Interventional Pulmonology

Respiration

Respiration 2013;85:486–492
DOI: 10.1159/000346987

Received: October 8, 2012
Accepted after revision: December 27, 2012
Published online: April 3, 2013

Rapid On-Site Cytologic Evaluation during Endobronchial Ultrasound-Guided Transbronchial Needle Aspiration for Diagnosing Lung Cancer: A Randomized Study

Masahide Oki[a] Hideo Saka[a] Chiyoe Kitagawa[a] Yoshihito Kogure[a]
Naohiko Murata[a] Takashi Adachi[a] Masahiko Ando[b]

[a]Department of Respiratory Medicine, Nagoya Medical Center, and [b]Center for Advanced Medicine and Clinical Research, Nagoya University Hospital, Nagoya, Japan

Key Words
Bronchoscopy · Diagnosis · Mediastinal lymph nodes · Staging

Abstract
Background: Although rapid on-site cytologic evaluation (ROSE) is widely used during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), its role remains unclear. ***Objectives:*** The purpose of the present study was to evaluate the efficacy of ROSE during EBUS-TBNA in the diagnosis of lung cancer. ***Methods:*** One hundred and twenty patients highly suspected of having lung cancer who had hilar/mediastinal lymphadenopathy or a tumor adjacent to the central airway were enrolled in this study and randomized to undergo EBUS-TBNA with or without ROSE. ***Results:*** Twelve patients with visible endobronchial lesions were excluded in the analysis. Thus, a total of 108 patients (55 in the ROSE group, 53 in the non-ROSE group) were analyzed. Additional procedures including EBUS-TBNA for lesions other than the main target lesion and/or transbronchial biopsy in the same setting were performed in 11% of patients in the ROSE group and 57% in the non-ROSE group ($p < 0.001$). Mean puncture number was significantly lower in the ROSE group (2.2 vs. 3.1 punctures, $p < 0.001$), and mean bronchoscopy time was similar between both groups (22.3 vs. 22.1 min, $p = 0.95$). The sensitivity and accuracy for diagnosing lung cancer were 88 and 89% in the ROSE group, and 86 and 89% in the non-ROSE group, respectively. No complications were associated with the procedures. ***Conclusions:*** ROSE during EBUS-TBNA is associated with a significantly lower need for additional bronchoscopic procedures and puncture number.

Introduction

Transbronchial needle aspiration (TBNA) is a well-established procedure for evaluating lesions adjacent to the central airway. Since the development of TBNA with a flexible bronchoscope in the late 1970s [1], the procedure has been improved with various techniques or devices to increase the diagnostic accuracy. Rapid on-site

Preliminary data were previously presented with slides at ERS 2012 Annual Meeting in Vienna. Trial Registration: UMIN-Clinical Trials Registry; Identifier: UMIN0000001334, http://www.umin.ac.jp/ctr/index.htm.

KARGER

E-Mail karger@karger.com
www.karger.com/res

0025–7931/13/0856–0486$38.00/0

Masahide Oki
Department of Respiratory Medicine, Nagoya Medical Center
4-1-1 Sannomaru, Naka-ku
Nagoya 460-0001 (Japan)
E-Mail masahideo@aol.com

cytologic evaluation (ROSE) during TBNA has been suggested as one such way. It has been reported to be effective, as it increases the diagnostic yield [2, 3], decreases the number of needle passes [4, 5], obviates the need for additional diagnostic procedures [4–7], reduces the complication rate of bronchoscopy [5] and reduces the cost [6]. Although its role is controversial [8], many investigators recommend the use of ROSE during TBNA [9, 10].

Development of an endobronchial ultrasound (EBUS) bronchoscope has enabled 'real-time' TBNA by confirming the position of the needle tip under EBUS imaging during the TBNA procedure, allowing for a more highly accurate TBNA procedure than by the conventional TBNA. Although EBUS-guided TBNA (EBUS-TBNA) is a relatively new procedure, many studies have reported its usefulness for hilar/mediastinal explorations [11–13], and it has been rapidly popularized. Many bronchoscopists use ROSE routinely during EBUS-TBNA as well as conventional TBNA in the current clinical practice [12, 13], and some authors recommend the use of ROSE during EBUS-TBNA [14]. However, no prospective comparative studies focused on the utility of ROSE during EBUS-TBNA have been reported, and so its role has remained unclear. We conducted this prospective randomized study to further clarify the role of ROSE during EBUS-TBNA in the diagnosis of lung cancer. The primary endpoint was the frequency with which additional bronchoscopic procedures can be eliminated in the same setting. Secondary endpoints were the diagnostic accuracy of EBUS-TBNA for lung cancer, the diagnostic yield of EBUS-TBNA, number of needle passes, time of the procedures, and the frequency of complications.

Patients and Methods

Patients

We carried out a prospective study which was approved by the institutional review board of Nagoya Medical Center (identifier: 2008-175) and registered with the UMIN-Clinical Trials Registry (identifier: UMIN000001334). Included in this study were 120 patients suspected of having lung cancer along with metastatic lymph nodes or tumors, 10 mm or greater in the shortest diameter on chest computed tomography, all of which were easily accessible with EBUS-TBNA. All patients with lung cancer diagnosed pathologically prior to bronchoscopy were excluded. Patients who had obviously bronchoscopically visible endobronchial lesions were also excluded. Randomization for EBUS-TBNA with or without ROSE was performed by minimization with stratification factors including lymph node location (subcarinal lymph node vs. other), lymph node size (20 mm or greater vs. less than 20 mm) and examiner experience (staff pulmonologists vs. pulmonary residents 5 years or less after receiving their MD). All patients provided their written informed consent.

Procedures

Bronchoscopic procedures were performed under local anesthesia with lidocaine and conscious sedation with intravenous midazolam by staff pulmonologists or supervised pulmonary residents. EBUS-TBNA was performed in the same manner we previously described [15, 16]. After insertion of the EBUS bronchoscope (BF-UC260F-OL8; Olympus, Tokyo, Japan) into the trachea directly or through an endotracheal tube, a balloon attached on the transducer was inflated with saline solution. The balloon was then brought into contact with the airway wall and moved in all directions to identify the lesions for sampling. When the target lesion was visualized by EBUS, a 21- or 22-gauge needle was passed through the working channel of the bronchoscope, which was then advanced through the tracheobronchial wall into the lesion under real-time EBUS visualization. After stylet removal, suction was applied using a syringe while manipulating the needle back and forth within the lesion. After the sampling, the suction was released slowly and the needle was retracted.

The specimen collected in the lumen of the needle was first pushed out with the central stylet and then blown by air with a syringe onto a glass slide. The visible tissue fragment on the glass slide was then collected and transferred into numbered separate containers filled with formalin for histologic examination. The remaining specimen on the glass slide was smeared with another glass slide, then the residual specimen stored at the lumen of the needle and catheter was then washed and flushed into saline for culture [15–17]. In patients assigned to the ROSE group, one glass slide was used for ROSE and another was submitted for permanent cytologic examination with Papanicolaou stain. For ROSE, a cytotechnologist evaluated the cell material of the air-dried smears on-site with a quick staining method (Diff-Quik; Kokusaishiyaku, Kobe, Japan). Additional passes were made after the ROSE result was identified. The decision as to termination or additional samplings was made by the examiner based on the ROSE results. In patients assigned to the non-ROSE group, all smeared cytologic specimens were fixed in 95% alcohol for cytologic examination. Three punctures were defined as a standard number in the study protocol, and additional punctures or additional bronchoscopic procedures such as EBUS-TBNA for other lesions or transbronchial biopsy (TBB) for peripheral pulmonary lesions were performed if the examiner considered it necessary. The location of the lymph node examined [18], the number of punctures and the time of the procedure were recorded.

Diagnosis

Each histologic and cytologic specimen was interpreted separately by an experienced pathologist. 'Suspicious' findings were regarded as negative in our analysis. The final diagnoses were established by pathological evidence from biopsy (e.g. bronchoscopic, radiological or surgical procedures), microbiological analysis or clinical follow-up. Benign diagnoses for patients without a definitive diagnosis by EBUS-TBNA were confirmed by radiological size stability and clinical compatibility during the follow-up period for at least 6 months after bronchoscopy.

Table 1. Characteristics of patients and lesions

Characteristics	ROSE	Non-ROSE	p value
Patients	55	53	
Male/female	44/11	39/14	0.50
Age, years	68.0±7.5 (51–84)	66.5±10.8 (34–84)	0.39
Smoking history			
Never-/ex-/current-smoker	9/18/28	4/20/29	0.37
Lesion size			
Mean, mm (range)	25.4±11.7 (10–60)	23.4±10.6 (10–67)	0.35
<20/≥20 mm	18/37	20/33	0.69
Location of lesion targeted			
2R	5	3	
2L	1	0	
3p	1	5	
4R	22	15	0.2
4L	1	3	
7	13	16	0.44
10R	1	2	
10L	2	2	
11R	6	5	0.8
11L	3	0	
12R	0	1	
Central parenchyma	0	1	
Lesions other than the main target lesion ≥10 mm accessible by EBUS-TBNA			
With/without	39/16	36/17	0.83
Side of suspected primary lesion			
Right/left	42/13	38/15	0.58
Primary disease			
Benign/malignant	2/53	7/46	0.09
Primary lung cancer/others	51/4	43/10	0.09
Bronchoscopy			
Initial bronchoscopy/previous nondiagnostic bronchoscopy	44/11	37/16	0.27
Examiner			
Staff pulmonologist/resident	50/5	49/4	1

Data are presented as n or means ± SD (range).

Statistical Analysis

Based on our own experience, we estimated that 33% of patients in the ROSE group and 75% of those in the non-ROSE group would have to undergo additional procedures. Demonstration of superiority with a statistical power of 90% at a two-sided significance level of 0.05 would require 66 patients. We considered that about 50% of the endoscopically visible lesions would be excluded from the analysis, and thus enrolled a total of around 120 patients with 60 in each group.

Means and percentages were presented as appropriate. Diagnostic yields, diagnostic sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated using the standard definitions on a per-patient basis. Dichotomous variables were analyzed using Pearson's χ^2 test or Fisher's exact test, and continuous variables were analyzed using Student's t test. Statistical analyses were performed using a statistical software program (PASW Statistics 18; SPSS Inc, Chicago, Ill., USA). Results were considered statistically significant when the p value was less than or equal to 0.05.

Results

Patients and Lesions

Between August 2008 and April 2011, a total of 120 patients were enrolled in this study and randomized to undergo EBUS-TBNA with or without ROSE. Twelve patients with a bronchoscopically visible endobronchial lesion were excluded from the analysis. Thus, a total of 108 patients (55 patients in ROSE group, 53 patients in non-ROSE group) were included in this analysis. Characteristics of patients and lesions in each group were summarized in table 1. There was no statistically significant difference in the baseline characteristics between the groups.

Table 2. Procedural details

Variables	ROSE (n = 55)	Non-ROSE (n = 53)	p value
Mean puncture number for main target lesion	2.2±0.9 (1–6)	3.1±0.4 (3–5)	<0.001
Additional procedures	6	30	<0.001
EBUS-TBNA for other lesions	2	26	
TBB for peripheral lesions	4	3	
EBUS-TBNA for other lesions and TBB for peripheral lesions	0	1	
Sole diagnosis provided by additional procedures	0	3	
Bronchoscopy time, min	22.3±15.9 (9–94)	22.1±7.7 (11–56)	0.95

Data are presented as n or means ± SD (range).

Table 3. Final diagnosis and EBUS-TBNA results

EBUS-TBNA findings	Patients (final diagnosis), n			
	ROSE (n = 55)		Non-ROSE (n = 53)	
Malignant				
Primary lung cancer				
Adenocarcinoma	10		14	
Squamous cell carcinoma	15		7	
Large cell carcinoma	1		0	
Non-small cell carcinoma	3		3	
Small cell carcinoma	16		13[a]	
Metastatic carcinoma	0		1	(renal cell carcinoma)
Malignant lymphoma	1		0	
Mediastinal tumor	0		1	(germ cell tumor)
Benign				
Epithelioid cell granuloma with/without necrosis	1	(1 tuberculosis)	1	(1 unspecified)
Nondiagnostic				
Epithelioid cell granuloma[b]	1	(1 lung cancer)	1	(1 lung cancer)
Nonrepresentative samples	7	(5 lung cancers, 1 amyloid tumor, 1 atypical carcinoid)	12	(5 lung cancers, 1 mediastinal cancer, 1 granuloma, 1 abscess, 4 unchanged with 8–30 months of follow-up)

[a] One was diagnosed by EBUS-TBNA for second target lesion. [b] Sarcoidal reaction.

Comparison of Procedures

Procedural details in each group are summarized in table 2. Punctures for the main target lesion were significantly fewer in the ROSE group than in the non-ROSE group (mean: 2.2 vs. 3.1 punctures, $p < 0.001$). In the ROSE group, 6 of 55 patients (11%) underwent additional procedures (2 EBUS-TBNA for other lesions, 4 TBB) in the same setting according to the negative result of ROSE, while in the non-ROSE group, 30 of 53 patients (57%) underwent additional procedures (26 EBUS-TBNA for other lesions, 3 TBB, 1 both EBUS-TBNA and TBB; $p < 0.001$). Of the 30 patients who underwent additional procedures in the non-ROSE group, 3 (10%) were diagnosed solely by the additional procedures. Mean bronchoscopy time was similar in each group (mean: 22.3 vs. 22.1 min, $p = 0.95$).

Diagnostic Performance

Pathological results of EBUS-TBNA and the final diagnosis per-patient basis are detailed in table 3. Two patients with a final diagnosis of lung cancer were given a histological diagnosis of epithelioid cell granuloma by EBUS-TBNA, which was suggested to be a sarcoidal reaction. The overall diagnostic yield of EBUS-TBNA in the ROSE-group and the non-ROSE group was 85% (47 of 55) and 75% (40 of 53), respectively ($p = 0.23$).

Table 4. Diagnostic value of EBUS-TBNA for lung cancer

	ROSE (n = 55)	Non-ROSE (n = 53)
Sensitivity	88	86
Specificity	100	100
Positive predictive value	100	100
Negative predictive value	40	63
Accuracy[a]	89	89

Data are presented as %. [a] $p = 0.95$ using χ^2 test.

The diagnostic accuracies of EBUS-TBNA in the diagnosis of lung cancer are shown in table 4. Of the 82 patients with lung cancer diagnosed by EBUS-TBNA, a positive EBUS-TBNA result was obtained from N3 lymph nodes in 11 patients, N2 lymph nodes in 59 patients, N1 lymph nodes in 11 patients and parenchyma in 1 patient.

Accuracy of ROSE

The diagnostic accuracy of ROSE as positive or negative in the diagnosis of malignancy for the final pathological diagnosis on per-lesion bases was calculated. Two false-positive cases and 2 false-negative cases resulted. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy were 96, 78, 96, 78 and 93%, respectively.

Safety

No complication was observed to be associated with bronchoscopy.

Discussion

To our knowledge, this is the first randomized study on the effect of ROSE during EBUS-TBNA in the diagnosis of lung cancer. This study demonstrated that during EBUS-TBNA ROSE reduced the puncture number or obviated the need for additional bronchoscopic procedures, but it was not associated with the total bronchoscopy time. We could not demonstrate differences in diagnostic accuracy or complication rate in this small study. Our study showed the usefulness of EBUS-TBNA as the initial diagnostic test for the pathological confirmation of lung cancer as well.

ROSE feeds back valuable information to the examiner on the adequacy of cytologic samples at the time of needle aspiration procedures, which indicates whether the procedure should be repeated or not. In conventional TBNA, many investigators have reported the usefulness of ROSE, but the role is controversial [8, 9]. For example, several authors have reported that ROSE increases the diagnostic yield [2, 3]. The examiner can modify the technique by changing the puncture site, puncture depth or angle based on the ROSE results, which might increase the diagnostic yield. The results of recent randomized studies contradicted the diagnostic efficacy of ROSE during conventional TBNA [5, 7]. In a randomized study including 168 patients, Trisolini et al. [5] demonstrated no significant difference between TBNA with and without ROSE in terms of diagnostic yield or sample adequacy. In addition, procedure time on TBNA with ROSE was significantly longer than TBNA without ROSE due to processing, and careful review of the slides despite the use of ROSE was associated with fewer biopsy sites. The same investigators noted that the benefit of ROSE during TBNA was avoidance of additional biopsy which was associated with complications. Yarmus et al. [7] also found similar results in their randomized study of 68 patients.

The value of ROSE during EBUS-TBNA may be smaller than that during conventional TBNA in terms of diagnostic yield because of the high diagnostic yields of EBUS-TBNA regardless of using ROSE. In fact, it was reported that 7 aspirates maximized the yield of conventional TBNA for the diagnosis and staging of lung cancer [19], while a study [20] concerning EBUS-TBNA demonstrated that 3 aspirates per lesion were sufficient to obtain optimal results for the staging of lung cancer. The result may suggest that the optimal yield is obtained by 3 aspirates regardless of using ROSE. Griffin et al. [21] also found that ROSE during EBUS-TBNA did not increase the diagnostic yield in their retrospective study. They also reported that ROSE during EBUS-TBNA did not decrease the number of lesions sampled per patient. To the contrary, our study demonstrated that during EBUS-TBNA ROSE reduced the puncture number per lesion or the number of lesions aspirated. In our clinical practice without ROSE, we prefer performing EBUS-TBNA for plural lesions to performing EBUS-TBNA for a single lesion to increase the diagnostic yield if there are multiple evaluable lesions [16]. If we use ROSE, we can judge the necessity of further needle passes or diagnostic procedures from the ROSE results. In our study, EBUS-TBNA for multiple lesions was performed in only 5% of patients with enlarged evaluable lesions other than the main target lesion in the ROSE group, against 75% of patients in the non-ROSE group. However, the clinical benefit might be limited. EBUS-TBNA is extremely safe, so the additional punctures can be performed without additional compli-

cations. In addition, ROSE could not shorten the bronchoscopy time because preparing and reviewing slides for ROSE took time.

Our study demonstrated the usefulness of EBUS-TBNA as the initial diagnostic test for lung cancer as well. Diagnosis of lung cancer as well as its staging is one of the common indications for EBUS-TBNA. We often encounter patients with a small peripheral primary lung cancer with bulky mediastinal lesions. In addition, some lung cancers, especially small cell lung cancers, present mediastinal masses without a distinct primary parenchymal lesion [22]. Furthermore, the result of EBUS-TBNA plays an important role not only for the diagnosis but also the mediastinal staging. Surgical resection is not the treatment of choice for most patients with the positive result of N3 lymph nodes, N2 lymph nodes or N1 lymph nodes in small cell lung cancer. While many investigators have reported the accuracy of EBUS-TBNA for the staging of lung cancer [11, 12], little has been reported on the role of the procedure in the diagnosis of lung cancer. Lee et al. [22] retrospectively evaluated the diagnostic accuracy of EBUS-TBNA for lung cancer. They reported excellent accuracy and sensitivity of 98 and 97%, respectively. Our study again demonstrated the high accuracy of EBUS-TBNA in the diagnosis of lung cancer with or without ROSE. Despite the high accuracy, we must carefully interpret the pathological findings of epithelioid cell granulomas. In our study, sarcoidal reaction at the target lesion was found in one patient with lung cancer in each group. It may be difficult to distinguish between sarcoidosis and sarcoidal reaction from only pathological samples. If a specimen is obtained with a sarcoid-like appearance from enlarged lymph node in patients with suspected lung cancer, another biopsy for the primary lesion should be performed.

The limitation of our study was that the primary endpoint was the frequency for eliminating the need for additional bronchoscopic procedures, but not the diagnostic sensitivity for lung cancer. Therefore, our study is clearly too small to compare the diagnostic yield of EBUS-TBNA with and without ROSE. At the time of making our study protocol, we expected the difference between the diagnostic accuracy of EBUS-TBNA with and without ROSE would be quite small, so the power calculation for demonstrating diagnostic superiority of EBUS-TBNA with ROSE seemed to be unrealistic. In fact, one review article [12], which analyzed 1,299 patients who underwent EBUS-TBNA for mediastinal staging of lung cancer, reported the pooled sensitivity of EBUS-TBNA with or without ROSE to be 0.97 and 0.92. However, the statistically significant difference could not be demonstrated even in such a large population. To show the diagnostic superiority of EBUS-TBNA with ROSE, thousands of patients in each arm would be required. In our study, although ROSE provided little clinical benefit in patients with high prevalence and probability, it might be useful in other populations. For staging purposes, the preprobability of metastasis may be lower, and thus more lymph nodes should be examined. In addition, the instantaneous results of ROSE during EBUS-TBNA in the staging of lung cancer have been reported to be useful for the decision-making following surgical resection [23]. More detailed elucidation of the role of ROSE during EBUS-TBNA in patients with lung cancer for staging purposes may be warranted in a further study.

In conclusion, ROSE during EBUS-TBNA in the initial diagnosis of lung cancer can reduce the puncture number or eliminate the need for additional bronchoscopic procedures.

Financial Disclosure and Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

References

1 Oho K, Kato H, Ogawa I, Hayashi N, Hayata Y: A new needle for transfiberoptic bronchoscopic use. Chest 1979;76:492.

2 Davenport RD: Rapid on-site evaluation of transbronchial aspirates. Chest 1990;98:59–61.

3 Diette GB, White P Jr, Terry P, Jenckes M, Rosenthal D, Rubin HR: Utility of on-site cytopathology assessment for bronchoscopic evaluation of lung masses and adenopathy. Chest 2000;117:1186–1190.

4 Baram D, Garcia RB, Richman PS: Impact of rapid on-site cytologic evaluation during transbronchial needle aspiration. Chest 2005;128:869–875.

5 Trisolini R, Cancellieri A, Tinelli C, Paioli D, Scudeller L, Casadei GP, Parri SF, Livi V, Bondi A, Boaron M, Patelli M: Rapid on-site evaluation of transbronchial aspirates in the diagnosis of hilar and mediastinal adenopathy: a randomized trial. Chest 2011;139:395–401.

6 Diacon AH, Schuurmans MM, Theron J, Louw M, Wright CA, Brundyn K, Bolliger CT: Utility of rapid on-site evaluation of transbronchial needle aspirates. Respiration 2005;72:182–188.

7 Yarmus L, Van der Kloot T, Lechtzin N, Napier M, Dressel D, Feller-Kopman D: Randomized prospective trial of the utility of rapid on-site evaluation of transbronchial needle aspirate specimens. J Bronchol Inter Pulmonol 2011;18:121–127.

8 Boyan W: On-site cytopathologic analysis of bronchoscopic needle aspiration: con: on-site analysis is not indicated. J Bronchol 2003;10:152–154.
9 Chin R Jr: On-site cytopathologic analysis of bronchoscopic needle aspiration: pro: on-site analysis is indicated. J Bronchol 2003;10:150–151.
10 Gasparini S: It is time for this 'ROSE' to flower. Respiration 2005;72:129–131.
11 Varela-Lema L, Fernández-Villar A, Ruano-Ravina A: Effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration: a systematic review. Eur Respir J 2009;33:1156–1164.
12 Gu P, Zhao YZ, Jiang LY, Zhang W, Xin Y, Han BH: Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: a systematic review and meta-analysis. Eur J Cancer 2009;45:1389–1396.
13 Ost DE, Ernst A, Lei X, Feller-Kopman D, Eapen GA, Kovitz KL, Herth FJ, Simoff M, AQuIRE Bronchoscopy Registry: Diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration: results of the AQuIRE Bronchoscopy Registry. Chest 2011;140:1557–1566.
14 Bulman W, Saqi A, Powell CA: Acquisition and processing of endobronchial ultrasound-guided transbronchial needle aspiration specimens in the era of targeted lung cancer chemotherapy. Am J Respir Crit Care Med 2012;185:606–611.
15 Oki M, Saka H, Kitagawa C, Tanaka S, Shimokata T, Kawata Y, Mori K, Kajikawa S, Ichihara S, Moritani S: Real-time endobronchial ultrasound-guided transbronchial needle aspiration is useful for diagnosing sarcoidosis. Respirology 2007;12:863–868.
16 Oki M, Saka H, Kitagawa C, Kogure Y, Murata N, Ichihara S, Moritani S: Prospective study of endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes versus transbronchial lung biopsy of lung tissue for diagnosis of sarcoidosis. J Thorac Cardiovasc Surg 2012;143:1324–1329.
17 Oki M, Saka H, Kitagawa C, Kogure Y, Murata N, Adachi T, Ichihara S, Moritani S: Transesophageal bronchoscopic ultrasound-guided fine needle aspiration for diagnosis of sarcoidosis. Respiration 2013;85:137–143.
18 Mountain CF, Dresler CM: Regional lymph node classification for lung cancer staging. Chest 1997;111:1718–1723.
19 Chin R Jr, McCain TW, Lucia MA, Cappellari JO, Adair NE, Lovato JF, Dunagan DP, Brooks MA, Clark HP, Haponik EF: Transbronchial needle aspiration in diagnosing and staging lung cancer: how many aspirates are needed? Am J Respir Crit Care Med 2002;166:377–381.
20 Lee HS, Lee GK, Lee HS, Kim MS, Lee JM, Kim HY, Nam BH, Zo JI, Hwangbo B: Real-time endobronchial ultrasound-guided transbronchial needle aspiration in mediastinal staging of non-small cell lung cancer: how many aspirations per target lymph node station? Chest 2008;134:368–374.
21 Griffin AC, Schwartz LE, Baloch ZW: Utility of on-site evaluation of endobronchial ultrasound-guided transbronchial needle aspiration specimens. Cytojournal 2011;8:20.
22 Lee JE, Kim HY, Lim KY, Lee SH, Lee GK, Lee HS, Hwangbo B: Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of lung cancer. Lung Cancer 2010;70:51–56.
23 Yasufuku K, Pierre A, Darling G, de Perrot M, Waddell T, Johnston M, da Cunha Santos G, Geddie W, Boerner S, Le LW, Keshavjee S: A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer. J Thorac Cardiovasc Surg 2011;142:1393–1400.