menopause represents a key turning point in the bone metabolism of a female's life cycle. The abrupt decline of estrogen levels leads to an imbalance between bone resorption and bone formation, resulting in rapid bone loss and deterioration of bone microstructure, which makes postmenopausal women a high-risk population for OVCF [13]. New-onset or aggravated postoperative intercostal neuralgia is an important complication affecting the early rehabilitation and quality of life of patients [6]; however, effective preoperative prediction tools remain limited. This study is the first to systematically evaluate the predictive value of perioperative multi-dimensional serological biomarkers for post-PVP intercostal neuralgia in postmenopausal OVCF patients. We acknowledge that intercostal neuralgia after PVP has not yet been uniformly recognized as a distinct complication in the existing literature. Therefore, our findings have been interpreted with caution when discussing their clinical implications. Our findings identified five independent predictors—postoperative fasting blood glucose (Glu), fracture location, postoperative albumin, preoperative 25(OH)D, and BMD T-score. The combined predictive model constructed with these five indicators demonstrated excellent discriminative ability (AUC = 0.82), good calibration, and clinical applicability, and provided a novel approach to identifying patients at increased risk for intercostal neuralgia.

Lower BMD T-score was significantly associated with an increased risk of intercostal neuralgia, suggesting that osteoporosis may contribute to postoperative neuralgia through biomechanical mechanisms. Severe osteoporosis is characterized by microstructural degeneration of bone, marked by trabecular thinning and connectivity loss [14], which collectively lead to a reduction in vertebral load-bearing capacity. Patients with low BMD often experience more severe vertebral compression and kyphosis after fracture; even with cement augmentation, spinal alignment may remain altered [15]. Kyphosis can lead to intervertebral

foraminal narrowing, resulting in mechanical compression of the intercostal nerves. Liu *et al*. [3] identified foraminal area and volume as independent factors associated with intercostal neuralgia in OVCF patients, with foraminal stenosis directly correlating with nerve compression severity. Fracture location was independently associated with intercostal neuralgia, with middle thoracic vertebrae (T5–T8) showing a higher risk than lower thoracic vertebrae (T9–T12). This finding aligns with previous studies. For instance, Chen *et al*. [16] reported that residual intercostal pain after PVP is associated with fracture location, noting a higher incidence of intercostal neuralgia in patients with middle thoracic fractures. They proposed that the unique biomechanical stress at the apex of thoracic kyphosis (typically T7) may lead to varying degrees of nerve compression following vertebral fractures. Our findings are consistent with this hypothesis.

Postoperative hyperglycemia and hypoalbuminemia together constitute a perioperative metabolic and nutritional state that is not conducive to nerve repair. Stress hyperglycemia can damage the microcirculation of the endoneurial nerve and directly damage nerve fibers by inducing oxidative stress and promoting the formation of advanced glycation end-products [17,18], thus hindering the functional recovery of the injured intercostal nerve. As an important nutrient reserve, carrier protein, and antioxidant, low albumin levels may reflect the poor overall nutritional status, reduced tissue repair capacity, and weakened endogenous anti-inflammatory ability in patients [19]. Together, these two indicators point to a physiological state of poor repair, making the nerve more susceptible to a pain response after damage. 25(OH)D appears as an independent protective factor in this model. Vitamin D deficiency is common in OVCF patients [20]. 25(OH)D possesses immunomodulatory and neurotrophic properties and can inhibit the excessive production of proinflammatory cytokines [21]. It may also support nerve repair by upregulating the expression of neurotrophic factors such as nerve growth factor [22]. Therefore, a lower preoperative 25(OH)D level may indicate a more significant inflammatory response and impaired nerve repair capacity, thereby increasing the risk of postoperative neuralgia.

Taken together, this study showed that the predictive model combining BMD T-score, lower thoracic vertebrae, postoperative Glu, postoperative albumin, and preoperative 25(OH)D demonstrated good predictive performance. By reflecting metabolic status (Glu), nutritional reserve (albumin), neuroimmune modulation (25(OH)D), bone quality (BMD T-score), and anatomical factors (fracture location), the model captures key pathophysiological processes driving postoperative neuralgia. The multiple pathophysiological processes driving postoperative neuralgia were included, and the calibration curve of the model showed that the predicted risk was in a high degree of agreement with the observed risk.

Several limitations of this study should be acknowledged. First, as a single-center retrospective study, the sample size is relatively limited, and the study population was restricted to hospitalized surgical patients. Second, the retrospective design might not be able to fully control for all potential confounders. In addition, this study mainly analyzed preoperative and early postoperative static indicators and failed to dynamically monitor the trend of changes of these indicators during the perioperative period, which may yield additional predictive information. Fourth, due to the lack of an external validation cohort, the model requires further validation in multicenter, large-sample prospective studies before clinical application. Finally, as with all observational studies, causality cannot be inferred from our findings, and the observed associations require confirmation in well-designed prospective trials. In addition to future external validation in multicenter, large-sample prospective cohorts, further attempts can be made to simplify it into a risk scoring tool for clinical use. Furthermore, it remains to be explored whether targeted interventions for high-risk patients, such as intensive anti-inflammatory therapy, glycemic control, nutritional support, and vitamin D supplementation, can effectively reduce the incidence of postoperative neuralgia, thereby strengthening the clinical translational value of this work.

Conclusions

Bone mineral density T-score, fracture location, postoperative fasting blood glucose, postoperative albumin, and preoperative 25(OH)D are independent predictors of post-PVP intercostal neuralgia in postmenopausal OVCF patients. A model integrating these indicators has a good predictive efficiency, providing an objective and multi-dimensional approach to enabling early risk stratification and guiding targeted perioperative management of this complication. Integrating bone quality, anatomical factors, metabolic status, and nutritional condition in clinical practice may represent an effective approach to improving perioperative management of PVP and enhancing postoperative rehabilitation outcomes. Despite the inherent limitations of a retrospective design, this study provides valuable preliminary evidence and identifies clear research directions for advancing precision medicine in this field.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

HC and GS designed the research study. HC and GS performed the research. HC analyzed the data. GS drafted the article. Both authors contributed to the critical revision of the manuscript for important intellectual content. Both authors read and approved the final manuscript. Both authors

have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study adhered to the principles of the Declaration of Helsinki, and the study protocol was approved by the ethics committee of Wenzhou TCM Hospital of Zhejiang Chinese Medical University (approval number: WZY2026-LW-001-01). Due to the retrospective nature of the study and the use of anonymized data, the requirement for written informed consent was formally waived by the ethics committee.

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Conflict of Interest

The authors declare no conflict of interest.

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