Asymptomatic systemic air embolism after CT-guided percutaneous transthoracic needle biopsy

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ABSTRACT

Purpose: We presented details and incidence of systemic arterial embolism (SAE) following a CT-guided percutaneous transthoracic needle biopsy (PTNB) and evaluated risk factors for SAEs.
Methods: We retrospectively evaluated 1014 PTNBs performed in our hospital from 2005 to 2017. SAE was identified in the pulmonary vein, left heart, coronary artery, and aorta by reviewing post-biopsy CT images. Limited post-biopsy CT scans only covering the region biopsied were available until the first case of SAE was identified (n = 503). Then, the entire thorax was scanned for further examination of SAE (n = 511). Eighteen-gauge automatic cutting needles were used in all procedures. When SAE was evident on post-biopsy CT, subsequent brain CT was performed in order to confirm the cerebral SAE.
Results: Nine patients (0.89%) developed SAEs. In the univariate analyses, the location of the needle tip relative to the lesion (outside or inside of the lesion) as well as accompanying pulmonary hemorrhage were significant risk factors for SAEs (P = 0.021 and 0.036, respectively). Two patients developed neurological symptoms with cerebral SAEs, and one of these had sequelae. In seven asymptomatic SAEs with no cerebral SAE, four patients were retrospectively-diagnosed cases and three patients were detected on post-biopsy CT images. All seven of these patients had no sequelae.
Conclusion: The incidence of SAE was higher than expected, due to radiologically detected asymptomatic SAEs. The location of the needle tip relative to the lesion and accompanying pulmonary hemorrhage were significant risk factors for the occurrence of SAEs. We proposed a guideline for treating asymptomatic SAEs.

1. Introduction

Computed tomography (CT)-guided percutaneous transthoracic needle biopsy (PTNB) is frequently performed to evaluate pulmonary and mediastinal lesions. This technique has several associated complications, most commonly simple pneumothorax (27%), intrapulmonary hemorrhage (11%) and hemoptysis (7%), which are usually mild and treated conservatively [1,2]. Systemic air embolism (SAE) is an extremely rare complication of a CT-guided PTNB, but one that is potentially fatal. The incidence of SAE is 0.02 to 0.07% [2–4]. However, this incidence is likely an underestimation due to undiagnosed asymptomatic patients. Indeed, some studies have recently reported a higher incidence rate [5–9].

The cause of death in patients with SAE-related complications is cardiac or cerebral infarction [10,11]. However, SAE is usually non-fatal and has no long-term morbidity if it is promptly recognized, and if immediate temporizing measures as well as a targeted management strategy are administered [12]. For these reasons, it is crucial for radiologists to diagnose SAE and recognize cardiac and neurological dysfunctions both during and after PTNB, since the patient is usually in the radiology department at the time of symptom onset, and may even still be on the CT table [12].

We evaluated incidence and risk factors of SAE following a CT-guided PTNB. In addition, we presented a clinical course on, and a guideline for treating asymptomatic SAE, which may be rare but fatal, to help less experienced chest or interventional radiologists.

2. Materials and methods

This study was approved by the institution's review board.

2.1. Study population and data collection

We performed a total of 1123 CT-guided PTNBs including lung needle marking in our hospital from March 2005 to February 2017. Eighty PTNBs for mediastinal or pleural lesions as well as 29 cases of lung needle marking with a hook wire were excluded. A total of 1014 PTNBs for lung lesions were included.

CT images obtained before, during, and after the procedure, patient charts, and procedure records for the 1014 patients were retrospectively reviewed by a thoracic radiologist with 16 years of experience aided by a radiology trainee. Multiple variables relating to the patients, lesions, procedures, and clinical course were collected. Patients' data included age and sex. Lesion data included size (maximum axial diameter of the lesion), lobar location of the lesion (upper, middle, or lower lobe), zonal location of the lesion (subpleural or peripheral), subtype of the lesion (solid nodule, subsolid nodule and consolidation), and presence of pulmonary emphysema or subpleural honeycombing cysts. On pre-biopsy target CT images for PTNB, the zonal location of each lesion led it to be classified as either a peripheral lesion separated from the pleura or a subpleural lesion attached to the pleura, depending on whether the aerated healthy lung tissue was traversed or not. In the subtype of the lesion, subsolid nodules included ground-glass nodules and part-solid ground-glass nodules. PTNB data included patient position (supine, prone, or oblique), use of a coaxial needle system, size of the biopsy needle used, needle angle to the pleura (right angle or not right angle), and depth of the needle tip (the distance between the pleural surface and the needle tip inserted). Additionally, on post-biopsy CT images, complications such as pneumothorax, pulmonary hemorrhage, and SAE were evaluated. In the cases where SAE was detected, further evaluation was done on the presence of dilated pulmonary vein located in the proximity to needle tip, occurrence of accompanying complications (pneumothorax or parenchymal hemorrhage), biopsy diagnosis of specimens obtained (malignancy or benign), and coughing during or after PTNB. A larger sized vein (compared to the normal vein of the surrounding lung) running toward the mass is defined as a dilated pulmonary vein. Data for clinical course included brain CT finding (presence of cerebral SAE), electrocardiogram (ECG) findings if available, optimal positioning on the CT table (supine with Trendelenburg position or prone position), immediate management (supportive treatment with 100% oxygen administration or hyperbaric oxygen therapy [HBOT]), and outcome (presence of permanent sequelae). We also reviewed follow-up brain and chest CT scans.

2.2. CT-guided PTNB procedure

All procedures were performed percutaneously under CT guidance by an experienced chest radiologist. Eighteen-gauge, 10 or 16-cm-automatic cutting needles (Magnum, Bard Biopsy System, Tempe, AZ, USA) were used in all procedures with either a non-coaxial needle system (n = 962) or coaxial needle system (n = 52).

Prior to PTNB, a pre-biopsy CT scan (Sensation 16, Siemens Medical Solutions, Forchheim, Germany) was obtained to help target the lesion. Patients were positioned differently depending on the determined location of the lesion. Most patients were positioned supine or prone, but the oblique decubitus position was used in some cases. PTNB was performed in suspended inspiration with local anesthesia. The needle path was chosen in order to traverse the least amount of lung parenchyma and to avoid visible bronchi and relatively large vessels. A limited post-biopsy chest CT scan through the region biopsied was obtained on each patient until the first case of SAE was identified (n = 503). After this first case, the entire thorax was scanned for the examination of SAEs (n = 511).

2.3. Post-biopsy CT image interpretation for SAE

When air bubbles were confirmed in the cardiovascular system (pulmonary vein, left atrium, left ventricle, coronary artery, and aorta) on the post-biopsy chest CT or cerebral system on the brain CT scan, we regarded the patient as a case with SAE. If SAEs were detected directly after PTNB on the CT table, immediate treatment was initiated, and subsequent brain CT was then performed for evaluation of cerebral SAE. In addition, in a case with delayed detection of SAE after the patient was moved to the ward, subsequent brain CT was performed. On the other hand, if SAEs were detected upon retrospective evaluation of the images, subsequent brain CT was not performed.

2.4. Statistical analysis

The descriptive data were compared between the SAE and non-SAE groups using the Wilcoxon rank sum test and Fisher's Exact test for numerical and categorical values, respectively. Descriptive statistics were used to define the baseline data (median and interquartile range (IQR; 25th–75th percentile) and N [%], as appropriate). Statistical analysis was performed using SAS 9.3 (Carey, NC). P values < 0.05 were considered to be statistically significant.

3. Results

The characteristics of total PTNB and SAE cases are summarized in Table 1. Nine (0.89%) patients among the 1014 included cases developed SAEs. In the univariate analyses of numerical and categorical variables, the location of the needle tip relative to the lesion (outside or inside of the lesion) and accompanying pulmonary hemorrhage during the procedure were significant risk factors for the development of SAE (P = 0.021 and 0.036). Accompanying pneumothorax was not associated with the occurrence of SAEs, statistically. Pneumothorax is the most common complication and pulmonary hemorrhage represents the second most common complication associated with PTNB. In fact, of 1014 patients with PTNBs, 528 patients had a pneumothorax by CT scan (52%, non-SAEs vs. SAEs = 51% vs. 77%) and 411 patients had a hemorrhage (40%, non-SAEs vs. SAEs = 40% vs. 77%).

The detailed features of the nine cases with SAE are presented in Table 2. The patients were six men and three women ranging in age from 55 to 74 years (with a mean age of 68 years). The lesions ranged in size from 11 to 70 mm. The distance between the pleural surface and where the needle tip was inserted (depth of the needle tip), varied from 0 to 50 mm. In two cases with subpleural lesions, we performed PTNB by placing the needle tip in the pleura or extrapleural regions to obtain the tissue properly in the lesion and measured the depth of the needle tip to 0 mm. Two patients had mild emphysema and another patient had extensive subpleural honeycombing cysts in both lungs. A dilated pulmonary vein located proximal to the needle tip was seen on post-biopsy CT images in six patients. The position used during PTNB was supine in two patients and prone in seven patients. A non-coaxial needle system was used in eight patients. PTNB-related other complications were pneumothorax and hemorrhage: five patients exhibited both, two exhibited pneumothorax only, and two exhibited hemorrhage only. Four patients experienced paroxysms of coughing during or immediately after the procedure. In seven patients, the specimens were confirmed to be malignant, and in two patients the specimens were confirmed to be benign.

The location of air bubbles were in the left atrium (n = 7), left ventricle (n = 2), right coronary artery (n = 2), aorta (n = 3), and pulmonary vein (n = 2) on post-biopsy CT images, and cerebral artery and vein (n = 2) on subsequent brain CT (Tables 3, 4). Subsequent brain CT was performed in two symptomatic patients and three asymptomatic patients with SAE found on the CT tables, and all of them underwent follow-up brain CT and chest CT.

Table 1
Characteristics of total PTNB by SAE cases.

		Total PTNB (n = 1014) N (%)	Non-SAE (n = 1005)	SAE (n = 9)	P-value
Age (years)					0.439 (a)
	Median (IQR)	66 (55–73)	66 (55–73)	67 (65–74)	
Sex					1.000 (b)
	Male	628 (61.93%)	622 (61.89%)	6 (66.67%)	
	Female	386 (38.07%)	383 (38.11%)	3 (33.33%)	
Zonal location of the lesion					0.723 (b)
	Peripheral	721 (71.10%)	715 (71.14%)	6 (66.67%)	
	Subpleural	293 (28.90%)	290 (28.860%)	3 (33.33%)	
Lobar location of the lesion					0.774 (b)
	Right upper lobe	262 (25.84%)	259 (25.77%)	3 (33.33%)	
	Right middle lobe	54 (5.33%)	53 (5.27%)	1 (11.11%)	
	Right lower lobe	259 (25.54%)	257 (25.57%)	2 (22.22%)	
	Left upper lobe	236 (23.27%)	234 (23.28%)	2 (22.22%)	
	Left lower lobe	203 (20.02%)	202 (20.10%)	1 (11.11%)	
Subtype of the lesion					0.053 (b)
	Solid nodule	835 (82.35%)	830 (82.59%)	5 (55.56%)	
	Subsolid nodule	61 (6.02%)	59 (5.87%)	2 (22.22%)	
	Consolidation	118 (11.64%)	116 (11.54%)	2 (22.22%)	
Associated findings					0.732 (b)
Emphysema	No	709 (69.92%)	702 (69.85%)	7 (77.78%)	
	Yes	305 (30.08%)	303 (30.15%)	2 (22.22%)	
					0.466 (b)
Honeycombing	No	946 (93.29%)	938 (93.33%)	8 (88.89%)	
	Yes	68 (6.71%)	67 (6.67%)	1 (11.11%)	
Size of the lesion (mm)					0.085 (b)
	0–10	22 (2.17%)	22 (2.17%)	0	
	11–30	423 (41.72%)	415 (40.93%)	8 (0.79%)	
	31–50	301 (29.68%)	301 (29.68%)	0	
	51–70	160 (15.78%)	159 (15.68%)	1 (0.1%)	
	> 70	108 (10.65%)	108 (10.65%)	0	
Position during the PTNB					0.774 (b)
	Supine	316 (31.16%)	314 (31.24%)	2 (22.22%)	
	Prone	677 (66.77%)	670 (66.67%)	7 (77.78%)	
	Oblique supine	15 (1.48%)	15 (1.49%)	0	
	Oblique prone	6 (0.59%)	6 (0.60%)	0	
Needle angle to the pleura					1.000 (b)
	Right angle	358 (35.31%)	355 (35.32%)	3 (33.33%)	
	Not right angle	656 (64.69%)	650 (64.68%)	6 (66.67%)	
Use of coaxial system					0.379 (b)
	No	962 (94.87%)	954 (94.93%)	8 (88.89%)	
	Yes	52 (5.13%)	51 (5.07%)	1 (11.11%)	
Location of needle tip to the lesion					0.021* (b)
	Inside the lesion	806 (79.49%)	802 (79.80%)	4 (44.44%)	
	Outside the lesion	208 (20.51%)	203 (20.20%)	5 (55.56%)	
Needle depth to the lesion (mm)					0.102 (b)
	0–10	177 (17.46%)	172 (16.96%)	5 (0.49%)	
	11–30	463 (45.66%)	460 (45.36%)	3 (0.30%)	
	31–50	272 (26.82%)	271 (26.73%)	1 (0.10%)	
	51–70	90 (8.88%)	90 (8.88%)	0	
	> 70	12 (1.18%)	12 (1.18%)	0	
Other complications					0.181 (b)
Pneumothorax	No	486 (47.93%)	484 (48.16%)	2 (22.22%)	
	Yes	528 (52.07%)	521 (51.84%)	7 (77.78%)	
					0.036* (b)
Hemorrhage	No	603 (59.47%)	601 (59.80%)	2 (22.22%)	
	Yes	411 (40.53%)	404 (40.20%)	7 (77.78%)	

(a): P-value by Wilcoxon rank sum test.
(b): P-value by Fisher's Exact test.
  * Statistically significant (P < 0.05).

3.1. Two symptomatic patients with SAEs

The presence of systemic air bubbles was missed in the initial post-biopsy chest CT images in the first two symptomatic patients. After moving to the ward, one patient (case 1) showed mental change and, left motor and sensory dysfuntion 2 h later. The other patient (case 2) showed similar symptoms, but only 10 min later while still on the CT table (Fig. 1). We performed immediate treatment with 100% oxygen administered through a mask and maintained the biopsy position (supine) of the patient with no positional change. Brain CT revealed gas within the cerebral artery and venous system in both cases. Follow-up chest and brain CT scans were taken after the patients had stabilized; the scans revealed no air bubbles in both cases. However, right cerebral infarction was seen in case 1; no sequelae was seen in case 2. Unfortunately, HBOT was not available in both patients. These results are presented in Table 3.

3.2. Seven asymptomatic patients with SAEs

After the experience with the first two symptomatic SAEs, we

Table 2
Detailed features in 9 cases of SAE.

Case no.	Age/sex	Size	Subtype	Dilated PV	Lobar/zonal location	Patient position	Coaxial system	Needle depth[a]	Needle tip[b]	Cough	PNX	HEMO
1	74/M	25 mm	Solid	Yes	RLL/SUB	Prone	No	8 mm	Outside	Yes	Yes	Yes
2	74/M	18 mm	Solid	Yes	RML/PPH	Supine	No	14 mm	Inside	Yes	Yes	Yes
3	65/M	70 mm	Consol	Yes	LUL/SUB	Supine	No	0 mm	Inside	Yes	Yes	No
4	67/M	24 mm	Solid	Yes	RLL/PPH	Prone	No	20 mm	Inside	Yes	Yes	No
5	67/M	11 mm	Consol	No	RUL/SUB	Prone	Yes	0 mm	Outside	No	No	Yes
6	66/M	18 mm	Subsolid	Yes	RUL/PPH	Prone	No	10 mm	Inside	No	Yes	Yes
7	65/F	24 mm	Solid	No	RUL/PPH	Prone	No	17 mm	Outside	No	No	Yes
8	55/F	11 mm	Solid	Yes	LLL/PPH	Prone	No	3 mm	Outside	No	Yes	Yes
9	74/F	25 mm	Subsolid	No	LUL/PPH	Prone	No	50 mm	Outside	No	Yes	Yes

Abbreviations: Consol, consolidation; PV, pulmonary vein, LLL, left lower lobe; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe; SUB, subpleural location of the lesion; PPH, peripheral location of the lesion; PNX, pneumothorax; HEMO, pulmonary hemorrhage.

[a] Needle depth measures distance between the pleural surface and the needle tip inserted.
[b] Needle tip indicates location of the needle tip relative to the lesion whether the needle tip is located inside or outside of the lesion.

subsequently identified seven asymptomatic SAEs. Four patients received no treatment and brain CT scan due to the diagnosis being retrospectively applied (Fig. 2). Conversely, the other three patients in whom the presence of SAE was confirmed by careful review of post-biopsy CT scan were placed in the supine with Trendelenburg position (case 3) or in the flat prone position (case 4, Fig. 3 and case 5) with no repositioning, and conservative treatment was begun immediately with administration of 100% oxygen through a mask. Brain CT was done subsequently. In addition, monitoring vital sign and ECG were performed. After confirming that there was no cerebral SAE on brain CT, patients were moved to the ward with no positional change, and follow-up chest and brain CT scans were done to check for remaining air bubbles. All three patients were resolved with no sequelae after the immediate and conservative therapy. HBOT was not available. These results are presented in Table 4.

4. Discussion

SAE is thought to be an extremely rare complication (0.02–0.07%) incurred during or after PTNB [2–4]. However, this incidence may be underestimated due to SAE in patients without cardiac or cerebral symptoms going undiagnosed. Some authors have previously reported non-fatal asymptomatic and symptomatic SAEs with an incidence of 0.21–0.45%, which is significantly higher than the commonly-accepted figure [5–7,9]. Freund et al. reported that the radiological incidence of SAE complicating PTNB was 3.8% (23/610 patients), whereas the clinically apparent incidence was 0.49% [8]. Interestingly, 17 of these cases were detected retrospectively when evaluating the images. Hiraki et al. attributed the high incidence to performed postprocedure CT scans in the whole thorax for the survey of SAE after encountering the first case of SAE, whereas it had been previously performed only at the target region [5]. Recent studies recommend that the post-biopsy CT should scan the entire thorax or aorto-cardiac region, because it is important to recognize radiologic asymptomatic SAEs before patients develop clinical symptoms, such as rapid deterioration of the neurological/cardiovascular state [5,7,8]. We also performed post-biopsy CT scans of the entire thorax to detect air bubbles in the pulmonary vein,

left heart, aorta, or coronary artery following the first case of SAE; the incidence of SAE after PTNB in our institution was found to be 0.89% (9 of 1014 biopsies), which is substantially higher than previously reported. In fact, after obtaining the post-biopsy CT scan of the entire thorax, one symptomatic patient and seven asymptomatic patients were discovered. Four of the seven patients with asymptomatic SAE were detected retrospectively when evaluating the post-biopsy CT images. Post-biopsy CT scan through the entire thorax helped us note SAE in a timely manner in the remaining three asymptomatic cases. In fact, the incidence of SAE in patients who underwent a post-biopsy CT scan of the entire thorax showed a higher incidence of 1.57% (8 of 511 biopsies).

Understanding the mechanisms of SAEs and identifying the risk factors for SAEs will facilitate the development and implementation of adequate preventive measures prior to and during biopsy. There are three possible ways that air can be introduced into the pulmonary venous system during PTNB [13,14]. The first is when the biopsy needle punctures a pulmonary vein, resulting in a direct connection with atmosphere. The second is when the needle traverses both a pulmonary vein and an adjacent airway, forming an iatrogenic bronchovenous fistula. The third is when the needle punctures a pulmonary artery and air in the pulmonary arterial circulation reaches the pulmonary venous circulation by traversing the pulmonary microvasculature. In all three scenarios, pulmonary venous air bubbles acquired from lung biopsy may reach the systemic arterial circulation through the left heart and aorta with potential embolization into multiple organs [12]. SAE into the coronary or cerebral arteries may result in severe morbidity or death [12,15]. Coronary artery air embolism may induce myocardial infarction and cerebral artery air embolism may cause permanent or transient neurologic deficit. Regarding the three mechanisms of SAE, several preventative considerations have been recommended. They include avoiding needle biopsy of cystic, cavitary, or bullous lung parenchyma; using a stylet or ensuring occlusion of the hollow needle at all times; educating the patient about the risk of coughing or straining during the procedure; and penetrating the least amount of lung parenchyma necessary for reaching the mass by choosing an appropriate entrance site [5,11,14,16,17]. In addition, placing the tip of the needle

Table 3
Clinical course and management in 2 cases of symptomatic SAE.

Case no.	Post-biopsy CT: location of SAE	Time of notice	Symptoms	Initial ECG	Initial brain CT: location of SAE	Supportive Tx with 100% O₂[a]	Outcome
1	Lt. atrium	At the ward (2 h later)	Mental change, Left hemiparesis	Non-available	Rt. cerebral artery, superior sagittal sinus	Yes	Rt. cerebral infarction
2	Ascending aorta, Lt. ventricle, Rt. coronary artery	On the CT table (10 min later)	Mental change, Left hemiparesis	ST elevation	Both cerebral arteries	Yes	No sequelae

Abbreviations: Lt., left; Rt., right; Tx, treatment.
[a] Hyperbaric oxygen therapy was not available.

Table 4
Clinical course and management in 7 cases of asymptomatic SAE.

Case no.	Post-biopsy CT: location of SAE	Time of notice	Initial ECG	Initial brain CT: location of SAE	Supportive Tx with 100% O$_2$[a]	Outcome
3	Ascending aorta, Lt. ventricle, Rt. coronary artery	On the CT table (immediately)	ST elevation	No SAE	Yes	No sequelae
4	Descending aorta, Lt. atrium, Lt. pulmonary vein	On the CT table (immediately)	Sinus bradycardia with 1st AV block	No SAE	Yes	No sequelae
5	Lt. atrium	On the CT table (immediately)	Non-available	No SAE	Yes	No sequelae
6	Lt. atrium	Retrospective	Non-available	Non-available	Non-available	No sequelae
7	Lt. atrium	Retrospective	Non-available	Non-available	Non-available	No sequelae
8	Lt. atrium	Retrospective	Non-available	Non-available	Non-available	No sequelae
9	Lt. atrium, Lt. pulmonary vein	Retrospective	Non-available	Non-available	Non-available	No sequelae

Abbreviations: AV block, atrioventricular block; Lt., left; Rt., right; Tx, treatment.
[a] Hyperbaric oxygen therapy was not available.

outside the target lesion should be avoided, thereby minimizing contact with a pulmonary vein or airway [8,14].

Perilesional bullous or cystic lung parenchymal finding was found in three of nine cases with SAEs (emphysema in two and subpleural honeycombing cysts in one). Patients with COPD and air-trapping may be at increased risk for secondary increased airway pressures [17].

Because the pulmonary vein pressure is normally low, any factor producing an increased pressure gradient between the airway and pulmonary vein may allow for the entrance of air into the vein, causing air embolism. Honeycombing cysts were thought to be associated with an increased risk of air embolism by similar mechanisms. However, our results showed that associated emphysema or honeycombing cysts are
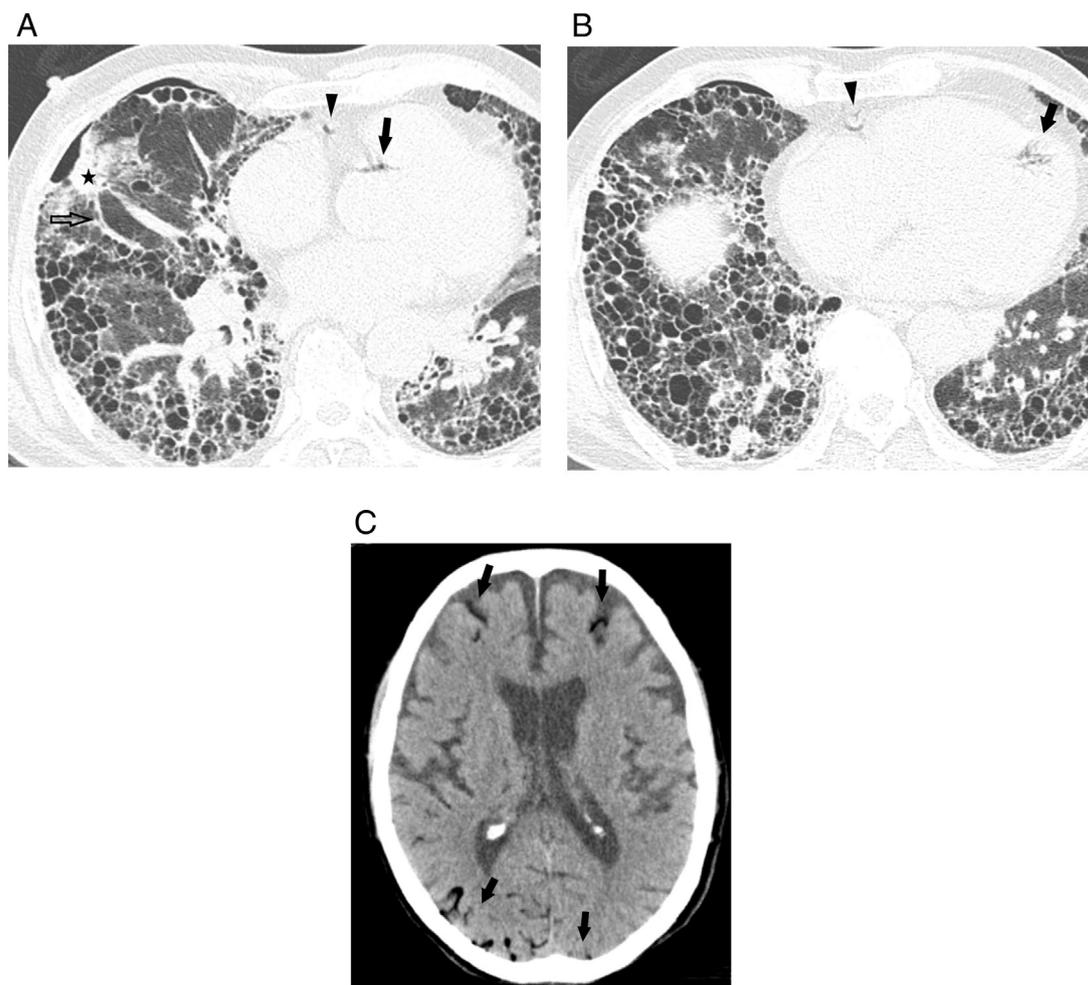

Fig. 1. A 74-year-old man with symptomatic SAE (case 2) after CT-guided PTNB of 18 mm peripheral solid nodule in right middle lobe. The patient had evidence of idiopathic pulmonary fibrosis. The lesion was confirmed as adenocarcinoma.
A. Post-biopsy CT image shows a small amount of air bubbles in the ascending aorta (arrow) and right coronary artery (arrowhead). A dilate pulmonary vein (white arrow) adjacent to nodule (asterisk) is clearly visible. A small amount of pneumothorax as well as hemorrhage around the nodule are also noted.
B. Post-biopsy CT image shows a small amount of air bubbles in the right coronary artery (arrowhead) and left ventricle (arrow).
C. Subsequent non-contrast brain CT image shows intra-arterial air bubbles (arrows) in both cerebral hemispheres, with substantially more in the right occipital area. Follow-up non-contrast brain CT performed four months later showed no abnormal findings with no air-bubbles present.
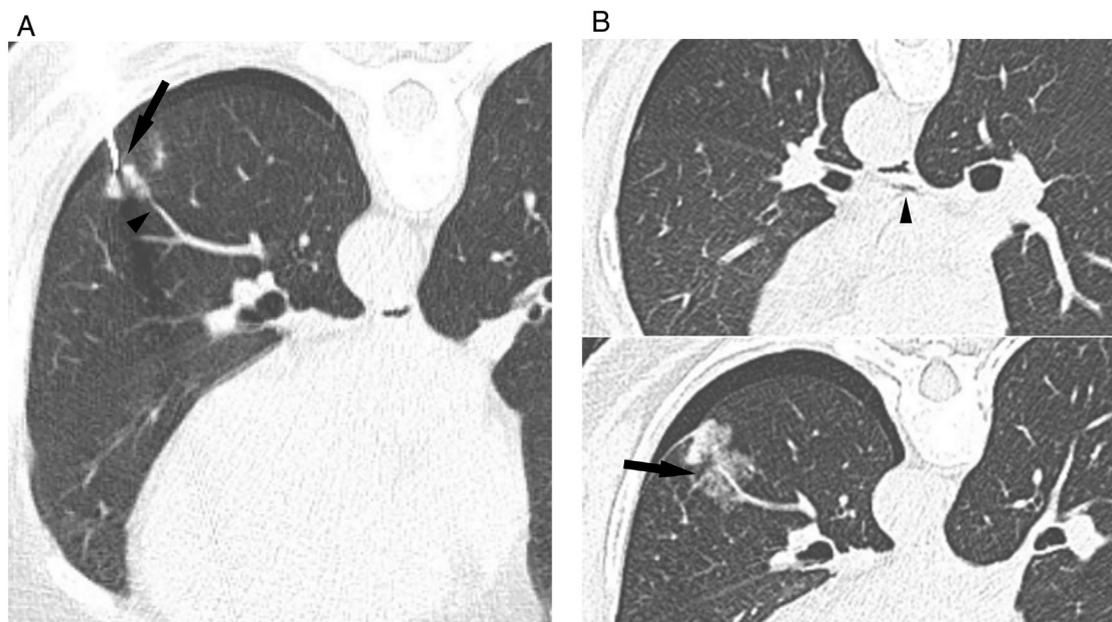
Fig. 2. A 55-year-old woman with asymptomatic SAE (case 8) after CT-guided PTNB of 11 mm peripheral solid nodule in left lower lobe. The lesion was confirmed as adenocarcinoma.

A. CT image obtained during biopsy with the patient in the prone position shows the pulmonary vein (arrowhead) is located adjacent to the needle tip (arrow). Note the small pneumothorax.

B. Post-biopsy CT images show a small amount of air bubbles in left atrium (arrowhead). Note the hemorrhage around the nodule (arrow).

not risk factors for SAEs (Table 1). We did not investigate the cause of honeycombing cysts in the total PTNB data, only their presence. One case of honeycombing cysts associated with SAE was due to idiopathic pulmonary fibrosis.

Four (cases 1–4) of nine cases with SAEs experienced paroxysms of coughing during or immediately after the procedure. During a cough, the airway pressure is higher than the pulmonary venous pressure. This might have facilitated the mechanisms of the development of SAEs. Therefore, educating patients not to cough and to hold their breath during the procedure is necessary before performing PTNB.

In a total of nine patients with SAEs, the size range of lesions was 11–25 mm, except for in the first case (70 mm), so the tip of the needle was often located outside of the target lesion (n = 5). We found that the location of the needle tip relative to the lesion is a significant risk factor for SAEs (Table 1). In other words, there was statistical significance in the occurrence of SAE when the tip of the needle was located outside of the target lesion. Increased frequency of CT screening increased the need for biopsy for smaller lung lesions. In particular, when performing procedures for nodules smaller than 2 cm, the possibility that the needle tip is to be located outside of the lesion increases. Even if the needle tip is located at the center, it is more likely to pass normal lung tissue, because we used an 18-gauge needle with a cutting length of 2.2 cm or 1.5 cm. Similarly to our result, Freund et al. [8] also found that the most important independent risk factor for the development of SAE within a single institution was needle penetration depth in the tumor; the deeper the tip of the needle was in the tumor, the lower the risk of SAEs.

Additionally, in six of our cases with SAE, dilated peripheral pulmonary veins were seen adjacent to all target lesions. We think that direct injury of the pulmonary vein or communication of injured pulmonary vein and bronchus occurred because the needle tip was in close proximity to the peripheral pulmonary vein. Therefore, if there are large pulmonary venous branches near the targeted lesion, a nearby needle trajectory during PTNB should be avoided if possible. Unfortunately, we retrospectively evaluated dilated pulmonary veins adjacent to the target lesions in SAE patients (n = 9) only and presumed it may be the risk factor of the SAE. However, we did not analyze the statistical significance, nor the exact diameter of the veins due to

the small size even though the veins were dilated. Furthermore, there is no record for the factor as dilated pulmonary vein in non-SAE patients (n = 1005), so then we did not investigate it as risk factor between SAE and non-SAE groups statistically.

In general, increased probability of SAE relates to the size of the needle and the coaxial techniques used, since larger needles have an increased risk of involving the pulmonary veins, and the coaxial method increases the risk of contact with the atmosphere after removal of the internal stylet [5,9,17]. On the other hand, no association has been reported concerning the size of the biopsy needle (17-gauge to 23-gauge) or the biopsy methods used, such as fine needle aspiration, core biopsy, and coaxial needle biopsy [12,14,18,19]. We used the same gauge needle (18-gauge) in every biopsy, the non-coaxial method in eight of nine cases with SAEs, and the coaxial method in the remaining case. Our results showed that use of the coaxial needle system is not a risk factor for SAEs (Table 1). In addition, the size of the needle cannot be determined as a risk factor for SAE in our institution.

A multicentric study by Ishii et al. [9] found parenchymal hemorrhage during the procedure may be risk factors for SAEs. We also found that accompanying pulmonary hemorrhage is significantly associated with the occurrence of SAEs (Table 1). Parenchymal hemorrhage may indicate injury of the pulmonary vessels. Alveolar air maybe introduced into the pulmonary vein through the injured venous wall [9]. Furthermore, parenchymal hemorrhage may promote the coughing up of blood that may facilitate the migration of alveolar air into the pulmonary vein as a result of the marked elevation of the pressure gradient [9]. In addition, study by Ishii et al. [9] found that location of the lesion in the lower lobe is another risk factor; the vessels are much larger in the lower lobes than those in other lobes, so then procedures performed in the lower lobe may pose a higher risk of injuring the veins and thereby causing SAE. They also suggested that lower lobar location of the lesion is related to prone position during the procedure because most of the patients with a lesion in the lower lobe were placed in the prone position. Unlike their results, we found that lobar location of the lesion was not significantly associated with SAEs (Table 1). Lesions were located in the upper lobes (n = 5), lower lobes (n = 3), and middle lobe (n = 1). Three patients with a lesion in the lower lobe were
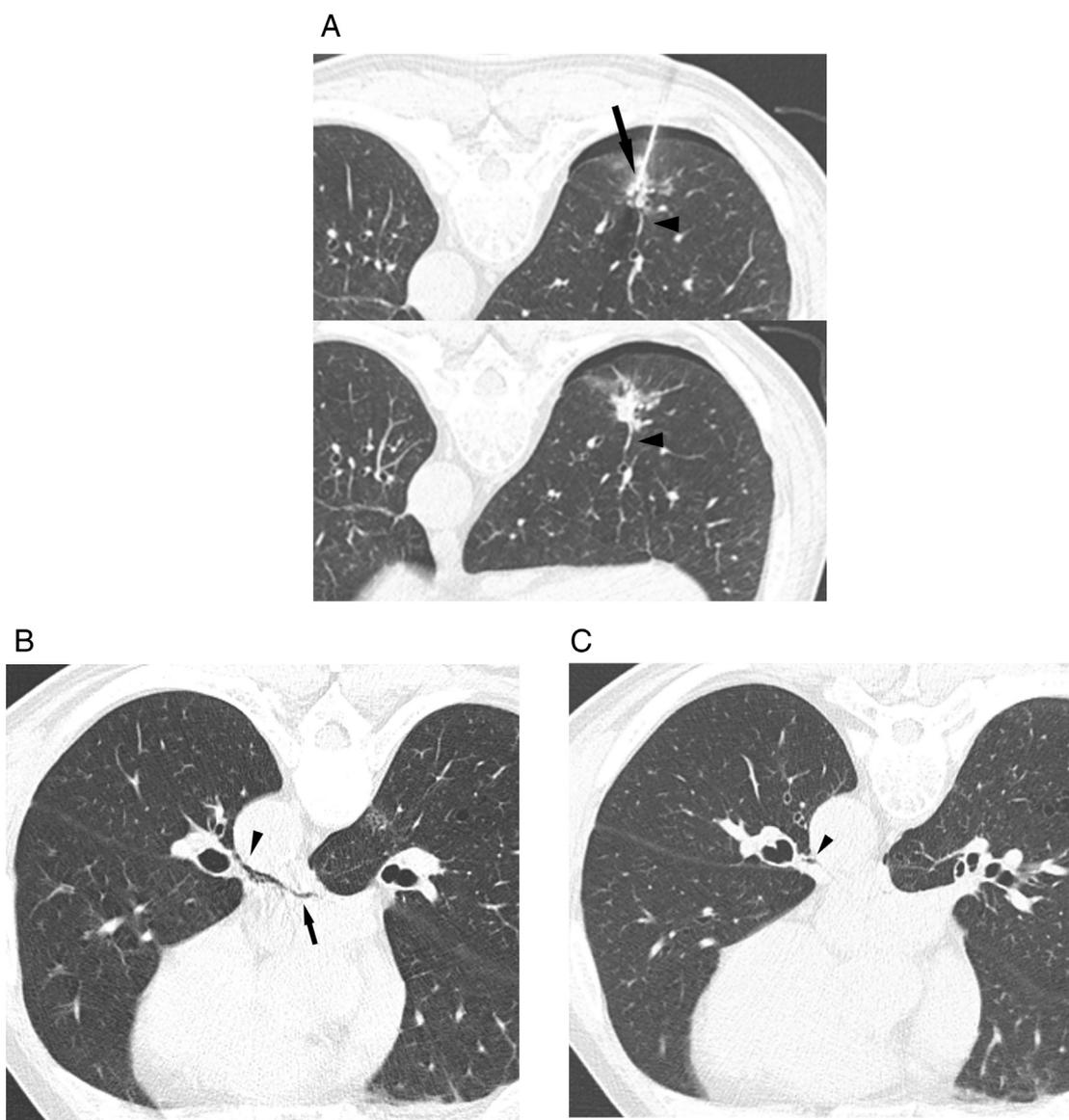
Fig. 3. A 67-year-old man with asymptomatic SAE (case 4) after CT-guided PTNB of 24 mm peripheral solid nodule in right lower lobe. The lesion was proven to be adenocarcinoma.

A. CT image obtained during biopsy with the patient in the prone position shows the pulmonary vein (arrowheads) is locating adjacent to the needle tip (arrow). Note the small pneumothorax.

B and C. Post-biopsy CT images reveal a small amount of air bubbles in left atrium (arrow), extending to left pulmonary vein (arrowheads).

placed in the prone position. Further studies are required to confirm relationship of lobar location and position for risk factor of SAEs.

We found that patient positioning is not significantly associated with the occurrence of SAEs (Table 1). Our result was similar to those of Ishii et al. [9]. However, whether the prone position is a risk factor for SAE is a question of debate [8,9]. Rott et al. [20] reviewed the literature including the studies cited and concluded that the prone position seems to be relevant for the development of SAE and should be considered a risk factor, at least as far as lesions in the lower parts of the lung area are concerned. Some authors [8,19,21] recommended ipsilateral dependent positioning of the patient during PTNB. However, many radiologists prefer, the supine or prone position to the lateral one whenever possible, as prone position is generally considered more stable and consistent [22,23]. Our results showed no association with SAE and position, but seven out of nine patients with SAEs were in the prone position during PTNBs. Further studies with a larger sample size are required to confirm the positional risk factor for SAE.

In several studies with coronary air embolism after PTNB, a correlation between the position of the patient and the location of the air in coronary artery was noted [6,10,24]. In air embolism of right coronary artery cases, patients were supine or left decubitus on the table at the time of biopsy. On the other hand, in air embolism of left coronary artery cases, patients were prone or right decubitus. In the present study, two patients (cases 2 and 3) had air embolism in right coronary artery after PTNB; both were supine. Both patients exhibited no cardiac symptoms, but ECG showed an ST elevation which normalized in 10 min after the application of 100% oxygen.

When asymptomatic SAE is detected on post-biopsy CT imaging, immediate management should be applied to the patient while they are still on the CT table. Vital signs should be monitored during this time and the administration of 100% high-flow oxygen is essential. The optimal position to minimize complication is still debatable. Some authors recommend the right lateral decubitus position and/or Trendelenburg position [12,17,25,26], while others recommend a flat supine position [15,27]. Turning a patient from prone to supine should be avoided as it can facilitate antegrade passage of air [27]. If SAEs

Table 5
Proposed management recommendations for asymptomatic SAE.

Prior PTNB:
Educating patient not to cough and hold breath during or after PTNB
During PTNB:
Radiologist's recognition of risk factors so they can be avoided
After PTNB:
Carefully reviewing the post-biopsy CT on the entire thorax for detection of air bubbles in pulmonary vein, left heart, coronary artery, and aorta
When detecting asymptomatic SAE on post-biopsy CT:
1. Immediate treatment: 100% oxygen administration.
2. Maintain the optimal position: supine with Trendelenburg position or flat prone position, with no repositioning of prone to supine.
3. Check the patient's cardiovascular and neurologic symptoms, vital signs, and/or ECG.
4. Perform the subsequent brain CT to confirm the cerebral SAE.
5. Asymptomatic patient with no cerebral SAE: move to the ward with no positional change and then conservatively treat. If clinically needed, HBOT is received.

were to occur in a patient in a prone position, this position should be maintained. We never changed a patient's position in the present study. If the patient was supine during PTNB, the supine and Trendelenburg position was maintained. If the patient was prone during PTNB, the flat prone position was maintained, because turning a patient from prone to supine can facilitate antegrade passage of air, as mentioned above. Subsequent brain CT was performed while the patient was on the CT table to assess for cerebral SAE. After confirming no cerebral SAE on brain CT, the patient could be moved to the ward with no positional change for conservative therapy with 100% oxygen administration. HBOT is the only proven effective treatment for SAE so far. HBOT not only dissolves the air within embolized bubbles by accelerated nitrogen resorption, but also improves oxygenation of ischemic tissues by providing 100% oxygen at high pressure [15]. However, not all institutions have the facilitiesnecessary to perform HBOT on patients, and conservative therapy with 100% oxygen administration is also effective [9]. HBOT was not available in our institution; one symptomatic and three asymptomatic patients with SAE, except for the first symptomatic case (case 1), were non-fatal with no sequelae. Based partly on our personal experience with nine cases of SAE following a CT-guided PTNB, we proposed a guideline for treating asymptomatic SAEs that will help less experienced chest or interventional radiologists (Table 5).

Our study has some limitations. Before the first case of SAE, limited post-biopsy chest CT scan of only the region biopsied was obtained in 569 PTNB cases. There is the possibility of the presence of air-bubbles in the extra field-of-view region of the thorax in some of these cases. If so, the incidence might have been underestimated. In addition, the incidence of SAE patients was too low to assess statistical risk factors. However, we evaluated risk factors of SAE using univariate statistical analysis only. If more cases are examined, we think a meaningful result can be ultimately obtained. We believe that more useful results will come from statistical studies such as multivariable analysis. Further studies on the relationship between non-SAE cases and SAE cases are needed insofar as nearby dilated pulmonary vein, patient positioning and lobar location.

In summary, SAE following a CT-guided PTNB was encountered more frequently than would be expected, due to radiologically detected asymptomatic SAEs. The location of the needle tip relative to the lesion and accompanying pulmonary hemorrhage were significant risk factors for the occurrence of SAEs. Post-biopsy chest CT scan should include the entire thorax to properly exclude SAE. Radiologists should concentrate on post-biopsy chest CT images for the prompt recognition and management of SAE, even if the patient is asymptomatic. When asymptomatic patients with SAE are detected on post-biopsy CT images, they should be administered 100% high-flow oxygen, and placed in the supine with Trendelenburg position or flat prone position with no repositioning.

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