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KLİNİK ÇALIŞMA
RESEARCH ARTICLE

Diagnostic utility of endobronchial ultrasound-guided transbronchial needle aspiration in elderly patients

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SUMMARY

Diagnostic utility of endobronchial ultrasound-guided transbronchial needle aspiration in elderly patients

Introduction: *In the elderly population, diagnosis and initial treatment should be considered as soon as possible because of co-morbidities and complications. We aimed to evaluate the findings of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) to determine the diagnostic utility of EBUS-TBNA in patients 65 years of age and older.*

Materials and Methods: *We retrospectively evaluated records of patients who underwent EBUS-TBNA from February 2014 to August 2017 for diagnosis and/or staging. The demographic data, clinical and EBUS findings, diagnostic procedures during EBUS-TBNA and the incidence of accurate diagnosis with EBUS-TBNA in patients 65 years of age and older and in younger patients were determined.*

Results: *A total of 496 patients [younger patients (< 65 years, n= 293, M/F: 198/95) and older patients (≥ 65 years, n= 203, M/F: 155/48)] who underwent EBUS-TBNA at our clinic were included. The mean age of the older patients was 69.7 ± 5.1 years, while the mean age of the younger patients was 51.4 ± 10.4 years. Overall, the diagnostic accuracy of EBUS-TBNA was 96.5% in the older patients and 98% in the younger patients. The diagnostic utility of EBUS-TBNA in the two study groups was similar (p= 0.191). While 196 (96.6%) of the older patients had no complications during EBUS-TBNA, 285 (97.3%) of the younger patients had no complications. Complication rates were not statistically different between the two groups (p= 0.389).*

Conclusion: *In general, EBUS-TBNA is a safe method. The results of this study demonstrated the high diagnostic value of EBUS-TBNA and its low complication rates in patients 65 years of age and older.*

Key words: *Endobronchial ultrasound; transbronchial needle aspiration; complications; diagnostic utility; elderly*

ÖZET

Yaşlı hastalarda endobronşiyal ultrason eşliğinde alınan transbronşiyal iğne aspirasyonunun tanı değeri

Giriş: *Yaşlı nüfusta, komorbidite ve komplikasyonlar nedeniyle tanı ve tedavi en kısa zamanda düşünülmelidir. Bu yazıda 65 yaş ve üzerindeki hastalarda endobronşiyal ultrasonografi eşliğinde alınan transbronşiyal iğne aspirasyonunun (EBUS-TBİA) kullanımı ve tanı başarısını değerlendirmeyi amaçladık.*

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Materyal ve Metod: *Şubat 2014-Ağustos 2017 tarihleri arasında tanı ve/veya evreleme amaçlı EBUS-TBİA uygulanan hastaların kayıtlarını retrospektif olarak değerlendirdik. Altmış beş yaş ve üzeri ve daha genç hastaların demografik verileri, klinik ve EBUS bulguları, EBUS-TBİA sırasında işlem bilgileri ve işlemin tanı değeri kaydedildi.*

Bulgular: *Kliniğimizde EBUS-TBİA uygulanan 496 hasta [genç hastalar (< 65 yaş, n= 293, E/K: 198/95) ve yaşlı hastalar (≥ 65 yaş, n= 203, M/F: 155/48)] dahil edildi. Yaşlı hastaların ortalama yaşı 69.7 ± 5.1 yıl iken, daha genç yaştaki hastaların yaş ortalaması 51.4 ± 10.4 idi. Genel olarak, EBUS-TBİA'nın tanısal doğruluğu yaşlı hastalarda %96.5, genç hastalarda %98'idi. Her iki grupta da EBUS-TBİA'nın tanı değeri benzerdi (p= 0.191). EBUS-TBİA sırasında yaşlı hastaların 196'sında (%96.6) herhangi bir komplikasyon görülmezken, genç hastaların 285'inde (%97.3) komplikasyon gelişmedi. Komplikasyon oranlarına bakıldığında iki grup arasında istatistiksel olarak anlamlı fark yoktu (p= 0.389).*

Sonuç: *Genel olarak, EBUS-TBİA güvenli bir yöntemdir. Bu çalışmanın sonuçları 65 yaş ve üstündeki hastalarda EBUS-TBİA'nın yüksek tanısal değerini ve düşük komplikasyon oranlarını ortaya koymuştur.*

Anahtar kelimeler: *Endobronşiyal ultrason; transbronşiyal iğne aspirasyonu; komplikasyonlar; tanı değeri; yaşlı*

INTRODUCTION

In the elderly population, co-morbidities, such as diabetes mellitus, renal failure, ischemic heart disease and congestive heart failure, are common, and cognitive problems, decreased social support, atypical clinical presentations and diagnostic issues make the approach to this population difficult. Similarly, structural, physiological and immunological changes that occur in the respiratory system with age may also cause loss of function. Due to these and similar problems in the elderly, the number of medications used increases. The risk of side effects increases as the number of medications increases, consequently, the approach to the elderly population becomes even more difficult (1).

Endobronchial ultrasonography (EBUS) is an ultrasound method developed to visualize structures in the mediastinum and hilum. It enables real-time transbronchial needle aspiration (TBNA) of the mediastinal and hilar lymph nodes (LNs) or lesions accessible via the major airways. Over the last decade, several studies have proved the high diagnostic accuracy, minimal invasiveness and wide accessibility of hilar and mediastinal nodes with the use of convex probe EBUS-TBNA. Usage of EBUS-TBNA is increasing because of its safety, simplicity and high diagnostic yield in both benign and malignant conditions (2). EBUS-TBNA is a well-tolerated procedure, and its complications are rare and similar to those of standard bronchoscopy and conventional TBNA, including fever, cardiac arrhythmias, nausea, vomiting, bleeding from major vessels, pneumomediastinum, mediastinitis, pneumothorax, bronchospasm and laryngospasm. Major complications are reported at lower than 0.1%. Bleeding complications are much less likely with EBUS-TBNA than with blind TBNA as the procedure is performed with real-time visualization of the needle (3).

To the best of our knowledge, very little work exists that examines the influence of age on EBUS in the elderly (4,5). The aim of this study is to describe the main indications, final diagnosis and complications of EBUS-TBNA in elderly patients as compared with younger patients.

MATERIALS and METHODS

This single-centre observational study was conducted retrospectively from February 2014 to August 2017. Patients referred to our department with hilar and mediastinal LNs and/or lesions adjacent to major air ways for diagnosis and/or staging were included the study. Patients who had a bleeding tendency, coagulation dysfunction or severe cardiac insufficiency were excluded. Patients were divided into two groups: those younger than 65 years of age and those 65 years of age and older. The indications were as follows: for diagnosis, staging and diagnosis + staging. Written informed consent was obtained from all patients prior to the procedure. In all cases, EBUS-TBNA was performed as an out-patient procedure in dedicated bronchoscopy suites using endoscopic ultrasound systems EB-1970UK-Pentax and HiVision Avius (Hitachi, Tokyo, Japan) and BF-UCI60F-OL8/ BF-LlC26OF-OL8 and EU-C60/EU-C200 (Olympus, Tokyo, Japan) with either 21 or 22 gauge needles GUS-21-18-021(Medi-Globe Corporation, Achenmühle, Germany) and NA-201SX-4022 (Olympus, Tokyo, Japan), respectively, to sample the LNs and/or lesions adjacent to major airways. As a routine application at our clinic, topical lidocaine spray and 0.07 mg/kg IV

midazolam, respectively, were offered to all patients by the bronchoscopist prior to the procedure for conscious sedation. Additional doses of 1 mg midazolam were given in 5-minute intervals to patients deemed to need them by the bronchoscopist. Flumazenil was available for the treatment of respiratory depression (6). Electrocardiogram, oxygen saturation and non-invasive blood pressure monitoring were performed throughout the procedure. Approximately three needle aspirations were performed for each target lesion. The short axis diameter of a lymph node or a lesion, station of the lymph node or lesion and the number of needle passes per subject and per lymph node or lesion were recorded for each subject. All cases were confirmed by pathological diagnosis. Rapid on site cytological examination (ROSE) was not available. Non-diagnostic findings were validated by mediastinoscopy, video-assisted thoracoscopic surgery (VATS) or thoracotomy. If a patient rejected these procedures, a minimum of six months of radiological follow-up was done.

Statistical Analysis

We described patient characteristics using proportions for categorical or ordinal values and means for continuous variables. Older and younger patients were compared. Chi-square tests were used to determine statistical significance. A value of $p< 0.05$ was assumed as statistically significant. Statistical analysis was accomplished using SPSS (PASW Statistics for Windows, Version 21.0; SPSSInc., Chicago, IL, USA) software.

RESULTS

From February 2014 to August 2017, a total of 496 patients underwent EBUS-TBNA. Younger patients (< 65 years, n= 293, M/F: 198/95) and older patients (≥ 65 years, n= 203, M/F: 155/48) with a total of 847 LNs or lesions adjacent to major airways (an average of 1.7 nodes per patient) were included in the study. The mean age of older patients was 69.7 ± 5.1 years, while the mean age of younger patients was 51.4 ± 10.4 years. While diagnosis was a more common indication (122 of 203, 60.1% in older patients; 224 of 293, 76.5% in younger patients, p= 0.002), staging (29 of 203, 14.3% in older patients; 25 of 293, 8.5% in younger patients, p= 0.04) and diagnosis + staging (52 of 203, 25.6% in older patients; 44 of 293, 15% in younger patients, p= 0.03) were also indications, respectively. Indications for EBUS-TBNA were significantly different between study groups. The mean short axes of the nodes were 18.1 ± 10.40 mm in older patients and 17.9 ± 9.60 in younger patients on the ultrasound. The mean procedure time was 15 ± 5 min in older patients and 14 ± 9 min in younger patients. The mean short axes and the mean procedure time were not statistically different between older and younger patients (p= 0.184). The localisation of the LNs or lesions adjacent to major airways is shown in Table 1. The most common sites of TBNA were the subcarinal station (95, 29.4% in older patients; 177, 33.8% in younger patients), followed by the lower right paratracheal station (84, 26.0% in older patients; 129, 24.6% in younger patients). There was no significant difference between older and younger patients in terms of the stations of the LNs or lesions (p= 0.271) (Table 1). There were 36 mass lesions in older patients (16 at the paratracheal station, 12 at the hilar station, 7 at the interlobar station, 1 at the subcarinal station). No mass lesions were detected in younger patients.

The final diagnoses in older patients were as follows: 15 (7.5%) patients had a diagnosis of small cell lung cancer, 18 (8.9%) patients had squamous cell carcinoma, 28 (13.8%) patients had adenocarcinoma,

Table 1. Nodal stations distributions

Stations of the lymph nodes/lesions adjacent to major airways	N (%) older patients	N (%) younger patients	p
7	95 (29.4)	177 (33.8)	0.271
4R	84 (26.0)	129 (24.6)	
11L	36 (11.2)	63 (12.0)	
11R	34 (10.5)	46 (8.8)	
4L	31 (9.6)	47(9.0)	
10R	22 (6.8)	33 (6.3)	
Others	21(6.5)	29 (5.5)	
Total	323(100)	524(100)	

25 (12.4%) patients had non-small cell lung carcinoma not otherwise specified (NSCLC-NOS), 35 (17.2%) patients had anthracotic lymph nodes, 18 (8.8%) patients had sarcoidosis, 16 (7.9%) patients had extrathoracic malignancy metastasis, 33 (16.2%) patients had reactive lymph node, 4 (1.9%) had tuberculosis, 3 (1.5%) had lymphoma, 1 (0.5%) had mesothelioma and 7 (3.4%) provided inadequate material (Table 2).

The final diagnoses in younger patients were as follows: 25 (8.4%) patients had a diagnosis of small cell lung cancer, 21 (7.2%) patients had squamous cell carcinoma, 34 (11.6%) patients had adenocarcinoma, 30 (10.2%) patients had NSCLC-NOS, 42 (14.2%) patients had anthracotic lymph nodes, 65 (22.3%) patients had sarcoidosis, 22 (7.5%) patients had extrathoracic malignancy metastasis, 41 (14%) patients had reactive lymph nodes, 3 (1.02%) patients had tuberculosis, 3 had (1.02%) lymphoma, 2 (0.6%) had mesothelioma and 5 (1.6%) provided inadequate material (Table 2).

No major complications, such as respiratory failure requiring interventions other than oxygen administration, fever lasting longer than 24 h, pneumothorax requiring intervention, prolonged bronchospasm, and haemorrhage not responsive to application of topical adrenaline and/or cold saline and requiring further intervention, were recorded after the procedure.

A total of 196 (96.6%) of the older patients had no complications during EBUS-TBNA, while 1 (0.5%) patient had mild respiratory depression requiring high flow oxygen administration, 1 (0.5%) patient had a haemorrhage that was controlled with a cold saline, 2 (1%) patients had agitation, 2 (1%) patients had a cardiovascular event (transient tachycardia) and 1 (0.5%) patient had fever (Table 3).

Table 2. Final diagnosis of patients

Diagnosis	N (%) older patients	N (%) younger patients
Small cell lung cancer	15 (7.5)	25 (8.4)
Squamous cell carcinoma	18 (8.9)	21 (7.2)
Adenocarcinoma	28 (13.8)	34 (11.6)
NSCLC-NOS	25 (12.4)	30 (10.2)
Anthracosis	35 (17.2)	42 (14.2)
Sarcoidosis	18 (8.8)	65 (22.3)
Tuberculosis	4 (1.9)	3 (1.02)
Normal lymph node	33 (16.2)	41 (14)
Extra thoracic malignancies	16 (7.9)	22 (7.5)
Lymphoma	3 (1.5)	3 (1.02)
Mesothelioma	1 (0.5)	2 (0.6)
Inadequate	7 (3.4)	5 (1.6)
Total	203 (100)	293 (100)

NSCLC-NOS: Non-small cell lung carcinoma-not otherwise specified.

Table 3. Complications during EBUS-TBNA

Complications	N (%) older patients	N (%) younger patients	p
No complications	196 (96.6)	285 (97.3)	0.389
Respiratory depression	1(0.5)	1 (0.3)	
Haemorrhage	1(0.5)	0 (0)	
Fever	1(0.5)	0 (0)	
Cardiovascular events	2 (1)	1 (0.3)	
Poor tolerance/Agitation	2 (1)	5 (1.7)	
Cough	0 (0)	1 (0.3)	

Of the younger patients, 285 (97.3%) had no complications during EBUS-TBNA, while 1(0.3%) patient had mild respiratory depression requiring high flow oxygen administration, 1 (0.3%) patient had a cardiovascular event (transient tachycardia), 5 (1.7%) patients had agitation and 1 (0.3%) patient had a cough (Table 3). Complication rates were not statistically different between the two groups (p= 0.389).

Two of the 7 elderly patients, who had inadequate material accepted mediastinoscopy. In the case where inadequate material was obtained due to agitation, the diagnosis was tuberculosis after mediastinoscopy. The other case was diagnosed as renal cell carcinoma metastasis after mediastinoscopy. This patient had a haemorrhage that was controlled with cold saline during the procedure. The remaining five cases did not accept invasive procedures or re-EBUS, but no radiological progression was observed after at least six months of follow-up. Overall, the diagnostic accuracy of EBUS-TBNA in older patients was 96.5%.

One of the five younger patients with inadequate material accepted mediastinoscopy. In this patient, EBUS was performed for staging. The lymph node was reported as non-metastatic after EBUS; however, post-operatively, it was reported as adenocarcinoma metastasis. The remaining four cases did not accept invasive procedures or re-EBUS, but no radiological progression was observed after a minimum of six months of follow-up. Overall, the diagnostic accuracy in younger patients was 98%. The diagnostic utility of EBUS-TBNA in the two study groups was similar (p= 0.191).

DISCUSSION

The main findings of the present study are the similar complication rates and diagnostic yield of EBUS-TBNA in older and younger patients. These findings suggest that the risk of adverse events related to EBUS-TBNA does not increase with age, and EBUS-TBNA should not be avoided in elderly patients when a clinical indication is found.

Convex probe EBUS-TBNA is a minimally invasive method increasingly used because it is safe and simple and produces a high diagnostic yield. It has also acquired importance considering cases in which surgical procedures are contraindicated or unnecessary (7).

Erdogan et al. reported that EBUS-TBNA had 92% diagnostic rate in distinguishing benign from malignant mediastinal and/or hilar LNs (8). In the study of Evision et al., patients were divided into younger than 70 (< 70 yr) or 70 and older (≥ 70 yr) age categories, and diagnostic accuracy was found to be significantly higher in those aged 70 yr or above (90.2% versus 96.0%; p= 0.02) for the nodal sampling in patients with confirmed or suspected lung cancer (4). This result was a surprise and most likely reflected a higher rate of false negative sampling in the younger cohort. Overall, we found the diagnostic accuracy of EBUS-TBNA was 96.5% in older patients and 98% in younger patients.

The EBUS procedure is usually performed as an outpatient procedure with local anaesthesia and conscious sedation. It can also be performed under general anaesthesia with rigid bronchoscopy, bronchoscopy through the intubation tube or laryngeal mask. EBUS-TBNA has indications in both benign and malignant conditions adjacent to airways (9). Indications for EBUS-TBNA were significantly different between older and younger patients in this study. When we looked at the final diagnoses, while younger patients had 46.8% malignant diseases, older patients had 52.2% malignant diseases. As in our study, the incidence of malign diseases increases with age (10). Sarcoidosis is a disease that is seen in the young population (average 35-45 years of age) (11). The findings of this study are consistent with the literature, and sarcoidosis was more frequently found in younger patients (22.3%) than in older patients (8.8%). On the other hand, anthracotic lymph nodes were more frequently found in older patients (17.2%) than in younger patients (14.2%). This can be attributed to a longer duration of exposure to indoor and outdoor air pollution in older patients as opposed to younger patients. Two of the 7 elderly patients, who had inadequate material accepted mediastinoscopy. One of them was diagnosed as tuberculosis, the other case was diagnosed as renal cell carcinoma metastasis after mediastinoscopy. This patient had a haemorrhage that was controlled with cold saline during the procedure. Renal cell carcinomas are frequently hypervascular haemorrhagic tumours (12). Presumably, because of this, we obtained inadequate fibrin material.

The cumulative number of clinical complications reported in large studies was 126 out of 12,351(1.02%) procedures (13). There is no uniform description or definition for EBUS complications. In the British Thoracic Society Bronchoscopy Guideline, major complications include major bleeding (defined as the need for resuscitation, transfusion, critical care

admission or death), cardiac arrhythmia requiring intervention, seizure, myocardial infarction or pulmonary edema, pneumothorax requiring intercostal chest drain or aspiration, over sedation requiring ventilator support or sedation reversal, unplanned hospital admission or death. Minor complications include mild or moderate bleeding (defined as the need for continual suctioning or vasoconstrictors), cardiac arrhythmia not requiring intervention, hypotension requiring intervention and poor tolerance of the procedure requiring early termination (14).

In the study of Evision et al., major complications, namely bleeding and prolonged post-procedure hypoxia in patients > 70 years of age were reported at 0.4%, and minor complications were reported at 6.7%. However, there was no significant difference in the rate of minor (p= 0.057) or major (p= 0.19) complications between the younger and older age groups, though poor procedural tolerance was significantly more common in the younger than 70 year old age group (p= 0.036), despite the higher levels of sedation (4).

Bleeding is the most common complication reported in large studies. The AQuIRE Registry reported higher complications in those aged > 70 years of age. In the same study, bleeding that required intervention occurred in three (0.2%) patients post-EBUS-TBNA, and resulted in one death due to major bleeding (5).

Elderly patients are potentially at increased risk of complications because of underlying co-morbidities. The hepatic metabolism of midazolam may decrease in the elderly population. However, several studies have shown that elderly patients tolerate the procedure well with no observed increased incidence of complications (6).

In a study by Casal et al., hypertension (six patients), tachy arrhythmia (three patients) and transient hypoxaemia (two patients) were the most common minor complications in those administered moderate sedation (15). In our study, 196 (96.6%) of the older patients had no complications during EBUS-TBNA, while 1 (0.5%) patient had mild respiratory depression requiring high flow oxygen administration, 1 (0.5%) patient had a haemorrhage that was controlled with cold saline, 2 (1%) patients had agitation, 2 (1%) patients had cardiovascular events (transient tachycardia) and 1 (0.5%) patient had fever. All patients received midazolam for moderate sedation, and there was no major complication associated with midazolam. A total of 285 (97.3%) younger patients had no complications during EBUS-TBNA, while 1 (0.3%) patient had mild respiratory depression requiring high flow oxygen administration, 1(0.3%) patient had a cardiovascular event (transient tachycardia), 5 (1.7%) patients had agitation and 1 (0.3%) patient had a cough. Complication rates were not statistically different between the two groups (p= 0.389). There was no mortality in our study.

There are some limitations in our study. First, it is a retrospective analysis. Second, these EBUS-TBNA results were single-centre results, and the sample size was relatively small. Finally, we reported only the complications occurring within 24 h of the procedure. Unfortunately, we have no records about complications after 24 h and up to two months post-procedure.

The most valuable aspect of the present study is the comparison of the general diagnostic utility of EBUS-TBNA between older and younger patients, which, to our knowledge, has not been previously demonstrated. In our study, the diagnostic utility of EBUS-TBNA in older and younger patients was similar (p= 0.191). The complication rates were not statistically different between the two groups (p= 0.389).

CONCLUSIONS

In conclusion, EBUS-TBNA is an important tool to use in the diagnosis of pulmonary diseases and should be considered in elderly patients whenever indicated. EBUS-TBNA can be performed safely with minor, self-limiting complications, regardless of the patient's age.

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