

P045 Risk of bleeding associated with transbronchial biopsy using flexible bronchoscopy in patients with suspected pulmonary hypertension

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Abstract

Background: The safety of endobronchial ultrasound-guided transbronchial biopsy (EBUS-TBB) in patients with a finding of pulmonary hypertension (PH) is controversial. Little is known about the relationship between the risk of bleeding associated with EBUS-TBB in the presence of PH suspected on echocardiography or chest CT.

Methods: To assess the risk of bleeding associated with EBUS-TBB in patients with presumed PH per echocardiography or chest CT, we retrospectively reviewed the medical records of 314 consecutive patients who underwent EBUS-TBB using a guide sheath (GS), as well as echocardiography and chest CT. A bleeding complication was defined as over one minute of suctioning, repeated wedging of the bronchoscope, instillation of cold saline, diluted vasoactive substances, or thrombin due to persistent bleeding. PH was defined as peak tricuspid regurgitation velocity (TRV) > 2.8 m/s on echocardiography or pulmonary artery to aorta ratio (PA:A ratio) > 0.9 on chest CT.

Results: In total, 35 (11.1%) patients developed bleeding and all cases were managed safely. Furthermore, 17 (5.4%) and 59 (18.8%) patients were suspected to have PH based on echocardiography and chest CT, respectively. Of the patients suspected to have PH on echocardiography, 5 (5/17=29.4%) patients developed bleeding. Of the patients suspected to have PH on chest CT, 11 (11/59=18.6%) patients developed bleeding. Univariate analysis revealed that long diameter (≥ 30 mm) of the lesion, lesion location (biopsy site was inner side than segmental bronchus), bronchoscopic diagnosis of malignancy, and additional biopsy were potential predictive factors of bleeding. The finding of PH on echocardiography correlated significantly with bleeding ($p=0.03$). On multivariate analysis, long diameter of the lesion ($p=0.021$) and finding of PH on echocardiography ($p=0.049$) were significantly associated with bleeding.

Conclusion: PH suspected based on echocardiography may be a risk factor of significant but manageable bleeding associated with EBUS-TBB using a GS.

Competing interests

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Background

- Endobronchial ultrasound (EBUS)-guided transbronchial biopsy (TBB) is an indispensable diagnostic procedure for peripheral lung lesions.¹
- Several previous studies have also reported the usefulness of EBUS with a guide sheath (GS), in which biopsy forceps covered with a GS can be delivered to the lesions under EBUS guidance, and biopsy and brushing specimens can be sequentially obtained by keeping the GS in the lesion.²
- Bleeding associated with EBUS-guided TBB using a GS (EBUS-GS-guided TBB) is rarely reported, but constitutes one of the most serious procedural emergencies in daily practice.
- Reported risk factors for bleeding associated with bronchoscopic procedures include immunosuppression, mechanical ventilation, thrombocytopenia, lung transplant, anticoagulant therapy, antiplatelet therapy, and liver or kidney disease.³
- A few clinical studies examined whether Pulmonary hypertension (PH) increases the risk of bleeding with TBB, but the results were contradictory.^{4,8}
- In daily clinical practice, it is rare to perform TBB on a patient already diagnosed with PH; however, it is not uncommon to see patients who happen to be suspected to have PH based on echocardiography or chest computer tomography (CT) performed prior to TBB.
- Little is known about the relationship between findings of PH on such imaging modalities and the risk of bleeding complications associated with TBB.

Aim

We conducted this retrospective study to assess the risk of bleeding associated with EBUS-GS-guided TBB in patients with suspected PH.

Materials and methods

- We retrospectively reviewed the medical records of 314 consecutive patients with EBUS-GS-guided TBB who underwent echocardiography between six months prior to and one month following bronchoscopy, at the Hokkaido University Hospital, Japan, from January 2018 to June 2020.
- A bleeding complication was defined as over one minute of suctioning, repeated wedging of the bronchoscope, instillation of cold saline, diluted vasoactive substances, or thrombin due to persistent bleeding.
- On echocardiography, we defined a finding of PH as peak tricuspid regurgitation velocity (TRV) > 2.8 m/s in accordance with previous reports.⁹
- On chest CT, we measured the diameter of the main pulmonary artery at the level of its bifurcation and measured the maximum diameter of the ascending aorta using the same images, in keeping with previous literature.¹⁰
- We defined a finding of PH as pulmonary artery to aorta ratio (PA:A ratio) > 0.9 in accordance with previous reports.¹¹



Results

Table 1. Characteristics of patients (n=314)

Characteristic	Value	Characteristic	Value
Age, years		Lesion location ^a	
Median (range)	71 (38-88)	Central	37 (11.8)
<75	222 (70.7)	Peripheral	277 (88.2)
≥ 75	92 (29.3)	Lesion location	
Sex		Right upper lobe	100 (31.8)
Male	192 (61.1)	Middle lobe	22 (7.0)
Female	122 (38.9)	Lower lobe	65 (20.7)
BMI, kg/m ²		Left upper lobe	68 (21.7)
Median (range)	23 (14.3-42.1)	Lower lobe	59 (18.8)
<25	215 (68.5)	Bronchoscopic diagnosis	
≥ 25	99 (31.5)	Lung cancer and other malignancy	182 (58.0)
Smoking		Benign	34 (10.8)
Former	163 (51.9)	Unspecific	98 (31.2)
Current	81 (25.8)	Final diagnosis	
Never	70 (22.3)	Lung adenocarcinoma	159 (50.6)
Antiplatelet agent administration ^a		Lung squamous cell carcinoma	42 (13.4)
Yes	58 (18.5)	Lung small cell carcinoma	12 (3.8)
No	256 (81.5)	Others (malignant)	39 (12.4)
Anticoagulant agent administration ^a		Others (benign)	62 (19.7)
Yes	19 (6.1)	Additional biopsy after GS removal ^c	
No	295 (93.9)	Yes	48 (15.3)
Lesion size (long diameter), mm		No	266 (84.7)
Median (range)	25 (7-92)		
<30	187 (59.6)		
≥ 30	127 (40.4)		

Values are No. (%) or as otherwise indicated. BMI = Body mass index; GS = guide sheath.

^a All cases set a drug holiday in accordance with regulations of our department.

^b Central lesion was defined as the lesion with bronchus sign positive localized inner than segmental bronchus.

^c Additional biopsy using a Radial Jaw 4 Standard Pulmonary Biopsy Forceps® 1.8mm (Boston Scientific, Natick, MA, USA) or a Cryotherapy instrument, ERBE-CRYO2® (ERBE, Tübingen, Germany), with a flexible cryoprobe (1.9 mm diameter and 1.150 mm in length) after GS removal.

Table 2. Complications associated with EBUS-GS-guided TBB

Complication	Value
Bleeding	35 (11.1)
Pneumothorax	7 (2.2) ^a
Infection	2 (0.6)

Values are No. (%) or as otherwise indicated. EBUS-GS-guided TBB = Endobronchial ultrasound with a guide sheath transbronchial biopsy.

^a No case required drainage.

> All cases of bleeding in this study were managed safely, 28 patients were treated with thrombin spray through the working channel and 7 patients were treated with repeated wedging of the bronchoscope.

Table 3. The results of peak tricuspid regurgitation velocity (TRV) in echocardiography and pulmonary artery to aorta ratio (PA:A ratio) in chest CT

	Total (n=314)	Non-bleeding (n=279)	Bleeding (n=35)
Peak TRV, m/s			
Median (range)	2.35 (1.00-4.27)		
Non-suspicious group (≤ 2.8)	297 (94.6)	267 (89.9)	30 (10.1)
Suspicious group (> 2.8)	17 (5.4)	12 (70.6)	5 (29.4)
PA:A ratio			
Median (range)	0.79 (0.50-1.21)		
Non-suspicious group (≤ 0.9)	255 (81.2)	231 (90.6)	24 (9.4)
Suspicious group (> 0.9)	59 (18.8)	48 (81.4)	11 (18.6)

Values are No. (%) or as otherwise indicated.

Table 4. The relationship between clinical factors and bleeding complication

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Age (≥ 75 years)	1.72 (0.83-3.55)	.168		
Sex (male)	0.56 (0.28-1.14)	.140		
BMI (≥ 25 kg/m ²)	1.74 (0.85-3.56)	.176		
Smoking (current or former smoker)	0.96 (0.42-2.23)	1.000		
Antiplatelet agent administration ^a (yes)	0.90 (0.36-2.29)	1.000		
Anticoagulant agent administration ^a (yes)	0.93 (0.21-4.22)	1.000		
Lesion size (≥ 30 mm)	4.34 (2.00-9.40)	< .001	2.78 (1.17-6.62)	.021
Lesion location ^b (central)	5.30 (2.36-11.91)	< .001	2.11 (0.81-5.49)	.125
Lesion location (upper or middle lobe)	1.49 (0.70-3.15)	.361		
Bronchoscopic diagnosis (malignancy)	2.27 (1.03-5.04)	.045	1.30 (0.54-3.14)	.565
Final diagnosis (malignancy)	1.57 (0.59-4.24)	.502		
Additional biopsy after GS removal ^c (yes)	3.52 (1.61-7.69)	.002	2.27 (0.96-5.41)	.063
TRV (> 2.8 m/s)	3.71 (1.22-11.25)	.030	3.44 (1.01-11.74)	.049
PA:A ratio (> 0.9)	2.21 (1.01-4.80)	.063		

BMI = Body mass index; GS = guide sheath; TRV = tricuspid regurgitation velocity; PA:A ratio = pulmonary artery to aorta ratio.

^a All cases set a drug holiday in accordance with regulations of our department.

^b Central lesion was defined as the lesion with bronchus sign positive localized inner than segmental bronchus.

^c Additional biopsy using a Radial Jaw 4 Standard Pulmonary Biopsy Forceps® 1.8mm (Boston Scientific, Natick, MA, USA) or a Cryotherapy instrument, ERBE-CRYO2® (ERBE, Tübingen, Germany), with a flexible cryoprobe (1.9 mm diameter and 1.150 mm in length) after GS removal.

Conclusions

- All cases of bleeding in the present study were managed safely.
- The risk of bleeding is moderately elevated when PH is suspected by echocardiography in patients undergoing EBUS-GS-guided TBB.

References

- Rivera MP, et al. Chest. 2013;143:e1425-e1655.
- Kikuchi E, et al. Eur Respir J. 2004;24:533-537.
- Bernasconi M, et al. ERJ Open Res. 2017;3:00084-2016.
- Waisdi MM, et al. Respiration. 2005;72:266-265.
- Diaz-Guzman E, et al. Respiration. 2009;77:292-297.
- Diaz-Fuentes G, et al. Respiration. 2016;92:182-187.
- Ishiwata T, et al. Respir Investig. 2019;57:73-78.
- Lashari BH, et al. Cureus. 2020;12:e9004.
- Sumimoto K, et al. Circ Res. 2020;23:625-629.
- Wells JM, et al. N Engl J Med. 2012;367:913-921.
- Yagi M, et al. Respirology. 2017;22:1393-1399.