A prospective study of selective pleural blood patching for pneumothorax due to computed tomography-guided percutaneous lung biopsy

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Research article

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Abstract

**Background:** We conducted a prospective study to investigate the efficacy of pleural blood patching to reduce the need for chest tube placement in pneumothorax of CT-guided percutaneous lung biopsy.

**Methods:** We enrolled each 77 patients in study and control groups. If the patient of study group developed pneumothorax ≥ 1 cm on post-biopsy CT, we drew 15 mL blood, then performed simple aspiration followed by pleural blood patching. In control group, we performed only simple aspiration or no interventions.

**Results:** Of the 77 patients of study group, 41 developed pneumothorax, 9 of which were ≥ 1 cm, and 8 patients underwent pleural blood patching. None of these 8 patients (0%) required chest tube placement. In comparison between study group and control group, pleural blood patching reduced the chest tube insertion rate from 23.1% to 11.1% in patients pneumothorax ≥ 1 cm, but not statistically significant (p=0.26)

**Conclusion:** Selective pleural blood patching reduced chest tube insertion rate in patients pneumothorax ≥ 1 cm, large-scale studies are warranted to confirm the result.

**Trial registration:** This study was registered in the UMIN Clinical Trials Registry (trial number: 000007586).

Background

CT-guided percutaneous lung biopsy is an established technique with a sensitivity of 85.7–93% for the diagnosis of suspected pulmonary malignancy [1–3]. Pneumothorax is the most common adverse event of this procedure, occurring in 24.3–54% of cases [1–4], 0.2–19% of which require temporal drainage or chest tube placement to manage the pneumothorax. Among the methods attempted to reduce the rate of drainage are manual aspiration immediately after development of complicated pneumothorax, breath-holding after forced expiration before biopsy needle removal, and rapid rotation to the biopsy-side-down position after biopsy [5–7]. Pleural blood patching is also reported to be a useful and safe method for pneumothorax and persistent pulmonary air leak after lung surgery [8–11]. However, it remains controversial whether routine pleural blood patching for all patients receiving CT-guided percutaneous lung biopsy can reduce the need for chest tube placement in pneumothorax. To date, four studies have concluded that routine pleural blood patching was useful [12–15], while another two reported that it was not useful [16, 17]. In addition, a retrospective study reported that selective pleural blood patching for patients with post-biopsy pneumothorax alone avoided further intervention and was associated with a significantly higher success rate than simple aspiration [18].

We conducted a prospective study to investigate the efficacy and safety of selective pleural blood patching to reduce the need for chest tube placement in pneumothorax caused by CT-guided percutaneous lung biopsy.
Methods

Subjects

This study was approved by the institutional review board of Toranomon Hospital (No. 575 and 1880) and was registered in the UMIN Clinical Trials Registry (trial number: 000007586). All procedures performed in this study were in accordance with the ethical standards of the institutional with the 1964 Helsinki declaration. All patients of study group provided written informed consent, and of control group were presented in the form of opt-out on the web-site.

Concerning study group, a prospective clinical study was conducted in our hospital from April 2012 to October 2013 at the end of case accumulation. In total, 77 patients scheduled for percutaneous CT-guided biopsy of lung lesions were enrolled. Patients were included if they were scheduled for CT-guided lung biopsy for lung lesions of undetermined cause. Exclusion criteria were the inability to obtain blood for patching, suspected active infectious lung disease, or if the patient was deemed inappropriate for the study by a physician. Active infectious lung diseases were excluded because empyema has been reported to be the most frequent adverse event of pleural blood patching for spontaneous pneumothorax with persistent air leak [19].

Control group included 77 sequential patients form September 2010 to June 2011 before introduction of pleural blood patching, who received CT-guided percutaneous lung biopsy of lung lesions. If they had pneumothorax after CT-guided percutaneous lung biopsy, they received simple manual aspiration or just be observed.

Procedure

Chest CT scans (slice thickness, 3 mm) were performed with an Aquilion S16 or 64 system (Toshiba Medical Systems, Ohtawara, Japan) before the procedure. CT-guided percutaneous lung biopsy was carried out with the patients in the supine or prone position, depending on the proximity of the lesion to the chest wall. After administering 1% lidocaine solution for local anesthesia, we made a small incision to facilitate entry of the 17-gauge guide needle of the co-axial system (Co-Axial Introducer Needle, Medical Device Technologies, Gainesville, FL), which was used for all coaxial biopsies. The cutting needle was inserted through the 17-gauge guide needle. Core biopsy was performed with an 18-gauge needle (Super Core Biopsy Instrument, Medical Device Technologies). Chest CT was performed immediately after removing the needle to check for pneumothorax or hemorrhage. If the patient developed pneumothorax ≥ 1 cm (maximum vertical distance between viscera and parietal pleura), which was considered as the minimal depth for intervention as observed on post-biopsy CT, we drew 15 mL peripheral blood. We inserted the introducer needle into the pleural space of the pneumothorax and performed simple aspiration [5], followed by intrapleural instillation of autologous blood (pleural blood patching). All 77 patients lay quietly in a supine position for at least 1 hour after biopsy before undergoing chest radiography. If moderate to severe pneumothorax remained, the treating physician performed chest tube
All patients were followed for a minimum of 1 week after CT-guided percutaneous lung biopsy.

**Data Collection**

The presence of chronic lung diseases, such as emphysema and interstitial pneumonia, the location, form, and long-axis size of the lesion, and its depth from the pleura were collected from imaging data. A lung mass was defined as an opacity ≥3 cm in long-axis diameter and a nodule as an opacity <3 cm in diameter. The number of passes, presence of pneumothorax, placement of a chest tube, and pathological and final diagnoses were determined by checking the medical records and pathological records for CT-guided percutaneous lung biopsy, surgery, and bronchoscopy. And, for investigating the effects of autologous pleural blood patching for surgery, we surveyed presence of adhesions and amount of blood loss of surgeries in pleural blood patching and control groups.

**Statistical Analysis**

For assuming a rate of chest tube placement after autologous blood patching, the estimated ratio (proportion) was defined as 13.6% and the threshold ratio (null proportion) was defined as 53.6% [18]; with a two-sided significance level of 0.05 and 90% power, the estimated accrual was 14 patients receiving pleural blood patching. Assuming a rate of 20% as pneumothorax requiring pleural blood patching after CT-guided TNB and adding 7 patients as possible deviation, we calculated that 77 patients were required for study group of this trial.

The primary endpoint was the rate of chest tube placement after autologous pleural blood patching. The secondary endpoints were the rate of pneumothorax associated with CT-guided percutaneous lung biopsy and the safety of the procedure. Statistical analysis was performed by SPSS ® v23 (SPSS Statistics, Chicago, IL). Fisher’s exact test, Chi-Square test and Wilcoxon signed-rank test were used for univariate analysis to compare study group and control group.

**Results**

Patient characteristics are summarized in Table 1. A total of 77 CT-guided percutaneous lung biopsy procedures were enrolled and performed in 77 patients in study group. No cases were excluded. Underlying diseases were emphysema in 19 patients and interstitial pneumonia in 10. Although CT-guided percutaneous lung biopsy passes of control group couldn't be collected because of retrospectivity, there were no statistical difference patients’ characteristic between study group and control group.
Table 1
Patient and Lesion Characteristics in study and control group

| Characteristic                              | Study group (N = 77) | Control group (N = 77) | P value |
|---------------------------------------------|---------------------|------------------------|---------|
| Sex, n                                      | Male                | 51                     | 50      | 0.342   |
|                                             | female              | 26                     | 27      |         |
| Age, years                                  | median (range)      | 69 (33–83)             | 69 (28–90) | 0.489   |
| Underlying disease, n                       | emphysema           | 19                     | 22      | 0.548   |
|                                             | interstitial        | 10                     | 8       | 0.587   |
|                                             | pneumonia           |                        |         |         |
| Lesion size, mm                             | median (range)      | 29 (4–94)              | 34 (10–123) | 0.458   |
| Lesion depth, mm                            | median (range)      | 10 (0–45)              | 5 (0–54) | 0.081   |
| Lesion location, n                          | right upper lobe    | 22                     | 23      | 0.604   |
|                                             | right middle lobe   | 7                      | 5       |         |
|                                             | right lower lobe    | 16                     | 19      |         |
|                                             | left upper lobe     | 18                     | 19      |         |
|                                             | left lower lobe     | 14                     | 11      |         |
| Lesion form, n                              | Nodule              | 40                     | 39      | 0.610   |
|                                             | Mass                | 33                     | 37      |         |
|                                             | consolidation       | 4                      | 1       |         |
| CT-guided percutaneous lung biopsy passes, n| median (range)      | 4 (1–9)                | NE      | NE      |

Regarding on study group, of the 41 patients (53.2%) who developed pneumothorax, 9 had pneumothorax ≥ 1 cm, 8 of whom underwent pleural blood patching (Fig. 1). The characteristics of the 8 patients were summarized in Table 2. None of these 8 patients (0%) required chest tube placement (the primary endpoint). Only 1 of 9 (11.1%) had pneumothorax ≥ 1 cm received chest tube insertion. The single patient who did not receive pleural blood patching, because we could not insert the introducer needle into the pleural space hidden behind a rib, required chest-tube placement. No adverse events due to pleural blood patching were observed (the secondary endpoint). Of the 32 patients who developed
pneumothorax < 1 cm, 3 also required chest tube placement. The overall chest tube insertion was a rate of 5.2% (4/77) (the secondary endpoint). All occurrences of pneumothorax improved within a few days, and no new cases of pneumothorax had developed by the day after CT-guided percutaneous lung biopsy.

### Table 2
Characteristics of 8 patients receiving blood patching

| Characteristic                              |   |
|--------------------------------------------|---|
| Sex, n                                      |   |
| Male                                       | 5 |
| female                                     | 3 |
| Age, years                                 |   |
| median (range)                             | 64.5 (33–78) |
| Underlying disease, n                      |   |
| emphysema                                  | 3 |
| interstitial pneumonia                     | 1 |
| Lesion size, mm                            |   |
| median (range)                             | 18 (4–31) |
| Lesion depth, mm                           |   |
| median (range)                             | 10 (3–19) |
| Lesion location, n                         |   |
| right upper lobe                           | 2 |
| right middle lobe                          | 0 |
| right lower lobe                           | 2 |
| left upper lobe                            | 2 |
| left lower lobe                            | 2 |
| Lesion form, n                             |   |
| Nodule                                     | 8 |
| Mass                                       | 0 |
| consolidation                              | 0 |
| CT-guided percutaneous lung biopsy passes, n |   |
| median (range)                             | 3 (2–4) |

As for control group, of the 43 patients (55.8%) who developed pneumothorax, 13 (16.9%) had pneumothorax ≥ 1 cm. 3 of these 13 patients (23.1%) having pneumothorax ≥ 1 cm, 1 of 30 (3.3%) patients having pneumothorax < 1 cm were required chest tube placement (Fig. 1). The overall chest tube insertion of control group was a rate of 5.2% (4/77).

In comparison between study group and control group, pleural blood patching reduced the chest tube insertion rate from 23.1–11.1% in patients pneumothorax ≥ 1 cm, but not statistically significant ($p = 0.26$). In addition, there were no statistical difference in overall chest tube insertion rate between study group and control group (5.2% vs 5.2%, $p = 1.000$).
Adverse events of CT-guided percutaneous lung biopsy aside from pneumothorax in study group were minor amounts of blood in the sputum in 20 patients (26.0%), 2 (2.6%) of whom were given an intravenous infusion of hemostatic medicine, and air embolism and cough in 1 case each.

In terms of surgery after pleural blood patching, 6 of 8 patients received surgery. Adhesions at first glance of surgery was seen in 2 of 6 (33.3%) patients, and median amount of blood loss was 100 (0-260) ml. As for control group, 13 of 77 patients received surgery after CT-guided percutaneous lung biopsy. Adhesions was seen in 8 of 13 (51.5%) patients, and median amount of blood loss was 150 (0-947) ml.

**Discussion**

In study group, 8 patients underwent pleural blood patching for ≥1-cm pneumothorax due to CT-guided percutaneous lung biopsy. None of 8 patients who received pleural blood patching required chest tube placement. The pleural blood patching reduced the chest tube insertion rate from 23.1–11.1% in patients pneumothorax ≥ 1 cm, but not statistically significant. There were no adverse events due to pleural blood patching. The pleural blood patching might not increase adhesions and blood loss during surgery after CT-guided percutaneous lung biopsy.

Temporal drainage or chest tube placement is required in 0.2–19% of patients who develop pneumothorax as an adverse event of CT-guided percutaneous lung biopsy [1–4]. Several procedures have been used in an attempt to reduce the occurrence of pneumothorax due to CT-guided percutaneous lung biopsy and the need for chest tube placement, with varying degrees of success. Breath-holding after forced expiration before removing the biopsy needle was reported to almost halve the rate of overall pneumothorax, but could not reduce the rate of chest tube placement [7]. Rapid needle-out, patient-rollover to the biopsy-side-down position not only reduced the rate of overall pneumothorax, from 37–23%, but also the rate of pneumothorax necessitating chest tube placement, from 10–4% [6]. Percutaneous manual aspiration of pneumothorax performed immediately after CT-guided percutaneous lung biopsy may prevent progressive pneumothorax and may lower the rate for chest tube placement to 3.2% [5].

Routine or selective pleural blood patching after CT-guided biopsies has also been reported. To investigate the effectiveness of this strategy, we divided the results of prospective studies on routine pleural blood patching into advantages and disadvantages. In terms of the advantages, Malone et al [13] showed that pleural blood patching reduced the rate of pneumothorax requiring chest tube replacement from 18–9% in patients receiving CT-guided biopsy, while Lang et al [12] reported a decrease in the rate of routine pleural blood patching from 47–9% in patients with deep lesions. Clayton et al [14] registered 434 CT-guided biopsy cases over 6 years, and presented decrease in the rate of pneumothorax requiring chest tube replacement from 16–4%. Finally, Graffy et al [15] retrospectively compared 472 patients with pleural blood patching after CT-guided biopsy and 352 patients without pleural blood patching, and showed pleural blood patching decrease the pneumothorax intervention rate including pleural blood patching from 24.1–8.9%. In contrast, two studies have shown that routine pleural blood patching was
not effective for decreasing the rates of pneumothorax and chest tube insertion after CT-guided biopsy [16, 17]. Recently, Huo et al [20] conducted a systematic review and meta-analysis to evaluate how to reduce pneumothorax after CT-guided biopsy, and showed the pleural blood patching reduced chest tube insertion rate to approximately one third. In terms of selective pleural blood patching, Wagner et al [18] reported in a retrospective study that, compared with simple aspiration, the rate of chest tube insertion and further interventions decreased from 53.3–13.6% ($p = 0.03$) for patients with significant pneumothorax after CT-guided percutaneous lung biopsy. This result motivated us to perform the present prospective study. But, the results of our study couldn't reach statistically significant, further cases were warranted to confirm the result. From a different perspective, selective pleural blood patching was more cost-effective than routine pleural blood patching, so might be a choice for patients pneumothorax $\geq 1$ cm after CT-guided.

The most common complication of pleural blood patching is empyema. Cagirici et al [19] administered 50 ml autologous blood for blood patching to patients with persistent air-leak spontaneous pneumothorax, and empyema developed in 3 cases (9%). Based on their report, we planned to exclude patients with active infectious lung disease from the present study, but no cases were excluded as a result. However, empyema has not been reported as an adverse event in studies of pleural blood patching for pneumothorax due to CT-guided percutaneous lung biopsy [12, 13, 16–18], possibly because of the small amounts of blood (< 15 ml) used in those studies. Therefore, in general, it is probably unnecessary to exclude patients with active infectious lung disease, but this should be examined in future studies.

Our study has several limitations. First and foremost ones were a single-center study and small number of patients with intervention. In addition, if we had also used the breath-holding after forced expiration before removing the biopsy needle [7] and/or rapid rotation of the patient to the biopsy-side-down position [6], we may have further reduced the rate of chest tube placement. The efficacy of these combined approaches warrants further study.

**Conclusions**

Our study showed possibility of reducing chest tube insertion rate in patients pneumothorax $\geq 1$ cm by selective pleural blood patching. Large-scale studies are warranted to confirm the result.

**List Of Abbreviations**

Computed tomography (CT)-guided percutaneous lung biopsy

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the institutional review board of Toranomon Hospital (No. 575 and 1880) and was registered in the UMIN Clinical Trials Registry (trial number: 000007586).
Date of registration

03/27/2012

URL of trial registry record

https://upload.umin.ac.jp/cgi-open-bin/ctr/ctr.cgi?
function=brows&action=brows&type=summary&recptno=R000008882&language=J

Consent for publication

All patients of study group provided written informed consent, and of control (no intervention) group were presented in the form of opt-out on the web-site. Opt-out method in retrospective study is legally accepted in Japan.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request due to the regulation by the institutional review board of Toranomon Hospital.

Competing interests

The authors have no potential conflict of interest related to this article.

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Authors’ contributions

HU; Conceptualization-Lead, Writing-original draft-Lead
HT; Project administration-Supporting
SM; Formal analysis-Lead
YT; Methodology-Lead
KO; Validation-Lead
KM; Supervision-Lead
SH; Visualization-Lead
AM; Investigation-Lead
NM; Project administration-Lead
All authors read and approved the final manuscript.

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**Figures**
Figure 1

Flow of Patients through the Study

Supplementary Files

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