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ORIGINAL ARTICLE

A 5-Item Prediction Model Incorporating Pain With Neuropathic Characteristics at 2 Weeks for Chronic Postsurgical Pain After Video-Assisted Thoracoscopic Lung Surgery: A Prospective Cohort Study

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ABSTRACT

Background: Chronic postsurgical pain (CPSP) after video-assisted thoracoscopic surgery (VATS) is common, yet clinicians lack tools to identify high-risk patients at routine follow-up. We hypothesized that pain with neuropathic characteristics at 2 weeks, signifying central sensitization, could stratify risk and guide precision analgesia.

Methods: This prospective cohort study enrolled 500 adults undergoing VATS lung resection. Two logistic models were developed: one using variables on postoperative day 1 (POD1), and another adding neuropathic pain features on POD14. The primary outcome was CPSP at 3 months, defined as a Numerical Rating Scale [NRS] score ≥ 1 for pain in the surgical region that was not present preoperatively and was not attributable to malignancy or infection; sensitivity analysis was conducted using NRS ≥ 3 . Discrimination (area under the curve [AUC]), calibration and decision curve analysis quantified predictive performance and potential clinical applicability.

Results: Of 483 patients analysed, 247 (51.1%) developed CPSP and 184 (38.1%) had 3-mon NRS ≥ 3 . The POD14 model (sex, surgery type, chest tube duration, pain intensity, pain with neuropathic characteristics) was superior (AUC 0.904, 95% CI: 0.872–0.936) to the POD1 model (AUC 0.865, 95% CI: 0.827–0.903). Neuropathic pain at 2 weeks was the strongest predictor (odds ratio 13.98, 95% CI: 2.90–67.38). Temporal validation confirmed discrimination with good calibration. Sensitivity analysis showed an AUC of 0.786 (95% CI: 0.737–0.835) for the POD14 model; pain with neuropathic characteristics retained strong predictive value.

Conclusions: This 5-item tool with neuropathic pain features at 2-week visit identifies patients at high risk for CPSP after VATS.

Significance Statement: Translating central sensitization from a theoretical mechanism to an actionable bedside tool, this study demonstrates that neuropathic pain features captured at routine two-week follow-up stratify risk for CPSP after VATS. This 5-item model is a first step toward individualized CPSP risk stratification after VATS and requires external validation before clinical implementation.

Wei Dou and Hai-jing Shi contributed equally to this work.

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1 | Introduction

Chronic postsurgical pain (CPSP) after video-assisted thoracoscopic surgery (VATS) affects 20%–47% of patients, driving long-term opioid use, disability, sleep disturbance and increased healthcare utilization (Carley et al. 2021; Chen et al. 2023; Moka et al. 2025; Pergolizzi et al. 2023; Weinrib et al. 2017). Evidence suggests that the transition from acute to chronic pain can begin within the first two postoperative weeks, making this period a critical window for preventive interventions (Chapman and Vierck 2017; Zhang et al. 2025). Thus, an objective bedside risk stratification tool is needed to guide precision analgesia after VATS.

Existing prediction models for CPSP have been derived from mixed surgical populations or retrospective data (Chen et al. 2023; van Driel et al. 2022; Wu et al. 2022), limiting their applicability to VATS patients who experience distinct nociceptive mechanisms, including intercostal nerve injury, pleural tube irritation and graded surgical resection. Although recent work by van Driel et al. has advanced the field by incorporating postoperative pain trajectories and neuropathic characteristics measured on postoperative day 1 (POD1) and POD 14, that model was developed and validated in a heterogeneous cohort spanning orthopaedic, abdominal and thoracic procedures (van Driel et al. 2022).

Because VATS entails a unique anatomical injury pattern and because thoracic surgery clinics require rapid, bedside-compatible tools, we prospectively developed and validated two clinical decision tools for CPSP prediction after VATS lung resection: a 5-item POD1 model for early risk awareness, and a 5-item POD14 model incorporating neuropathic features to guide actionable decisions at the 2-week visit. We hypothesized that: (i) including VATS-specific variables such as chest tube duration and anatomical resection grade would capture the unique risk profile of VATS within this homogeneous population and (ii) dynamic pain phenotypes, especially pain with neuropathic characteristics on POD14, would dominate prediction by capturing early altered central-peripheral processing unique to intercostal nerve trauma, and thus the POD14 tool would demonstrate superior discrimination to the POD1 model.

2 | Methods

2.1 | Study Design and Ethics

This single-center prospective cohort study was conducted at the First Affiliated Hospital of Soochow University from December 2022 to September 2023. The protocol was approved by institutional Ethics Committee (Approval No. 2022-442) and registered at the Chinese Clinical Trial Registry (<http://www.chictr.org.cn>, identifier: ChiCTR2200066122; principal investigator: Ke Peng; registered November 24, 2022). The detailed study protocol was previously published (Hu et al. 2023).

Given a monthly volume of over 100 elective VATS procedures at our center and a dedicated research team, we completed the

enrollment of 500 patients over 10 months. All participants provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and reported following the Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) guideline (Collins et al. 2024, 2015). The completed checklist is provided in Appendix S1.

2.2 | Participants

Consecutive adults (aged ≥ 18 years) scheduled for elective VATS lung resection with ASA physical status I–III were screened. Exclusion criteria were: (1) chronic pain before surgery, defined as pain lasting > 3 months prior to the current surgery; (2) previous thoracic surgery (because prior pleural adhesions and subclinical sensory changes could confound the attribution of CPSP to the index procedure); (3) language or communication barriers and (4) conversion to thoracotomy or reoperation within 3 months. Patients were enrolled on the day before surgery and followed up for 3 months postoperatively.

2.3 | Anaesthesia and Pain Management

All patients received standard monitoring and general anaesthesia. Perioperative pain management was at the discretion of attending anesthesiologist or ward physician. Flurbiprofen axetil was routinely administered intravenously (50 mg during surgery and twice daily for two postoperative days). Postoperative analgesic regimens were classified as follows: (i) regional nerve block (intercostal nerve block or erector spinae plane block); (ii) patient-controlled intravenous analgesia (PCIA) with sufentanil; (iii) both or (iv) neither. Postoperative rescue analgesia was provided using intravenous tramadol or dezocine. Detailed opioid consumption or cumulative dosing was not systematically documented.

2.4 | Outcomes

The primary outcome was CPSP, defined as a Numerical Rating Scale (NRS) score ≥ 1 at 3 months that was not present preoperatively and could not be attributed to malignancy or infection (Wu et al. 2022). NRS was collected by ward visit on POD1 and by telephone at POD14 and 3 months (POD90) by a trained researcher who was not involved in perioperative care and was blinded to anaesthesia and surgical details. To minimize potential bias, this researcher conducted all NRS assessments to ensure consistency, using a standardized script: ‘On a scale of 0 to 10, where 0 is no pain and 10 is the worst pain imaginable, what is your average pain level over the last 24 h?’ Leading questions (e.g., ‘Is your pain better than last time?’) were avoided. The first number provided by the patient was recorded. Patients reporting any pain at 3 months were asked to confirm (i) that the pain was located in the surgical region (the chest wall and surgical field of the index procedure) and (ii) whether the pain had been present before surgery; only new-onset pain localized to the surgical region was classified as CPSP. This definition is consistent with the IASP classification of chronic postsurgical pain for ICD-11 (Schug

et al. 2019), which requires pain that develops or increases in intensity after surgery, persists for at least 3 months, is localized to the surgical field or its innervation territory, and is not better explained by another cause such as infection, malignancy, or a pre-existing pain condition. The complete standardized interview script is provided in Appendix S2.

2.5 | Predictors

Candidate predictors were selected a priori according to literature review (Chen et al. 2021; Fregoso et al. 2019; Glare et al. 2019; Macrae 2008; Pak et al. 2018; Werner et al. 2010) and clinical expertise (involving thoracic surgeons, anesthesiologists and pain specialists at our institution), which has been reported in our published study protocol (Hu et al. 2023). Preoperative factors included age, sex, body mass index (BMI), smoking history, comorbidities (age-adjusted Charlson Comorbidity Index [aCCI]) (Liu et al. 2022), preoperative anxiety (4-item Amsterdam Preoperative Anxiety And Information Scale [APAIS]) (Moerman et al. 1996), frailty (FRAIL scale) (Kojima 2018) and pulmonary function. Intraoperative factors included type of surgery (biopsy/exploration, wedge resection, segmentectomy, lobectomy, pneumonectomy), analgesic regimen and duration of surgery. Postoperative factors included duration of chest tube drainage, pain intensity (Prince-Henry scale 0–4) on POD1 and POD14 (Qiu et al. 2021; Xiao et al. 2022), and pain with neuropathic characteristics on POD1 and POD14.

Pain with neuropathic characteristics within the surgical area over the preceding 24 h was assessed using the Douleur Neuropathique 4 (DN4) questionnaire by a trained researcher. This questionnaire consists of seven self-report items about pain descriptors (burning, painful cold, electric shocks, tingling, pins and needles, numbness, itching) and three items relating to sensory examination (hypoesthesia to touch, hypoesthesia to pinprick, pain caused by brushing); each item was scored as present (1) or absent (0). On POD1, the full 10-item DN4 was used via ward visit, with a cut-off of ≥ 4 ; on POD 14, the 7-item DN4-interview including pain descriptors only was used during telephone follow-up, with a cut-off of ≥ 3 (Aho et al. 2020; Bouhassira et al. 2005, 2008). Because the DN4 has not been formally validated in acute postoperative pain, we treated the score as a composite phenotypic marker of neuropathic features rather than a diagnostic tool.

2.6 | Sample Size

The target sample size of 500 patients was determined a priori in the published protocol (Hu et al. 2023). Based on the 10 events-per-variable (EPV) principle (Wynants et al. 2015), 14 candidate predictors and an anticipated CPSP incidence of 40% required at least 350 patients for the development cohort ($14 \times 10/0.4$). An additional 150 patients were planned for temporal validation in a subsequent recruitment block, yielding a total target of 500. The actual development cohort comprised 338 patients and the temporal validation cohort 145 patients after 17 exclusions. Preoperative pulmonary function was excluded due to $> 5\%$ missing data, leaving 13 candidate predictors and an actual EPV of 13.7 in the development cohort.

2.7 | Statistical Analysis

Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile range [IQR]); categorical variables are summarized as n (%). Univariable logistic regression was performed for all 13 candidate predictors; variables with $p < 0.10$ were advanced to the multivariable stage. Multivariable logistic models were built separately for POD1 and POD14 using forward stepwise selection. Nomograms for both models are provided to facilitate bedside probability estimation. A sensitivity analysis defining CPSP as NRS ≥ 3 at 3 months was conducted to assess robustness across pain severity thresholds.

For internal validation, over-fitting-corrected performance was estimated from 1000 bootstrap resamples drawn with replacement from the development cohort (Grant et al. 2018). The discriminative ability was quantified with the area under the receiver operating characteristics curve (AUC) and 95% confidence interval (CI), and calibration plots were constructed to assess agreement between predicted probabilities and observed frequencies. For temporal validation, the final coefficients were applied without re-estimation to the temporal cohort recruited during a subsequent 3-month block. Discrimination (AUC), calibration (Hosmer-Lemeshow test, Brier score) and decision curve analysis (DCA; net benefit across 1%–99% risk thresholds) were computed on complete cases (Van Calster et al. 2018; Vickers et al. 2016). SHapley Additive exPlanations (SHAP) was used to quantify each feature's contribution to individual predictions (Nohara et al. 2022; Ponce-Bobadilla et al. 2024). For each prediction, SHAP calculates how much each variable pushes the predicted probability upward (positive SHAP value, increased risk) or downward (negative SHAP value, decreased risk) relative to the model's baseline probability. The sum of SHAP values across all features equals the difference between the individual prediction and the average prediction.

All analyses were performed using R software (version 4.5.1; www.R-project.org) and SPSS (IBM, version 30.0). Missing values $\leq 5\%$ were handled by multiple imputation using chained equations in the mice package. Predictive mean matching was used for continuous variables, logistic regression for binary variables and proportional odds models for ordinal variables. Twenty imputed datasets were generated with 50 iterations per chain, and estimates were pooled using Rubin's rules. Variables with $> 5\%$ missing were excluded. A two-tailed $p < 0.05$ was considered statistically significant.

3 | Results

3.1 | Study Flow and Perioperative Data

Of 500 adults enrolled, 17 were excluded (11 lost to follow-up, 2 converted to thoracotomy, 4 reoperated within 3 months), leaving 483 patients in the analysis (Figure 1). The development cohort comprised 338 patients enrolled during the first 7 months (December 2022–June 2023) and the temporal validation cohort included 145 patients during the final 3 months (July 2023–September 2023).

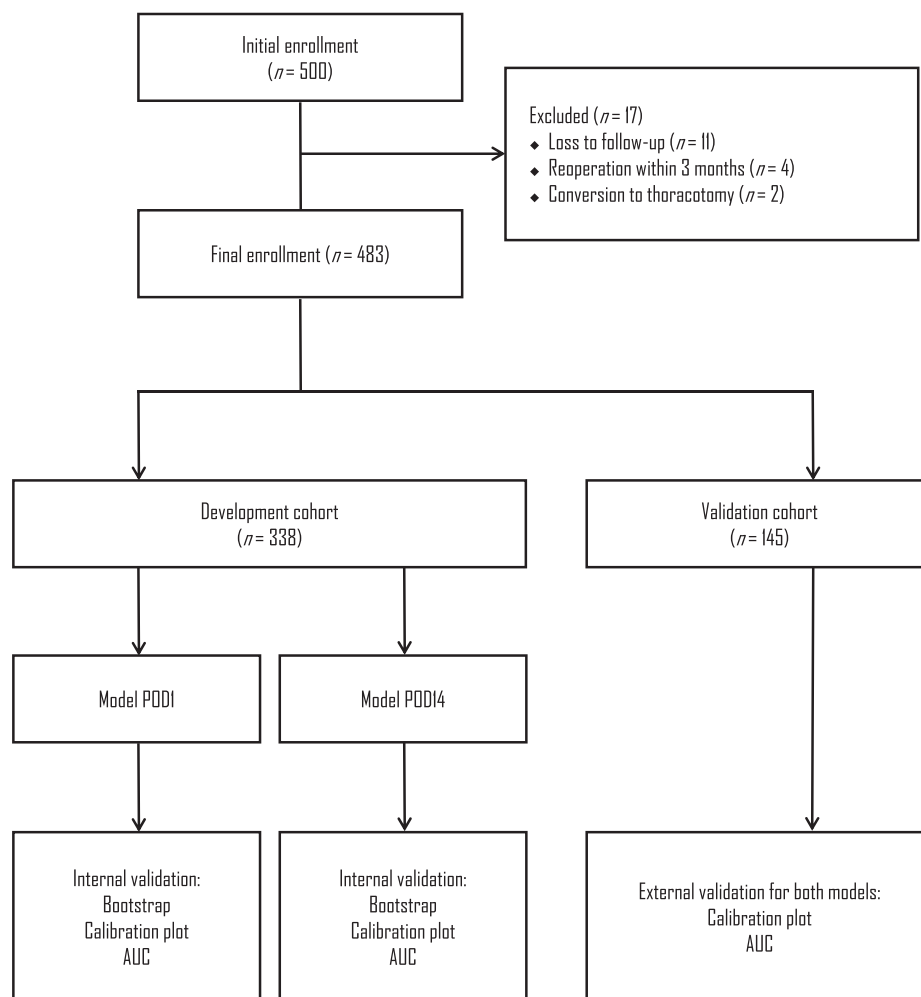


FIGURE 1 | Study flowchart. AUC, area under the curve; POD, postoperative day.

Demographic and perioperative characteristics were similar between cohorts (Table 1). Median (IQR) age was 56 (45–65) years in the development cohort and 52 (43–65) years in the validation cohort. Preoperative pulmonary function was excluded from analysis due to missing data exceeding the 5% threshold. In the development cohort, pulmonary function data were missing in 41 patients (12.1%); in the validation cohort, 18 patients (12.4%) were missing.

Approximately 50% of patients underwent wedge resection, with a median surgical duration of ~120 min. Approximately 35% received a regional block and/or PCIA. Median duration of chest tube drainage was 4 days in both cohorts. Pain with neuropathic characteristics was present in 6%–7% of patients on POD1 and 10%–12% on POD14.

3.2 | Occurrence of CPSP and Selection of Predictors

Three months after surgery, 178 (52.6%) patients in the development cohort and 69 (47.5%) in the validation cohort experienced

CPSP. Univariable analysis is shown in Table S1. Significant risk factors included older age ($p < 0.001$), female sex ($p < 0.001$), higher aCCI scores ($p = 0.003$), major surgery ($p < 0.001$), absence of nerve block or PCIA ($p = 0.028$), longer surgical time ($p < 0.001$), prolonged chest tube drainage ($p < 0.001$), higher pain intensity on POD1 ($p < 0.001$) and POD14 ($p < 0.001$) and pain with neuropathic characteristics on POD1 ($p < 0.001$) and POD14 ($p < 0.001$).

3.3 | Prediction of CPSP on POD1

For the POD1 model, multivariable logistic regression retained sex, BMI, surgery type, chest tube duration and pain intensity on POD1 (Table 2). An example nomogram is shown in Figure 2. The AUC was 0.865 (95% CI: 0.827–0.903) in the development cohort and 0.748 (95% CI: 0.664–0.832) in the temporal validation cohort (Figure 3A). Calibration plots showed good agreement between predicted and observed CPSP in the development cohort (Brier score 0.166; Figure 3B) and validation cohort (Brier score 0.224; Figure 3C). DCA confirmed positive net benefit (Figure S1). SHAP analysis identified pain intensity on POD1 as the dominant contributor (Figure S2).

TABLE 1 | Demographic and perioperative data.

	Development cohort		Validation cohort	
	Total (<i>n</i> = 338)	Missing values, <i>n</i> (%)	Total (<i>n</i> = 145)	Missing values, <i>n</i> (%)
Preoperative				
Age (year)	56 (45, 65)	0	52 (43, 65)	0
Male sex	123 (36.3%)	0	63 (43.4%)	0
BMI (kg/m ²)	23.5 (21.6, 25.3)	0	23.9 (22.0, 25.4)	0
Smoking history	84 (24.9%)	5 (1.5%)	43 (29.7%)	3 (2.0%)
ASA physical status				
I	84 (24.8%)	0	35 (24.1%)	0
II	193 (57.1%)		96 (66.2%)	
III	61 (18.1%)		14 (9.7%)	
Comorbidities (aCCI)	3 (2, 5)	0	3 (2, 5)	0
Preoperative anxiety (4-item APAIS)	6 (4, 8)	0	6 (4, 8)	0
Preoperative frailty				
Not frail	260 (76.9%)	0	121 (83.4%)	0
Prefrail	70 (20.7%)		23 (15.8%)	
Frail	8 (2.3%)		1 (0.6%)	
Intraoperative				
Type of surgery				
Biopsy and exploration	2 (0.6%)	0	2 (1.4%)	0
Wedge resection	159 (47.1%)		74 (51.0%)	
Segmentectomy	89 (26.3%)		35 (24.1%)	
Lobectomy	87 (25.7%)		34 (23.5%)	
Pneumonectomy	1 (0.3%)		0 (0%)	
Duration of surgery (min)	115 (75, 162)	0	120 (75, 180)	0
Analgesic regimen				
Regional blocks	23 (6.8%)	0	15 (10.4%)	0
PCIA	76 (22.5%)		30 (20.7%)	
Both	17 (5.0%)		5 (3.4%)	
Neither	222 (65.7%)		95 (65.5%)	
Postoperative				
Duration of chest tube drainage (day)	4 (3, 6)	2 (0.6%)	4 (3, 5)	5 (3.5%)
Prince-Henry pain score on POD1				
0	3 (0.9%)	0	5 (3.4%)	0
1	13 (3.8%)		2 (1.4%)	
2	107 (31.7%)		54 (37.3%)	
3	124 (36.7%)		56 (38.6%)	
4	91 (26.9%)		28 (19.3%)	

(Continues)

TABLE 1 | (Continued)

	Development cohort		Validation cohort	
	Total (n = 338)	Missing values, n (%)	Total (n = 145)	Missing values, n (%)
Prince-Henry pain score on POD14				
0	5 (1.5%)	0	2 (1.4%)	0
1	63 (18.6%)		27 (18.6%)	
2	125 (36.9%)		63 (43.4%)	
3	111 (32.9%)		41 (28.3%)	
4	34 (10.1%)		12 (8.3%)	
Pain with neuropathic characteristics on POD1	20 (5.9%)	0	10 (6.8%)	0
Pain with neuropathic characteristics on POD14	41 (12.1%)	0	15 (10.3%)	0

Note: Data are median (interquartile range) or n (%).

Abbreviations: aCCI, age-adjusted Charlson Comorbidity Index; APAIS, Amsterdam Preoperative Anxiety and Information Scale; BMI, body mass index; PCIA, patient-controlled intravenous analgesia; POD, postoperative day.

3.4 | Prediction of CPSP on POD14

Sex, type of surgery, duration of chest tube drainage, pain intensity, and pain with neuropathic characteristics on POD14 were included in the POD14 model (Table 2). Pain with neuropathic characteristics at 2 weeks emerged as the strongest predictor (odds ratio [OR] 13.98, 95% CI: 2.90–67.38). An example nomogram is presented in Figure 2.

The AUC was 0.904 (95% CI: 0.872–0.936) in the development cohort and 0.796 (95% CI: 0.724–0.869) in the temporal validation cohort (Figure 3D). Calibration plots showed excellent agreement, with Brier scores of 0.137 in the development cohort (Figure 3E) and 0.202 in the validation cohort (Figure 3F). DCA indicated greater net benefit than the POD1 model (Figure S1). SHAP analysis showed pain intensity on POD14 remained the leading contributor, while pain with neuropathic characteristics significantly amplified CPSP probability (Figure S3).

3.5 | Sensitivity Analysis

When CPSP was defined as NRS ≥ 3 , 184 of 483 patients (38.1%) met the criterion. The POD14 model retained acceptable discrimination (AUC 0.786, 95% CI: 0.737–0.835) (Figure S4). Pain with neuropathic characteristics at 2 weeks remained the strongest predictor (OR 4.03, 95% CI: 1.83–8.84), with age and chest tube duration also entering the model (Table S2).

4 | Discussion

In this prospective cohort, we developed two parsimonious, 5-item models for predicting CPSP after VATS; the POD14 model, incorporating pain with neuropathic characteristics at 2 weeks, showed the highest discrimination in temporal validation.

These models represent a first step toward risk stratification at the routine 2-week visit. However, as they were derived from single-center data and validated only temporally, external validation in independent multicenter cohorts is required before they can be used in clinical routine.

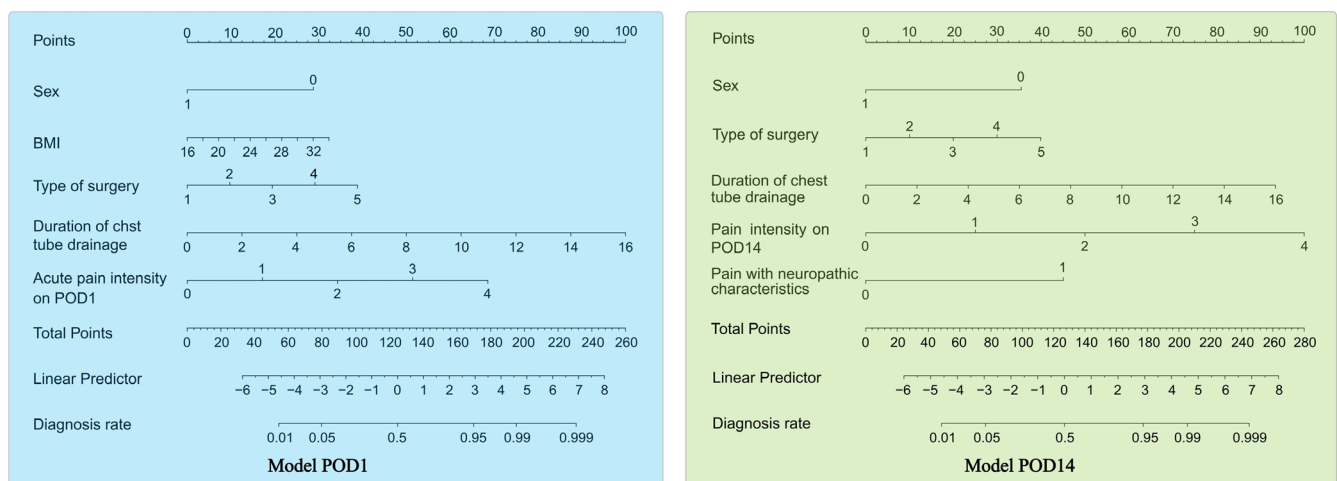
Female sex and prolonged chest tube drainage remained independent predictors in both models, corroborating previous thoracic surgery data (Peng et al. 2014; Pergolizzi et al. 2023; Rivera-Ramos et al. 2025). Although previous studies have reported an association between age and CPSP (Kim et al. 2018; Li et al. 2025; van Dijk et al. 2021), the absence of age in our models probably reflects collinearity with comorbidity indices and the relatively narrow age distribution of our cohort. Higher BMI has been associated with increased postoperative pain (Chen et al. 2022; Majchrzak et al. 2019; Sun et al. 2020); we found BMI was retained only in the POD1 model, suggesting its influence is mediated through early surgical-site inflammation rather than sustained nociceptive drive. Anatomical resections (lobectomy/segmentectomy) conferred higher CPSP risk than wedge resection, reflecting the graded burden of tissue and intercostal nerve injury (Jiang et al. 2025). In the POD14 model, the presence of pain with neuropathic characteristics, reflecting surgically induced nerve injury and sustained immune-mediated sensitization (Costigan et al. 2009), emerged as an independent driver of CPSP, aligning with population data showing that neuropathic features markedly increase the risk of chronicity (Bouhassira et al. 2008).

We elected to use the total DN4 score as a composite predictor rather than individual items for three reasons. First, the DN4 was designed and validated as a composite screening instrument (Bouhassira et al. 2005); its total score captures the cumulative presence of sensory descriptors and objective signs, providing a more robust phenotype marker than any single item. Second, entering multiple individual items into the multivariable model would substantially increase the risk of overfitting in our

TABLE 2 | Final prediction models for chronic postsurgical pain.

Predictor	Model POD1			Model POD14		
	β coefficients	OR (95% CI)	<i>p</i>	β coefficients	OR (95% CI)	<i>p</i>
Intercept	−8.771	0.000 (0.000, 0.001)	<0.001	−5.933	0.003 (0.001, 0.014)	<0.001
Sex	−1.878	0.153 (0.080, 0.294)	<0.001	−2.076	0.125 (0.062, 0.253)	<0.001
BMI	0.117	1.124 (1.002, 1.262)	0.046	—	—	—
Type of surgery	0.634	1.885 (1.324, 2.683)	<0.001	0.584	1.793 (1.232, 2.611)	0.002
Duration of chest tube drainage	0.408	1.503 (1.279, 1.768)	<0.001	0.342	1.408 (1.197, 1.655)	<0.001
Pain intensity on POD1	1.118	3.060 (2.141, 4.375)	<0.001	—	—	—
Pain intensity on POD14	—	—	—	1.463	4.321 (2.850, 6.553)	<0.001
Pain with neuropathic characteristics on POD14	—	—	—	2.637	13.978 (2.901, 67.375)	0.001

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; POD, postoperative day.



To estimate an individual patient's risk of developing CPSP on POD1 and POD14, nomogram-based calculations were performed.

For example, a female patient with a BMI of 24 underwent video-assisted thoracoscopic segmentectomy. The chest tube was retained for 8 days. The acute pain intensity score was 4 on POD1 and 3 on POD14, and pain with neuropathic characteristics was present on POD14. Based on the Model POD1 nomogram, the total score for this patient was 181 points, corresponding to an estimated postoperative pain probability of 96.5%. Using the POD14 nomogram, the total score was 221 points, also corresponding to an estimated probability of 99.4%.

FIGURE 2 | Predicting a patient's individual risk of developing CPSP with an example using nomograms of Model POD1 and Model POD14. CPSP, chronic postsurgical pain; POD, postoperative day.

development cohort. Third, a single binary variable preserves the clinical feasibility of the final 5-item bedside tool. Notably, van Driel et al. (2022) adopted the same approach, using the total DN4 score as a composite marker.

Strengths include the prospective design, protocol registration and adherence to the TRIPOD guideline. The POD14 AUC of 0.90 compares favourably with recently published CPSP models

derived from mixed surgical cohorts (AUC 0.64–0.82) (van Driel et al. 2022; Wu et al. 2022). We acknowledge that direct comparison of AUC values across studies should be interpreted cautiously owing to differences in cohort characteristics, outcome definitions and validation strategies. Several factors may explain the apparent improvement in discrimination observed in our cohort. First, our model was developed and validated in a homogeneous, prospective VATS lung resection cohort, whereas

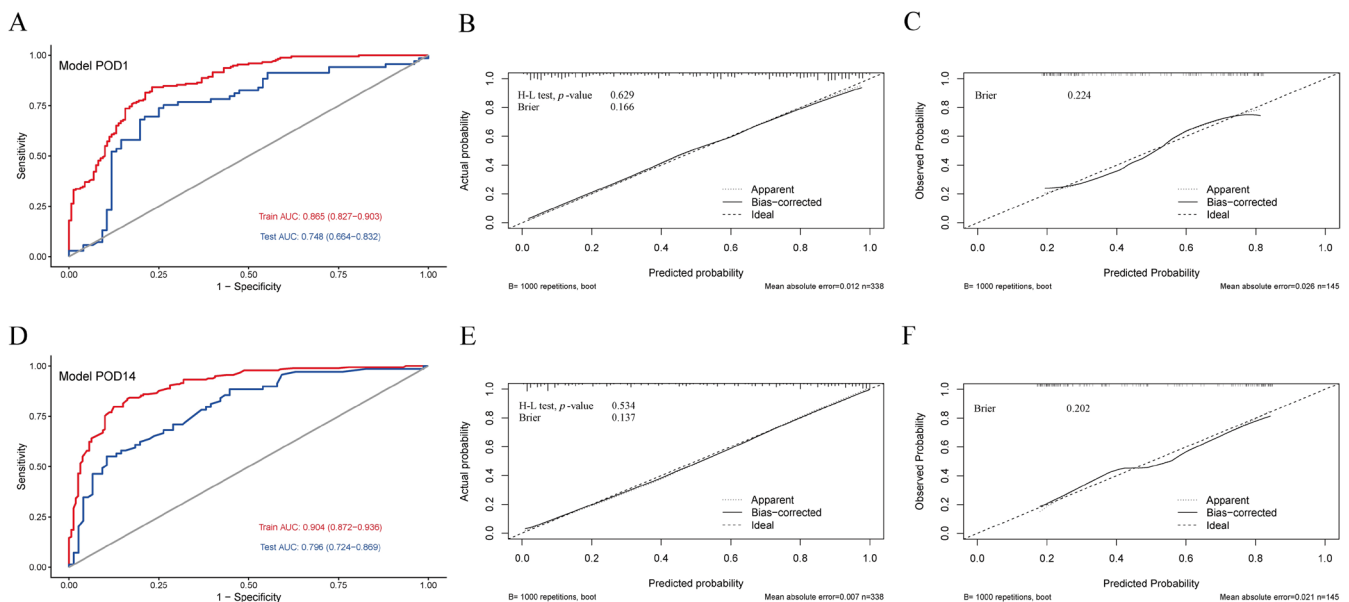


FIGURE 3 | Internal and temporal validation of Model POD1 and Model POD14. (A) AUC for Model POD1; (B) calibration plot of internal validation for Model POD1; (C) calibration plot of temporal validation for Model POD1; (D) AUC for Model POD14; (E) calibration plot of internal validation for Model POD14; (F) calibration plot of temporal validation for Model POD14. AUC, area under the curve; POD, postoperative day.

existing tools were derived from mixed surgical populations (orthopaedic, abdominal and thoracic procedures) or retrospective data. This specificity allows thoracic-specific predictors (chest tube duration, intercostal nerve injury) to emerge with greater precision by eliminating inter-surgical heterogeneity in pain mechanisms. Second, we designed two parsimonious 5-item models for distinct clinical timepoints: POD1 for early ward-based risk awareness and POD14 for actionable decision-making at the routine outpatient visit. Although van Driel et al. also collected dynamic postoperative data in a mixed population, the predictive signal of VATS-specific trajectories may be diluted by non-thoracic cases (van Driel et al. 2022); Wu et al. (2022) relied exclusively on preoperative and intraoperative variables, missing the critical postoperative window during which the acute-to-chronic transition occurs. Third, the integration of pain with neuropathic characteristics at POD14 represents a key differentiator. In our VATS cohort, this phenotype yielded an odds ratio of 13.98, likely reflecting the high burden of intercostal nerve trauma and sustained chest tube-related sensitization characteristic of thoracoscopic surgery, a mechanistic specificity that is attenuated in mixed surgical cohorts where nociceptive pain predominates. We emphasize, however, that these represent potential advantages supported by single-center data; definitive evidence requires prospective multicenter external validation and clinical impact studies.

Several limitations should be noted. First, the single-center design and temporal validation limit generalizability; our models must be validated externally in independent, prospective multicenter cohorts before clinical implementation. Second, defining CPSP as NRS ≥ 1 increases sensitivity may capture mild pain of limited functional impact. Our sensitivity analysis using the more stringent NRS ≥ 3 threshold confirmed that pain with neuropathic characteristics at POD14 remains a robust predictor, supporting the biological validity

of our findings across the severity spectrum. Third, genetic, psychosocial and quantitative sensory testing variables were unavailable, potentially leaving additional explanatory power untapped. Fourth, the DN4 was originally validated in chronic neuropathic pain conditions and has not been validated for the diagnosis of acute neuropathic pain. Fifth, the DN4 was not administered at the 3-month follow-up; therefore, the neuropathic quality of the pain reported at 3 months could not be determined, and our POD14 model predicts CPSP in general rather than neuropathic CPSP specifically. Future studies should incorporate neuropathic pain screening at long-term follow-up to test whether early neuropathic phenotypes preferentially predict neuropathic CPSP. Finally, we did not explore whether individual DN4 descriptors (e.g., cold hypersensitivity, burning) carry differential predictive value compared with the total score. Future multicenter studies should determine whether specific items outperform the composite score in acute postoperative settings.

In conclusion, two 5-item models incorporating routinely collected perioperative variables predicted CPSP after VATS with good discrimination in temporal validation; the POD14 model, incorporating pain with neuropathic characteristics at 2 weeks, performed better. These findings provide a basis for future individualized risk stratification after VATS, but prospective multicenter external validation is required before any clinical implementation can be considered.

Author Contributions

Study design: W.D., H.S., J.H. and K.P. Data acquisition: W.D., H.S. and J.H. Statistical analysis: W.D., H.S. and J.H. Data interpretation: all authors. Manuscript drafting: W.D., H.S., J.L. and Y.Z. Manuscript revision: H.L., J.H., K.P. Final approval of the version to be published: all authors.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

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

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Decision curve analysis. **Figure S2:** SHAP analysis of POD1. (A) Variable importance plot: the mean absolute SHAP value for each predictor; longer bars indicate greater overall influence on model predictions. (B) Waterfall plot for a single representative patient: each bar shows how a specific variable pushes the predicted probability higher (yellow, positive SHAP value, increased risk) from the base value (population average) to the final predicted probability. (C) Bee swarm plot: each dot represents one patient;

the horizontal position shows the SHAP value, and the colour gradient (purple to yellow) indicates the feature value from low to high. **Figure S3:** SHAP analysis of POD14. (A) Variable importance plot: the mean absolute SHAP value for each predictor; longer bars indicate greater overall influence on model predictions. (B) Waterfall plot for a single representative patient: each bar shows how a specific variable pushes the predicted probability higher (yellow, positive SHAP value, increased risk) or lower (purple, negative SHAP value, decreased risk) from the base value (population average) to the final predicted probability. (C) Bee swarm plot: each dot represents one patient; the horizontal position shows the SHAP value, and the colour gradient (purple to yellow) indicates the feature value from low to high. **Figure S4:** Predicting chronic postsurgical pain with NRS ≥ 3 using the models of POD1 and POD14. (A) AUC for POD1; (B) AUC for POD14. AUC, area under the curve; NRS, numerical rating scale; POD, postoperative day. **Table S1:** Preliminary predictor screening by univariate analysis. **Table S2:** Prediction models for chronic postsurgical pain with NRS ≥ 3 . **Appendix S1:** TRIPOD-checklist-completed. **Appendix S2:** Standardized interview scripts and pain assessment instruments. Part 1: Telephone interview script at 3-month follow-up (POD90) including Numerical Rating Scale (NRS) question, pain localization confirmation, and pre-existence verification. Part 2: Prince-Henry Pain Scale instructions and scoring criteria for POD1 and POD14. Part 3: Full 10-item Douleur Neuropathique 4 (DN4) questionnaire for POD1 ward visit. Part 4: 7-item DN4-interview for POD14 telephone follow-up. **Appendix S3:** STROBE statement—checklist of items that should be included in reports of observational studies.