Diagn Interv Radiol 2026; DOI: 10.4274/dir.2026.264149

GENERAL RADIOLOGY

ORIGINAL ARTICLE

Analysis of risk factors and construction of a nomogram prediction model for early hemoptysis following ^{125}I seed implantation in patients with advanced lung cancer

YiJie Yan[1]
XiaoYuan Yang[2]
Jun Zhang[1]
FanJie Meng[3]
ZhiYu Guan[1]

[1]The Second Hospital of Tianjin Medical University, Department of Thoracic Surgery, Tianjin, China

[2]Tianjin Institute of Medical Science and Technology Information, Tianjin, China

[3]Beijing Chao-Yang Hospital, Capital Medical University, Department of Thoracic Surgery, Beijing, China

PURPOSE

To identify risk factors for hemoptysis following iodine-125 (^{125}I) seed implantation in patients with advanced lung cancer and to develop a nomogram-based prediction model.

METHODS

This retrospective study included patients who underwent ^{125}I seed implantation at the Second Hospital of Tianjin Medical University between August 2023 and May 2025. Patients were divided into a hemoptysis group (n = 31) and a non-hemoptysis group (n = 102) based on the occurrence of postoperative hemoptysis. Clinical characteristics were compared between groups. Binary logistic regression was used to identify independent risk factors, and a nomogram prediction model was constructed. Model performance was evaluated using receiver operating characteristic (ROC) analysis, calibration curves, and decision curve analysis (DCA).

RESULTS

Of the 133 enrolled patients, 31 (23.3%) developed postoperative hemoptysis. Logistic regression analysis identified right hilar lesion location [odds ratio (OR): 10.831, 95% confidence interval (CI): 2.537–46.232], history of chemotherapy (OR: 3.138, 95% CI: 1.160–8.488), and intrathoracic bleeding (OR: 2.666, 95% CI: 1.016–6.993) as independent risk factors. Prothrombin time (PT) showed a negative correlation in the multivariate analysis (OR: 0.507, 95% CI: 0.280–0.918). However, as both sets of values fall within the normal range and the difference is minimal, the clinical significance is limited, and the results should be interpreted with caution. The nomogram demonstrated good discriminative ability, with an area under the ROC curve of 0.830 (95% CI: 0.753–0.907). At a cutoff probability of 0.155, the model achieved a sensitivity of 93.5% and a specificity of 65.7%. Calibration analysis showed good agreement between predicted and observed outcomes, and DCA indicated significant net clinical benefit across a threshold probability range of 0.02–0.70.

CONCLUSIONS

Lesion location, chemotherapy history, intrathoracic bleeding, and PT are independently associated with hemoptysis following ^{125}I seed implantation in advanced lung cancer. The proposed nomogram demonstrates favorable predictive performance and may help identify patients at high risk early, guiding preventive strategies.

CLINICAL SIGNIFICANCE

This nomogram enables early post-procedural identification of high-risk patients, particularly those with right hilar lesions, and its high sensitivity supports its use as a screening tool to guide preventive hemostatic strategies.

KEYWORDS

Iodine radioisotopes, hemoptysis, risk factors, nomograms

Handling editor: Onur Taydaş

Corresponding author: ZhiYu Guan

E-mail: guanzy69@163.com

Received 21 May 2026; revision requested 04 June 2026; last revision requested 26 June 2026; accepted 01 July 2026.

Epub: 14.09.2026

DOI: 10.4274/dir.2026.264149

You may cite this article as: Yan Y, Yang X, Zhang J, Meng F, Guan Z. Analysis of risk factors and construction of a nomogram prediction model for early hemoptysis following ^{125}I seed implantation in patients with advanced lung cancer. *Diagn Interv Radiol*. 14 September 2026 DOI: 10.4274/dir.2026.264149 [Epub Ahead of Print].

Lung cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide. Approximately 2.5 million new cases are diagnosed each year, accounting for more than 1.6 million deaths annually.[1] The majority of patients are diagnosed at an advanced stage, at which point surgical resection is no longer feasible.[2] Although chemotherapy and radiotherapy are commonly used for advanced disease, their therapeutic benefit is often limited,[3] and some patients are unable to tolerate standard treatments due to poor overall state or comorbidities.[4] With the development of image-guided techniques and three-dimensional treatment planning systems, radioactive seed implantation has become increasingly employed in oncology.[5,6] Compared with external beam radiotherapy, brachytherapy is minimally invasive, is associated with fewer complications, and has demonstrated favorable safety and efficacy profiles.[7] It allows for precise delivery of radiation to tumor tissues while minimizing damage to surrounding normal structures.[8] However, hemoptysis is a relatively common and potentially life-threatening complication following iodine-125 (^{125}I) seed implantation.[9] Severe postoperative hemoptysis may severely affect prognosis and quality of life. Therefore, early identification of patients at high risk and prevention of postoperative hemoptysis are important clinical priorities. Currently, studies investigating risk factors and predictive models for hemoptysis following ^{125}I seed implantation in patients with advanced lung cancer are limited. Therefore, this study aimed to identify independent risk factors associated with hemoptysis following ^{125}I seed implantation and to develop a nomogram-based prediction model to facilitate early risk stratification and optimize clinical management.

Materials and methods

Study population

This retrospective study included 133 patients with lung cancer who underwent ^{125}I seed implantation at the Department of Thoracic Surgery, The Second Hospital of Tianjin Medical University, between August 2023 and May 2025. Patients were divided into a hemoptysis group (n = 31) and a non-hemoptysis group (n = 102) based on the occurrence of postoperative hemoptysis. The inclusion criteria were as follows: (1) histologically confirmed lung cancer, age ≥ 18 years, and suitability for ^{125}I seed implantation; (2) presence of metastatic disease, recurrence after surgery, or inability to tolerate surgical resection; (3) selection of ^{125}I seed implantation based on the characteristics of the lesions or patient condition; and (4) Eastern Cooperative Oncology Group (ECOG) performance status of 0–3 and ability to cooperate with treatment. Exclusion criteria included (1) use of anticoagulant agents or traditional Chinese medicines with blood-activating and stasis-resolving properties following implantation, which might interfere with hemoptysis assessment; (2) cachexia, severe dysfunction of major organs (liver, kidney, heart, lung, or brain), severe anemia, dehydration, or uncorrectable metabolic disorders; and (3) incomplete clinical data. Of the 187 cases initially screened, 54 were excluded for various reasons (including 22 with missing clinical data, 18 using anticoagulants, 9 lost to follow-up, and 5 not meeting inclusion criteria), leaving 133 cases for final analysis.

This study was approved by the Ethics Committee of the Second Hospital of Tianjin Medical University (approval number: KY2025K482, date: 24.12.2025). Due to the retrospective nature of the study, the ethics committee waived the requirement for informed consent. The inclusion and exclusion criteria are shown in Figure 1.

The ^{125}I seed implantation procedure

The patient's position (supine, lateral, or prone) was determined according to tumor size and location. Local anesthesia with lidocaine was administered before the procedure. Tumor volume was measured using a Siemens 64-slice spiral computed tomography (CT) scanner (Siemens Healthineers, Erlangen, Germany), and preoperative treatment planning was performed using a three-dimensional treatment planning system (KL-SIRPS-3D, developed by Beihang University of Aeronautics and Astronautics, Beijing, China). Commercially available ^{125}I seeds (Saide Biopharmaceutical Co., Ltd., Tianjin, China) were used, with a half-life of 60.2 days, an activity of 0.7 mCi per seed, gamma-ray energy of 27–35 keV, and an effective tissue penetration distance of 1.7 cm. A coplanar template-guided approach with disposable implantation needles was employed. The prescribed radiation dose was 120 Gy. Two certified physicians delineated the target volume and developed the implantation plan based on preoperative chest CT images. All procedures were performed under CT guidance according to the preoperative plan. Immediate postoperative CT imaging was conducted to verify dose distribution. If inadequate dose coverage was detected, supplementary seeds were implanted. Chest radiography was routinely performed on the first postoperative day, and appropriate symptomatic management, including anti-infective and hemostatic therapy, was provided when necessary.

Observation indicators

The collected clinical and treatment-related variables included demographic and clinical factors [age, sex, lesion location, pathological type, preoperative tumor–

Main points

- Right hilar lesion, prior chemotherapy, and intrathoracic bleeding are independent risk factors for hemoptysis.
- The nomogram model enables effective peri-procedural risk assessment.
- With a sensitivity of up to 93.5%, this model can be used for the rapid early identification of individuals at high risk of haemoptysis.

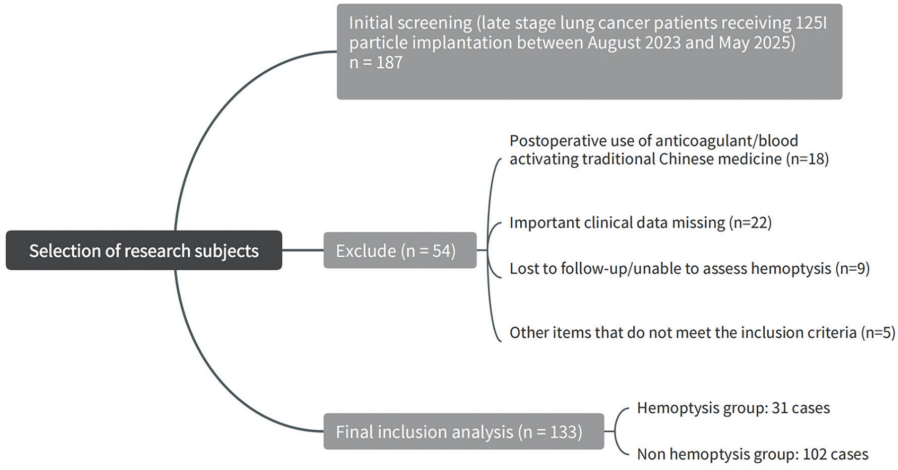

Figure 1. Flowchart of patient selection.

node–metastasis (TNM) stage, presence of distant metastasis, and ECOG performance status]; preoperative treatment history (radical surgery, chemotherapy, radiotherapy, and targeted therapy); laboratory parameters (liver and renal function, blood coagulation profile, and platelet count); coagulation parameters, including and targeted therapy); laboratory parameters [liver function parameters, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST); renal function parameters; coagulation parameters, including activated partial thromboplastin time (APTT); and platelet count]; postoperative complications (pneumothorax, intrathoracic hemorrhage, and other adverse events); and brachytherapy-related parameters (number of implanted seedsand number of needle insertions).

Outcome definition

In this study, hemoptysis was defined as any respiratory tract bleeding occurring within 48 hours after ^{125}I particle implantation, including blood streaks, clots, or fresh blood in sputum. This specific 48-hour window was selected primarily to strictly differentiate acute traumatic hemorrhage directly induced by the interventional puncture procedure from spontaneous hemoptysis resulting from later tumor progression or vascular erosion. In confining the outcome assessment to this immediate post-procedural period, the aim was to minimize etiological confounding and ensure that the endpoint was specifically attributed to the surgical intervention rather than to the natural disease course. Hemoptysis was graded according to the Common Terminology Criteria for Adverse Events Version 5.0:[10] Grade 1 was blood-streaked sputum; Grade 2 was moderate hemoptysis not requiring urgent intervention; Grade 3 and above was massive hemoptysis (≥ 10 mL per episode) or requiring bronchoscopy or interventional hemostasis. This study defines the occurrence of hemoptysis of any grade (≥ Grade 1) as the outcome event; as there were no cases of Grade 3 or higher, no subgroup analysis was performed for Grades 1 and 2.

Statistical analysis

Statistical analyses were performed using SPSS version 22.0. Continuous variables with normal distributions were presented as mean ± standard deviation and compared using the independent-samples t-test. Non-normally distributed variables were reported as median (Q1, Q3) and analyzed using the Mann–Whitney U test. Categorical variables were presented as frequencies and percentages and were compared using the chi-square (χ^2) test. This study analyzed only the 133 cases with complete data; missing data were not imputed. Binary logistic regression analysis was conducted to identify independent risk factors for postoperative hemoptysis. A nomogram prediction model was developed using R software (version 4.5.2). Model performance was evaluated using receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA). The optimal cut-off probability for predicting hemoptysis using the nomogram model was determined by applying the principle of maximizing the Youden index (Youden index = sensitivity + specificity − 1). A two-sided P value < 0.05 was considered statistically significant.

Results

Demographic characteristics and laboratory parameters

A total of 133 patients were included in the study, comprising 86 men and 47 women, with ages ranging from 43 to 87 years. Postoperative hemoptysis occurred in 31 patients, an incidence of 23.3% (31/133). As shown in Table 1, there were no statistically significant differences between the two groups in terms of age, sex, ECOG score, ALT, AST, total protein, albumin, creatinine, platelet count, activated partial thromboplastin time, or D-dimer (all $P > 0.05$); however, there was a statistically significant difference between the two groups in prothrombin time (PT) ($P < 0.05$).

Tumor characteristics, treatment history, and surgery-related parameters

As shown in Table 2, there were no statistically significant differences between the two groups in terms of tumor size, histological

Table 1. Comparison of clinical characteristics between the hemoptysis and non-hemoptysis groups

Variable	No Hemoptysis (n = 102)	Hemoptysis (n = 31)	t/Z/χ^2	*P* value
Age (years)	70 (62, 74.25)	68 (60, 72)	1.689	0.091
Sex [n (%)]			0.168	0.682
Male	65 (63.7)	21 (67.7)		
Female	37 (36.3)	10 (32.3)		
ECOG performance status	2 (1, 2)	1 (1, 2)	1.174	0.240
ALT (IU/L)	14 (11.35, 21.75)	15 (12, 19.6)	0.346	0.729
AST (IU/L)	21.85 (17.08, 26.68)	21.7 (15, 27.3)	0.343	0.731
Total protein (g/L)	64.96 ± 6.11	65.91 ± 7.49	0.643	0.524
Albumin (g/L)	34.81 ± 4.24	35.64 ± 4.98	0.920	0.359
Creatinine (μmol/L)	62.75 (51.98, 81.05)	62.8 (58.8, 81)	0.628	0.530
Platelet count (×10^9/L)	232 (173, 298.75)	217 (186, 279)	0.106	0.915
Prothrombin time (s)	13.5 (12.8, 14.0)	13.0 (12.6, 13.3)	3.372	0.001
Activated partial thromboplastin time (s)	35.6 (33.7, 38.2)	35.9 (32.9, 38.4)	0.362	0.717
D-dimer (mg/L)	0.80 (0.50, 1.80)	0.78 (0.36, 1.55)	0.865	0.387

Data are presented as median (IQR), mean ± SD, or n (%), as appropriate. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECOG, Eastern Cooperative Oncology Group. t, Z, and χ^2 denote Student's t-test, Mann-Whitney U test, and Pearson's Chi-squared test, respectively, selected based on data type and distribution. P < 0.05 was considered statistically significant. SD, standard deviation; IQR, interquartile range. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ECOG, Eastern Cooperative Oncology Group.

type, TNM staging, history of radical surgery, history of radiotherapy or history of targeted therapy (all $P > 0.05$); however, there were statistically significant differences between the two groups in terms of lesion location and history of chemotherapy (all $P < 0.05$).

As shown in Table 3, there were no statistically significant differences between the two groups in terms of the number of implanted particles, the number of needle punctures, or the incidence of pneumothorax (all $P > 0.05$); however, there was a statistically significant difference in the incidence of intrathoracic hemorrhage ($P < 0.05$).

Risk factors for hemoptysis following iodine-125 seed implantation

Binary logistic regression analysis was performed to identify independent factors associated with postoperative hemoptysis. Lesion location in the right hilum [odds ratio (OR): 10.831, 95% confidence interval (CI): 2.537–46.232, $P = 0.001$], history of chemotherapy (OR: 3.138, 95% CI: 1.160–8.488, $P = 0.024$), and intrathoracic bleeding (OR: 2.666, 95% CI: 1.016–6.993, $P = 0.046$) were identified as independent risk factors for postoperative hemoptysis (Table 4). PT also showed a negative correlation in the multivariate analysis (OR: 0.507, 95% CI: 0.280–0.918, $P = 0.025$); however, the difference in median values between the two groups was only 0.5 seconds (13.5 vs. 13.0 seconds), and both fell within the normal range, so the clinical significance of this association is unclear.

Construction and validation of the nomogram prediction model

A nomogram prediction model was constructed based on the four independent factors identified via logistic regression (Figure 2). As the scatter plot in Figure 2 shows, the scores for each variable were summed to obtain a total score, which was plotted on the risk axis below to determine the probability of hemoptysis. The area under the receiver operating characteristic curve (AUC) for the model was 0.830 (95% CI: 0.753–0.907), indicating good discriminative ability (Figure 3). In accordance with the principle of maximizing Youden's index, at a cut-off probability of 0.155, the model achieved a sensitivity of 93.5% and a specificity of 65.7%. The calibration curve demonstrated good agreement between predicted and observed probabilities, and the Hosmer–Lemeshow goodness-of-fit test showed no evidence of poor fit ($\chi^2 = 6.25$, $P = 0.62$) (Figure 4). The DCA further demonstrated a favorable net clinical benefit across a threshold probability range of 0.02–0.70 (Figure 5), supporting the model's potential clinical utility.

Discussion

Management of advanced-stage lung cancer remains challenging. For patients who are not candidates for surgical resection, multimodal therapies, including chemotherapy, radiotherapy, targeted therapy, and immunotherapy, have traditionally been used to prolong survival, alleviate symptoms, and improve quality of life.[11] In recent years, ^{125}I seed implantation has emerged as an effective alternative for patients who are unable or unwilling to undergo surgery, those with recurrence following chemoradiotherapy, or individuals unsuitable for targeted therapy or immunotherapy.[12] This technique delivers localized radiation directly to tumor tissue, inducing apoptosis and inhibiting angiogenesis.[13] The primary target of therapeutic radiation is tumor DNA, and radiation-induced DNA damage results in tumor cell death while altering the tumor microen-

Table 2. Tumor characteristics and treatment history

Variable	No hemoptysis (n = 102)	Hemoptysis (n = 31)	t/Z/χ^2	*P* value
Tumor size (cm)	4.35 (2.70, 5.62)	4.10 (3.40, 4.80)	0.016	0.987
Tumor location [n (%)]			18.657	< 0.001
Hilum of the left lung	9 (8.8)	6 (19.4)		
Left lung	42 (41.2)	6 (19.4)		
Hilum of the right lung	7 (6.9)	10 (32.3)		
Right lung	44 (43.1)	9 (29.0)		
Pathological type [n (%)]			1.539	0.463
Squamous cell carcinoma	48 (47.1)	12 (38.7)		
Adenocarcinoma	22 (21.6)	10 (32.3)		
Metastatic lung cancer	32 (31.4)	9 (29.0)		
TNM stage [n (%)]			0.070	0.791
Stage IIIB	22 (21.6)	6 (19.4)		
Stage IV	80 (78.4)	25 (80.6)		
Radical surgery [n (%)]			0.067	0.795
Yes	24 (23.5)	8 (25.8)		
No	78 (76.5)	23 (74.2)		
Adjuvant therapy [n (%)]				
Radiotherapy	12 (11.8)	1 (3.2)	1.117	0.291
Chemotherapy	37 (36.3)	19 (61.3)	6.103	0.013
Targeted therapy	12 (11.8)	4 (12.9)	0.000	1.000
None	47 (46.1)	9 (29.0)	2.834	0.092

TNM is tumor–node–metastasis staging, which here follows the 8th edition of the International Association for the Study of Lung Cancer guidelines. Data are presented as median (interquartile range) or number (%), as appropriate. t, Z, and χ^2 denote Student's t-test, Mann-Whitney U test, and Pearson's Chi-squared test, respectively, selected based on data type and distribution. P < 0.05 was considered statistically significant.

Table 3. Surgical-related indicators and complications

Variable	No hemoptysis (n = 102)	Hemoptysis (n = 31)	t/Z/χ^2	*P* value
Number of particles implanted	58.5 (30, 78.25)	58 (47, 80)	1.282	0.200
Number of puncture needles	9 (6, 14)	11 (8, 12)	0.926	0.354
Pneumothorax [n (%)]			3.397	0.065
Yes	37 (36.3)	17 (54.8)		
No	65 (63.7)	14 (45.2)		
Intrathoracic hemorrhage [n (%)]			9.136	0.003
Yes	29 (28.4)	18 (58.1)		
No	73 (71.6)	13 (41.9)		

Data are presented as median (interquartile range), mean ± standard deviation, or number (%), as appropriate. t, Z, and χ^2 denote Student's t-test, Mann-Whitney U test, and Pearson's Chi-squared test, respectively, selected based on data type and distribution. P < 0.05 was considered statistically significant.

Table 4. Multivariate logistic regression analysis of factors associated with hemoptysis

Variable	B	SE	Wald χ^2	*P* value	OR	95% CI
Prothrombin time (s)	−0.680	0.303	5.035	0.025	0.507	0.280–0.918
Tumor location						
Hilum of the left lung	1.144	0.730	2.455	0.117	3.140	0.751–13.134
Hilum of the right lung	2.382	0.740	10.352	0.001	10.831	2.537–46.232
Right lung	0.178	0.624	0.081	0.775	1.195	0.352–4.056
Chemotherapy	1.144	0.508	5.072	0.024	3.138	1.160–8.488
Intrathoracic hemorrhage	0.981	0.492	3.970	0.046	2.666	1.016–6.993

Logistic regression analysis was performed to identify independent factors associated with hemoptysis. The left lung (non-hilar region) was used as the reference group for the lesion site. B, regression coefficient; SE, standard error; Wald χ^2, Wald Chi-squared statistic; OR, odds ratio; CI, confidence interval.

vironment.[14] A recent meta-analysis further confirmed the efficacy and safety of ^{125}I seed implantation in patients with inoperable early-stage non–small cell lung cancer.[15]

Pneumothorax and hemoptysis are common complications associated with percutaneous lung procedures. In this study, the incidence of pneumothorax was 40.6% (54/133); however, most cases were mild and resolved on their own without invasive intervention. Hemoptysis is potentially life-threatening and requires prompt identification and management. Our analysis identified lesion location in the right hilum, history of chemotherapy, and intrathoracic bleeding as independent risk factors for postoperative hemoptysis. This study defines hemoptysis occurring within 48 hours post-surgery as procedure-related hemoptysis. This time window is based on the clinical patterns of procedure-related bleeding following percutaneous lung biopsy and effectively excludes spontaneous hemoptysis in patients with advanced lung cancer caused by tumor invasion of blood vessels or tumor necrosis. Consequently, this model predicts the risk of acute hemoptysis directly associated with ^{125}I seed implantation, rather than hemoptysis arising from the natural progression of the tumor.

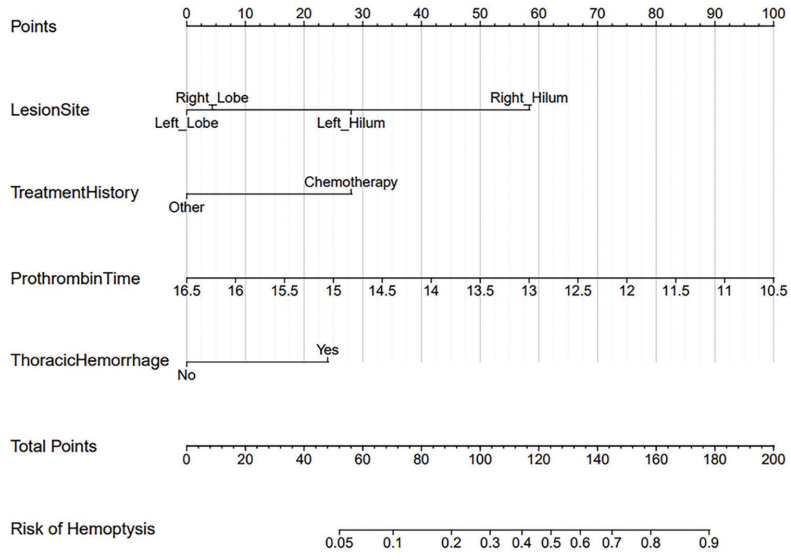

Figure 2. Nomogram for prediction of hemoptysis risk.

It is worth noting that ^{125}I seed implantation has a dual effect on hemoptysis. On the one hand, brachytherapy with ^{125}I seed can shrink the tumor and induce local tissue fibrosis, thereby alleviating hemoptysis caused by tumor invasion of blood vessels; existing studies have confirmed its definite hemostatic effect in patients with lung cancer accompanied by hemoptysis.[16] On the other hand, hemoptysis is also a common complication of CT-guided ^{125}I seed implantation; the literature reports an incidence ranging from 34.2% to 66.7%.[17,18] The two are not mutually exclusive: the former represents the long-term therapeutic effect of the particles (tumor shrinkage → hemostasis); the latter refers to acute hemoptysis triggered by the puncture procedure in patients with un-

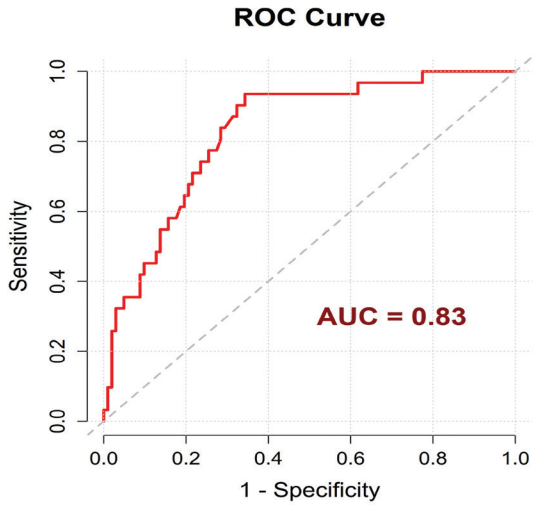

Figure 3. Receiver operating characteristic (ROC) curve of the prediction model. AUC, area under the curve.

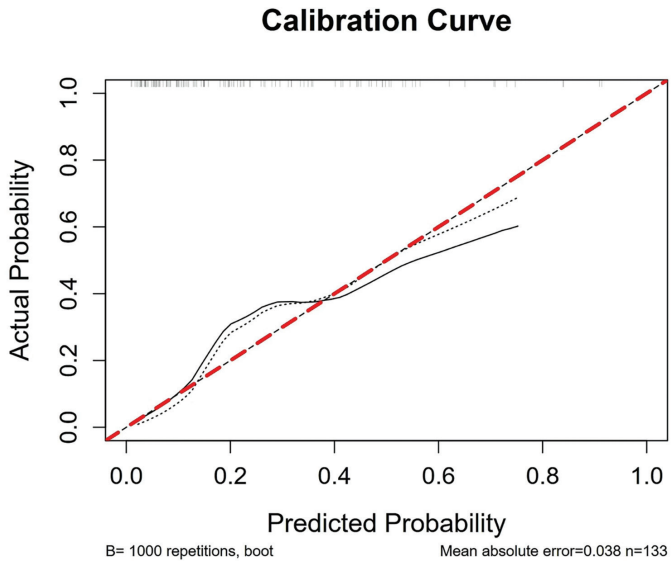

Figure 4. Calibration curve of the prediction model.

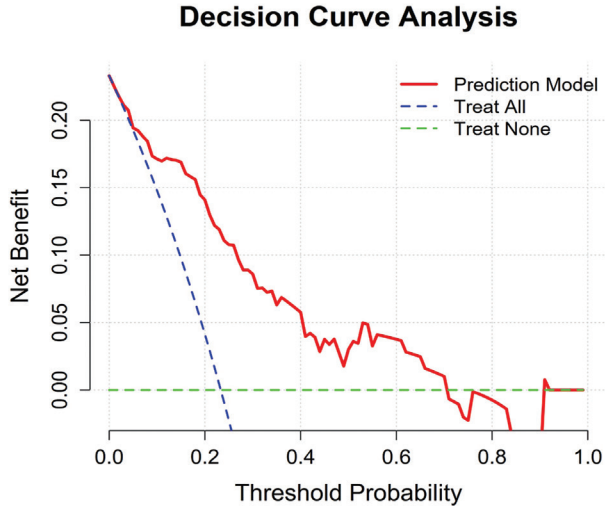

Figure 5. Decision curve analysis of the prediction model.

derlying vascular vulnerability (puncture → vascular injury → hemoptysis). This indicates that the occurrence of hemoptysis depends more on the patient's own anatomical vulnerability or vascular pathology. Therefore, this study does not negate the therapeutic value of ^{125}I particles.

A history of chemotherapy was also associated with increased hemoptysis risk. Chemotherapy-induced vascular endothelial injury and tumor necrosis may make vessels more fragile and susceptible to bleeding.[19,20] Furthermore, puncture-related damage to small pulmonary arterial branches or subpleural vessels may simultaneously result in intrathoracic bleeding and rupture of bronchial mucosal vessels, increasing the risk of hemoptysis.[21,22]

Regarding lesion location, the significantly increased risk associated with right hilar tumors (OR: 10.831) may be explained by anatomical features. The right pulmonary artery is typically 1.2–1.5-times wider than the left and forms a smaller branching angle with the bronchus (approximately 30°), which may increase the risk of vascular injury during CT-guided puncture procedures.[23] As this study restricted the timeframe for hemoptysis to within 48 hours post-surgery, the hemoptysis in question was an acute event induced by the puncture procedure, rather than vascular necrosis caused by long-term particle radiotherapy. Due to the unique anatomical structure of the right hilum, the vessels there are more vulnerable, making puncture procedures more likely to induce hemoptysis in such patients.

In this study, PT was negatively associated in the multivariate analysis (OR: 0.507, 95% CI: 0.280–0.918, P = 0.025); however, this result should be interpreted with extreme caution. First, the median PTs in the two groups were 13.5 seconds (non-hemoptysis group) and 13.0 seconds (hemoptysis group), respectively, a difference of only 0.5 seconds, and both fell within the clinically normal reference range (11–13.5 seconds).[24] Furthermore, clinically, a PT exceeding the normal control value by more than 3 seconds is generally considered a clinically significant prolongation,[25] and the mean PT values in both groups in this study were well below this threshold. Second, from a physiological perspective, a prolonged PT typically indicates a defect in the extrinsic coagulation pathway; theoretically, this should increase rather than decrease the risk of bleeding. Studies have indicated that isolated PT prolongation is rarely clinically significant, and

the degree of prolongation is not correlated with the severity of coagulation factor deficiency. For example, previous research has shown that a single coagulation factor deficiency typically requires a level below 35% of normal to significantly prolong PT, whereas the combined effect of mild deficiencies in multiple factors may lead to prolonged PT; however, this is not always associated with a clinical risk of bleeding.[26] Furthermore, certain drugs, such as daptomycin, may cause a false prolongation of PT that does not reflect an actual deficiency in clotting factors or a risk of bleeding.[27] This finding supports the view that there is no direct correlation between prolonged PT and the degree of clotting factor deficiency. Finally, patients with advanced lung cancer often present with a hypercoagulable state; theoretically, a mildly prolonged PT may partially offset this hypercoagulable tendency, thereby reducing the risk of thrombus-related vascular rupture and severe hemodynamic fluctuations during surgery.[28] Consequently, the negative correlation observed in this study may also be attributable to selection bias inherent in retrospective studies. Future research should employ propensity score matching or a prospective design to clarify the true association between PT and postoperative hemoptysis. Nevertheless, the possibility of a subtle biological effect cannot be ruled out. This conclusion requires further validation through larger, multicenter studies, and it is not currently recommended as an independent basis for clinical decision-making.

To the best of our knowledge, no previous predictive model specifically addressing hemoptysis following ^{125}I seed implantation in lung cancer has been reported. The nomogram developed in this study demonstrated good discrimination (AUC: 0.830) and satisfactory calibration, suggesting potential clinical utility in preoperative risk assessment and individualized management. Regarding clinical recommendations, the nomogram can be used to calculate the probability of haemoptysis during or immediately after the procedure. When the risk threshold exceeds 0.155, it is recommended to enhance planning of the puncture trajectory during surgery, monitor the patient closely for 48 hours postoperatively, and ensure that hemostatic agents or facilities for interventional hemostasis are readily available.

This study has certain limitations. First, as a single-center retrospective study, the sample size in the hemoptysis group was relatively small (31 cases), which may introduce selection bias and preclude subgroup analysis. Furthermore, the imbalance in sample sizes between the case and control groups may affect the stability of the model. Although the internal validation results are favorable, external validation using a multicenter, large-sample prospective cohort is required to assess the model's generalizability. Moreover, this study did not include a control group of patients with advanced lung cancer who did not receive ^{125}I seed implantation; therefore, it is not possible to rule out a confounding effect of the seeds themselves in preventing hemoptysis (e.g., some patients in the non-hemoptysis group may have benefited from the long-term tumor shrinkage and hemostatic effects of the seeds). Furthermore, the predictive conclusions of this model are limited to the risk of acute hemoptysis within 48 hours post-surgery and do not involve an evaluation of the long-term efficacy of the seeds. Additionally, this strict 48-hour time window, although clinically rational, constitutes a secondary limitation. Rare, delayed iatrogenic hemoptysis occurring beyond this threshold might be missed, and such cases could be inadvertently misclassified into the non-hemoptysis group, potentially leading to a slight underestimation of the true procedure-related bleeding risk. Future research could further explore the combined predictive value of preoperative radiomic features (e.g., vascular patterns and tumor vascularization as shown on CT angiography) and procedure-related variables (e.g., the length of the puncture path and whether the interlobar fissure was traversed) to improve the model's performance.

Lesion location in the right hilum, history of chemotherapy, and intrathoracic bleeding are significantly associated with the occurrence of hemoptysis following ^{125}I seed implantation in patients with advanced lung cancer. A nomogram incorporating these variables demonstrated good predictive performance and may assist in early identification of patients at high risk, facilitating timely preventive interventions. Comprehensive preoperative evaluation, careful puncture planning to avoid major vessels and bronchi, meticulous procedural technique, and prompt management of intrathoracic bleeding are recommended to reduce the risk of hemoptysis. Future studies should explore additional imaging and procedural predictors and develop more robust, externally validated models to improve risk stratification in clinical practice.

Acknowledgments

The successful completion of this study would not have been possible without the support and collaboration of multiple individuals and institutions. We sincerely thank all patients and their families for their trust and participation, which formed the foundation of this research. We are grateful to the Ethics Committee of The Second Hospital of Tianjin Medical University for reviewing and guiding the study protocol to ensure compliance with ethical standards. We also thank the imaging team for their expertise in CT scanning and localization, and the nursing staff for their dedicated perioperative care.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

Funding

This study was supported by the Beijing Postdoctoral Research Foundation (number: 2023-ZZ-042).

References

1. Shroff GS, Sheshadri A, Altan M, Truong MT, Erasmus LT, Vlahos I. Drug-induced lung disease in the oncology patient: from cytotoxic agents to immunotherapy. *Clin Chest Med*. 2024;45(2):325-337. [Crossref]
2. Chen K, He Y, Wang W, Yuan X, Carbone DP, Yang F. Development of new techniques and clinical applications of liquid biopsy in lung cancer management. *Sci Bull (Beijing)*. 2024;69(10):1556-1568. [Crossref]
3. Lammers A, Slatore CG, Fromme EK, Vranas KC, Sullivan DR. Association of early palliative care with chemotherapy intensity in patients with advanced stage lung cancer: a national cohort study. *J Thorac Oncol*. 2019;14(2):176-183. [Crossref]
4. Ding T, Ge X, Hao S, Wang Z, Zhang W, Zhang G. Nomogram prediction model for overall survival of late-stage lung cancer patients undergoing iodine-125 particle implantation brachytherapy. *J Contemp Brachytherapy*. 2024;16(6):410-427. [Crossref]
5. Ruge MI, Simon T, Suchorska B, et al. Stereotactic brachytherapy with iodine-125 seeds for the treatment of inoperable low-grade gliomas in children: long-term outcome. *J Clin Oncol*. 2011;29(31):4151-4159. [Crossref]
6. Ding T, Hao S, Wang Z, Zhang W, Zhang G. Analysis of risk factors for pneumothorax after particle implantation in the treatment of advanced lung cancer after surgery and establishment of a nomogram prediction model. *Front Med (Lausanne)*. 2024;11:1428456. [Crossref]
7. Tang F, Cao XJ, Gong T, Huang XY, Ya-Qing K, Xiang Z. Bronchial arterial

chemoembolization/infusion combined with iodine-125 brachytherapy in advanced non-small cell lung cancer: a promising salvage therapy after standard treatment failure. *BMC Cancer*. 2025;25(1):750. [Crossref]

8. Yao H, ZhuGe Y, Jin S, et al. The efficacy of coaxial percutaneous iodine-125 seed implantation combined with arterial infusion chemotherapy for advanced pancreatic cancer: a randomized clinical trial. *Int J Radiat Biol*. 2024;100(7):1041-1050. [Crossref]
9. Li Z, Hu Z, Xiong X, Song X. A review of the efficacy and safety of iodine-125 seed implantation for lung cancer treatment. *Cancer Treat Res Commun*. 2024;41:100844. [Crossref]
10. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 [Internet]. Bethesda (MD): National Institutes of Health; 2017 Nov 27 [cited 2026 Jun 16]. [Crossref]
11. Jabbour SK, Berman AT, Decker RH, et al. Phase 1 trial of pembrolizumab administered concurrently with chemoradiotherapy for locally advanced non-small cell lung cancer: a nonrandomized controlled trial. *JAMA Oncol*. 2020;6(6):848-855. [Crossref]
12. Guibin D, Xiaolan S, Wei Z, Xiaoli L, Liu D. Prediction of iodine-125 seed implantation efficacy in lung cancer using an enhanced CT-based nomogram model. *PLoS One*. 2024;19(11):e0313570. [Crossref]
13. Tang M, Lin X, Zhu L, et al. The efficacy and safety of percutaneous CT-guided iodine-125 brachytherapy combined with standard chemotherapy and brachytherapy alone for lung malignant nodule: a retrospective comparative cohort study. *J Thorac Dis*. 2024;16(1):573-580. [Crossref]
14. Chargari C, Deutsch E, Blanchard P, et al. Brachytherapy: an overview for clinicians. *CA Cancer J Clin*. 2019;69(5):386-401. [Crossref]
15. Chen E, Wang J, Zhang H, et al. Analysis of the efficacy and safety of iodine-125 seeds implantation in the treatment of patients with inoperable early-stage non-small cell lung cancer. *J Contemp Brachytherapy*. 2021;13(3):347-357. [Crossref]
16. Cheng G, Wang Y, Dong D, Zhang W, Wang L, Wan Z. To evaluate the efficacy and safety of 125I seed implantation in SCLC as second line therapy. *Medicine (Baltimore)*. 2022;101(29):e29251. [Crossref]
17. Lu M, Pu D, Zhang W, et al. Trans-bronchoscopy with implantation of ^{125}I radioactive seeds in patients with pulmonary atelectasis induced by lung cancer. *Oncol Lett*. 2015;10(1):216-222. [Crossref]
18. Ran L, Liang H, Chen J, et al. Evaluating the efficacy of 8Spheres microsphere combined with Iodine-125 seeds in the treatment of advanced lung squamous cell carcinoma presenting with hemoptysis: A retrospective study. *Eur J Radiol*. 2025;191:112295. [Crossref]
19. Yang W, Yuan Q, Bai Y, et al. Comparative safety and efficacy of single-agent chemotherapy combined with microwave ablation versus radioactive seed brachytherapy in elderly patients with advanced NSCLC: a ten-year retrospective study. *Am J Cancer Res*. 2025;15(7):3063-3078. [Crossref]
20. Hanotin C, Salvayre R, Lassalle L, et al. Predictive factors for recurrent hemoptysis after bronchial artery embolization in patients with lung cancer. *J Vasc Interv Radiol*. 2024;35(9):1296-1303. [Crossref]
21. Yucel S, Sayit AT, Tomak L, Celenk C. Frequency of complications and risk factors associated with computed tomography guided core needle lung biopsies. *Ann Saudi Med*. 2021;41(2):78-85. [Crossref]
22. Zhang X, An J, Wu J, Jing X, Lu H, Tian Y. Effect of saline sealing after CT-guided lung biopsy on pneumothorax and hemoptysis. *J Comput Assist Tomogr*. 2025;49(4):640-645. [Crossref]
23. Ding T, Hao S, Wang Z, Zhang W, Zhang G. Analysis of risk factors for pneumothorax after particle implantation in the treatment of advanced lung cancer after surgery and establishment of a nomogram prediction model. *Front Med (Lausanne)*. 2024;11:1428456. [Crossref]
24. Levy JH, Szlam F, Wolberg AS, Winkler A. Clinical use of the activated partial thromboplastin time and prothrombin time for screening: a review of the literature and current guidelines for testing. *Clin Lab Med*. 2014;34(3):453-477. [Crossref]
25. Fritsma GA. Reference Intervals for PT and PTT. The Fritsma Factor. 2010. [Crossref]
26. Burns ER, Goldberg SN, Wenz B. Paradoxic effect of multiple mild coagulation factor deficiencies on the prothrombin time and activated partial thromboplastin time. *Am J Clin Pathol*. 1993;100(2):94-98. [Crossref]
27. Yamada T, Kato R, Oda K, et al. False prolongation of prothrombin time in the presence of a high blood concentration of daptomycin. *Basic Clin Pharmacol Toxicol*. 2016;119(4):353-359. [Crossref]
28. Novelli PM, Tublin JM, Orons PD. Correcting coagulopathy for image-guided procedures. *Semin Intervent Radiol*. 2022;39(4):428-434. [Crossref]