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INTERVENTIONAL RADIOLOGY

REVIEW

Risk factors for air embolism following computed tomography-guided percutaneous transthoracic needle biopsy: a systematic review and meta-analysis

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ABSTRACT

To quantitatively analyze the risk factors for air embolism following computed tomography (CT)-guided percutaneous transthoracic needle biopsy (PTNB) and qualitatively review their characteristics.

The databases of PubMed, Embase, Web of Science, Wanfang Data, VIP information, and China National Knowledge Infrastructure were searched on January 4, 2021, for studies reporting the occurrence of air embolisms following CT-guided PTNB. After study selection, data extraction, and quality assessment, the characteristics of the included cases were qualitatively and quantitatively analyzed.

A total of 154 cases of air embolism following CT-guided PTNB were reported. The reported incidence was 0.06% to 4.80%, and 35 (22.73%) patients were asymptomatic. An unconscious or unresponsive state was the most common symptom (29.87%). Air was most commonly found in the left ventricle (44.81%), and 104 (67.53%) patients recovered without sequelae. Air location ($P < 0.001$), emphysema ($P = 0.061$), and cough ($P = 0.076$) were associated with clinical symptoms. Air location ($P = 0.015$) and symptoms ($P < 0.001$) were significantly associated with prognosis. Lesion location [odds ratio (OR): 1.85, $P = 0.017$], lesion subtype (OR: 3.78, $P = 0.01$), pneumothorax (OR: 2.16, $P = 0.003$), hemorrhage (OR: 3.20, $P < 0.001$), and lesions located above the left atrium (OR: 4.35, $P = 0.042$) were significant risk factors for air embolism.

Based on the current evidence, a subsolid lesion, being located in the lower lobe, the presence of pneumothorax or hemorrhage, and lesions located above the left atrium were significant risk factors for air embolism.

KEYWORDS

Air embolism, CT-guided PTNB, meta-analysis, risk factor

Lung cancer is the leading cause of cancer incidence and mortality worldwide; with 2.1 million new cases and 1.8 million deaths in 2018, it represents approximately 18.4% of all cancer deaths.[1] As 70% of lung cancers are discovered in advanced stages and are unresectable, needle biopsy techniques are the primary diagnostic methods.[2] These techniques include computed tomography- (CT) or ultrasound-guided percutaneous transthoracic needle biopsy (PTNB) and endobronchial ultrasound-guided biopsy.[3] Endobronchial ultrasound-guided biopsy is best suited to central lesions. The use of ultrasound-guided PTNB is limited by its low resolution and is suitable only for lesions of the peripheral lung, chest wall, and mediastinum.[4] CT-guided PTNB is the most widely used technique due to its high-resolution display of lung lesions, its wide availability to both central and peripheral lung lesions, and its minimal invasiveness and high accuracy.[5,6]

The most common complications of CT-guided PTNB are pneumothorax and hemorrhage.[7,8] Air embolisms are rare but potentially fatal complications.[7,9] The direct injection of

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2 mL of air into the cerebral circulation is enough to be fatal, and just 0.5–1.0 mL of air injected into a coronary artery can cause cardiac arrest.[10] The clinical features of air embolism vary from confusion to stroke, arrhythmia, cardiac ischemic features, loss of consciousness, and death.

As the incidence of air embolism is rare, few studies have systematically reported the characteristics and risk factors for air embolism following CT-guided PTNB. Thus, we conducted this systematic review and meta-analysis to qualitatively summarize the characteristics of air embolism following CT-guided PTNB and quantitatively analyze its risk factors.

Methods

This manuscript was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[11] Ethical approval was not required.

Search strategy

A literature search was performed on January 4, 2021, on the PubMed, Embase, and Web of Science databases and on three Chinese databases (Wanfang Data, VIP information, and China National Knowledge Infrastructure) using combinations of the following search terms and their synonyms and variations without time and language restrictions: "lung," "chest," "biopsy," "air embolism," and "systematic air embolism." Medical subject headings were applied if available. The reference lists of the retrieved articles, including reviews, were searched manually for other relevant studies. Two authors performed the search independently and reviewed all the identified publications for inclusion using predetermined criteria.

Main points

- Air embolism is a rare but potentially fatal complication of computed tomography-guided percutaneous transthoracic needle biopsy.
- The most common symptoms of air embolism were an unconscious or unresponsive state, hemiplegia, hypotension, and cardiopulmonary arrest; the air was most commonly located in the left ventricle, aorta, and cerebral artery.
- Patients with emphysema, cough, and air located in the left heart, aorta, cerebral artery, and coronary artery were more likely to develop clinical symptoms than patients without these conditions; air location and symptoms were significantly related to patient prognosis.
- Lesion location (lower lung lobe), lesion subtype (subsolid), pneumothorax, hemorrhage, and lesions located above the left atrium were significant risk factors for air embolism.

Inclusion criteria

The inclusion criteria were (a) air embolism defined as air density in the cardiovascular system found on CT images and (b) if air embolism was found during, immediately after, or at least in a clear temporal coincidence with CT-guided PTNB. The exclusion criteria were (a) air embolism caused by trauma, transbronchial lung biopsy, CT-guided marking of lung lesions, or CT-guided radiofrequency ablation other than CT-guided biopsy; (b) comments and review articles in which the exact data of patients with air embolism could not be extracted; and (c) studies reported neither in Chinese nor in English.

Data extraction and quality assessment

A standardized extraction form was used to collect the characteristics of the study: (a) study characteristics, including the first author, publication year, and country; (b) patient characteristics, including age and sex; (c) lesion characteristics, including location (upper, middle, or lower lobe), diameter (maximum axial diameter of the lesion), and cavity contained in the lesion; (d) CT-guided biopsy characteristics, including the number of biopsies, the diameter of the biopsy needle, patient's position when biopsied, and the use of the coaxial biopsy technique; (e) complications, including pneumothorax, pulmonary hemorrhage or hemoptysis, and cough, and (f) the location of air in the cardiovascular system (the air location in each patient was analyzed individually), clinical symptoms, treatments, and prognoses.

The methodological quality of the studies included in the meta-analysis was assessed using the Newcastle–Ottawa Scale.[12] Data extraction and quality assessment were performed independently by two reviewers, and any disagreement was resolved by consensus.

Statistical analysis

Information about the number of air embolism cases, patient characteristics, lesions, biopsy processes, treatments, and prognoses was extracted from the individual cases in the included studies. These clinical characteristics were reported as mean ± standard values or proportions according to whether they were continuous or categorical variables. Differences in these variables in different symptomatic groups and prognostic groups were compared, and a two-sided value of $P < 0.05$ was considered statistically significant. A chi-squared test or Fisher's exact test was used for nominal variables, while a Mann–Whitney test was used for continuous variables with an abnormal distribution. The above statistical analyses were performed using SPSS 21.0 software (IBM).

Odds ratios (ORs) and corresponding 95% confidence intervals (CIs) were used to assess the strength of the association between the different factors and the occurrence of air embolism. Heterogeneity between different studies was evaluated by an I^2 test, with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively. A random-effects model (the DerSimonian–Laird model) was used if $I^2 > 50\%$ or $P \leq 0.01$. Otherwise, a fixed-effects model (the Mantel–Haenszel model) was used. Publication bias was evaluated using a Begg's funnel plot. Differences were considered statistically significant if $P > 0.05$. Statistical analyses were performed using STATA 12.0 (StataCorp).

Results

Study selection and characteristics

Figure 1 presents this study's PRISMA flow diagram, which summarizes the screening process and the reasons for exclusion. A total of 104 studies[13-116] that reported the characteristics of air embolism after CT-guided PTNB were included in the systematic review (Supplementary Table 1). Five studies[99-101,117,118] that reported the risk factors for air embolism were included in the quantitative meta-analysis (Supplementary Table 2).

Qualitative analysis

A total of 154 patients from 104 studies were included. The reported incidence of air embolism after CT-guided PTNB ranged from 0.06% to 4.80%. The most common symptoms were an unconscious or unresponsive state (29.87%), hemiplegia (16.23%), hypotension (14.29%), and cardiopulmonary arrest (14.29%) (Supplementary Table 3). Thirty-five patients (22.73%) were asymptomatic. Air was most commonly found in the left ventricle (44.81%), aorta (40.91%), cerebral artery (29.87%), coronary artery (22.73%), and left atrium (14.94%) (Supplementary Table 4). Air is not always present in one site alone, but in multiple locations at the same time.

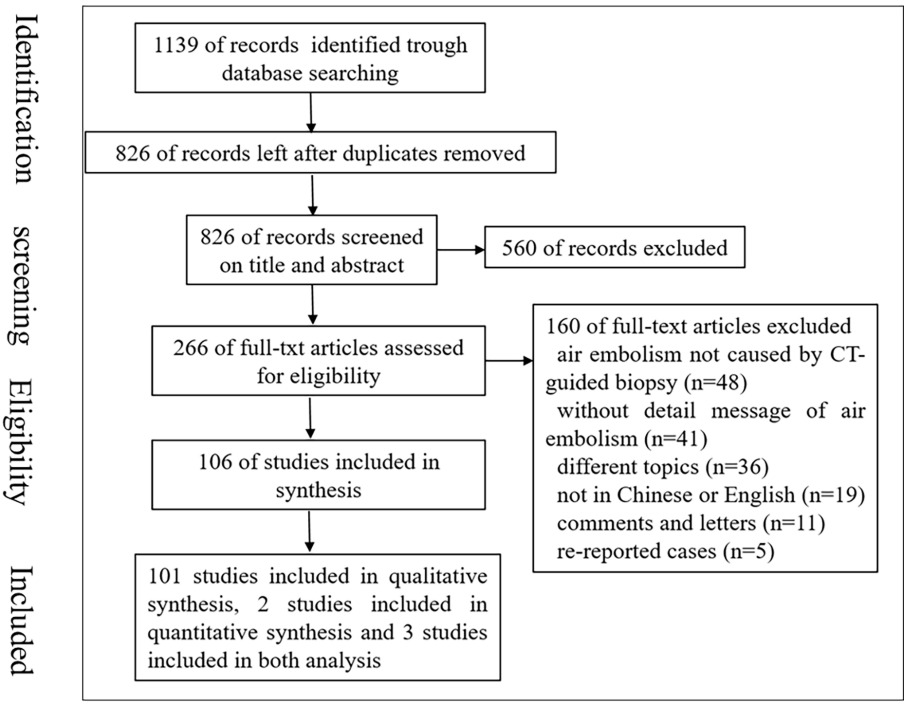

Figure 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram of the study selection process. CT, computed tomography.

Air location was significantly associated with the occurrence of clinical symptoms ($P < 0.001$) (Table 1), with air located in the cerebral artery, coronary artery, aorta, and left heart the most likely to result in clinical symptoms. Similarly, patients with emphysema and cough were the most likely to develop clinical symptoms ($P = 0.061$ and 0.076, respectively). Air location ($P = 0.015$) and symptoms ($P < 0.001$) were also significantly associated with prognosis (Table 2), with air located in the pulmonary vein/artery (100%), left heart (86.42%), aorta (78.94%), and right heart (75%) most likely to have the best outcomes. Of the 154 patients, 144 reported clinical outcomes, 104 (67.53%) recovered without sequelae, 21 (13.63%) patients recovered with sequelae, and 19 (12.34%) patients died. All asymptomatic patients recovered without sequelae.

Quantitative analysis

As shown in Table 3, the risk factors for air embolism following CT-guided PTNB were quantitatively analyzed. Data from 7.811 patients were extracted[99-101,118] to analyze the relationship between air embolism and lesion location. The pooled OR was 1.85 (95% CI: 1.12–3.05, $P = 0.017$) (Figure 2). Data from 5.798 patients[99-101,118] were extracted to analyze the relationship between air embolism and lesion subtype. The pooled OR was 3.78 (95% CI: 1.37–10.45, $P = 0.01$) (Figure 3). Data from 7.633 patients[99-101,117,118] were extracted to analyze the relationship between pneumothorax and air embolism. The pooled OR was 2.16 (95% CI: 1.31–3.57, $P = 0.003$) (Figure 4). Data from 7.397 patients[99-101,117,118] were extracted to analyze the relationship between air embolism and hemorrhage. The pooled OR was 3.20 (95% CI: 1.95–5.26, $P < 0.001$) (Figure 5). Data from 4.464 patients were extracted[99,117,118] to analyze the relationship between air embolism and lesion location above the level of the left atrium. The pooled OR was 4.35 (95% CI: 1.06–17.86, $P = 0.042$) (Figure 6). The funnel plots did not reveal any publication bias.

Data from five studies[99-101,117,118] were used to analyze the relationship between air embolism and patient gender; the pooled OR was 0.99 (95% CI: 0.64–1.54, $P = 0.979$). The relationship between emphysema and air embolism was analyzed in data from four studies;[99-101,118] the pooled OR was 0.96 (95% CI: 0.58–1.61, $P = 0.884$). Data from five studies[99-101,117,118] were used to analyze the relationship between air embolism and biopsy position; the pooled OR was 1.10 (95% CI: 0.24–5.16, $P = 0.901$). Data from three studies[99-101] were used to analyze the relationship between air embolism and the use of the coaxial method; the pooled OR was 1.93 (95% CI: 0.66–5.64, $P = 0.228$). Data from two studies (100,118) were used to analyze the relationship between air embolism and needle-tip location; the pooled OR was 0.46 (95% CI: 0.11–1.94, $P = 0.293$).

Discussion

This study qualitatively summarized the characteristics of air embolism after CT-guided PTNB and quantitatively analyzed the risk factors for air embolism. The most common symptoms of air embolism were an unconscious or unresponsive state, hemiplegia, hypotension, and cardiopulmonary arrest. Air was most commonly found in the left ventricle, aorta, cerebral artery, and coronary artery. Patients with emphysema, cough, and air located in the left heart, aorta, cerebral artery, and coronary artery were more likely to develop clinical symptoms than patients without these conditions, and air location and symptoms were also significantly related to patient prognosis. Lesion location (lower lung lobe), lesion subtype (subsolid), pneumothorax, hemorrhage, and lesions located above the left atrium were significant risk factors for air embolism.

The reported incidence of air embolism after CT-guided PTNB was 0.06% to 4.80%. This varied because the controlled CT scan after CT-guided PTNB was limited to the target area, and some asymptomatic air embolism cases were not found. A study led by Monnin-Bares showed that by limiting the volume of the post-procedure CT scan to the target area, the rate of air embolism detection was just 1% instead of 4.8%.[118] However, the good news is that, usually, these asymptomatic air embolisms will not have serious consequences. Therefore, doctors should weigh up the risk of increased radiation exposure from an enlarged scanning area against the expected benefits of an early diagnosis.

The CT-guided PTNB of lesions in the lower lobe is more likely to result in air embolism than a biopsy performed in other lobes. This difference may be due to gravity, resulting in larger vessels in the lower lobes and a more obvious respiratory motion. Thus, procedures performed in the lower lobe may pose a higher risk of injuring the veins and causing air embolism.[101] Additionally, the respiratory motion of the lung may complicate the procedure and necessitate a high number of needle redirections to reach the lesion, leading to increased injury of the pulmonary vein and airway.[101] Usually, a prone or lateral position with lesions on the upper side is selected to perform a CT-guided PTNB of lesions in the lower lobe. In areas higher than the left atrium, the pressure in both the pulmonary artery and alveoli is greater than that in the pulmonary vein.[119] If a bronchopulmonary venous fistula or an alveolopulmonary vein fistula forms, the air is more likely to enter the

Table 1. Characteristics of asymptomatic and symptomatic air embolism following computed tomography-guided percutaneous transthoracic needle biopsy

Characteristics	Asymptomatic	Symptomatic	*P*
Gender			
Male	11	79	0.325
Female	8	35	
NA	16	5	
Age (years)	61.28 (27–75)	64.21 (25–85)	0.397
Lesion location			
Up and middle	9	38	0.430
Lower	9	57	
NA	17	24	
Lesion density			
Solid	13	47	0.213
Subsolid	3	4	
NA	18	69	
Cavity			
Yes	0	4	0.565
No	16	47	
NA	18	69	
Emphysema			
Yes	0	4	0.061
No	5	2	
NA	29	114	
Puncture needle diameter			
>18 gauge	8	43	0. 668
≤18 gauge	10	43	
NA	18	32	
Position			
Supine	4	23	0.318
Lateral	2	20	
Prone	12	39	
NA	17	37	
Cough			
Yes	7	33	0.076
No	8	13	
NA	19	74	
Pneumothorax			
Yes	6	27	0.413
No	3	7	
NA	25	86	
Hemorrhage			
Yes	12	34	0.655
No	2	4	
NA	21	81	
Coaxial			
Yes	16	60	0.448
No	1	12	
NA	18	47	
Air location			
Left heart	33	55	<0.001
Right heart	1	4	
Aorta	11	62	
Cerebral artery	2	54	
Coronary artery	3	41	
Pulmonary vein/artery	3	11	
Other arteries	2	6	

NA, not applicable.

Table 2. Risk factors for prognosis of air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy

Characteristics	Without sequelae	With sequelae	Death	*P*
Gender				
Male	54	16	14	0.342
Female	30	4	5	
NA	20	1	0	
Age (years)	65.63 (27–82)	62.4 (32–85)	59.42 (35–75)	0.192
Lesion location				
Up and middle	30	11	4	0.197
Lower	46	7	8	
NA	28	3	7	
Lesion density				
Solid	42	9	7	0.314
Subsolid	5	0	2	
NA	57	12	10	
Cavity				
Yes	6	2	1	0.729
No	41	7	8	
NA	57	12	10	
Emphysema				
Yes	4	0	0	0.428
No	6	1	0	
NA	94	20	19	
Puncture needle diameter				
≥18 gauge	36	10	4	0.597
<18 gauge	36	8	7	
NA	32	3	8	
Position				
Supine	19	3	3	0.715
Lateral	13	5	2	
Prone	38	6	5	
NA	34	7	9	
Cough				
Yes	27	7	5	0.608
No	14	2	4	
NA	63	12	10	
Pneumothorax				
Yes	24	4	5	0.730
No	6	2	2	
NA	74	15	12	
Hemorrhage				
Yes	33	9	5	0.299
No	3	1	2	
NA	68	11	12	
Coaxial				
Yes	56	11	6	0.708
No	9	2	2	
NA	39	8	11	
Air location				
Left heart	70	7	4	0.015
Right heart	3	0	1	
Aorta	45	6	6	
Cerebral artery	23	10	8	
Coronary artery	21	3	8	
Pulmonary vein/artery	10	0	0	
Other arteries	6	1	2	
Hyperbaric oxygen therapy				
Yes	27	8	4	0.305
No	63	9	5	
NA	14	4	10	
Trendelenburg position				
Yes	7	2	1	0.801
No	3	1	0	
NA	94	8	28	
Symptomatic				
Yes	69	21	19	<0.001
No	35	0	0	

NA, not applicable.

Table 3. Pooled analysis of risk factors for air embolism following computed tomography-guided percutaneous transthoracic needle biopsy

Risk factors	Air embolism	Non-air embolism	OR (95% CI)	Model chosen for meta-analysis (fixed/random)	Publication bias (*P* value)
Lesion location					
Lower lung lobe	33	2.439	1.85 (1.12–3.05)	Fixed (I^2: 0, P = 0.408)	0.308
Upper and middle lung lobe	32	5.307			
Lesion subtype					
Subsolid	23	823	3.78 (1.37–10.45)	Random (I^2: 61.7%, P = 0.050)	0.734
Solid	42	4.910			
Pneumothorax					
Yes	29	2.144	2.16 (1.31–3.57)	Fixed (I^2: 0, P = 0.965)	0.462
No	58	5.402			
Hemorrhage					
Yes	65	3.841	3.20 (1.95–5.26)	Fixed (I^2: 0, P = 0.438)	>0.990
No	22	3.469			
Lesion located above the level of left atrium					
Yes	61	2.260	4.35 (1.06–17.86)	Random (I^2: 75.5%, P = 0.025)	>0.990
No	10	2.131			
Gender					
Male	53	4.617	0.99 (0.64–1.54)	Fixed (I^2: 0, P = 0.543)	0.609
Female	34	2.986			
Emphysema					
Yes	41	3.790	0.96 (0.58–1.61)	Fixed (I^2: 0, P = 0.804)	0.017
No	24	1.943			
Biopsy position					
Prone and lateral	54	4.555	1.10 (0.24–5.16)	Random (I^2: 89.6%, P = 0)	0.580
Supine	36	3.043			
Coaxial method					
Yes	27	3.557	1.93 (0.66–5.64)	Fixed (I^2: 0, P = 0.721)	0.599
No	11	1.595			
Location of needle tip					
Inside lesion	22	1.159	0.46 (0.11–1.94)	Random (I^2: 70.8%, P = 0.064)	0.620
Outside lesion	14	360			

OR, odds ratio; CI, confidence interval.

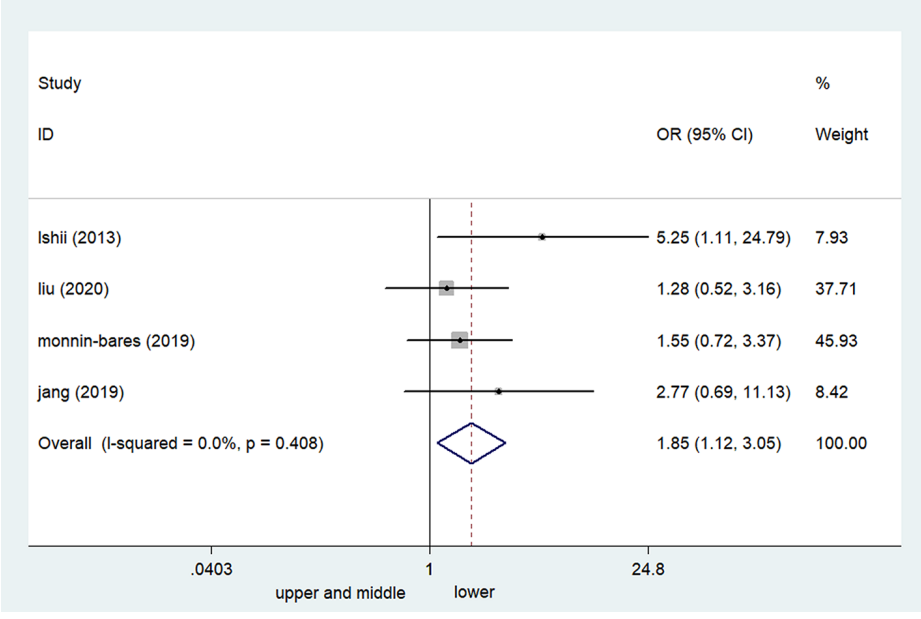

Figure 2. Forest plots of the relationship between lesion location (upper and middle lobe vs. lower lobe) and air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy. CI, confidence interval; OR, odds ratio.

pulmonary vein, resulting in air embolism. In fact, our study found that lesions located above the level of the left atrium are a risk factor for air embolism.

Some studies recommend transthoracic biopsy with the patient in an ipsilateral-dependent position to prevent air embolism.[117] Even though this approach has been shown to decrease the rate of pneumothorax, it is related to increased alveolar hemorrhage.[117] Additionally, this position may complicate the biopsy process, as the biopsy must pass through more lung area. The choice of the transthoracic biopsy position is still debatable, and we must consider the accuracy and safety of the procedure comprehensively.

Pneumothorax and hemorrhage are also risk factors. There may be two explanations for this: the first is that the presence of pneumothorax and hemorrhage means that alveolar, bronchial, or pulmonary vessels are injured. This injury can lead to a bronchovenous fistula, increasing the risk of air embolism. The second is that when hemorrhage is accompanied by cough, the intrapulmonic pressure is increased, resulting in air embolism.[111] Therefore, when a lung biopsy is performed, patients should try to avoid cough-

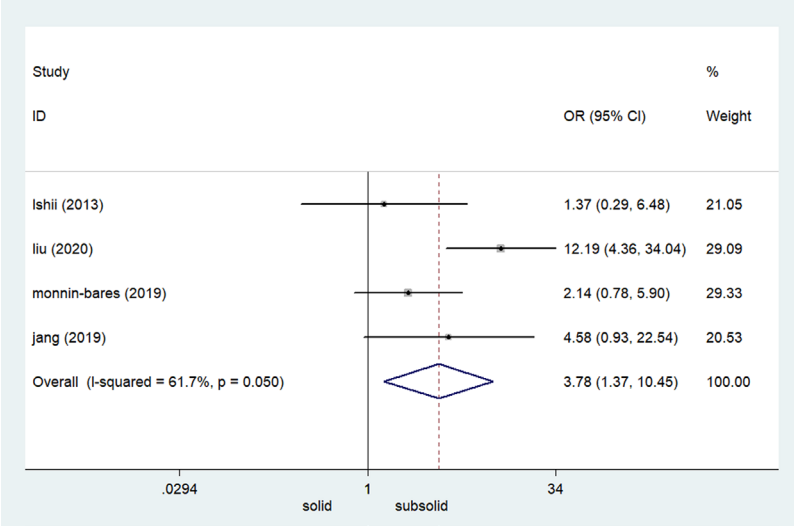

Figure 3. Forest plots of the relationship between lesion subtype (solid vs. subsolid) and air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy. CI, confidence interval; OR, odds ratio.

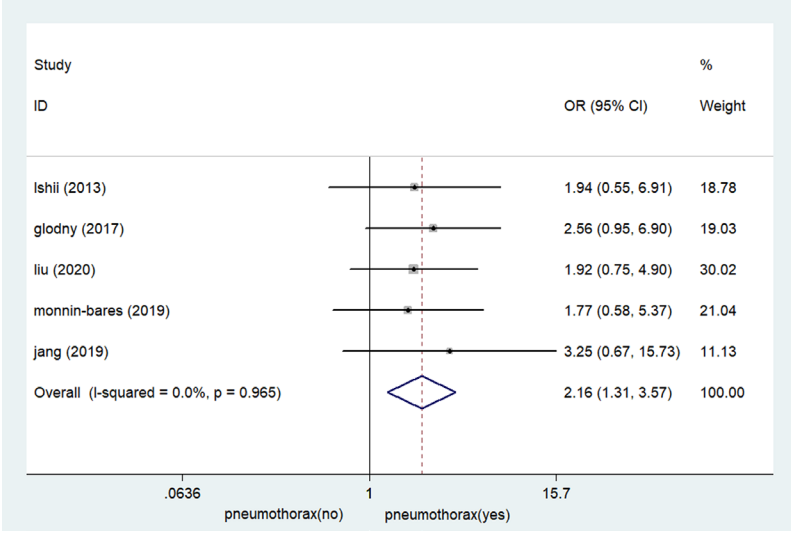

Figure 4. Forest plots of the relationship between pneumothorax and air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy. CI, confidence interval; OR, odds ratio.

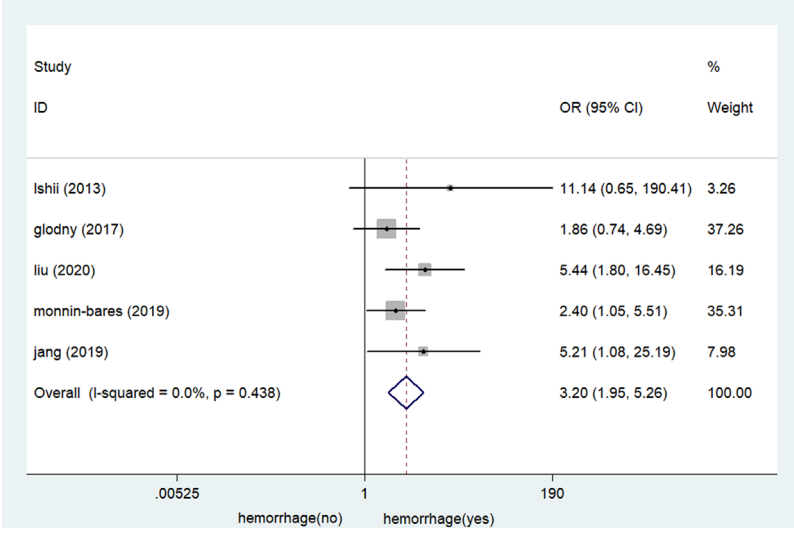

Figure 5. Forest plots of the relationship between hemorrhage and air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy. CI, confidence interval; OR, odds ratio.

ing or cough as little as possible during and after the procedure. For patients who cough frequently, medicine can be used to control their coughing before biopsy.

The lesion subtype is another risk factor. Subsolid nodules contain ground-glass opacities, which do not cover the normal parenchymal structures, including the airways and vessels, and can be visualized on chest CT images.[120] These normal parenchymal structures in the nodules increase the opportunity for air embolism during the biopsy.

Only three studies analyzed if the coaxial method was a risk for air embolism, with the results showing that it was unrelated to air embolism. In addition, only two studies analyzed if the needle-tip location was a risk factor for air embolism. Our analysis showed that it was not a risk factor; however, future studies should investigate this further.

The optimal positioning of patients following air embolism is controversial.[100] Some patients were placed in the right lateral decubitus or Trendelenburg position when air embolism occurred, while some studies recommend not changing the biopsy position. However, turning a patient from a prone position to a supine position should be avoided, as it can facilitate the antegrade passage of air.[121] In addition to position, 100% oxygen should be administered promptly to assist nitrogen–oxygen exchange within the air bubbles and accelerate their resorption.[122] The most effective treatment for air embolism is hyperbaric oxygen therapy, which can improve the oxygenation of the affected tissue and dissolve emboli by increasing nitrogen reabsorption.[81] In our analysis, the Trendelenburg position and hyperbaric oxygen therapy were not related to patient outcome; however, further studies are required on this topic.

Our study has some limitations. First, because of limited access to all the databases and the language barrier to understanding literature not published in English or Chinese, we searched only the databases suggested by the Cochrane Reviewer's Handbook and evaluated literature published only in English and Chinese. Second, the number of studies suitable for quantitative analysis was limited, and they differed in terms of factors related to air embolism; therefore, some factors were not quantitatively analyzed. Some factors, for example, the proximity of the targeted lesion to the segmental or subsegmental airways or vascular structures (especially the pulmonary veins), may relate to air embolism but

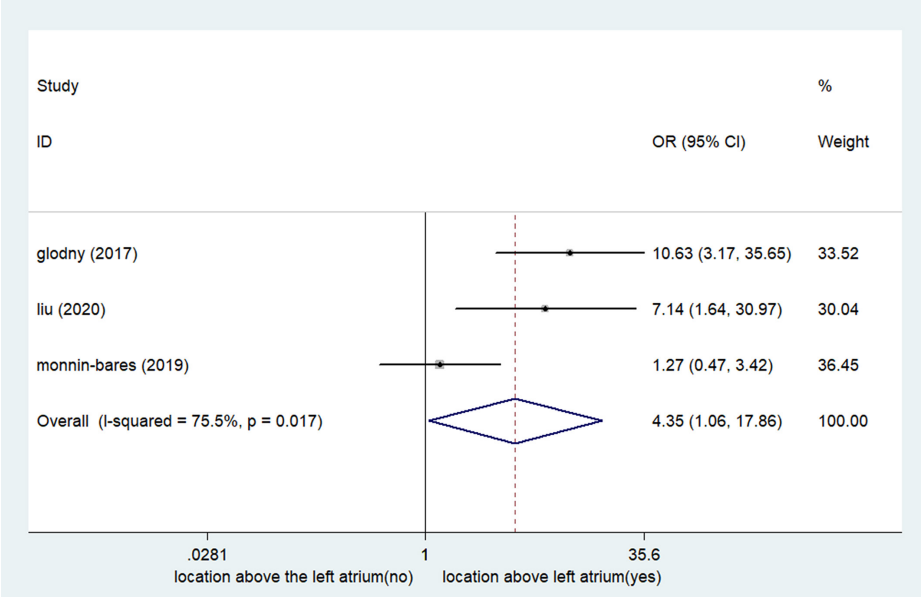

Figure 6. Forest plots of lesion location above the level of the left atrium. CI, confidence interval; OR, odds ratio.

were not evaluated in the original studies. Third, most studies included were case reports; hence, data from these studies were incomplete. Fourth, in most institutions, the extent of the post-procedure CT scan was limited to the target nodule area, so some asymptomatic air embolisms may not have been found. This may have introduced bias when analyzing the risks related to asymptomatic and symptomatic air embolism following CT-guided PTNB. Finally, we analyzed only air embolism following CT-guided PTNB without considering other techniques (e.g., ultrasound-guided PTNB); as the techniques are used for different types of lung lesions, the complication rates may also differ. Additional studies can be undertaken to analyze the characteristics and risk factors for air embolism with other techniques.

Conclusion

Based on current evidence, lesion location (lower lobe) and subtype (subsolid), pneumothorax, hemorrhage, and lesions located above the left atrium were significant risk factors for air embolism following CT-guided PTNB. The most common symptoms of air embolism were an unconscious or unresponsive state, hemiplegia, hypotension, and cardiopulmonary arrest. The air was most commonly located in the left ventricle, aorta, cerebral artery, and coronary artery. Emphysema, cough, and air location were related to patient symptoms, and air location and symptoms were significantly associated with patient outcomes.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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Supplementary Table 1. Characteristics of studies included in the systematic review

No	Studies	Country	Study design	No of patients with air embolism	Age (years)	Gender	Symptomatic	Outcomes
1	Wu et al.[13] 2012	China	Case report	1	NA	F	No	Without sequelae
2	Kawaji et al.[14] 2012	Japan	Case report	1	77	M	Yes	Without sequelae
3	Dalal and Varma[15] 2012	U.S.A.	Case report	1	46	M	No	Without sequelae
4	Al-Ali et al.[16] 2012	New Zealand	Case report	1	54	F	Yes	With sequelae
5	Thomas et al.[17] 2011	India	Case report	1	25	F	Yes	Died
6	Singh et al.[18] 2011	U.S.A.	Case report	1	75	M	Yes	Without sequelae
7	Shroff et al.[19] 2011	U.S.A.	Case report	1	58	M	Yes	Died
8	Mokart et al.[20] 2011	NA	Case report	1	57	M	Yes	Without sequelae
9	Kuo et al.[21] 2010	China	Case series	2	44, 74	M	1 yes, 1 no	Without sequelae
10	Cheng et al.[22] 2010	China	Case report	1	35	M	1	Died
11	Bou-Assaly et al.[23] 2010	U.S.A.	Case report	1	76	M	Yes	Died
12	Um et al.[24] 2009	Korea	Case series	4	40–75	3 M, 1 F	Yes	2 without sequelae, 2 died
13	Ishikawa et al.[25] 2009	Japan	Case report	1	51	M	Yes	Without sequelae
14	Hsi et al.[26] 2009	U.S.A.	Case report	1	67	M	Yes	Without sequelae
15	Ibukuro et al.[27] 2009	Japan	Case report	3	59–72	1 M, 2 F	Yes	Without sequelae
16	Bhatia[28] 2009	U.S.A.	Case report	1	NA	F	Yes	Without sequelae
17	Tomabechi et al.[29] 2008	Japan	Case report	1	71	M	Yes	Without sequelae
18	Kau et al.[30] 2008	Austria	Case report	1	50	M	Yes	With sequelae
19	Hiraki et al.[31] 2007	Japan	Case report	1	69	F	Yes	With sequelae
20	Ghafoori and Varedi[32] 2008	Iran	Case report	1	50	F	Yes	Died
21	Lattin et al.[33] 2006	U.S.A.	Case report	1	47	M	No	Without sequelae
22	Mansour et al.[34] 2005	Jordan	Case report	1	52	M	Yes	NA
23	Chakravarti et al.[35] 2004	India	Case report	1	63	M	Yes	NA
24	Ashizawa et al.[36] 2004	Japan	Case report	1	65	M	Yes	Without sequelae
25	Mokhlesi et al.[37] 2002	U.S.A.	Case report	1	77	M	Yes	Without sequelae
26	Arnold and Zwiebel[38] 2002	U.S.A.	Case report	1	60	M	Yes	Died
27	Ohashi et al.[39] 2001	Japan	Case report	1	75	M	Yes	Without sequelae
28	King et al.[40] 2013	U.S.A.	Case report	1	60	M	Yes	With sequelae
29	Kok et al.[41] 2013	Ireland	Case report	1	83	F	Yes	Without sequelae
30	Shi et al.[42] 2013	China	Case report	1	85	M	Yes	With sequelae
31	Chang and Yang[43] 2018	China	Case report	1	73	M	No	Without sequelae
32	Smit et al.[44] 2013	Netherlands	Case report	1	71	M	Yes	Without sequelae
33	Suzuki et al.[45] 2013	Japan	Case report	1	75	F	Yes	Without sequelae
34	Franke et al.[46] 2014	Germany	Case report	1	69	M	Yes	Died
35	Ramaswamy et al.[47] 2014	U.S.A.	Case report	1	75	F	Yes	Without sequelae
36	Shin et al.[48] 2014	Korea	Case report	1	70	F	Yes	Without sequelae
37	Hung et al.[49] 2015	China	Case report	1	63	M	Yes	Without sequelae
38	Olgun et al.[50] 2015	Turkey	Case report	1	69	M	Yes	Without sequelae
39	Pando Sandoval et al.[51] 2015	Spain	Case series	2	67, 69	M	Yes	With sequelae
40	Rocha et al.[52] 2015	Brazil	Case report	1	NA	NA	Yes	With sequelae
41	Kazimirko et al.[53] 2016	America	Case report	1	65	M	Yes	Without sequelae
42	Sun et al.[54] 2015	China	Case report	1	53	F	Yes	Died
43	Rahman et al.[55] 2016	U.S.A.	Case report	1	82	F	Yes	Without sequelae
44	Yamamoto et al.[56] 2016	Japan	Case report	1	74	F	Yes	Without sequelae
45	Fintelmann et al.[57] 2017	England	Case report	1	75	M	Yes	Died
46	Fiore et al.[58] 2017	Brazil	Case report	1	57	F	Yes	Without sequelae

Supplementary Table 1. Continued

47	Galvis et al.[59] 2017	U.S.A.	Case report	1	60	M	Yes	Without sequelae
48	Ialongo et al.[60] 2017	Italy	Case report	1	57	M	Yes	Died
49	April et al.[61] 2017	U.S.A.	Case report	1	65	M	No	Without sequelae
50	Kukuljan et al.[62] 2018	Croatia	Case report	1	60	NA	Yes	Without sequelae
51	Lang et al.[63] 2018	Austria	Case report	1	69	M	Yes	Without sequelae
52	Ren and Zavodni[64] 2018	Canada	Case report	1	68	F	Yes	Without sequelae
53	Ornelas et al.[65] 2018	Spain	Case report	1	70	F	Yes	NA
54	Matsuura et al.[66] 2017	Japan	Case report	1	74	M	Yes	Without sequelae
55	Sakatani et al.[67] 2018	Japan	Case report	1	72	M	Yes	Without sequelae
56	Tavare et al.[68] 2018	England	Case report	1	58	M	Yes	Without sequelae
57	Viqas et al.[69] 2018	Pakistan	Case report	1	67	M	Yes	With sequelae
58	Abid et al.[70] 2018	U.S.A.	Case report	1	61	M	Yes	Without sequelae
59	Beliaev et al.[71] 2019	New Zealand	Case report	1	69	M	Yes	With sequelae
60	Edwards et al.[72] 2017	England	Case report	1	75	M	Yes	Died
61	Li et al.[73] 2019	China	Case report	1	50	F	Yes	Died
62	Lonni and Ceruti[74] 2019	NA	Case report	1	70	M	Yes	Without sequelae
63	Marchak et al.[75] 2019	U.S.A.	Case report	1	78	F	Yes	Without sequelae
64	De Oliveira et al.[76] 2019	Brazil	Case report	1	69	M	Yes	Died
65	Deshmukh et al.[77] 2019	India	Case report	1	52	M	Yes	Without sequelae
66	El Homsi et al.[78] 2019	Lebanon	Case report	1	57	M	Yes	Without sequelae
67	Hellinger et al.[79] 2019	Germany	Case report	1	74	M	Yes	NA
68	Hare et al.[80] 2011	France	Case series	4	63–73	2 W, 2 F	2 yes, 2 no	Without sequelae
69	Warren et al.[81] 2019	U.S.A.	Case report	1	60	M	Yes	Without sequelae
70	Rott and Boecker[82] 2014	Germany	Case report	1	57	M	Yes	With sequelae
71	Lederer et al.[83] 2011	Austria	Case report	1	27	M	No	Without sequelae
72	Khalid et al.[84] 2018	U.S.A.	Case report	1	61	M	Yes	Without sequelae
73	Tomiyama et al.[85] 2006	Japan	Case series	6	57–75	4 M, 2 F	Yes	1 died, 1 with sequelae, 4 without sequelae
74	Piccoli et al.[86] 2019	Italy	Case report	1	36	M	Yes	Without sequelae
75	Oh et al.[87] 2020	Korea	Case report	1	81	M	Yes	With sequelae
76	Ko et al.[88] 2019	Korea	Case report	1	78	M	Yes	NA
77	Grandjean et al.[89] 2020	France	Case report	1	62	M	Yes	Without sequelae
78	Regge et al.[90] 1997	Italy	Case report	1	40	F	Yes	Without sequelae
79	Khatri[91] 1997	Italy	Case report	1	54	M	Yes	Without sequelae
80	Wong et al.[92] 1995	U.S.A.	Case report	1	62	M	Yes	With sequelae
81	Tolly et al.[93] 1988	U.S.A.	Case report	1	32	M	Yes	With sequelae
82	Baker and Awwad[94] 1988	U.S.A.	Case report	1	39	M	Yes	NA
83	Cianci et al.[95] 1987	U.S.A.	Case report	1	63	F	Yes	With sequelae
84	Aberle et al.[96] 1987	U.S.A.	Case report	1	60	M	Yes	Died
85	Matz et al.[97] 1980	Israel	Case report	1	70	M	Yes	Died
86	Omenaas et al.[98] 1989	Norway	Case report	1	54	M	Yes	Without sequelae
87	Liu et al.[99] 2020	China	Retrospective	19	NA	NA	3 yes, 16 no	Without sequelae
88	Jang et al.[100] 2019	Korea	Retrospective	9	55–74	6 M, 3 F	2 yes, 7 no	1 without and 8 with sequelae
89	Ishii et al.[101] 2014	Japan	Case control	10	53–80	5 M and 5 F	5 yes and 5 no	1 without and 9 with sequelae
90	Kogut et al.[102] 2012	U.S.A.	Case report	1	76	M	Yes	Without sequelae
91	Thapa et al.[103] 2013	U.S.A.	Case report	1	66	M	Yes	NA
92	Khalid et al.[104] 2016	U.S.A.	Case report	1	76	M	Yes	NA
93	Martins et al.[105] 2012	Portugal	Case report	1	64	M	Yes	Without sequelae
94	Wang and Gao[106] 2007	China	Case report	1	29	M	Yes	With sequelae

Supplementary Table 1. Continued

95	Luo and Yu[107] 2015	China	Case report	1	58	M	Yes	Without sequelae
96	Song et al.[108] 2016	China	Case report	1	58	M	Yes	Without sequelae
97	Wu et al.[109] 2016	China	Case report	1	57	M	Yes	With sequelae
98	Li[110] 2017	China	Case report	1	60	M	Yes	Without sequelae
99	Liu et al.[111] 2018	China	Case report	1	67	F	Yes	Without sequelae
100	Niu et al.[112] 2018	China	Case report	1	58	M	Yes	With sequelae
101	Milano-Johnson et al.[113] 2017	U.S.A.	Case report	1	65	M	Yes	NA
102	Njuguna[114] 2019	U.S.A.	Case report	1	60	M	Yes	Died
103	Shamsid-Deen et al.[115] 2017	U.S.A.	Case report	1	80	M	Yes	Without sequelae
104	Espinal et al.[116] 2019	U.S.A.	Case report	1	70	F	Yes	NA

NA, not applicable; male; F, female.

Supplementary Table 2. Characteristics of the studies included for quantitative meta-analysis

Studies	Country	Study design	Patients with air embolism	Patients without air embolism	Overall quality
Liu et al.[99] 2020	China	Retrospective	19	2.007	7
Jang et al.[100] 2019	Korea	Retrospective	9	1.005	7
Ishii et al.[101] 2014	Japan	Case control	10	2.206	7
Monnin-Bares et al.[118] 2019	France	Retrospective	24	532	7
Glodny et al.[117] 2017	Austria	Retrospective	25	1.853	7

Supplementary Table 3. Clinical symptoms and signs of patients with air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy

Clinical symptoms and signs	Number of patients (%)
Asymptomatic	35 (22.73)
Unconscious or unresponsive state	46 (29.87)
Hemiplegia	25 (16.23)
Cardiopulmonary arrest	22 (14.29)
Hypotension	22 (14.29)
Chest pain	17 (11.04)
Arrhythmia	14 (9.09)
Hemianopsia or conjugate eye deviation	11 (7.14)
ST segment elevation	10 (6.49)
Seizure	9 (5.84)
Aphasia or facioplegia	8 (5.819
Bradycardia	9 (5.84)
Dyspnea	6 (3.90)
Dizziness	5 (3.25)
Hypertension	4 (2.60)
Tachycardia	2 (1.30)
Urine incontinence	3 (1.95)
Tachypnea	2 (1.30)
Abdominal pain	2 (1.30)
Pulselessness	2 (1.30)
Altered mental status	1 (0.65)

Supplementary Table 4. Air location in patients with air embolism following computed tomography-guided percutaneous transthoracic lung needle biopsy

Location	Number of patients (%)
Left ventricle	69 (44.81)
Aorta	63 (40.91)
Cerebral artery	46 (29.87)
Coronary artery	35 (22.73)
Left atrium	23 (14.94)
Pulmonary vein	11 (7.14)
Right atrium	4 (2.60)
Right ventricle	3 (1.95)
Pulmonary artery	3 (1.95)
Renal artery	1 (0.65)
Intercostal artery	1 (0.65)
Spinal cord artery	1 (0.65)
Superior vena vein	1 (0.65)
Subclavian vein	1 (0.65)
Vertebral artery	1 (0.65)
Subclavian artery	1 (0.65)
Vertebral artery	1 (0.65)
Left subclavian artery	1 (0.65)
Truncus brachiocephalicus	1 (0.65)
Internal carotid artery	1 (0.65)
Unclear	7 (4.55)