Conventional vs. endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal lymphadenopathies

Zeliha ARSLAN[1], Ahmet ILGAZLI[1], Meryem BAKIR[1], Kürşat YILDIZ[2], Salih TOPÇU[3]

[1] Kocaeli Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, Kocaeli,
[2] Kocaeli Üniversitesi Tıp Fakültesi, Patoloji Anabilim Dalı, Kocaeli,
[3] Kocaeli Üniversitesi Tıp Fakültesi, Göğüs Cerrahisi Anabilim Dalı, Kocaeli.

ÖZET

Mediastinal lenfadenopati değerlendirmesinde transbronşiyal iğne aspirasyonu: Konvensiyonel mi, endobronşiyal ultrasonla mı?

Çalışmanın amacı; mediastinal lenfadenopati değerlendirmesinde geleneksel ve radyal prob-endobronşiyal ultrason (EBUS) kılavuzluğunda yapılan standart iğne aspirasyon sonuçlarını kıyaslamak ve EBUS'un katkısını değerlendirmektir. Çalışmada transbronşiyal iğne aspirasyonu yapılması planlanan hastalar prospektif olarak iki gruba randomize edildi. Birinci grupta işlem geleneksel körleme yöntemle, ikinci grupta ise işlem EBUS eşliğinde yapıldı. Her iki işlemle aspirasyon yapılan lenf nodu istasyonları subkarinal bölge ve diğer mediastinal lenf nodları olarak ikiye ayrıldı. 21 G aspirasyon iğnesi kullanıldı. Sitolojide sonuç alındı demek için ya spesifik tanı ya da lenfositlerin görülmesi pozitif kabul edildi. Çalışmaya 60 hasta dahil edildi (48'i erkek, 12'si kadın). Yaş ortalaması 56.15 ± 15.32 yıldı. Tüm hastalar değerlendirildiğinde geleneksel yöntemle tanı oranı %33.3, EBUS ile %66.7 idi. Subkarinal bölgede EBUS ile hastaların %62.5'inde geleneksel yöntemle %33.3'ünde pozitif sonuç elde edildi (p= 0.199). Diğer ulaşılabilir mediastinal lenf nodlarında EBUS ile %68.2 hastada, geleneksel yöntemle ise %33.3 hastada pozitif sonuç elde edildi (p= 0.028). Bu sonuçlar EBUS eşliğinde transbronşiyal iğne aspirasyonunun subkarinal bölge dışındaki mediastinal lenf nodlarında anlamlı daha iyi sonuç verdiğini göstermektedir. Mediastinal değerlendirmede, eğer varsa, EBUS'un rutin olarak kullanılması gerektiğini düşünüyoruz.

Anahtar Kelimeler: *Endobronşiyal ultrason (EBUS), transbronşiyal iğne aspirasyonu, mediastinal inceleme, mediastinal lenf nodları.*

SUMMARY

Conventional vs. endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of mediastinal lymphadenopathies

Zeliha ARSLAN[1], Ahmet ILGAZLI[1], Meryem BAKIR[1], Kürşat YILDIZ[2], Salih TOPÇU[3]

[1] Department of Chest Diseases, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey,
[2] Department of Pathology, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey,
[3] Department of Chest Surgery, Faculty of Medicine, Kocaeli University, Kocaeli, Turkey.

Yazışma Adresi (Address for Correspondence):

Dr. Zeliha ARSLAN, Firuzköy Pehlivan Caddesi Şafak Sokak No: 63 Avcılar,
34800 İSTANBUL - TURKEY
e-mail: zelihaar@yahoo.com

The aim of this study was to determine whether or not radial probe endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) is superior to conventional TBNA in the diagnosis of mediastinal lymphadenopathies in routine clinical practice. Consecutive patients, who were referred for TBNA, were randomized to conventional TBNA and EBUS-guided TBNA groups. Patients were also grouped according to the anatomic location of the pathologic lymph nodes to evaluate if there was a difference in the diagnostic yield with respect to lymph node station. Patients with subcarinal lymph nodes were designated as group A and patients with lymph nodes at station 2 (upper paratracheal), 3 (prevascular and retrotracheal), and 4 (lower paratracheal) were designated as group B. A 21-G aspiration needle was used during the procedure. Sixty patients with a mean age of 56.15 ± 15.32 years were included in the study. Thirty patients each underwent EBUS-TBNA and conventional TBNA. The overall diagnostic yield of conventional TBNA was 33.3% (10/30), while EBUS-TBNA had a yield of 66.7% (20/30; p= 0.010). In patients with subcarinal lymph nodes, the yield of conventional TBNA was 33.3% (4/12) compared to 62.5% (5/8) in the EBUS-guided group (p= 0.362). In patients with mediastinal lymph nodes other than subcarinal lymph nodes, EBUS-TBNA had a significantly higher yield compared to conventional TBNA [33.3% (6/18) vs. 68.2% (15/22) for conventional and EBUS-TBNA groups, respectively; p= 0.028]. In conclusion, the diagnostic yield of EBUS-TBNA was superior to the yield of conventional TBNA at stations other than subcarinal region. We suggest that EBUS is a useful tool to guide TBNA in the evaluation of mediastinal lymph nodes.

Key Words: *Endobronchial ultrasound (EBUS), transbronchial needle aspiration (TBNA), mediastinal evaluation, mediastinal lymph nodes.*

Transbronchial needle aspiration (TBNA) is a well-established technique that allows sampling of parabronchial and paratracheal lymph nodes (1,2). Recently, the indications for TBNA have been extended to the sampling of hilar and mediastinal lymph nodes with the development of flexible cytology needles. The diagnostic yield of TBNA varies widely, ranging from 20%-89%. The yield of TBNA is related to the size and location of the lesion, as well as the individual experience of the physician (3,4). Although TBNA has been shown to be effective in mediastinal lung cancer staging, TBNA is underutilized and is not formally taught in training programs (2,5). Although rapid on-site evaluation (ROSE) and obtaining ≤ 7 aspirates have been proposed to improve the yield, ROSE often requires expensive and sophisticated instrumentation (6). The guidance of fluoroscopy, computed tomography (CT), or endobronchial ultrasound (EBUS) have also been shown to increase the yield (7-9).

Kocaeli University is one of the first institutions in Turkey to use EBUS-TBNA sampling of mediastinal lymphadenopathies in clinical practice. The current study was conducted to determine whether or not EBUS-TBNA is superior to conventional TBNA in the diagnosis of mediastinal lymphadenopathies in routine clinical practice.

MATERIALS and METHODS

Sixty patients who had indications for TBNA of enlarged mediastinal lymph nodes were randomized into either the EBUS or conventional TBNA group between July 2006 and October 2007. Enlarged mediastinal lymph nodes were defined as ≥ 2 cm in the short axis diameter on CT. Lymph node stations were classified according to the American Thoracic Society mapping system (10). Informed consent was obtained from all patients before the study was initiated. Patients were also grouped according to the anatomic location of the pathologic lymph nodes to evaluate if there was a difference in the diagnostic yield with respect to lymph node station. Patients with subcarinal lymph nodes were designated as group A and patients with lymph nodes at station 2 (upper paratracheal), 3 (prevascular and retrotracheal), and 4 (lower paratracheal) were designated as group B. Bronchoscopy was performed in standard fashion under general anesthesia for combined rigid and flexible examinations or conscious sedation for flexible bronchoscopy. TBNA and EBUS were performed as detailed below. Prior to bronchoscopy, mediastinal lymph nodes were identified on thoracic CT. EBUS and TBNA were performed by pulmonologists routinely performing both procedures.

Endobronchial Ultrasound

EBUS was performed, as previously described in detail (11,12). Through a video-bronchoscope (Type BF 1T240; Olympus, Tokyo, Japan), a flexible ultrasound probe with a 20 MHz transducer (UM-BS 20-26R with an EU M30S processor; Olympus) was introduced. The exact location of the target lymph nodes and their relationship to the tracheobronchial tree were noted. The probe then was removed from the working channel, and TBNA was performed.

Transbronchial Needle Aspiration

TBNA was performed as previously described (2-4). Only cytology specimens were obtained with 21-gauge needles (NA-401 D1321; Olympus). The “jab-

bing" method (2) was used for all punctures, i.e., the needle was thrust through the intercartilaginous space with a quick, firm jab to the catheter, while the scope was fixed at the nose or the mouth. A minimum of 2 and a maximum of 6 needle passes were made at each lymph node station.

Cytology specimens were air-dried on site before being sent to the Pathology Department. No ROSE was used, and the pathologist was blinded to the method used for sampling.

Statistical Analysis

Statistical analysis was conducted using SPSS for Windows (version 10.0; SPSS Inc., Chicago, IL, USA). Data are presented as the mean ± standard deviation or N (%), as appropriate. Data were compared using the Student's t-test and a chi-square test at a confidence interval of 95%. A p value < 0.05 was considered statistically significant.

RESULTS

Sixty patients (12 women and 48 men) with a mean age of 56.15 ± 15.32 years (range, 19-85 years) were included in the study. Thirty patients each underwent EBUS-TBNA and conventional TBNA. The main indication for TBNA was the diagnosis of enlarged lymph nodes of unknown origin.

There were no significant differences between the EBUS-TBNA and conventional TBNA groups with respect to the male: female ratio (26:4 vs. 22:8 for conventional and EBUS-TBNA groups, respectively; p= 0.197) and age (54.97 ± 13.74 years vs. 57.33 ± 16.91 years for conventional and EBUS-TBNA groups, respectively; p= 0.595).

The overall diagnostic yield of conventional TBNA was 33.3% (10/30), while EBUS-TBNA had a yield of 66.7% (20/30; p= 0.010). In group A (patients with subcarinal lymph nodes), the yield of conventional TBNA was 33.3% (4/12) compared to 62.5% (5/8) in the EBUS-guided group, but the difference did not reach statistical significance (p= 0.362). In group B, however, EBUS-TBNA had a significantly higher yield compared to conventional TBNA (33.3% (6/18) vs. 68.2% (15/22) for conventional and EBUS-TBNA groups, respectively; p= 0.028].

A definitive diagnosis was established in 30.0% (9/30) and 56.7% (17/30) of the patients in the conventional TBNA and EBUS-TBNA groups, respectively (p= 0.037). In group A, a definitive diagnosis was established in 33.3% (4/12) of the patients in the conventional TBNA group, while 50.0% (4/8) of the patients had a definitive diagnosis in the EBUS-TBNA group (p= 0.648). In group B, 27.8% (5/18) of the patients in the conventional TBNA group, and 59.1% [13/22) of the patients in the EBUS-TBNA group had a definitive diagnosis (p= 0.048, Table 1).

While 17 patients were diagnosed with non-small cell lung carcinoma, small cell lung carcinoma, sarcoidosis, and salivary gland tumor metastasis were diagnosed in 6, 2, and 1 patients, respectively. Cytologic examinations of biopsy specimens of 4 patients revealed normal lymph nodes (Table 2).

The average number of needle passes was four. No complications related to the procedure or to bronchoscopic damage were observed with the use of EBUS and/or TBNA.

Table 1. Diagnostic yields and definitive diagnoses obtained with EBUS-TBNA and conventional TBNA.

	Conventional TBNA	EBUS-TBNA	p
Overall			
Diagnostic yield	10/30 (33.3%)	20/30 (66.7%)	0.010
Definitive diagnosis	9/30 (30.0%)	17/30 (56.7%)	0.037
Group A*			
Diagnostic yield	4/12 (33.3%)	5/8 (62.5%)	0.362
Definitive diagnosis	4/12 (33.3%)	4/8 (50.0%)	0.648
Group B**			
Diagnostic yield	6/18 (33.3%)	15/22 (68.2%)	0.028
Definitive diagnosis	5/18 (27.8%)	13/22 (59.1%)	0.048

* Patients with subcarinal lymph nodes were designated as group A.

** Patients with lymph nodes at station 2 (upper paratracheal), 3 (prevascular and retrotracheal), and 4 (lower paratracheal) were designated as group B.

TBNA: Transbronchial needle aspiration, EBUS: Endobronchial ultrasound.

Table 2. Definitive diagnoses obtained with EBUS-TBNA and conventional TBNA.

	Conventional TBNA (n= 30)	EBUS-TBNA (n= 30)
Non-small cell lung carcinoma	7	10
Small cell lung carcinoma	2	4
Sarcoidosis	-	2
Normal lymph nodes	1	3
Others	-	Metastatic salivary gland carcinoma

TBNA: Transbronchial needle aspiration, EBUS: Endobronchial ultrasound.

DISCUSSION

TBNA is a well-established bronchoscopic technique, but remains underutilized (5). Conventional TBNA is a relatively blind technique, thus preventing target visualization and making smaller lymph nodes and nodes at some specific stations more difficult to access. Limited options currently exist to improve the yield of TBNA, like use of ROSE, increasing the number of needle passes, and utilization of imaging techniques (6-9). EBUS is one of the alternative imaging techniques that permits imaging of the airway and parabronchial structures during bronchoscopy (11-13). In the current study, we aimed to determine whether or not EBUS-TBNA is superior to conventional TBNA in the diagnosis of mediastinal lymphadenopathies and found that the diagnostic yield of EBUS-TBNA was superior to the yield of conventional TBNA at stations other than subcarinal region, in patients with enlarged mediastinal lymph nodes. Moreover, EBUS-TBNA was superior in ability to establish a definitive diagnosis. Although, there was a trend in favor of EBUS-TBNA for the diagnosis of enlarged subcarinal lymph nodes, the difference between the two groups did not reach statistical significance. These findings are in agreement with the findings of Herth et al., who reported that EBUS-TBNA was superior to conventional TBNA at stations other than subcarinal region (84% vs. 58%, respectively) compared to the subcarinal region (86% vs. 74%, respectively), in their randomized study of 200 patients with suspected non-small cell lung carcinoma (14). The lack of significance between the two groups in terms of diagnostic yield at subcarinal region is likely to reflect the relative technical ease of conventional TBNA for subcarinal lymph nodes. Although Shannon et al. in 1996, reported in their randomized, controlled trial that there were no significant differences between EBUS-TBNA and conventional TBNA in terms of sensitivity (82.6% vs. 90.5%), specificity (100% for both), and diagnostic accuracy (86.7% vs. 91.7%), recent evidence indicates that EBUS-TBNA has a higher sensitivity than conventional TBNA (15). In a recent systematic review, Toloza et al. reported a pooled sensitivity of 76%, a pooled specificity of 96%, and a negative predictive value of 71% of TBNA for staging of lung cancer (16). On the other hand, Yasufuku et al. reported a sensitivity of 94.6%, a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 89.5%, and a diagnostic accuracy rate of 96.3% of EBUS-TBNA for staging of lung cancer (17). Similarly, in a study of 502 patients with mediastinal or hilar lymphadenopathies, the sensitivity for EBUS-TBNA was 94%, the specificity was 100% and the diagnostic accuracy was 94% (18). Of note, the lack of significant difference in the study of Shannon et al. might have resulted from the use of ROSE masking the beneficial effect of EBUS guidance (16).

EBUS is safe and minimally invasive technique, and does not require general anesthesia or hospitalization (12,13). The complication rate is extremely low and several studies have not reported any complications at all (9,11,12,19). Ernst et al. reported no complications with EBUS-TBNA, in their study, which compared real-time EBUS-TBNA and mediastinoscopy for pathologic staging in patients with mediastinal adenopathy and suspected non-small cell lung carcinoma, and suggested that EBUS might prevent rare complications associated with conventional TBNA such as inadvertent vascular and mediastinal injury (20). In the current study as well, no complications were noted.

There were some potential limitations to the current study, including a small sample size, the lack of surgical confirmation, and the lack of data regarding the clinical diagnosis established with other methods in patients, in whom a diagnosis could not be established with conventional/EBUS TBNA.

In conclusion, the diagnostic yield of EBUS-TBNA was superior to the yield of conventional TBNA at stations other than subcarinal region. In our institution, we are routinely performing EBUS-TBNA for the diag-

nosis of mediastinal lymphadenopathies at stations other than subcarinal region, and we strongly recommend its use.

CONFLICT of INTEREST

None declared.

REFERENCES

1. *Arroliga AC, Matthay RA. The role of bronchoscopy in lung cancer. Clin Chest Med 1993; 14: 87-98.*
2. *Mehta AC, Kavuru MS, Meeker DP, Gephardt GN, Nunez C. Transbronchial needle aspiration for histology specimens. Chest 1989; 96: 1228-32.*
3. *Wang KP, Brower R, Haponik EF, Siegelman S. Flexible transbronchial needle aspiration for staging of bronchogenic carcinoma. Chest 1983; 84: 571-6.*
4. *Gasparini S, Zuccatosta L, DeNictolis M. Transbronchial needle aspiration of mediastinal lesions. Monaldi Arch Chest Dis 2000; 55: 29-32.*
5. *Haponik EF, Shure D. Underutilization of transbronchial needle aspiration: experiences of current pulmonary fellows. Chest 1997; 112: 251-3.*
6. *Chin R Jr, McCain TW, Lucia MA, Cappellari JO, Adair NE, Lovato JF, et al. Transbronchial needle aspiration in diagnosing and staging lung cancer: how many aspirates are needed? Am J Respir Crit Care Med 2002; 166: 377-81.*
7. *Garpestad E, Goldberg S, Herth F, Garland R, LoCicero J 3rd, Thurer R, et al. CT fluoroscopy guidance for transbronchial needle aspiration: an experience in 35 patients. Chest 2001; 119: 329-32.*
8. *Herth FJF, Becker HD, Ernst A. Ultrasound guided transbronchial needle aspiration (TBNA): an experience in 242 patients. Chest 2003; 123: 604-7.*
9. *Okamoto H, Watanabe K, Nagatomo A, Kunikane H, Aono H, Yamagata T, et al. Endobronchial ultrasonography for mediastinal and hilar lymph node metastases of lung cancer. Chest 2002; 121: 1498-506.*
10. *Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. Chest 1997; 111: 1718-23.*
11. *Becker HD, Herth F. Endobronchial ultrasound of the airways and the mediastinum. In: Bolliger CT, Mathur PN (eds). Interventional bronchoscopy. Progress in respiratory research, vol 30. Basel, Karger, 2000; 80-93.*
12. *Herth F, Becker HD. Endobronchial ultrasound (EBUS): assessment of a new diagnostic tool in bronchoscopy for staging of lung cancer. Onkologie 2001; 24:151-4.*
13. *Kurimoto N, Murayama M, Morita K, Kobayashi A, Uomoto M, Nishizaka T. Clinical applications of endobronchial ultrasonography in lung diseases. Endoscopy 1998; 30 (Suppl 1): S8-12.*
14. *Herth F, Becker HD, Ernst A. Conventional vs. endobronchial ultrasound-guided transbronchial needle aspiration: a randomized trial. Chest 2004; 125: 322-5.*
15. *Shannon JJ, Bude RO, Orens JB, Becker FS, Whyte RI, Rubin JM, et al. Endobronchial ultrasound-guided needle aspiration of mediastinal adenopathy. Am J Respir Crit Care Med 1996; 153: 1424-30.*
16. *Toloza EM, Harpole L, Detterbeck F, McCrory DC. Invasive staging of non-small cell lung cancer: a review of the current evidence. Chest 2003; 123: 157S-166S.*
17. *Yasufuku K, Chiyo M, Koh E, Moriya Y, Iyoda A, Sekine Y, et al. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer. Lung Cancer 2005; 50: 347-54.*
18. *Herth FJ, Eberhardt R, Vilmann P, Krasnik M, Ernst A. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. Thorax 2006; 61: 795-8.*
19. *Herth F, Becker HD. Endobronchial ultrasound of the airways and the mediastinum. Monaldi Arch Chest Dis 2000; 55: 36-44.*
20. *Ernst A, Anantham D, Eberhardt R, Krasnik M, Herth FJ. Diagnosis of mediastinal adenopathy-real-time endobronchial ultrasound guided needle aspiration versus mediastinoscopy. J Thorac Oncol 2008; 3: 577-82.*