



# Contrast-enhanced computed tomography prior to percutaneous transthoracic needle biopsy reduces the incidence of hemorrhage

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**Background:** Hemorrhage is the second most common complication of percutaneous transthoracic needle biopsy (PTNB), and at present, there is no effective prevention strategy. Contrast-enhanced computed tomography (CECT) has the advantage of clearly visualizing blood supply within the lesion and aiding in the imaging of blood vessels, which can reduce hemorrhage complicating PTNB. As no large-sample studies were evaluating whether CECT could reduce hemorrhage, we conducted the present retrospective study.

**Methods:** From November 2011 to February 2016, 1,282 biopsies at Jinling Hospital were retrospectively reviewed; 555 underwent CECT, and 727 underwent non-contrast computed tomography (CT). Factors associated with hemorrhage were defined, and hemorrhage rates were compared between the 2 groups.

**Results:** We found that pre-biopsy CECT was associated with a reduced incidence of biopsy-related hemorrhage compared to non-contrast CT (16.4% vs. 23.1%,  $P=0.003$ ). Propensity score matching (PSM) analysis also showed that the incidence of hemorrhage in the CECT group was lower than that of the non-contrast CT group at a ratio of 1:1 ( $P=0.039$ ), 1:2 ( $P=0.028$ ), or 1:3 ( $P=0.013$ ). In the multivariate analysis, CECT before PTNB was found to be significantly associated with a reduced risk of hemorrhage [odds ratio (OR): 0.671, 95% confidence interval (CI): 0.499–0.902,  $P=0.008$ ]. Puncture position, lesion size, depth of needle tract, and the number of punctures were also found to be associated with hemorrhage (all  $P<0.05$ ).

**Conclusions:** Compared with non-contrast CT, CECT significantly reduced the risk of post-biopsy pulmonary hemorrhage, which suggests that CECT should be performed before PTNB.

**Keywords:** Percutaneous transthoracic needle biopsy (PTNB); contrast-enhanced computed tomography (CECT); hemorrhage

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## Introduction

Percutaneous transthoracic needle biopsy (PTNB) is a minimally invasive and safe procedure widely used for diagnosing lung lesions and the analysis of molecular alterations in clinical practice (1-5). Up to 2.9–54.5% of patients who undergo PTNB develop hemorrhage (3,6-10). Reported risk factors for pulmonary hemorrhage include penetration of blood vessels in the lung (11,12). Although most pulmonary hemorrhage is mild and self-limiting, severe hemorrhage might also occur during PTNB (8,13).

Contrast-enhanced computed tomography (CECT) has the advantage of clearly visualizing blood supply within the lesion and aiding in blood vessels' imaging. We, therefore, postulate that CECT could be used to reduce hemorrhage. The British Thoracic Society guidelines recommend performing computed tomography (CT) scan before lung biopsy (14), but do not mention whether or not CECT scans should be performed. Compared with non-contrast CT, CECT facilitates more accurate blood vessel imaging, particularly small vessels (15). Previous reports have indicated that most patients undergo CECT scans before the intervention to evaluate the feasibility of biopsy (10,16), but no large cohort study evaluating the effect of pre-biopsy CECT on hemorrhage after a biopsy has been conducted. Therefore, we assessed the efficacy of pre-biopsy CECT in reducing PTNB-related hemorrhage. In the present study, we compared hemorrhage rates between the non-contrast CT and the CECT groups and identified the risk factors associated with pulmonary hemorrhage during the biopsy.

We present the following article following the STROBE reporting checklist (available at <http://dx.doi.org/10.21037/atm-20-4384>).

## Methods

Although the present study was a retrospective study, the propensity score matching (PSM) method matched confounding factors, making the results more reliable.

### Participants

We retrospectively reviewed 1,430 biopsy procedures, which were performed on 1,370 patients between November 2011 and February 2016 in Jinling Hospital, Nanjing, China. To avoid the impact of repeat puncture targeting the same lesion on hemorrhage rates, for cases with repeated

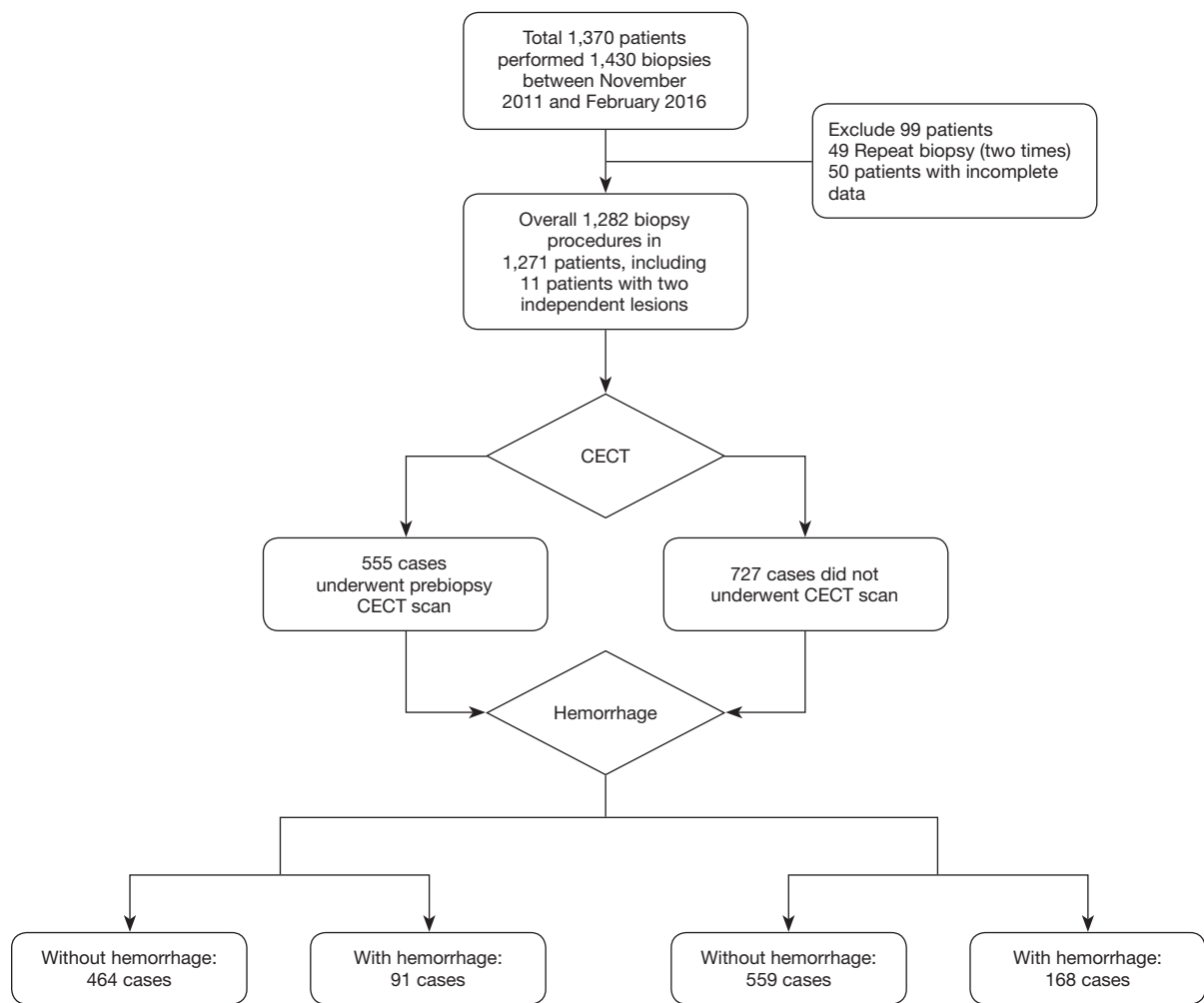
biopsies (49 patients), only the first biopsy was included in the analysis. Fifty patients with incomplete medical data were also excluded. Finally, a total of 1,271 patients (1,282 biopsies) were enrolled, including 11 patients with 2 independent lesions; the second biopsies were defined as independent incidences (*Figure 1*). The present study was conducted following the Declaration of Helsinki (as revised in 2013) and approved by the institutional review board of Jinling Hospital (No. 2017NZHX-022). All data were retrieved from a prospectively collected electronic database. Informed consent from individuals was waived due to the retrospective, observational, and anonymous nature of the current study.

### Inclusion criteria for biopsy

Patients included in the present study had focal lung lesions appearing as a nodule or a mass. Laboratory indices relevant to the hemorrhage complication, such as prothrombin time, activated partial thromboplastin time, international normalized ratio, and platelet count within 1 week of undergoing PTNB, were normal. Patients with a medical history of anticoagulant or antiplatelet medication use were required to stop taking medication at least 5 days before puncture, and those patients have also included if re-examination of coagulation was normal. Those who could not follow verbal or visual instruction and/or accept procedure-related risks were excluded from the study.

### Biopsy procedure

A helical CT scanner (SOMATOM Spirit; Siemens Medical Systems, Forchheim, Germany) and BARD MAGNUM 18-gauge cutting needles (Bard Peripheral Vascular, Inc., Tempe, Arizona, USA) were used. All patients underwent either chest CECT or non-contrast CT before the biopsy. Following a review of the pre-biopsy CT images, the optimal needle path was planned to perforate the least amount of aerated lung. Following sterilization and local anesthesia, a coaxial 18-gauge needle was inserted through the chest wall and moved towards the lesion. CT images were instantly procured to evaluate the biopsy needle and pulmonary nodule's position at the desired depth. The procedure was continued only if the needle was at an appropriate site within or near the lesions, and the operator triggered the biopsy switch to trap the tissue specimens. Biopsy specimens were then preserved in 10% buffered



**Figure 1** Flow diagram of patient inclusion and exclusion criteria.

formalin for pathological examination. After withdrawing the biopsy needle, a post-biopsy CT scan was immediately performed to assess possible complications, and the patient was required to stay in the supine position for at least 6 h. A chest radiograph was generally performed the following day. All patients who underwent PTNB were inpatients, and if required after the biopsy, received oxygen therapy or hemostatic drugs, or underwent chest drainage or pulmonary artery embolization.

### Definitions

The needle tracts' depths were calculated as the distance from the pleura to the center of the pulmonary lesions. Internal vessels were defined as vessels present at the edge and interior of the lesions, and others were considered

peripheral vessels. Pulmonary hemorrhage was defined as any new haziness observed in the post-biopsy CT images. Bloody sputum was also considered a part of pulmonary hemorrhage. Mild hemorrhage was defined as hemorrhage that occurred in the pulmonary parenchyma or bloody sputum ( $\leq 5$  mL), and severe hemorrhage was defined as hemoptysis complicating hemodynamic instability. The rest, exception of mild and severe hemorrhage, was defined as moderate hemorrhage.

### Statistical analysis

All statistical analyses were performed using SPSS version 17 (SPSS, Chicago, IL, USA). Univariate analyses of categorical variables, such as sex and biopsy positions, were performed using  $\chi^2$ -test and Fisher's exact test, and

continuous variables with skewed distributions were compared using the Mann-Whitney *U*-test. Multivariate logistic regression analyses of selected variables were performed to evaluate the effect of pre-biopsy CECT on hemorrhage rates and to determine the risk factors associated with hemorrhage. To demonstrate the effect of pre-biopsy CECT on hemorrhage rates, PSM was conducted by MatchIt package in R with nearest-neighbor 1:1, 2:1, and 3:1 matching. Differences and associations were considered significant when  $P < 0.05$ .

## Results

### *Patient characteristics*

A total of 1,271 patients (1,282 biopsies) were enrolled in the present study (854 males and 417 females), with a mean age of  $59.0 \pm 2.72$  years. Of all 1,282 biopsies, the majority (65.1%,  $n=834$ ) had a  $>3$  cm lesion size. Malignant and benign lesions accounted for 64% ( $n=820$ ) and 29.7% ( $n=381$ ), respectively. The most common lesion location was the upper lobe (51.1%,  $n=655$ ), and the prone position was the main puncture position (53.4%,  $n=684$ ). Also, 555 underwent CECT and 727 underwent non-contrast CT. Baseline characteristics, such as age, sex, smoking history, lesion size, and puncture position were not different between the CECT group and the non-contrast CT group ( $P > 0.05$ ) (Table 1).

### *Association of CECT with the reduced incidence of post-biopsy hemorrhage*

Of the 1,282 PTNB, pulmonary hemorrhage occurred in 259 (20.2%) biopsies. Hemorrhage rates in the CECT and the non-contrast CT were 16.4% (91/555) and 23.1% (168/721), respectively, which indicated that CECT before PTNB could reduce the incidence of biopsy-related hemorrhage ( $P=0.003$ ). However, there was no statistical difference in hemorrhage grade (mild, moderate/severe) between the CECT and non-contrast CT groups ( $P=1.000$ ). Of the 91 patients with hemorrhage in the CECT group, 95.6% (87/91) were classified as mild-grade hemorrhage, while 4.4% (4/91) as moderate/severe grade. In the non-contrast CT group, 95.2% (160/168) were classified as mild hemorrhage, and 4.8% (8/168) were classified as moderate/severe hemorrhage (Table 2).

Also, vessel distribution observed by CECT, either in the peripheral ( $P=0.016$ ) or internal ( $P=0.000$ ) lesion, was

associated with post-biopsy hemorrhage (Table 3).

### *PSM analysis confirming the positive effects of CECT on reducing hemorrhage*

To reduce bias, PSM analysis was performed. In the CECT and the non-contrast CT groups, the following factors were matched by the MatchIt package in R, with nearest-neighbor 1:1, 2:1, and 3:1 matching: sex, age, smoking history, lesion location, puncture position, size of the lesion, number of punctures, and depth of the needle tract (Table 4). According to 1:1 matching of hemorrhage and non-hemorrhage cases, the distribution of the propensity score is shown in Figure 2A. A significant negative relationship was found between pre-biopsy CECT and pulmonary hemorrhage ( $P=0.039$ ). Figure 2B,C shows the distribution of the propensity score from matching at a ratio of 1:2 ( $P=0.028$ ) and 1:3 ( $P=0.013$ ), respectively.

### *Univariate analysis of factors associated with hemorrhage*

We further analyzed factors that were assumed to be associated with post-biopsy hemorrhage; the results are summarized in Table 5. The data showed that females ( $P=0.039$ ), patients with a lesion size  $\leq 3$  cm ( $P=0.024$ ), supine puncture position ( $P=0.008$ ), repeated punctures ( $\geq 2$ ,  $P=0.006$ ), and depth of the needle tract  $>4$  cm ( $P=0.012$ ) were prone to hemorrhage. Hemorrhage was not found to be correlated with age, site of the lesion, and pathological results ( $P=0.160$ ,  $P=0.155$ , and  $P=0.539$ , respectively).

### *Multivariate logistic regression analysis for risk factors of hemorrhage*

A further multivariate logistic regression model was established. We found that the incidence of post-biopsy hemorrhage was remarkably reduced in patients who underwent pre-biopsy CECT scans [odds ratio (OR): 0.671, 95% confidence interval (CI): 0.499–0.902,  $P=0.008$ ]. In addition, smaller lesion size (OR: 0.990, 95% CI: 0.983–0.997,  $P=0.005$ ), supine position during puncture (OR: 2.734, 95% CI: 1.207–6.194,  $P=0.016$ ), increased number of punctures ( $n=2$ , OR: 1.546, 95% CI: 1.065–2.244,  $P=0.022$ ;  $n=3$ , OR: 1.673, 95% CI: 1.082–2.588,  $P=0.021$ ;  $n=4$ , OR: 8.746, 95% CI: 2.891–26.456,  $P < 0.001$ ), and increased depth of the needle tract (OR: 1.017, 95% CI: 1.009–1.025,  $P=0.000$ ) were all associated with upregulated risk of pulmonary hemorrhage (Table 6).

**Table 1** Patient demographics and lesion characteristics

Characteristic	CECT (n=555)		Non-contrast CT (n=727)	
	Number of biopsies	%	Number of biopsies	%
Age (years)				
<65	357	64.3	468	64.4
≥65	198	35.7	259	35.6
Sex				
Male	365	65.8	494	68.0
Female	190	34.2	233	32.0
Smoking history (year package)				
≤20	375	67.5	472	64.9
>20	180	32.5	255	35.1
Puncture position				
Supine	229	41.3	293	40.3
Prone	295	53.2	389	53.5
Lateral	31	5.5	45	6.2
Lesion location				
Upper lobe	268	48.3	387	53.2
Middle lobe	43	7.7	31	4.3
Lower lobe	244	44.0	309	42.5
Lesion size (cm)				
≤3	183	33.0	265	36.5
>3	372	67.0	462	63.5
Pathology				
Malignant	363	65.4	457	62.9
Benign	159	28.6	222	30.5
Non-diagnostic	33	6.0	48	6.6

CECT, contrast-enhanced computed tomography; CT, computed tomography.

## Discussion

To the best of our knowledge, the present study is the first large-sample comparative study to assess if pre-biopsy CECT could reduce hemorrhage incidence. We retrospectively reviewed 1,282 PTNB and found that pre-biopsy CECT was associated with a reduced incidence of biopsy-related hemorrhage compared with non-contrast CT (16.4% *vs.* 23.1%,  $P=0.003$ ). CECT before PTNB could also reduce post-biopsy hemorrhage risk (OR: 0.671, 95% CI: 0.499–0.902,  $P=0.008$ ).

CECT has been used to distinguish malignant lung lesions from benign lung lesions, evaluate indeterminate pulmonary nodules, and predict lung adenocarcinoma pathological grades (17-20). In the present study, the risk of pulmonary hemorrhage remarkably decreased when pre-biopsy CECT was performed, demonstrating the advantages of pre-biopsy CECT in the assessment of vascular distribution. To minimize hemorrhage caused by needle biopsy, Wu *et al.* suggested that major central blood vessels and systemic arteries should be avoided (7). A previous report showed that blood vessels that are not visible on non-

**Table 2** Grade of hemorrhage complication after percutaneous transthoracic needle biopsy (PTNB) between CECT group and non-contrast CT group

Grade	CECT (n=555)	Non-contrast CT (n=727)	P value
No hemorrhage	464	559	0.003**
Hemorrhage	91	168	
Mild	87	160	1.000
Moderate/severe	4	8	

\*\* , P<0.01. CECT, contrast-enhanced computed tomography.

**Table 3** Hemorrhage and vessels distribution observed by contrast-enhanced computed tomography (CECT)

Vessels distribution	CECT (n=555)		P value
	No hemorrhage (n=464)	Hemorrhage (n=91)	
Peripheral of lesion			0.016*
Y	263	64	
N	201	27	
Internal of lesion			0.000***
Y	174	61	
N	290	30	

\*, P<0.05; \*\*\*, P<0.001.

**Table 4** The difference of hemorrhage incidence between non-contrast CT group and CECT group after matching hemorrhage and non-hemorrhage cases in variable proportions

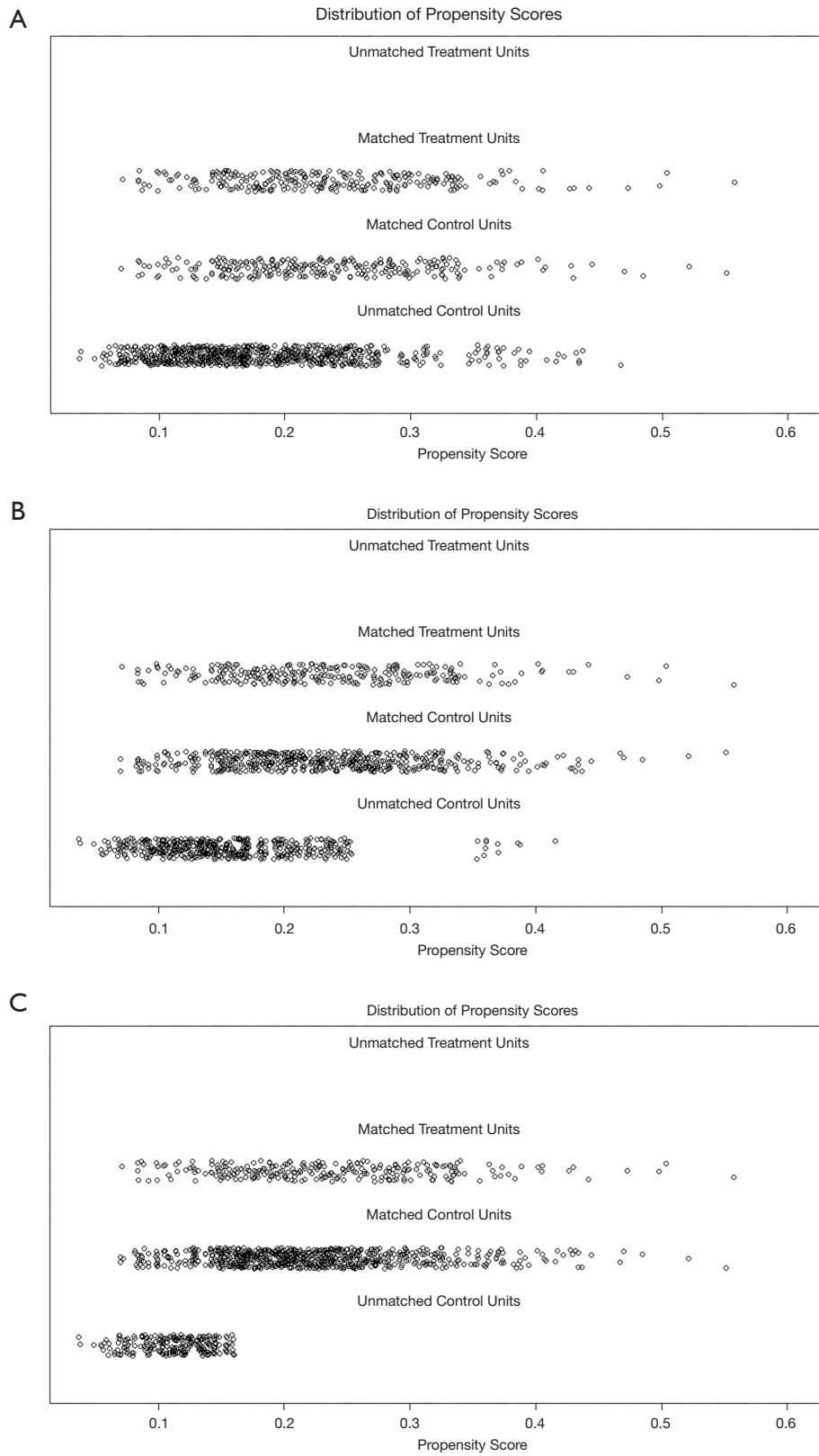
Proportion (hemorrhage: non-hemorrhage)	Non-contrast CT (n)	CECT (n)	P value
1:1	144	115	0.039*
	168	91	
1:2	292	226	0.028*
	168	91	
1:3	434	343	0.013*
	168	91	

\*, P<0.05. CECT, contrast-enhanced computed tomography.

contrast CT images might be visible on CECT images (15). Nour-Eldin *et al.* showed that needle tracks across pulmonary blood vessels could increase hemorrhage risk (11). Similarly, the incidence of hemorrhage increased in the presence of abundant internal blood vessels or margins surrounded by blood vessels in the present study. The present study also confirmed that small blood vessels were significantly enhanced in arterial and venous phases on CECT images, facilitating more accurate identification of

suitable puncture routes that avoid blood vessels.

Baadh *et al.* showed that using a track embolization technique with absorbable hemostat gelatin powder reduces hemorrhage (21). A limitation of this method was that the duration of the overall procedure, which was extended by approximately 1–2 min, potentially increased the risk of pneumothorax. Khan *et al.* also showed that pneumothorax rates significantly increased with an increase in puncture time. Compared with track embolization techniques, pre-



**Figure 2** Propensity score distribution of hemorrhage and non-hemorrhage patients after matching at different ratios. (A) 1:1; (B) 1:2; (C) 1:3.

**Table 5** Univariate analysis of risk factors associated with hemorrhage after percutaneous transthoracic needle biopsy (PTNB)

Variables	No hemorrhage, n (%)	Hemorrhage, n (%)	P value
Age (years)	58.7±12.80	60±12.35	0.160
Sex			0.039*
Male	701 (68.5)	160 (61.8)	
Female	322 (31.5)	99 (38.2)	
Lesion location			0.155
Upper lobe	517 (50.5)	138 (53.3)	
Middle lobe	54 (5.3)	20 (7.7)	
Lower lobe	452 (44.2)	101 (39.0)	
Lesion size (cm)			0.024*
≤3	342 (33.4)	106 (40.9)	
>3	681 (66.6)	153 (59.1)	
Puncture position			0.008**
Supine	400 (39.1)	122 (47.1)	
Prone	554 (54.2)	130 (50.2)	
Lateral	69 (6.7)	7 (2.7)	
Number of puncture			0.006**
1	275 (26.9)	48 (18.5)	
≥2	748 (73.1)	211 (81.5)	
Depth of needle tract (cm)			0.012*
≤4	157 (15.3)	24 (9.2)	
>4	866 (84.7)	235 (90.8)	
Pathology			0.539
Malignant	647 (63.2)	173 (66.8)	
Benign	309 (30.2)	72 (27.8)	
Non-diagnostic	67 (6.5)	14 (5.4)	

\*, P<0.05; \*\*, P<0.01.

biopsy CECT does not potentially increase the incidence of complications associated with puncture. The risks associated with the administration of intravenous injection iodine-based contrast agents, such as impaired renal function, contrast extravasation, and allergic reactions, were low if a full medical history and a history of allergies were provided. Therefore, we recommend using this convenient and safe technique before the biopsy to reduce pulmonary hemorrhage, which is the second most prevalent complication of PTNB.

As reported in previous studies, pulmonary hemorrhage

is affected by factors, such as sex, site of the lesion, size of the lesion, and depth of the needle tract (22-24). Our PSM analysis excluded the effects of confounding factors and confirmed that pre-biopsy CECT reduced PTNB-related hemorrhage. Significant differences in hemorrhage ratios between the pre-biopsy CECT and the non-CECT groups were observed in 1:1, 1:2, and 1:3 matching analyses, providing further evidence pre-biopsy CECT reduces the hemorrhage rate in patients undergoing PTNB. Previous research assessing risk factors of hemorrhage complicating needle biopsy did not involve methods, such as PSM, to



**Table 6** Multivariate logistic regression analysis for risk factors of hemorrhage

Variables	OR (95% CI)	P value
CECT		
Y	0.671 (0.499–0.902)	0.008**
N	Reference	
Lesion size (cm)		
	0.990 (0.983–0.997)	0.005**
Puncture position		
Supine	2.734 (1.207–6.194)	0.016*
Prone	2.107 (0.932–4.764)	0.073
Lateral	Reference	
Number of puncture		
1	Reference	
2	1.546 (1.065–2.244)	0.022*
3	1.673 (1.082–2.588)	0.021*
4	8.746 (2.891–26.456)	0.000***
Depth of needle tract (cm)	1.017 (1.009–1.025)	0.000***

\*, P<0.05; \*\*, P<0.01; \*\*\*, P<0.001. OR, odd ratio; CI, confidence interval; CECT, contrast-enhanced computed tomography.

control the influence of confounding factors. Therefore, to our knowledge, the present study is the first large-sample study to convincingly demonstrate that pre-biopsy CECT scans can be used to reduce the risk of pulmonary hemorrhage complications in patients undergoing PTNB.

Although our research has significant clinical value, it has several limitations. Biopsy procedures were conducted by experienced Operators, the differences between operators were not considered, which might affect the incidence of complication.

Second, it was a retrospective and single-center study, which could introduce unavoidable bias. For example, at the early stage, the role of CECT may not be recognized and the proportion of performing CECT was relatively low compared to the later stage, which might introduce distribution bias. Our findings should be validated in future studies with larger cohorts from multi-centers.

## Conclusions

The present study confirmed that pre-biopsy CECT was an effective tool to prevent pulmonary hemorrhage. Further studies are required to establish CECT as a routine pre-

biopsy procedure in patients scheduled to undergo PTNB.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at: <http://dx.doi.org/10.21037/atm-20-4384>

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*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/atm-20-4384>). The 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. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the institutional review board of Jinling Hospital (No. 2017NZHX-022). Informed consent from individuals for this retrospective analysis was waived.

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