

Safety of bronchoscopy in patients with hematologic disorders

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Abstract

Background: To evaluate the safety of bronchoscopy and describe factors affecting its complication rate in patients with hematologic disorders.

Methods: Between January 2009 and December 2018, 316 bronchoscopies in 282 patients with hematologic disorders and pulmonary lesions were performed at our institution. The bronchoscopic procedure used and its complications were evaluated.

Results: The most common underlying disease was acute myeloid leukemia (134/282 patients, 47.5%). Platelet transfusion was performed the day before or the day of bronchoscopy in 42.4%, supplemental oxygen was administered before the procedure in 23.1%, and midazolam was used in 74.4%. Two patients (0.6%) were intubated within 48 hour of the procedure and prolonged oxygen desaturation (>48 hour) occurred in 3.8%. Multivariate analysis showed that only use of midazolam significantly reduced the risk of prolonged oxygen desaturation ($p = 0.01$, hazard ratio 0.23, 95% confidence interval 0.07–0.75).

Conclusions: Bronchoscopy is relatively safe in patients with hematologic disorders. Sedation with midazolam may reduce the risk of prolonged oxygen desaturation.

Background

Pulmonary complications occur in up to 40–60% of patients with hematologic diseases and have a considerable influence on morbidity and mortality [1]. These complications include infiltration of underlying disease, opportunistic infections, and various pulmonary lesions after hematopoietic stem cell transplantation (HSCT), such as idiopathic pneumonia syndrome. Several studies have demonstrated the utility of bronchoscopy in patients with hematologic disorders [2–6], but the factors affecting the safety of bronchoscopy in such patients have not been well described. Here, we evaluated the safety of bronchoscopy at our institution and its complication rate with the aim of elucidating these factors.

Subjects And Methods

Subjects

The institutional review board of our Hospital approved this study (No. 1845). This retrospective study involved patients with hematologic disorders and pulmonary lesions who underwent bronchoscopy between January 2009 and December 2018 in a fully equipped endoscopy room in the Department of Respiratory Medicine, Toranomon Hospital, Tokyo, Japan. Bronchoscopies performed in another ward or in the intensive care unit were excluded from the analysis. The need for bronchoscopy was discussed at weekly multidisciplinary team meetings that included hematologists, infectious diseases specialists, and pulmonologists. Bronchoscopy was contraindicated in patients with severe disseminated intravascular

coagulation or bleeding tendency. The bronchoscopic procedure used and its complications were evaluated.

Bronchoscopy Procedure

Chest computed tomography was performed using an Aquilion 16 or 64 system (Toshiba Medical Systems, Otawara, Japan) before bronchoscopy. The bronchoscopic procedures were performed using a 4.9-mm bronchoscope (LTF-260; Olympus, Tokyo, Japan). All patients inhaled 5 mL nebulized 1% lidocaine solution before the procedure, and lidocaine was applied transbronchially during the procedure. Use of midazolam for sedation during bronchoscopy at our institution was started primarily from the beginning of 2011, which was in the middle of the study period. All procedures were performed by pulmonologists. Bronchoalveolar lavage was performed using 100–150 mL of normal saline at room temperature and bronchial washing was performed with 10–50 mL of saline. All patients were placed in the supine position for at least 1 h after biopsy before undergoing chest radiography. The attending physician then evaluated the severity of pneumothorax and the need for placement of a chest tube.

Statistical Analysis

Univariate analysis was performed using Fisher's exact test and the Mann-Whitney *U* test and multivariate analysis using multiple logistic regression. Variables with a p-value <0.2 in the univariate analysis were entered into the multivariate analysis by the variable increase method. All statistical analyses were performed using SPSS statistical software (version 18.0, IBM Corp., Armonk, NY).

Results

A total of 207 men and 75 women of median age 61 years were included in this study. Bronchoscopy was performed twice in 30 patients and 3 times in 2 patients, giving a total of 316 bronchoscopies in 282 patients. The most common underlying disease was acute myeloid leukemia (AML) including myelodysplastic syndromes (MDS)-overt AML ($n = 134$, 47.5%). One hundred and thirty-two patients had undergone HSCT (cord blood transplantation, $n = 69$; unrelated [transplantation = 35] or related [$n = 1$] bone marrow transplantation; autologous [$n = 15$] or related [$n = 12$] peripheral blood stem cell transplantation). Median platelet count was 91,000/ μL (3,000–568,000) in all patients, 125,000/ μL (9,000–561,000) in patients who underwent bronchoscopy with transbronchial lung biopsy (TBLB), and 68,000/ μL (3,000–568,000) in those who did not undergo TBLB. Platelet transfusion was performed the day before or the day of the bronchoscopy in 134 procedures (42.4%). Median neutrophil count was 2,840/ μL . Supplemental oxygen was administered before bronchoscopy at a rate of 0.5–6 L/min in 73 bronchoscopies (23.1%). Bronchial washing was included in 201 (63.6%) bronchoscopies, bronchoalveolar lavage in 104 (32.9%), TBLB in 119 (37.7%), transbronchial biopsy in 6 (1.9%), bronchial curettage in 6 (1.9%), and endobronchial ultrasound-guided transbronchial needle aspiration in 2 (0.6%). Pethidine was used in 261 bronchoscopies (82.6%) and midazolam in 235 (74.4%).

Thirty-five bronchoscopies (11.1%) were complicated by hemoptysis and 7 patients developed pneumothorax, 4 of whom required thoracic drainage. Two patients (0.6%) were intubated within 48 hour of the procedure. The first patient was intubated on the day after the procedure and died the following month; the second patient was intubated just after the procedure and underwent extubation the following day (Table 1). The oxygen desaturation data are summarized in Figure 1. Prolonged oxygen desaturation (>48 h) occurred after 12 of the 316 bronchoscopies (3.8%). Oxygen desaturation did not recover in 5 of these 12 patients and was ultimately fatal. The data for these 12 patients are summarized in Table 1. Oxygen desaturation recovered in 7 patients (including 2 with organizing pneumonia, 2 with invasion of underlying disease, and 1 with pneumocystis pneumonia). The 5 patients with no recovery of oxygen desaturation included 2 patients with aspergillosis and 2 with cytomegalovirus pneumonia.

Univariate and multivariate analyses were performed to identify risk factors for prolonged oxygen desaturation (>48 hour) after bronchoscopy. Factors identified as statistically significant in univariate analysis were platelet count $\leq 20 \times 10^3/\mu\text{l}$, TBLB not performed, and midazolam not administered (Table 2). The multivariate analysis showed that only midazolam significantly reduced the risk of prolonged oxygen desaturation ($p = 0.01$, hazard ratio 0.23, 95% confidence interval 0.07–0.75; Table 3).

Discussion

We performed 316 bronchoscopies in 282 patients with hematologic disorders and pulmonary lesions over a period of 10 years. Acute myeloid leukemia accounted for about half of the underlying diseases. Two patients were intubated within 48 hour of the procedure and 12 experienced prolonged oxygen desaturation. Multivariate analysis showed that midazolam significantly reduced the risk of prolonged oxygen desaturation by approximately a quarter.

A review by Harris et al. [6] identified the following complications of bronchoscopy after HSCT: bleeding (1.5–15%), pneumothorax (0–4%), and hypoxemia. Yanik et al. [7] retrospectively assessed 444 patients who underwent bronchoscopy after HSCT and reported that complications developed in 3.6% of patients; 1.8% had low oxygen, 1.7% had bleeding, 0.2% had low blood pressure, and 2% required mechanical ventilation within 2 days. Our results are consistent with the previous studies. In our study, 4 of 5 patients in whom oxygen desaturation did not recover had severe infection (aspergillosis or cytomegalovirus pneumonia), suggesting that their prolonged oxygen desaturation was likely a consequence of severe lung disease rather than a complication of bronchoscopy.

Our study identified use of midazolam to be a favorable factor for reducing the risk of prolonged oxygen desaturation. Midazolam was used as the main agent for sedation during bronchoscopy at our institution starting from the beginning of 2011. Sedation with midazolam improve patients' comfort and increased their ability to tolerate the procedure without significant hemodynamic changes or respiratory depression [8–10]. Our study shows that the results of the previous studies are applicable to bronchoscopy in patients with a hematologic disorder.

This study had several limitations, stemming mainly from its retrospective single-center design. Furthermore, given that midazolam was started in the middle of the study period, we cannot rule out “time-window bias”.

Conclusion

Bronchoscopy is relatively safe in patients with hematologic disorders provided that respiratory status is monitored carefully after the procedure. Sedation with midazolam may reduce the risk of prolonged oxygen desaturation.

Abbreviations

HSCT; hematopoietic stem cell transplantation

AML; acute myeloid leukemia

MDS; myelodysplastic syndromes

TBLB; transbronchial lung biopsy

Declarations

Ethics approval and consent to participate

The institutional review board of our Hospital approved this study (No. 1845).

Consent for publication

Informed consent was obtained 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 analysed during the current study are available from the corresponding author on reasonable request.

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

TS; Data curation-Lead

AN; Formal analysis-Lead

NU; Methodology-Lead

MT; Investigation-Lead

SM; Project administration-Lead

YT; Project administration-Supporting

KO; Resources-Lead

KM; Resources-Supporting

SH; Supervision-Lead

HT; Writing-review & editing-Supporting

AM; Validation-Supporting

NM; Validation-Lead

MK; Visualization-Supporting

HA; Visualization-Lead

RT; Supervision-Supporting

YA-M; Funding acquisition-Lead

AW; Funding acquisition-Equal

ST; Writing-review & editing-Supporting

KK; Writing-review & editing-Lead

All authors read and approved the final manuscript.

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No

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Tables

Due to technical limitations, the tables are only available as a download in the supplemental files section.

Figures

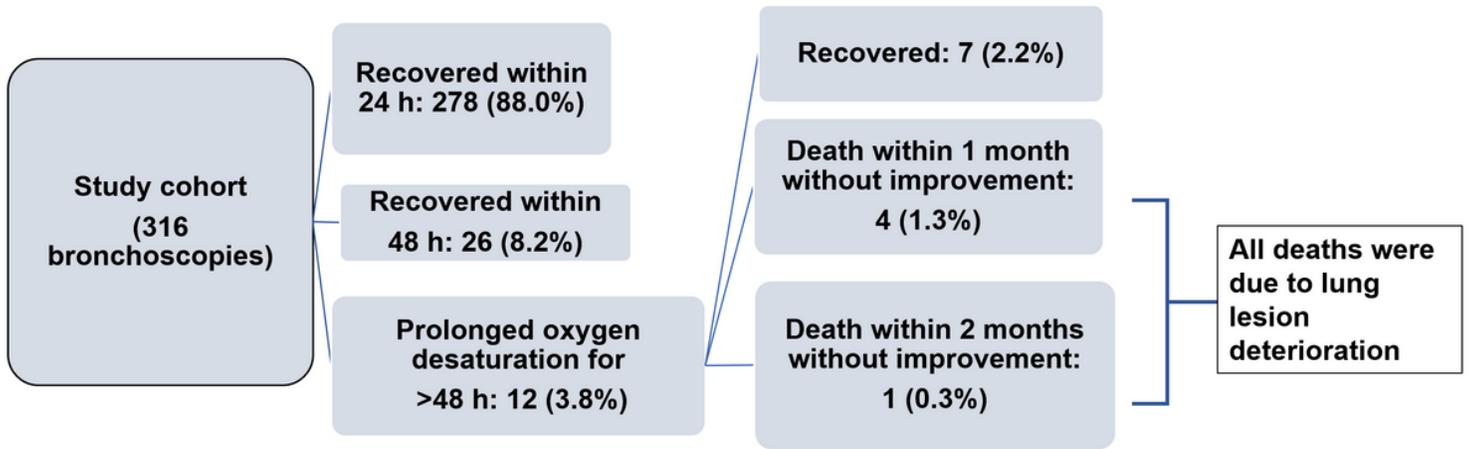


Figure 1

Flowchart of patients with the complication of oxygen desaturation after bronchoscopy.

Supplementary Files

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- [Tables2020.4.5.docx](#)