

The Incidence of Hemorrhagic Complications Was Lower With the Guide Sheath Than With the Conventional Forceps Biopsy Method

Results of Bronchoscopy in the 2016 Nationwide Survey by the Japan Society for Respiratory Endoscopy

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Background: The Japan Society for Respiratory Endoscopy performed a nationwide survey to evaluate the current status and complications of bronchoscopy. Data on deaths due to bronchoscopy, complications after bronchoscopy, and particularly, complications of forceps biopsy were surveyed.

Methods: The survey form was mailed to 532 facilities accredited by the society. The numbers of procedures, complications, and deaths were investigated.

Results: The response rate was 79.1% (421 facilities). Deaths attributable to diagnostic bronchoscopy occurred in 11 (0.011%) of 98,497 cases. In regards to forceps biopsy, the guide sheath method was applied in 23,916 cases and the conventional method in 31,419 cases was done with conventional method. Complications of forceps biopsy developed in 1019 cases in total, with an incidence rate of 1.84%. The most frequent complication was pneumothorax (0.70%), followed by pneumonia/pleurisy (0.46%) and hemorrhage (0.45%). The incidence of hemorrhagic complication was significantly lower in the guide sheath group than in the non-guide sheath group (0.29% vs. 0.58%; $P < 0.001$). The overall incidence of complications (1.63% vs. 2.00%; $P = 0.002$) and the mortality rate (0% vs. 0.02%; $P = 0.04$) were significantly lower in the guide sheath group.

Conclusion: The incidence of hemorrhagic complications in forceps biopsy of peripheral pulmonary lesions was lower when the guide sheath method was applied. It is necessary to increase the awareness for safety control in diagnostic bronchoscopy for new procedures.

Key Words: bronchoscopy, endobronchial ultrasound, interventional pulmonology, guide sheath, lung cancer, mortality/morbidity, transbronchial biopsy

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Diagnostic and therapeutic bronchoscopy is considered an invasive clinical procedure. Various complications associated with bronchoscopy have been reported. Accordingly, preventive measures and methods to deal with complications have been developed.

The Japan Society for Respiratory Endoscopy (JSRE) conducts periodically nationwide surveys

on the safety of bronchoscopy. A number of examinations by procedure were surveyed in 2000, 2006,¹ and 2010.² New diagnostic procedures for mediastinal lymph nodes and small peripheral lesions, such as endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA),³ virtual bronchoscopic navigation, and endobronchial ultrasonography with a guide sheath method, have been introduced since.⁴⁻⁶ With the progression of genetic analysis of lung cancer samples for precision medicine, the importance of tissue collection using bronchoscopy has recently increased.

An increasing number of evidences indicate that EBUS-guided transbronchial biopsy (TBB) is a powerful diagnostic tool for small peripheral pulmonary lesions.⁷⁻¹¹

The guide sheath method was introduced by Dr Kurimoto's group to improve the diagnostic yield in small peripheral nodules. In this method, after identifying the nodule by radial ultrasound probe, the guide sheath is then advanced into the responsible bronchiole to the nodular lesion, and the lesion is biopsied multiple times until ample specimen is retrieved.⁵ This method is advantageous in that biopsy can be reliably and repeatedly applied to a lesion.^{5,6} Although no prospective study has been performed to compare the diagnostic rate between EBUS-TBB with and without a guide sheath, there are several articles that adopted the benefit of the guide sheath method for peripheral lung lesions.^{5,6,12-14}

Endobronchial bleeding caused by TBB usually stops spontaneously. However, massive bleeding is noted as one of the complications of diagnostic bronchoscopy.^{15,16} There is a report that described the massive bleeding cases caused by forceps biopsy with the guide sheath.¹⁴ Hayama et al¹⁷ suggested that wedging the guide sheath in the target bronchus may have helped to stop the bleeding during TBB, in addition to the advantage of sufficient specimen procurement.

Thus the fourth nationwide survey on respiratory endoscopy was performed in 2017 to evaluate the practice pattern and complications that occurred during diagnostic and therapeutic bronchoscopy. The questionnaire sheet was edited and approved by the safety management committee of JSRE and the data collection period was set from January 1, 2016 to December 31, 2016. In this study, we analyzed the results of the survey.

MATERIALS AND METHODS

This was a retrospective, nationwide study of bronchoscopic procedures. The study was approved (approval number A28-14) by the Ethics Committee of Saitama City Hospital in 2016 as a retrospective observational study, and subsequently, by the board of directors of the JSRE. The survey forms were mailed to 532 JSRE-accredited facilities throughout Japan. The survey items were divided into 2 parts: in the first part, the actual conditions in clinical practice in the field of bronchoscopy were surveyed as multiple choice questions. In the second part the actual state of bronchoscopy cases was surveyed using an enclosed inventory in the form of a table. The inventory was filled out by the representative of each facility using data extracted from each facility's own medical records. The survey period was from January 1, 2016 through December 31, 2016. After completion, questionnaire sheets were sent back to the secretariat office. In this survey, no incentives were offered. A complete list of the accredited hospitals is available at the official website of the JSRE (www.jsre.org/senmon/sisetu.html).

Data Collection

The total numbers of diagnostic bronchoscopy cases, peripheral solitary lesions, and mediastinal lymph node lesions were surveyed individually. In addition, the number of examinations, and complications were surveyed by procedure type, namely forceps biopsy of peripheral solitary lesions using a guide sheath (guide sheath group), and without a guide sheath (nonguide sheath group).

In addition, the survey items included questions on the number of deaths attributable to bronchoscopy, numbers of EBUS-TBNA cases and complications, and breakage of bronchoscope during the procedures.

Definitions

The definition of complication was defined in the 2010 survey.² Briefly, asthma attack was defined when clinical sign and symptom emerged and necessitated additional treatments. Central airway obstruction was defined when airway continuity was lost during bronchoscopy due to foreign body, bleeding, or edema. Circulatory adverse event was defined as severe alteration of circulatory status during bronchoscopy. Hemorrhage was defined as >300 mL blood loss or the case that necessitated blood transfusion. Lidocaine toxicity was defined as an unfavorable reaction after administration of lidocaine that necessitated additional therapeutic measures. Perforation was defined as the disruption of the continuity of tracheobronchial tree. Pulmonary

infection included pneumonia and pleuritis. Pneumonia/pleurisy was defined when infiltration or pleural effusion on the chest film was detected or exacerbated with evident clinical symptoms. Pneumothorax was defined as the free air space observed on the chest film. When a complication was caused by applying several procedures, the procedure most likely to be the cause was regarded as the cause.

Statistical Analysis

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation For Statistical Computing, Vienna, Austria). More precisely, it is a modified version of the R commander designed to add statistical functions frequently used in biostatistics.¹⁸ Between-group comparison was performed using the χ^2 test with Yates correction or the Fisher exact test. When multiple procedures and treatment were applied to 1 lesion, it was included in the number of applications of each procedure.

RESULTS

The case survey form was recovered from 421 facilities, and the response rate was 79.1%. The list of the cooperated hospitals is shown in Appendix 1 (Supplemental Digital Content, <http://links.lww.com/LBR/A201>).

Diagnostic Bronchoscopy

Number of Procedures

Diagnostic bronchoscopy was performed in 98,497 in total and 0 to 1044 per facility (mean: 243, median: 200) during the survey period. EBUS-TBNA of hilar and mediastinal lymph node lesions was performed in 9713 cases in total.

Forceps biopsy of peripheral solitary lesions was performed in 55,335 cases in 2016. Conventional forceps biopsy was performed in 31,419 of these in total and 0 to 563 per facility (mean: 80.8, median: 50). Forceps biopsy using a guide sheath was performed in 23,916 in total and 0 to 550 per facility (mean: 65.5, median: 35).

Deaths

Deaths from diagnostic bronchoscopy occurred in 11 cases (0.011%): hemorrhage during examination resulted in death in 4, postbronchoscopy cardiovascular complication caused death in 2, acute aggravation of interstitial pneumonia after bronchoscopy for the purpose of investigating interstitial pulmonary diseases resulted in death in 2, death after bronchoscopy for the evaluation of advanced lung cancer

caused death in 2, and intractable pneumothorax developed and resulted in death in 1 case.

From the viewpoint of procedures, the condition aggravated upon biopsy in 9 cases. One patient died after EBUS-TBNA due to mediastinal and systemic infection/sepsis. One patient with brain metastasis deteriorated neurologically during bronchoscopy and died of brain herniation.

Complications

Complications of Forceps Biopsy. The number of complications in all cases of forceps biopsy of peripheral solitary lesions was 1019 (1.84%). The most frequent complication was pneumothorax with an incidence of 0.70%, followed by pneumonia/pleurisy (0.46%), and hemorrhage (0.45%). The incidence of complication was significantly lower in the guide sheath group than in the nonguide sheath group for bleeding (0.29% vs. 0.58%; $P < 0.001$), and respiratory failure (0.03% vs. 0.09%; $P = 0.007$). The overall incidence of complications (1.63% vs. 2.00%; $P = 0.002$) and mortality (0% vs. 0.02%; $P = 0.04$) were significantly lower in the guide sheath than in the nonguide sheath group, respectively (Table 1).

TABLE 1. Frequency of Complications Associated With Forceps Biopsy for Peripheral Solitary Lesions

	Total (%)	Guide Sheath Group (%)	Nonguide Sheath Group (%)	P
No. forceps biopsy	55,335	23,916	31,419	
PTX	389 (0.70)	178 (0.74)	211 (0.67)	0.33
Hemo	251 (0.45)	70 (0.29)	181 (0.58)	<0.001
PI	254 (0.46)	102 (0.43)	152 (0.48)	0.36
BA	40 (0.07)	14 (0.06)	26 (0.08)	0.37
RF	36 (0.07)	7 (0.03)	29 (0.09)	0.007
LTX	16 (0.03)	7 (0.03)	9 (0.03)	1
CVE	32 (0.06)	13 (0.05)	19 (0.06)	0.91
CAO	1 (0.00)	0 (0.00)	1 (0.00)	1
PF	0 (0.00)	0 (0.00)	0 (0.00)	1
Total complications	1019 (1.84)	391 (1.63)	628 (2.00)	0.002
Death	6 (0.01)	0 (0.00)	6 (0.02)	0.04

Results are number (%) of cases.

BA indicates bronchial asthma (asthmal attack was defined when clinical sign and symptom emerged and necessitated additional treatments); CAO, central airway obstruction (airway stenosis was defined when airway continuity was lost during bronchoscopy due to bleeding/edema); CVE, cardiovascular event (circulatory adverse event was defined severe alteration of circulatory status during bronchoscopy); Hemo, massive hemorrhage (Hemorrhage was defined as > 300 mL blood loss or the case that necessitated blood transfusion); LTX, lidocaine toxicity (lidocaine toxicity was defined as an unfavorable reaction after administration of lidocaine that necessitated additional therapeutic measures); PF, perforation (continuity of tracheobronchial tree was broken); PI, pulmonary infection (pneumonia was defined when infiltration on the chest film was detected or exacerbated with evident clinical symptoms and/or pleuritis); PTX, pneumothorax (pneumothorax was defined as the free air space observed).

TABLE 2. Breakage of Bronchoscopes and Devices

	Number
Bronchoscope breakage	269 facilities
Patients biting	162 cases
Needle perforation of forceps channel	109 cases
Dysfunction by heat or by mis-charge of high-energy devices	6 cases
Other causes	135 cases
Difficulty in opening/closing or removing the biopsy forceps	98 cases
Curette breakage	54 cases

Complications of EBUS-TBNA. Complications of EBUS-TBNA were as follows in the order of frequency: hemorrhage in 39 cases (0.40%), pneumonia/pleurisy in 16 (0.16%), asthmatic attack in 5 (0.05%), pneumothorax in 4 (0.04%), respiratory failure in 2 (0.02%), cardiovascular event in 2 (0.02%), and aggravation of airway obstruction in one (0.01%). One case was fatal.

Breakage of Devices

Breakages and malfunctions of bronchoscopes were reported from 269 (67.6%) of 398 facilities (Table 2).

DISCUSSION

JSRE periodically conducts a nationwide survey of the practice of bronchoscopy. The 2016 nationwide survey of bronchoscopy in Japan contained a wide range of items. Among all, we focused on the rapidly spreading EBUS-TBNA and forceps biopsy for peripheral pulmonary lesions, particularly the guide sheath method.

Regarding forceps biopsy of peripheral lesions, identification of their location, and biopsy procedure for peripheral solitary lesions using radial-type ultrasonographic imaging were developed around 2002^{7,8} and have become widely used worldwide. An excellent diagnostic rate was reported.⁷⁻¹⁰ EBUS using the guide sheath method was subsequently introduced by Dr Kurimoto's group⁵ and there have been several studies, although their nature was either a single arm study or a retrospective study.¹²⁻¹⁴

This was the first nationwide survey after the guide sheath method has been accepted as one of the biopsy methods. Cases employing the guide sheath method accounted for 43.2% of all forceps biopsy cases, witnessing the rapid spread of this method. In the 2010 survey, forceps biopsy of peripheral solitary lesions was performed in 37,485 cases,² and the number markedly increased by 1.5 times in the present survey. This increase is considered to be due

to the change in the environment of diagnostic bronchoscopy. After the previous survey in 2010, many small peripheral lesions have been identifiable due to improved imaging modality. Moreover, physicians have been requested more often to reach proper diagnosis and get enough specimens for molecular analysis from small peripheral lung lesions. To procure ample volume of specimen, repeated biopsy was often necessary. In the guide sheath method, biopsy and scraping cytology of a small peripheral lesion can be repeatedly performed while the bronchus involved in the lesion is wedged. To accomplish this task, many physicians have applied the guide sheath method, and although several reports have been published, the results regarding the diagnostic rate are inconsistent.^{5,6,12,14}

Regarding the complication of the guide sheath method, Hayama et al¹⁷ reported that pneumothorax and pulmonary infection developed in 0.8% and 0.5% of 965 cases, respectively, but no significant hemorrhage was observed. However, it was a single-center study, and it was not clearly concluded whether the guide sheath method decreased complications. Previous studies indicated that massive hemorrhage during diagnostic bronchoscopy was an important complication to deal with.^{15,16} The present large-scale nationwide survey clarified that the incidence of hemorrhage in biopsy was significantly lower in the guide sheath group. The incidence of hemorrhagic complication in the nonguide sheath group was 0.58%, being similar to that in the previous survey, and the incidence in the guide sheath group was 0.29%. Meanwhile, the incidence of hemorrhagic complications among all forceps biopsy cases was 0.45%, being lower than the incidence of pneumothorax. In this study, we did not survey the hemorrhage volume and clinical sequel of hemorrhagic complication cases; further scrutinized studies will be necessary.

In this survey, a peripheral pulmonary lesion was the inclusion criteria of the target of forceps biopsy. This criterion allowed variety of target size and diseases. There were also many confounding factors such as selection bias, operators' bias, and recall bias. Therefore, we have to pay attention when we evaluate the results of group comparisons.

Although many limitations existed, incidence of complications of forceps biopsy with guide sheath was lower than those of forceps biopsy without guide sheath in regards to hemorrhage and respiratory failure. This was a retrospective survey and it is necessary to perform a prospective study to prove the hypothesis as clinical evidence. However, considering about the prospective study, when hemorrhage

occurrence rate is assumed 0.5% and 0.25% in 2 groups, α error is 0.05, and β error is 0.1, the study volume should be > 30,000 cases for each group to demonstrate a significant difference. It seems difficult to perform this kind of large prospective study with regards to the registration of cases, study administration and funding.

The incidences of hemorrhage and pneumonia/pleurisy in EBUS-TBNA cases were 0.40% and 0.16%, respectively, being not markedly different from those in the 2010 survey² and 2012 survey on EBUS-TBNA.¹⁹ To prevent these complications and promote safety, it is important to apply the procedure in consideration of the risk in individual cases.^{20–23}

There were 11 fatal cases of diagnostic bronchoscopy among the 98,497 cases. It may be difficult to clearly distinguish deaths by direct cause of bronchoscopy from deaths by aggravation of underlying disease.

Regarding breakage of bronchoscopes and peripheral devices, the frequency of curette breakage tended to be low but this may have been due to the decreased use. The number of incidents was similar to that in the previous survey. The causes of breakage were divided into inappropriate use and patient-related issues. The incidence of needle perforation of forceps channels could be controlled by calling the attention of operating physicians and assistants.

The present nationwide survey on bronchoscopy involved facilities accredited by JSRE. As bronchoscopy performed at facilities not belonging to JSRE was very limited, this survey reflected the current state of bronchoscopy in Japan. The numbers of cases and complications indicated that the facilities generally performed bronchoscopy safely, but based on the findings, it is still necessary for the JSRE to enforce safety control for diagnostic bronchoscopy, particularly for new procedures.

On the basis of the results of this survey, diagnostic bronchoscopy can be considered a safe procedure. However, considering the cause of deaths, precautions before examination are important, such as control of the risk of bleeding, detailed evaluation of cardiovascular status, prevention of acute exacerbation of interstitial pulmonary diseases. In the recent years, there have been more cases with recurrent lung cancer or with progressive disease. For those patients, we are often requested to get the ample tissue specimen which is necessary for the molecular evaluation. In these cases, risk of complication

may be high when physicians try to perform diagnostic bronchoscopy. The more elaborative risk evaluation and criteria for the candidate of diagnostic bronchoscopy should be pursued.

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