Original Article

Development a predictive nomogram for spontaneous pleurodesis in patients with non-small cell lung cancer and malignant pleural effusion

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Background: Indwelling pleural catheter (IPC) insertion is associated with fewer subsequent procedures and higher rates of spontaneous pleurodesis (SP) in patients with malignant pleural effusion (MPE). However, long-term pleural drains may cause psychological and physical distress. Additionally, only a portion of patients can benefit from IPC insertion and ultimately have them removed. The nomogram reflects the influence of different factors on outcome visually, enabling clinics to assess the optimal population. Thus, the objective of this study was to develop and validate a novel nomogram to predict successful SP in non-small cell lung cancer (NSCLC) patients with MPE treated with IPC.

Methods: We reviewed data on the use of IPC insertion for MPE in patients with NSCLC and allocated them randomly to development (60%) and validation (40%) sets. A static and dynamic nomogram was developed based on multivariate logistic regression to evaluate SP occurrence in the development set. Receiver operating characteristic (ROC) curves, calibration curves, decision curve analysis (DCA), and Nelson-Aalen cumulative risk curves were used to validate the predictive accuracy of the nomogram.

Results: In total, 331 patients (development set: n=199; validation set: n=132) were selected for this study. Medical thoracoscopy, septated effusion, and effusion volume were the strongest predictors of SP. Other predictors included gender, systemic treatment, and serum neutrophil-to-lymphocyte ratio. The prediction nomogram was demonstrated good predictive ability in the development and validation sets (area under the curve: 0.745 and 0.720, respectively). The DCA indicated that the model had a certain clinical application value. Nelson-Aalen cumulative risk curves showed that the more favorable group received successful SP than did the less favorable group (P<0.001).

Conclusions: We developed an accurate and practicable nomogram for successfully predicting SP. These results may benefit clinicians in optimizing treatment decisions, improving the probability of SP, and relieving the long-term discomfort caused by IPC.

Keywords: Indwelling pleural catheter (IPC); malignant pleural effusion (MPE); nomogram; non-small cell lung cancer (NSCLC); spontaneous pleurodesis (SP)

Submitted Jan 06, 2025. Accepted for publication Feb 19, 2025. Published online Feb 27, 2025.
doi: 10.21037/jtd-2025-31
View this article at: https://dx.doi.org/10.21037/jtd-2025-31

Introduction

Malignant pleural effusion (MPE) occurs in up to 40% of patients with advanced non-small cell lung cancer (NSCLC) (1) and is associated with a short life expectancy (3–11 months) (1-3). Moreover, MPE is related to debilitating dyspnea, cachexia, and worsening quality of life (4,5). As one of the conventional management options for MPE, indwelling pleural catheter (IPC) insertion is an effective and safe procedure that relieves symptoms and reduces subsequent effusion-directed procedures and hospital stays (6-13). However, 24.0% to 65.0% of patients with MPE achieve spontaneous pleurodesis (SP) and can undergo IPC removal (7,9,11,14-17).

Previous studies have evaluated the local factors associated with SP in patients with pleural effusion, including medical thoracoscopy and pleural effusion above the hilum (8,18,19). And patients who experienced prolonged survival had more opportunities and longer time to achieve SP (7). Compared with chemotherapy, targeted therapy and immunotherapy have improved tumor response and survival rates in advanced NSCLC patients (20,21). Meanwhile, a recent study indicated that *EGFR* targeted therapy is associated with increased rates of SP in patients with NSCLC (7). Thus, SP is closely related to systemic and local factors. However, previous predictions based only on local or systemic factors are insufficient for constructing a stable model, it is necessary to develop an integrated, accurate, and visualized SP predictive model that incorporates the most relevant variables.

Therefore, in this study, we aimed to construct a novel nomogram based on the predictive factors to identify the optimal population for IPC treatment. The key purpose of this predictive nomogram is to predict which patients will achieve SP and subsequent removal of their IPC. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-31/rc).

Highlight box

Key findings

- This study developed an accurate and practical nomogram for successfully predicting the occurrence of spontaneous pleurodesis (SP) in patient who receive an indwelling pleural catheter (IPC).
- Through use of a novel and validated nomogram, clinicians can identify the optimal population for IPC insertion and improve the rate of SP in patients with malignant pleural effusion (MPE).

What is known and what is new?

- IPC insertion is associated with fewer subsequent procedures and with SP in patients with MPE. However, previous studies have reported that 24.0% to 65.0% of patients achieved SP. Moreover, the optimal population to achieve SP by IPC insertion is currently unknown.
- The study reviewed the available clinical data and constructed and validated a novel nomogram from the predictive factors to identify the optimal population for IPC insertion that would allow patients to engage in normal daily activities as soon as possible.

What is the implication, and what should change now?

- Through retrospective analysis, we found that medical thoracoscopy, systemic treatment, septated effusion, effusion volume, gender, and serum neutrophil-to-lymphocyte ratio were predictors of SP.
- Using these predictors, we developed a valid nomogram which could help clinicians in identifying optimal populations, improve SP, and relieve long-term discomfort caused by IPC.

Methods

Study design, patients, and clinical data collection

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of West China Hospital (No. 2023-818) and individual consent for this retrospective analysis was waived. Patients were recruited at West China Hospital of Sichuan University between January 2015 and December 2022. All available data were used to maximize the power and generalizability of the results. Lung cancer was diagnosed via histology based on the 2015 World Health Organization classification of lung tumors (22). The clinical stage was evaluated based on the eighth edition of the Tumor Node Metastasis (TNM) staging system (23). MPE was diagnosed by pleural fluid cytology, histology from a pleural biopsy, or malignancy was presumed based on the presence of a recurrent, large, exudative pleural effusion along with a histologically proven malignancy with confirmed metastatic disease elsewhere (24).

The key eligibility criteria were pathologically confirmed NSCLC, diagnosis of MPE and treatment with IPC, and no history of IPC placement. The exclusion criteria were previously attempted chemical pleurodesis, intrathoracic chemotherapy, previous IPC placement, pleural space infection, chylous effusion, respiratory failure requiring mechanical ventilation, catheter removal due to complications related to the catheter, and received less than 2 treatment cycles. Thus, 331 of the 524 initial patients were included and allocated randomly to development (60%) and validation (40%) sets via the caret R package. Patients were divided into two subgroups based on whether they had SP at 60 days after IPC insertion.

Outcomes and variables

The primary outcome was the SP success rate after 60 days of IPC insertion. Successful SP was defined as elective IPC removal due to minimal drainage (<50 mL/day) on three consecutive drainages and decreased pleural effusion on radiographic evaluation: chest radiography, computed tomography (CT) imaging, or ultrasound (7,12,24-27). No sclerosing agent was administered though the IPC (12). The classification of SP is as follows (28,29): (I) complete response—relief of symptoms related to the effusion, with absence of re-accumulation of fluid on radiographic evaluation; (II) partial response—diminution of dyspnea related to the effusion, with only partial re-accumulation of fluid and no requirement for pleural interventions; (III) failed SP—lack of success. IPC removed for pain, infection, or other reasons were excluded from the analysis. Patients who did not meet the successful SP criteria, who died before removal of IPC, or who experienced MPE recurrence requiring additional pleural interventions including replacement of other types of drainage tubes or other interventions, were considered to not have achieved pleurodesis. SP was reached with either complete response or partial response (16). The secondary outcomes included the time to SP, from the placement of the first IPC to its removal.

We collected relevant clinical data based on prior analyses and review, which included Eastern Cooperative Oncology Group performance status (ECOG PS), actionable mutational status, chest imaging, oncological treatments while the IPC was *in situ*, and pleural fluid analysis at the time of insertion. Moderate to large pleural effusions means more than 2 intercostal space (ICS) occupied by effusion (ultrasound) or more than 20% of the hemithorax (CT scan) (30,31). Septated effusion is defined as pleural fluid collections that is limited in extent by pleural adhesions (32). Trapped lung was characterized by the persistence of a residual intrathoracic cavity and the absence of the lung to fully expand in an advanced state (18). In this study, we mainly refer to septated effusion and trapped lung that existed before IPC insertion. Some patients underwent medical thoracoscopy for tissue biopsy to diagnosis and ancillary testing (8,18). The procedure was performed in the endoscopy suite with moderate conscious sedation. Using ultrasonographic guidance to mark the appropriate entry site, the skin was anesthetized with lidocaine, Kelly forceps were used to dissect to the pleural space, and an 8 mm disposable trocar was inserted. A semirigid pleuroscope was inserted through the trocar and all fluid was aspirated. Only biopsy of parietal pleural abnormalities was performed, rather than treatment with any sclerosing agent. An IPC was inserted at the end of the procedure. If patients underwent medical thoracoscopy between the time the pleural effusion occurred and IPC inserted, it will be documented. Chest imaging was assessed at baseline and every 2 months, after which the degree of lung expansion was recorded. Clinical data at the time of treatment initiation, 60 days after IPC insertion, and other information on clinical follow-up were collected through medical records. All patients underwent DNA-based next-generation sequencing (NGS) and immunohistochemistry to detect *EGFR* mutations or *ALK/ROS1* fusions. The samples used for actionable genetic testing included histological specimens and MPE samples. The actionable mutation group included patients with *EGFR* mutations or *ALK/ROS1* fusions.

Clinical practice

Systemic anticancer therapy was administered according to the established guidelines (33,34). The radiological response of the tumor was evaluated every 8–10 weeks by radiologists and clinicians. The cutoff date was March 2023, with a median follow-up time of 244 days. Patients with suspected NSCLC with MPE were referred to the Department of Pulmonary and Critical Care Medicine at West China Hospital of Sichuan University and assessed for unified IPC insertion in outpatient clinics, on the inpatient wards, or at the time of medical thoracoscopy in the endoscopy suite by clinicians. All patients were followed up daily, after which they were followed up each week. If the amount of IPC drainage was less than 50 mL per day on three consecutive drainages and there was no increase in pleural effusion

size on the follow-up chest imaging and ultrasound, the IPC was removed in the ward or emergency department. This information will be recorded by the hospital and can be retrospectively analyzed through medical records. Clinicians would determine additional pleural interventions for patients in cases in which SP failed to occur.

Statistical analyses, model development, and nomogram construction

Continuous variables are presented as the median and interquartile range (IQR), while categorical variables are presented as frequencies and percentages. Baseline characteristics were compared between patients who had successful SP using independent sample *t*-tests, Chi-squared tests, or Fisher's exact tests. The associations of clinical variables with successful SP were assessed via univariate and multivariate logistic regression for both categorical and continuous variables. Variables with P<0.20 were retained in the final multivariate models, which effectively avoids the omission of important variables (35-38). Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

We used the independent predictive variables in the multivariate analysis to construct a predictive, static and dynamic nomogram for SP to maximize the predictive ability of the model. The factor that had the greatest impact on the outcome was assigned a maximum of 100 points, and the other variables were assigned lower maximum points that were proportional to the size of the impact. Calibration plots were generated to evaluate the concordance between the nomogram-predicted probability and the actual probability of SP at 60 days. The power of the model, discrimination, and prediction were assessed by Harrell concordance index (C-index) statistics. The closer the area under the curve (AUC) was to 1, the more accurate and powerful the prediction was considered. The net reclassification index (NRI) and integrated discrimination improvement (IDI) are two alternatives to AUC to assess improvement in risk prediction and measure the usefulness of a new model (39,40). They were used to evaluate the clinical benefits and utility of the nomogram compared with previous models. The decision curve analysis (DCA) was generated to evaluate the predictors' net clinical benefits. The model's clinical decision was more advantageous at greater distances from the "treat-all" or "treat-none" strategies (41). To estimate the performance of the nomogram, we used a validation set. The Nelson-Aalen curve was another non-parametric survival curve that plots the cumulative hazard function over time. The cumulative hazard function was the complement to the survival function and directly reflects the cumulative risk of an event occurrence. It was used to illustrate the cumulative hazard of incidence of SP, and their difference among different groups was compared with Gray's test.

The data were analyzed using SPSS 26 statistical software (IBM Corp., Armonk, NY, USA) and R version 4.2.3 (The R Foundation for Statistical Computing). The R package caret and seed were used to allocated data set randomly to development and validation sets. Statistical tests were two-tailed, and P<0.05 indicated statistical significance.

Results

Participant characteristics

We reviewed 524 patients with NSCLC and MPE. Ultimately, 331 patients treated with IPC were reviewed in the final analysis (Figure S1), and the median age was 61.3 years. Males and non-smokers accounted for 55.9% and non-smokers accounted for 62.5% of the study population, respectively. The baseline patient characteristics of patients in the development and validation sets are shown in *Table 1*. There were no significant differences in age, gender, smoking status, ECOG PS, or disease stage between the development and validation sets. Thus, they were comparable in terms of demographic and clinical characteristics (P>0.05). The success rate of SP was nearly 64.3% at 60 days following IPC insertion. The median time to achieving SP was 11 (IQR, 7.0–19.0) days.

Univariate and multivariate analysis of SP in the development set

The results of the univariate and multivariate logistic regression analyses are shown in *Table 2*. Univariate analyses revealed that the factor associated with successful SP were systemic treatment within 30 days of IPC insertion (OR, 1.671; 95% CI: 0.869–3.212; P=0.12), immune checkpoint inhibitors (ICIs) plus chemotherapy (OR, 2.730; 95% CI: 0.894–8.338; P=0.08), targeted therapy (OR, 1.790; 95% CI: 0.737–4.350; P=0.20), and medical thoracoscopy (OR, 14.398; 95% CI: 1.876–110.493; P=0.01). Meanwhile, the factors associated with a decreased SP success rate were male gender (OR, 0.692; 95% CI: 0.392–1.222; P=0.20),

Table 1 Baseline demographics of patients with NSCLC and MPE that received IPC insertion

Clinical characteristic	Total (N=331)	Development set (N=199)	Validation set (N=132)	P value
Age				0.95
<65 years	185 (55.9)	112 (56.3)	73 (55.3)	
≥65 years	146 (44.1)	87 (43.7)	59 (44.7)	
Gender				0.54
Female	146 (44.1)	91 (45.7)	55 (41.7)	
Male	185 (55.9)	108 (54.3)	77 (58.3)	
Smoking status				>0.99
Non-smoker	207 (62.5)	124 (62.3)	83 (62.9)	
Current/ex-smoker	124 (37.5)	75 (37.7)	49 (37.1)	
Type of pathology				0.61
Adenocarcinoma	310 (93.7)	188 (94.5)	122 (92.4)	
Squamous cell carcinoma	21 (6.3)	11 (5.5)	10 (7.6)	
ECOG PS				0.55
0–1	260 (78.5)	159 (79.9)	101 (76.5)	
2–4	71 (21.5)	40 (20.1)	31 (23.5)	
Metastasis number				
<3	249 (75.2)	156 (78.4)	93 (70.5)	0.13
≥3	82 (24.8)	43 (21.6)	39 (29.5)	
8th edition TNM stage				0.36
IVA	219 (66.2)	136 (68.3)	83 (62.9)	
IVB	112 (33.8)	63 (31.7)	49 (37.1)	

Data are presented as n (%). BMI, body mass index; ECOG PS, Eastern Cooperative Oncology Group performance status; IPC, indwelling pleural catheter; MPE, malignant pleural effusion; NSCLC, non-small cell lung cancer; TNM, Tumor Node Metastasis.

moderate to large pleural effusion (OR, 0.312; 95% CI: 0.135–0.724; P=0.007), septated effusion (OR, 0.274; 95% CI: 0.113–0.666; P=0.004), and a higher serum neutrophil-to-lymphocyte ratio (sNLR) (≥2.68) (OR, 0.405; 95% CI: 0.203–0.810; P=0.01) (*Table 2*). Neither pleural fluid location, BMI, nor trapped lung (P=0.28) was independently associated with SP.

According to the multivariate analysis, medical thoracoscopy was associated with successful SP (OR, 17.087; 95% CI: 1.952–149.540; P=0.01). Moreover, associations of systemic treatment within 30 days of IPC insertion, ICI plus chemotherapy, and targeted therapy with successful SP were indicated, but these were not significant (P>0.05). Meanwhile, a decreased SP success rate was associated with male gender (OR, 0.672, 95% CI: 0.354–1.275; P=0.22), moderate to large pleural effusion (OR, 0.367; 95% CI: 0.148–0.911; P=0.03), septated effusion (OR, 0.256, 95% CI: 0.095–0.690; P=0.007), and higher sNLR (≥2.68) (OR, 0.413; 95% CI: 0.192–0.888; P=0.02) (*Figure 1*).

Development of a nomogram for predicting successful SP

According to the results of the multivariate logistic analysis, seven characteristics (male sex, systemic treatment within 30 days of IPC insertion, systemic treatment, medical thoracoscopy, moderate to large pleural effusion, septated effusion, and higher sNLR) were incorporated into the predictive nomogram in the development set, as seen in *Figure 2A*; in the nomogram, the values of each characteristic are projected onto the positions

Table 2 Univariate and multivariate logistic regression of clinical factors predicting successful SP

Clinical factor	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (*vs.* <65 years)				
≥65 years	1.257 (0.711–2.222)	0.43	–	–
Gender (*vs.* female)				
Male	0.692 (0.392–1.222)	0.20	0.672 (0.354–1.275)	0.22
Smoking status (*vs.* non-smoker)				
Current/ex-smoker	0.815 (0.457–1.454)	0.49	–	–
ECOG PS (*vs.* 0–1)				
2–4	1.121 (0.553–2.271)	0.75	–	–
BMI (*vs.* <18.5 kg/m^2)				
18.5–23.9 kg/m^2	0.844 (0.290–2.455)	0.76	–	–
24–27.9 kg/m^2	0.583 (0.191–1.780)	0.34	–	–
≥28 kg/m^2	1.364 (0.200–9.282)	0.75	–	–
Unknown	0.327 (0.057–1.870)	0.21	–	–
N stage (*vs.* N0–N1)				
N2–N3	0.968 (0.614–1.530)	0.89	–	–
Metastasis number (*vs.* <3)				
≥3	1.150 (0.751–1.750)	0.53	–	–
Type of pathology (*vs.* adenocarcinoma)				
Squamous cell carcinoma	1.296 (0.367–4.579)	0.69	–	–
Systemic treatment within 30 days of IPC insertion (*vs.* no)				
Yes	1.671 (0.869–3.212)	0.12	1.422 (0.689–2.933)	0.34
Pleural fluid volume[†] (*vs.* little)				
Moderate to large	0.312 (0.135–0.724)	0.007	0.367 (0.148–0.911)	0.03
Systemic treatment (*vs.* chemotherapy)				
ICI plus chemotherapy	2.730 (0.894–8.338)	0.08	2.454 (0.699–8.610)	0.16
Targeted therapy	1.790 (0.737–4.350)	0.20	1.266 (0.476–3.368)	0.64
Pleural fluid location (*vs.* single)				
Bilateral	0.822 (0.286–2.364)	0.72	–	–
Trapped lung (*vs.* no)				
Yes	0.731 (0.413–1.294)	0.28	–	–
Septated pleural effusion[‡] (*vs.* no)				
Yes	0.274 (0.113–0.666)	0.004	0.256 (0.095–0.690)	0.007
Medical thoracoscopy[§] (*vs.* no)				
Yes	14.398 (1.876–110.493)	0.01	17.087 (1.952–149.540)	0.01
sNLR (*vs.* <2.68)				
≥2.68	0.405 (0.203–0.810)	0.01	0.413 (0.192–0.888)	0.02

[†], definition of pleural effusion volume: moderate to large pleural effusions means more than 2 ICS occupied by effusion (ultrasound) or more than 20% of the hemithorax (CT scan); [‡], septated effusion: it is defined as pleural fluid collections that are limited in extent by pleural adhesions prior to the IPC insertion; [§], medical thoracoscopy: it defines whether the patient undergoes medical thoracoscopy and IPC was inserted at the end of the procedure. BMI, body mass index; CI, confidence interval; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; ICS, intercostal space; IPC, Indwelling pleural catheter; OR, odds ratio; sNLR, serum neutrophil-to-lymphocyte ratio; SP, spontaneous pleurodesis.

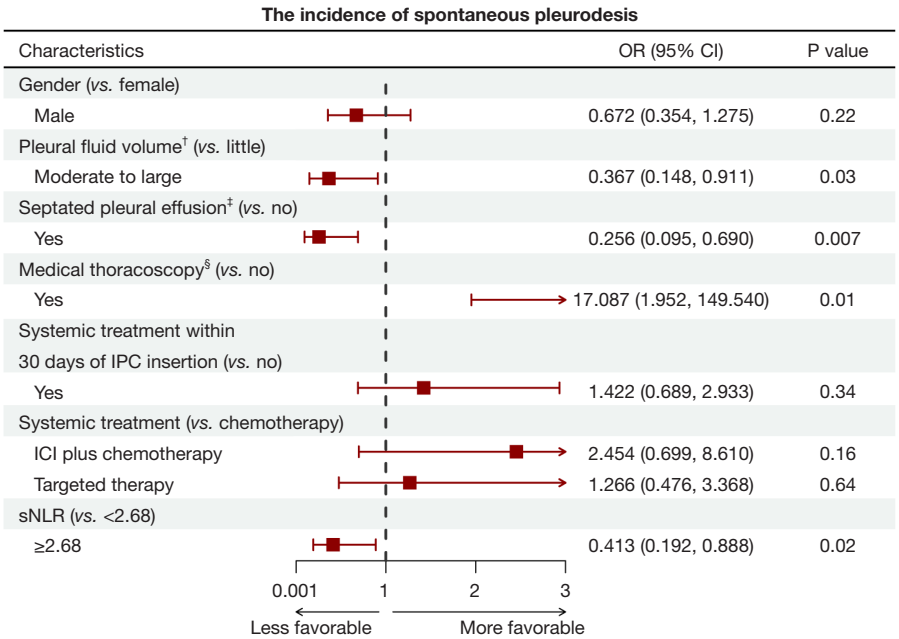

Figure 1 Forest plot showing the ORs from multivariable logistic regression in the modelling group. †, definition of pleural effusion volume: moderate to large pleural effusions means more than 2 ICS occupied by effusion (ultrasound) or more than 20% of the hemithorax (CT scan); ‡, septated effusion: it is defined as pleural fluid collections that are limited in extent by pleural adhesions prior to the IPC insertion; §, medical thoracoscopy: it defines whether the patient undergoes medical thoracoscopy and IPC was inserted at the end of the procedure. OR, odds ratio; CI, confidence interval; IPC, indwelling pleural catheter; ICI, immune checkpoint inhibitor; sNLR, serum neutrophil-to-lymphocyte ratio; ICS, intercostal space; CT, computed tomography.

corresponding to the line of "Points", and the total points are summed. Based on the total points projected into the last row, the rate of SP is calculated. A higher point total indicates an elevated success rate of SP. To facilitate clinical practice, we constructed a web-based dynamic online nomogram (*Figure 2B*), which can be accessed at https://sunshine3036.shinyapps.io/dynnomapp/.

Prediction model validation

For the prediction model, the AUCs of logistic regression were 0.745 (95% CI: 0.678–0.812) and 0.720 (95% CI: 0.631–0.809) in the development and validation sets, respectively, which indicated a good discrimination ability of the model (*Figure 3A*,*3B*). To assess the calibration of the predictive nomogram, we compared the predicted probability of successful SP with the corresponding actual observations. The calibration curve of the successful SP nomogram showed favorable agreement (*Figure 3A*,*3B*). Moreover, DCA was performed to evaluate the clinical application of the nomogram by quantifying the net benefits at different threshold probabilities. The DCA showed that, especially when the threshold probability was >0.27, the positive net benefit of this model for SP probability prediction was more obvious compared with the 'all' or 'none' scheme in development set (*Figure 3C*). And it demonstrated a favorable net benefit in the range of 0.38–0.85 for validation set, which indicated that the model possesses certain clinical application value, as shown in *Figure 3D*. Compared with that of other prediction models (7,8), the AUC of the SP predictive nomogram (model 1) was larger, indicating its superiority in predicting SP (*Figure 4A*). The curve corresponding to the SP predictive nomogram (model 1) index is above, using model 1 to predict SP added more benefit than non-treatment or all-treatment (*Figure 4B*). DCA showed that the SP predictive nomogram was superior to other prediction models in predicting SP. While compared with model 2 and model 3, the NRI of model 1 were 0.589 (95% CI: 0.328–0.851; P<0.001) and 0.724 (95% CI: 0.468–0.979; P<0.001), and the IDI were 0.088 (95% CI: 0.046–0.129; P<0.001) and 0.159 (95% CI: 0.106–0.212; P<0.001), indicating that the

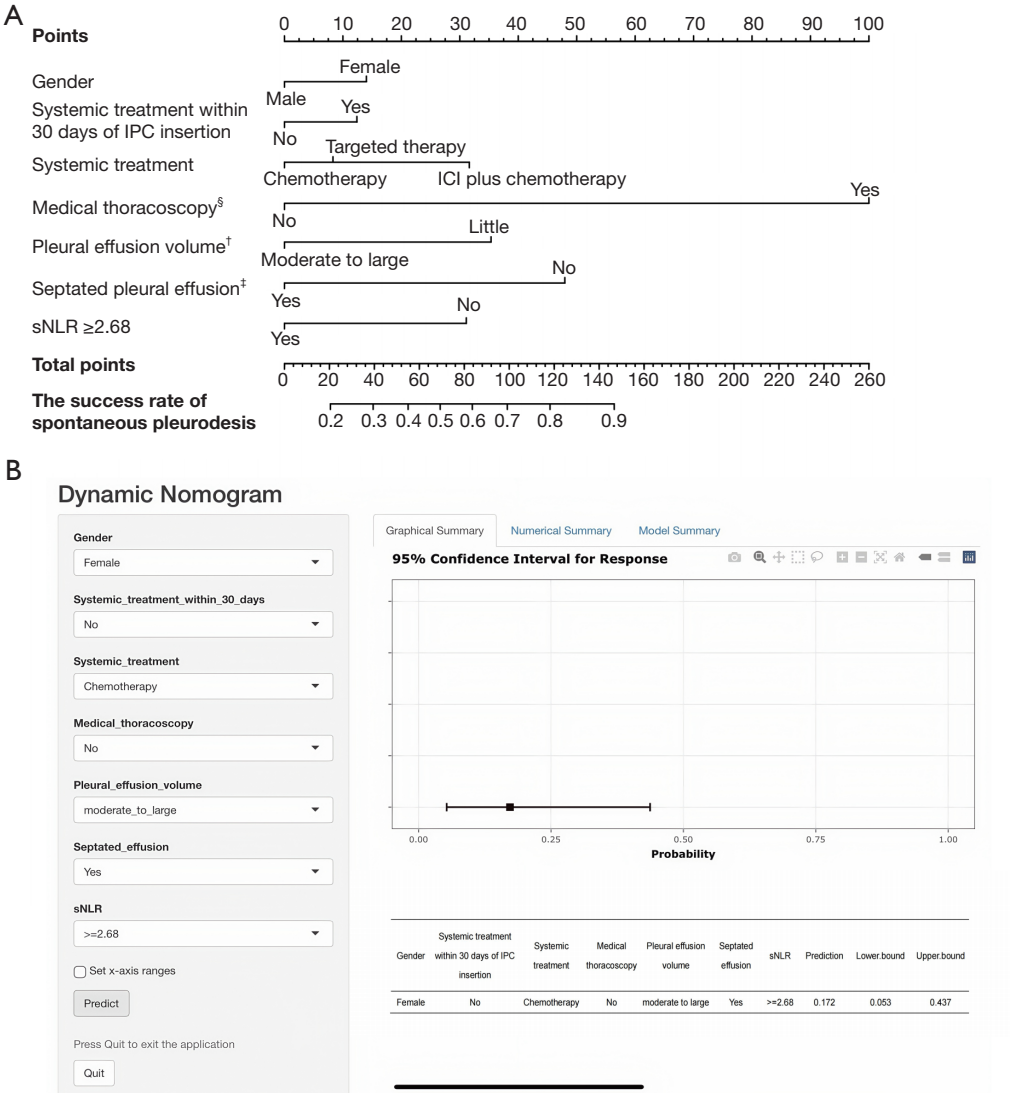

Figure 2 Nomogram for the prediction of successful spontaneous pleurodesis and its predictive performance. (A) The static nomogram for the prediction of successful spontaneous pleurodesis. (B) The web-based dynamic online nomogram, depicting an example for predicting the probability of spontaneous pleurodesis for a female participant received chemotherapy, with moderate to large pleural effusion, septated effusion and sNLR ≥2.68. And she did not receive medical thoracoscopy or systemic treatment within 30 days of IPC insertion. After selecting the values of each item of the dynamic nomogram on the web page and clicking "Predict", the risk of predicted spontaneous pleurodesis was 0.172 shown in the prediction probability graph on the right. Finally, the patient failed spontaneous pleurodesis. The SP prediction nomogram was developed with predictors including gender, systemic treatment within 30 days of IPC insertion, systemic treatment, medical thoracoscopy, the pleural effusion volume, septated effusion, and the sNLR. †, definition of pleural effusion volume: moderate to large pleural effusions means more than 2 ICS occupied by effusion (ultrasound) or more than 20% of the hemithorax (CT scan); ‡, septated effusion: it is defined as pleural fluid collections that are limited in extent by pleural adhesions prior to the IPC insertion; §, medical thoracoscopy: it defines whether the patient undergoes medical thoracoscopy and IPC was inserted at the end of the procedure. CT, computed tomography; ICI, immune checkpoint inhibitors; ICS, intercostal space; IPC, Indwelling pleural catheter; sNLR, serum neutrophil-to-lymphocyte ratio; SP, spontaneous pleurodesis.

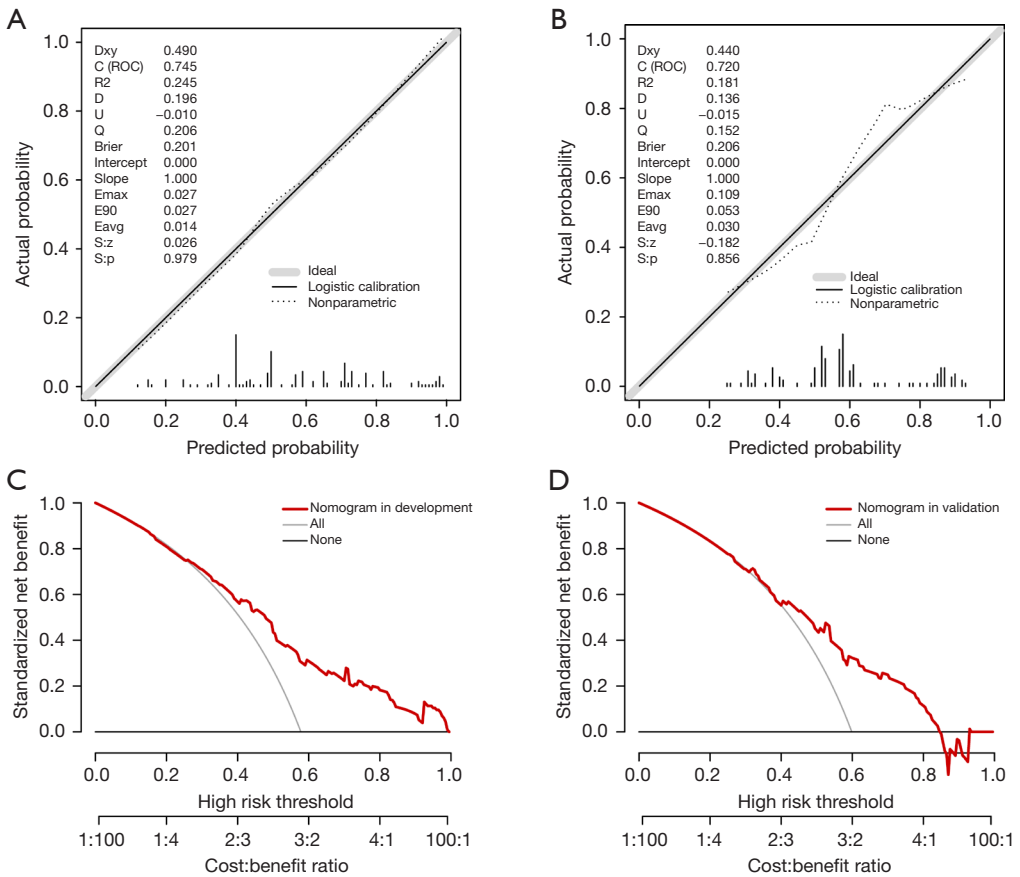

Figure 3 Prediction performance of nomogram for predicting the probability of spontaneous pleurodesis in the development set and validation set. (A) Calibration curves of the spontaneous pleurodesis nomogram prediction in the development set. (B) Calibration curves of the spontaneous pleurodesis nomogram prediction in the validation set. (C) DCA for evaluating the net benefit of nomogram for predicting spontaneous pleurodesis in the development set. (D) DCA for evaluating the net benefit of nomogram for predicting spontaneous pleurodesis in the validation set. DCA, decision curve analysis; ROC, receiver operating characteristic curve.

model 1 predicted SP with greater accuracy than other models (*Table 3*).

As mentioned above, the nomogram was shown to have a good ability to predict SP occurrence. To further validate the efficacy of the nomogram in predicting SP, we calculated the prediction point based on the seven factors in the nomogram. A median cutoff value was used to subdivide patients into groups that were more favorable to achieve SP group (total points >100.607) and those that were less favorable group to achieve SP (total score ≤100.607). The Nelson-Aalen cumulative risk curves indicated that the cumulative incidence of SP in the more favorable group was significantly greater than that in the less favorable group in the development and validation sets, as shown in *Figure 5* (P<0.001). The success rate of SP at 60 days of more favorable group and less favorable patients in the development set was 80.1% and 46.7%, respectively (*Figure 5A*). Due to the limited number of patients in the validation set, we calculated the success rate of SP at 30 days of more favorable group and less favorable patients was 79.8% and 56.6% (*Figure 5B*).

Discussion

In this study, we examined 331 patients with NSCLC who were treated with IPC insertion due to symptomatic MPE. As expected, patient response to the management of IPC was associated with varying outcomes. Our results identified important clinical factors associated with SP and developed and validated a predictive nomogram for the rate

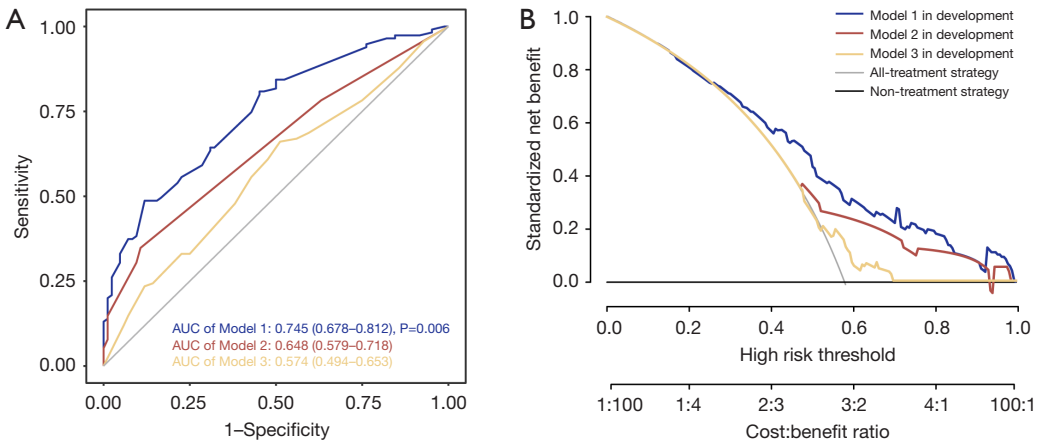

Figure 4 ROC and DCA of our nomogram model and previous published model for predicting spontaneous pleurodesis in patients with MPE. (A) ROC of our nomogram model compared with previous published models for predicting spontaneous pleurodesis. (B) DCA of our nomogram model compared with previous published models for predicting spontaneous pleurodesis. Model 1: the spontaneous pleurodesis predictive nomogram model was developed with predictors including gender, systemic treatment within 30 days of IPC insertion, systemic treatment, medical thoracoscopy, pleural effusion volume, septated effusion, and the sNLR. Model 2: the spontaneous pleurodesis predictive nomogram model was developed with predictors including Eastern Cooperative Oncology Group performance status, medical thoracoscopy, and the volume of pleural fluid. Model 3: the spontaneous pleurodesis predictive nomogram model was developed with predictors including gender, Eastern Cooperative Oncology Group performance status, distant metastasis, and targeted therapy. AUC, area under the curve; DCA, decision curve analysis; IPC, indwelling pleural catheter; MPE, malignant pleural effusion; ROC, receiver operating characteristic curve; sNLR, serum neutrophil-to-lymphocyte ratio.

Table 3 NRI and IDI of the nomogram compared with other models in spontaneous pleurodesis prediction for patients with NSCLC and MPE that received IPC insertion

Index	Estimate	95% CI	P value
NRI (model 1)			
vs. model 2	0.589	0.328–0.851	<0.001
vs. model 3	0.724	0.468–0.979	<0.001
IDI (model 1)			
vs. model 2	0.088	0.046–0.129	<0.001
vs. model 3	0.159	0.106–0.212	<0.001

Model 1: the spontaneous pleurodesis predictive nomogram model was developed with predictors including gender, systemic treatment within 30 days of IPC insertion, systemic treatment, medical thoracoscopy, pleural effusion volume, septated effusion, and the sNLR. Model 2: the spontaneous pleurodesis predictive nomogram model was developed with predictors including Eastern Cooperative Oncology Group performance status, medical thoracoscopy, and the volume of pleural fluid. Model 3: the spontaneous pleurodesis predictive nomogram model was developed with predictors including gender, Eastern Cooperative Oncology Group performance status, distant metastasis, and targeted therapy. CI, confidence interval; IDI, integrated discrimination improvement; IPC, Indwelling pleural catheter; MPE, malignant pleural effusion; NRI, net reclassification index; NSCLC, non-small cell lung cancer; sNLR, serum neutrophil-to-lymphocyte ratio.

of SP in patients with NSCLC and MPE. All independent predictors included in the predictive nomogram showed good internal validation and were readily available in the clinic. Therefore, our results may be particularly valuable for clinicians in identifying patients with MPE who are likely to achieve SP and removal of IPC.

Thoracic drainage has long been used for patients with MPE to drain the pleural space and achieve SP (6,9). It is thought that pleural procedures induce inflammation and drains the space for apposition between the visceral pleura and parietal pleural surfaces (42). Coagulation cascade and a decrease in pleural fibrinolytic activity may have certain effects on pleurodesis (42). However, research has failed to demonstrate any association between anticoagulation therapy and the time to pleurodesis (24), and the exact mechanism of pleurodesis is unclear.

The rate of SP in patients with MPE has been reported to range from 24.0% to 65.0% (7,9,11,14-17), with SP typically being achieved after a mean duration of 26 to 56 days after IPC insertion (9,14,43,44). In our study, the rate of SP was nearly 64.3% in the development set. We hypothesize that a greater SP rate may be associated with the administration of systemic antitumor treatment within

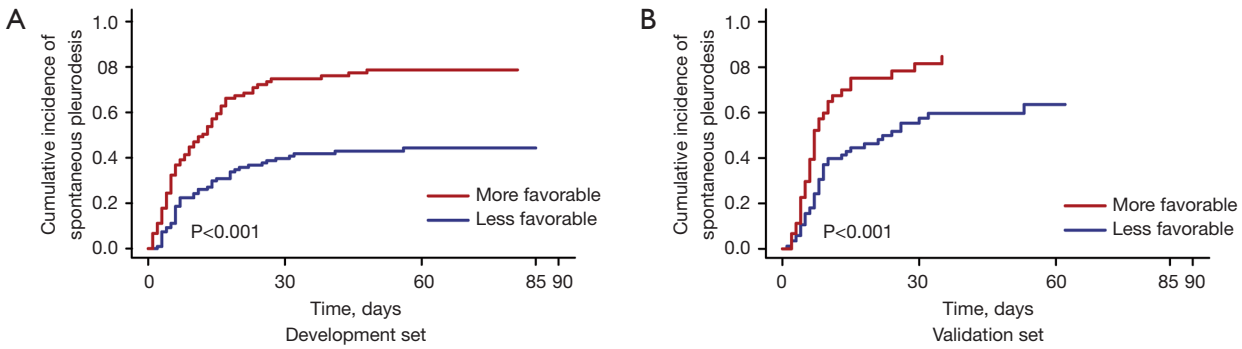

Figure 5 Spontaneous pleurodesis curves of patients who had a number of points associated with higher success rates of spontaneous pleurodesis compared to those of patients in the development set (A) and validation set (B).

30 days of IPC insertion in nearly 63.7% (211/331) of patients. In a recent study, systemic antitumor treatment was associated with increased rates of IPC removal, and patients who experienced prolonged survival had more opportunities and a longer time to achieve SP (7).

Predictions based only on the most basic clinical characteristics are insufficient for constructing a stable model. The pleural effusion volume, septated effusion, and medical thoracoscopy were included to generate an improved model. In our study, we found that female gender, systemic treatment within 30 days of IPC insertion, immunotherapy or targeted therapy, lower sNLR, and medical thoracoscopy were associated with success SP. Meanwhile, a decreased SP success rate was associated with moderate to large pleural effusion and septated effusion. In other studies, pleural effusion above the hilum was found to predict delayed pleurodesis (8,45) likely because it indicates a faster rate of fluid synthesis and recurrence of pleural effusion (45-47). Further studies indicated that a larger volume of fluid may predict the necessity for definitive therapy and reintervention (45,48).

We found that septated effusion decreased the rate of pleurodesis, which is similar to the findings of prior studies. For instance, 33.3–40.0% of patients with MPE were diagnosed with septated effusion (49,50). An increasing volume of septated pleural effusion has been associated with persistent dyspnea and a lack of effective effusion drainage to achieve pleurodesis (51-53). The presence of septations has also been associated with poor survival and nonclinical benefits from the use of urokinase via chest drainage (52). Previous studies have shown that a trapped lung is associated with a lower rate of pleurodesis and a greater chance of persistent drainage (11,18). In our study, trapped lungs were associated with a lower rate of SP, but this difference was not statistically significant in the univariate analysis.

Many patients may undergo thoracoscopy to rule out other pleural diseases. Medical thoracoscopy likely facilitates SP as the pleural biopsies and introduction of air into the pleural space, which may facilitate an inflammatory response (8). Thoracoscopy also allows for the removal of pleural effusion under visualization and the separation of pleural adhesions (19,54). Other studies reported that patients who underwent combined medical thoracoscopy and pleural catheter insertion had significantly greater SP success rates and earlier catheter removal than did other patients (18,19). Moreover, closed drainage after medical thoracoscopy with the addition of negative pressure suction was shown to help expel the residual gas and pleural fluid caused by tumor infiltration or thoracoscopic stimulation (18,55).

In our study, we found that a higher sNLR was correlated with a decreased SP rate. A higher sNLR indicates an increased abundance of neutrophils relative to that of lymphocytes. According to previous studies, neutrophils, especially tumor-associated neutrophils, are associated with tumor cell invasion, metastasis, and immune suppression (56,57). Lymphocytes play a key antitumor role by remodeling the tumor microenvironment and inhibiting tumor proliferation (58). Therefore, the sNLR is believed to reflect systemic inflammation induced by cancer and to be a prognostic marker for poor survival, early disease progression, and MPE recurrence in patients with MPE (59-62). Thus, the sNLR may be a potential indicator for predicting successful SP.

Based on prior research, we identified factors associated with successful SP and then used our development set to develop a predictive nomogram. Meanwhile, in order to

further improve the clinical convenience and practicality of the nomogram, we also developed a web-based dynamic online nomogram, which can quickly calculate the occurrence probability of SP by selecting the corresponding factors and clicking the "Predict" button on the web page. This nomogram is able to identify patients with a low rate of SP, which will have long-term pleural procedures serving. It may empower remaining patients to reminder their terminal cancer and be troubled and anxious about daily activities including sleeping and showers (63,64). Such patients will require longer supportive care and other treatment options as appropriate. How to provide more favorable care to patients needs to be explored in subsequent studies.

We then constructed a calibration plot to separately examine the agreement between the predicted probabilities of the decision rule with the observed SP outcome. Perfect predictions would lie on the 45-degree line for agreement with the SP in the calibration plot. The DCA shows that the positive net benefit of our model for SP prediction was obvious in the rate of SP. Additionally, Nelson-Aalen cumulative risk curves grouped by the median cutoff value of the total points demonstrated the predictive power of the nomogram. Compared with that of other prediction models (7,8), our SP predictive nomogram model had the highest AUC. In addition, DCA proved that our nomogram predicted SP with better clinical benefit and utility than the prior prediction models. The positive NRI and IDI of the nomogram versus other prediction models indicated that our SP predictive nomogram had better predictive capability. The strength of our nomogram is that it mainly consists of readily available clinical factors for estimating SP probability and thus identifying the optimal population. To our knowledge, this is the best model for predicting SP occurrence.

However, there were also certain limitations to this study which should be mentioned. Firstly, the nomogram is only internally validated in the same database and not externally in other databases. Its efficacy is dependent on systemic treatment practices in the region and accurate baseline data. Therefore, the predictive power of the nomogram needs to be validated in other databases or multi-center study in the future. Secondly, our study was an observational retrospective study, and the application of the model identified in this study in patients' treatment plans needs further exploration. In addition, some of the factors we needed to use such as frequency of IPC drainage and time from diagnosis to treatment were not available, which brought irreparable regret to the study. All these shortcomings need to be continued to be improved in future studies, so that the model can better serve the clinical work. Despite the limitations of this study, we identified the relevant clinical factors and developed a nomogram to predict the success rate of SP. Our model exhibited predictive power and clinical application value.

Conclusions

We developed and validated a novel nomogram with relatively satisfactory accuracy to help clinicians identify the population most suited for IPC insertion and to improve the rate of SP among patients with NSCLC and MPE. The SP prediction nomogram, which included the volume of pleural fluid, septated effusion, sNLR, medical thoracoscopy, and systemic treatment within 30 days of IPC insertion, is highly accessible and convenient to use. Additional large prospective cohort studies are needed to verify these results and elucidate the underlying mechanism of IPC induced SP.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-31/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-31/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-31/prf

Funding: This work was supported by the National Natural Science Foundation of China (No. 82473213 to P.T., 82470099 to Y.L., 92159302 to W.L.), Noncommunicable Chronic Diseases-National Science and Technology Major Project of China (Nos. 2023ZD0506106 and 2023ZD0506100 to W.L.).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-31/coif). J.M.A. serves as an unpaid editorial board member of *Journal of Thoracic*

Disease from October 2023 to September 2025. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of West China Hospital (No. 2023-818) and individual consent for this retrospective analysis was waived.

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Cite this article as: Tan S, Zeng H, Huang Q, Pu X, Li W, Ali JM, Nayak R, Bhagat M, Li Y, Tian P. Development a predictive nomogram for spontaneous pleurodesis in patients with non-small cell lung cancer and malignant pleural effusion. J Thorac Dis 2025;17(2):1013-1027. doi: 10.21037/jtd-2025-31

