Risk factors for pulmonary hemorrhage following ultrasound-guided percutaneous biopsy of peripheral lung lesions

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Lung cancer is a leading cause of cancer-associated death worldwide, and the morbidity and mortality of lung cancer have increased over the past few decades. Imaging techniques are limited in providing a definitive diagnosis, which requires a tissue sample for pathologic evaluation. Adenocarcinomas account for 40% of all lung cancers and tend to occur peripherally in the lung,[1] making them amenable to ultrasound-guided percutaneous biopsy for pathologic diagnosis. Peripheral lung cancers are usually close to the pleura, enabling ultrasound to clearly show the internal structure of the lesion, its blood supply, and its relationship with surrounding tissues.

Although ultrasound-guided transthoracic cutting needle biopsy is considered a safe and efficient method for obtaining a definitive pathologic diagnosis, the technique is associated with several complications, including air embolism, pneumothorax, pulmonary hemorrhage, and tumor seeding.[1] Severe hemoptysis can necessitate endobronchial tamponade, arterial embolization, or surgery and can be life-threatening.[2] Data regarding the risk factors for pulmonary hemorrhage after ultrasound-guided percutaneous lung biopsy are scarce.

The purpose of this study was to identify risk factors associated with pulmonary hemorrhage following ultrasound-guided transthoracic needle biopsy of peripheral lung lesions. This retrospective analysis included patients who underwent ultrasound-guided transthoracic needle biopsy between June 2010 and June 2016 at the Department of Ultrasound, the First Affiliated Hospital of Guangxi Medical University, China. This study was approved by the Ethics Committee of The First Affiliated Hospital of Guangxi Medical University [No. 2021(KYE-199)], and the requirement to obtain informed consent was waived because of the retrospective design. The inclusion criteria were (1) chest X-ray, magnetic resonance imaging

(MRI), or computerized tomography (CT) showing peripheral lung lesions, (2) the lesions were focally adherent to the pleura, (3) the patient underwent ultrasound-guided transthoracic needle biopsy, and (4) all data required for the analysis, including relevant images, reports, and pathologic diagnosis, were available from the medical records. The exclusion criteria were (1) severe lung and/or heart dysfunction, (2) severe arrhythmia, (3) susceptibility to bleeding, and (4) unable to undergo ultrasound-guided transthoracic needle biopsy due to cough or hemoptysis.

The biopsy procedure was the same as that described in a previous study.[3] All procedures were performed by two radiologists experienced in ultrasound diagnosis and proficient in percutaneous lung biopsy techniques. First, sonography was performed with reference to the chest CT data to investigate the sizes, locations, and sonographic features of the pulmonary lesions. The examinations were performed using Logiq E9 (GE Healthcare, Waukesha, WI, USA) or AcusonS2000 (Siemens, Erlangen, Germany) with a convex array probe at 2.5–4.0 MHz or 3.5–5.5 MHz, or a Preirus or EUB6500 ultrasound diagnostic instrument, special puncture probe with a frequency of 1–5 MHz or 2–5 MHz (model EUP-B715 or EUB6500) (Hitachi, Tokyo, Japan). The lesions were measured using the maximum diameter of superficial to deep lesions on sagittal sectional ultrasound images. The biopsy procedure was performed under ultrasound guidance using the Hitachi Preirus ultrasound system and Logiq E9 3.5–5.0 MHz convex-array probe. Color Doppler imaging was routinely used to delineate large vessels and abnormal arteries so that the operator could avoid puncturing them during the biopsy. Classification of blood flow in peripheral lung lesions was based on the Adler blood flow classification. Biopsy was performed using an 18-gauge automatic cutting needle (Bard Magnum Biopsy Instrument; Covington, GA, USA).

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After careful planning, the skin was sterilized, and 2% lidocaine (Yimin, Yichang, China) was applied for local anesthesia.

The following clinical data were extracted from the medical records: age, sex, absence/presence of bronchus sign, target lesion position, target lesion size (longest diameter), target lesion blood flow, number of punctures during the biopsy, and lesion pathologic characteristics. Target lesion size was categorized as small (longest diameter ≤2 cm), intermediate (>2 cm and ≤5 cm), or large (longest diameter >5 cm). Target lesion position was categorized as left upper lung, left lower lung, right upper lung, right middle lung, or right lower lung. Target lesion blood flow was categorized as rich or poor according to the characteristics of the color blood flow signals of the peripheral lung lesions.[4] Based on the pathology results, the lesion was defined as malignant tumor, benign tumor, or inflammatory disease.

All patients were followed up for 1 week after the biopsy, with careful monitoring for complications, such as chest pain, shortness of breath, or hemoptysis. According to the patient's symptoms and blood routine judgment after a needle biopsy, if the patient presented with chest pain, dyspnea, hemoptysis, hemoglobin decline, and other conditions, and suspected complications, such as pneumothorax and hemothorax, CT examination was performed to confirm the diagnosis. Pulmonary hemorrhage was defined as new ground-glass opacities on post-biopsy CT imaging (indicating alveolar hemorrhage), hemoptysis, bloody sputum, or hemothorax necessitating intervention.

Statistical analysis was performed using SPSS 21.0 (IBM, Armonk, NY, USA). The patients were grouped according to pulmonary hemorrhage. Data were presented as n (%) and compared between groups using the Chi-square test or Fisher's exact test. Binary logistic regression analyses were performed to identify factors independently associated with pulmonary hemorrhage. Variables with $P < 0.05$ in univariable analysis were entered into the multivariable logistic regression analysis using the forward (likelihood ratio) method, and odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated. $P < 0.05$ was considered to indicate a statistically significant difference.

A total of 914 patients (661 men, 72.32%) aged 54.27 ± 14.44 years (range, 14–87 years) were included in the final analysis. The range of the target lesion size was 7–138 mm. Four hundred and twelve patients were diagnosed with a malignant lesion by pathology (45.08%). A benign tumor was diagnosed in 76 patients (8.32%), and an inflammatory lesion was found in 426 patients (46.61%).

Post-biopsy pulmonary hemorrhage occurred in 105 patients (11.49%), including hemoptysis in 35 patients (3.83%), bloody sputum in 28 patients (3.06%), hemothorax in 2 patients (0.22%), and alveolar hemorrhage (diagnosed by post-biopsy CT) in 40 patients (4.38%). Representative sonographic images from a patient who experienced hemoptysis during biopsy and a patient who experienced hemothorax during the biopsy are presented

in Supplementary Figure 1, http://links.lww.com/CM9/A777. All patients with postoperative hemorrhage recovered after symptomatic treatment.

The clinical characteristics of the patients in the two groups (those with pulmonary hemorrhage during/after biopsy and those without pulmonary hemorrhage during/after biopsy) are shown in Supplementary Table 1, http://links.lww.com/CM9/A777. Patients with post-biopsy pulmonary hemorrhage had a significantly higher proportion of smaller lesions ($\chi^2 = 25.365$, $P < 0.001$), and a significantly higher proportion of lesions with a rich blood supply ($\chi^2 = 10.811$, $P = 0.001$).

The multivariable analysis revealed that lesion size (OR, 0.418; 95% CI: 0.298–0.588; $P < 0.001$) and a rich blood supply to the lesion (OR, 2.238; 95% CI: 1.363–3.247; $P = 0.001$) were independently associated with pulmonary hemorrhage.

In this study, pulmonary hemorrhage was observed in 105 of 914 patients who underwent ultrasound-guided lung biopsy (11.49%), which is consistent with the finding of Yildirim et al.[5] However, the incidence of pulmonary hemorrhage in our study was significantly lower than that reported previously for CT-guided lung biopsy (19.6–45.4%).

Among the 105 patients with pulmonary hemorrhage after biopsy, pathologic examination demonstrated a malignant tumor in 41 patients (39.05%), an inflammatory lesion in 57 patients (54.29%), and a benign tumor in seven patients (6.67%). Inflammatory lesions can exhibit intralesional vascular remodeling and increased collateral circulation, while malignant tumors can contain a substantial number of newly generated vessels. Therefore, these lesion types are particularly susceptible to puncture-induced vascular damage and pulmonary hemorrhage, resulting in hemoptysis, bloody sputum, and hemothorax.

Lesion size was negatively related to post-biopsy pulmonary hemorrhage. Before and during ultrasound-guided lung biopsy, color Doppler flow imaging was used to evaluate the lesion, the optimal puncture approach was determined according to the blood flow in the lesion, and puncture was performed to avoid the major vessels, which may have minimized the incidence of pulmonary hemorrhage. For the prevention of hemorrhage in small lesions, real-time ultrasound monitoring should be performed during the whole process. When the tip is not clearly displayed, the path should be adjusted properly until the tip is clearly displayed. The needle can be inserted at a large angle or in a direction parallel to the chest wall, and the sampling at the oblique diameter of the lesion can increase the sampling volume and reduce the number of passes.

There is a higher risk of damage and hemorrhage with an increased number of needle passes. The largest number of punctures in our study was 4, but there was no significant difference in the incidence of pulmonary hemorrhage between patients with a single puncture, two or three punctures and those with four punctures. It indicates that biopsies avoiding major vessels or lesions with a positive

bronchus sign are safe if the number of passes is four or fewer. In the present study, lesion location, bronchus sign, age, and gender were not related to pulmonary hemorrhage after lung biopsy.

Although ultrasound-guided biopsy of peripheral lung lesions is a highly useful tool for diagnosing lung cancer, it is nonetheless associated with some complications, including pulmonary hemorrhage. Based on our findings, we speculate that the following measures may be helpful to reduce the risk of pulmonary hemorrhage after biopsy: (1) clinicians should communicate effectively with patients to reduce their anxiety; (2) the disease condition should be carefully evaluated before biopsy, and indications and contraindications should be applied; (3) the depth of puncture should be strictly controlled, and the distance between the needle tip and lesion center should be shorter than the depth of puncture to help avoid puncture through the back wall of the lesion and pulmonary hemorrhage; and (4) care should be taken to avoid blood vessels during puncture, particularly for lesions with a rich blood supply. Small-amount hemoptysis or phlegm with blood filaments can stop by itself. If the amount of bleeding is large and the hemoglobin is decreased, hemostatic drugs should be used. If hemoglobin is still decreased after hemostatic drug use, surgical treatment should be performed.

In conclusion, we have found that rich lesion blood supply and small lesion size are factors associated with pulmonary hemorrhage during or after ultrasound-guided biopsy of peripheral lung lesions. These findings may help to reduce the risk of pulmonary hemorrhage during and after lung biopsy and improve technical safety.

Conflicts of interest

None.

References

1. Winokur RS, Pua BB, Sullivan BW, Madoff DC. Percutaneous lung biopsy: technique, efficacy, and complications. Semin Intervent Radiol 2013;30:121–127. doi: 10.1055/s-0033-1342952.
2. Tai R, Dunne RM, Trotman-Dickenson B, Jacobson FL, Madan R, Kumamaru KK, et al. Frequency and severity of pulmonary hemorrhage in patients undergoing percutaneous CT-guided transthoracic lung biopsy: single-institution experience of 1175 cases. Radiology 2016;279:287–296. doi: 10.1148/radiol.2015150381.
3. Wang S, Yang W, Zhang H, Xu Q, Yan K. The role of contrast-enhanced ultrasound in selection indication and improveing diagnosis for transthoracic biopsy in peripheral pulmonary and mediastinal lesions. Biomed Res Int 2015;2015:231782. doi: 10.1155/2015/231782.
4. Adler DD, Carson PL, Rubin JM, Quinn-Reid D. Doppler ultrasound color flow imaging in the study of breast cancer: preliminary findings. Ultrasound Med Biol 1990;16:553–559. doi: 10.1016/0301-5629(90)90020-d.
5. Yildirim E, Kirbas I, Harman A, Ozyer U, Tore HG, Aytekin C, et al. CT-guided cutting needle lung biopsy using modified coaxial technique: factors effecting risk of complications. Eur J Radiol 2009;70:57–60. doi: 10.1016/j.ejrad.20*08.01.006.