The Diagnostic Yield of Endobronchial Ultrasound Transbronchial Needle Aspiration (EBUS-TBNA) in Respiratory Compromised Patients under General Anesthesia

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ABSTRACT

Background: Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) is a frequently used method for obtaining tissue samples for the diagnosis of various respiratory conditions, including lung cancer staging. In most cases, EBUS-TBNA is performed under moderate sedation (MS). However, in cases of respiratory compromised patients, if this procedure is performed, it is conducted under general anesthesia (GA).

Objective: To assess the diagnostic yield of EBUS-TBNA among respiratory compromised patients.

Methods: Data of consecutive patients (n=191) who underwent EBUS-TBNA at our medical center between January 2019 and December 2019 were retrospectively analyzed. Respiratory compromised patients underwent GA and patients without respiratory compromise were mostly moderately sedated (MS). Characteristics, diagnostic yield, and complication rates were compared.

Results: Diagnostic yield was similar between the two sedation modes (89% in GA group and 78% in the MS group, P = 0.11). The number of total samples obtained per procedure was significantly higher in the GA vs. the MS group (4.1 ± 2.1 vs. 2.1 ± 1.33, P < 0.01). The overall complication rate was 13% and 20.9% in the GA vs. the MS groups, respectively (P = 0.14), with the most frequent complication being minor bleeding. Interestingly, while the number of brushings, bronchoalveolar lavage, and endobronchial biopsy were similar, the percent of subjects who underwent transbronchial biopsy was significantly higher in the GA group (49% vs. 24.2%, P < 0.01).

Conclusion: EBUS-TBNA performed under GA among respiratory compromised patients is safe and has similar diagnostic yield to that of patients without a respiratory compromise.

IMAJ 2022; 24: 225–228

KEY WORDS: anesthesia, diagnostic yield, endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA), interventional pulmonology

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Rapid diagnosis and accurate staging are crucial in subjects with mediastinal lymphadenopathy, especially in those with suspected lung malignancy [1,2]. Although new tests are being explored [3,4], histological staging is indispensable in selecting candidates for surgical resection [5,6]. Endobronchial ultrasound transbronchial needle aspiration (EBUS-TBNA) allows reaching the same areas accessible to mediastinoscopy, as well as to hilar and smaller nodes [1,2,7,8], with a high safety profile [1,8]. It also reduces expenditures when compared to mediastinoscopy [5], while achieving similar results [2,5,8]. Therefore, the American College of Chest Physicians (ACCP) guidelines for lung cancer recommended it as the first-line for invasive mediastinal staging [9,10].

The two main types of sedation for EBUS-TBNA are moderate sedation (MS) and general anesthesia (GA) [11-13]. Nevertheless, since GA is not readily available, MS is more frequently used. In our experience, since many patients present with respiratory co-morbidities such as advanced chronic obstructive pulmonary disease (COPD), pulmonary fibrosis with severe dyspnea and even hypercapnia [14-16], they pose an increased anesthetic and operative risk. Therefore, these subjects usually undergo the procedure under GA. In this study, we assessed these relatively severe cases, their diagnostic yield and outcomes following EBUS-TBNA.

PATIENTS AND METHODS

STUDY POPULATION

Data from all subjects with severe respiratory co-morbidities (e.g., COPD, idiopathic pulmonary fibrosis) who underwent EBUS-TBNA were extracted from electronic medical records. Data were anonymized and coded by sequential numbering and divided according to sedation-type groups (MS and GA) for further analysis.

EBUS-TBNA PROCEDURES

All procedures were performed by the interventional pulmonology staff. A flexible real-time ultrasound/optic fiber bronchoscope was used (BF-UC180F; Olympus Medical Systems, Tokyo, Japan).

Ultrasound imaging was conducted using a linear ultrasound transducer (EU-ME1; Olympus Medical Systems, Tokyo, Japan). Transbronchial needle biopsies were taken with a compatible 21 or 22-G needle (NA-201SX; Olympus Medical Systems, Tokyo, Japan).

SEDATION TYPES

GA subjects were sedated in the OR by an anesthesiologist as customary. In all the GA procedures, a laryngeal mask was used. The MS subjects were induced by intravenous boluses of midazolam (3–10 mg) and fentanyl (80–200 μg) given by the operating pulmonologist. Propofol was used when needed.

CRITERIA FOR EBUS-TBNA USING GA

All subjects with severe COPD (FEV1% below 50%), high level of PCO_2 (above 55 mmHg), tachypnea above 20 breaths/min, severe congestive heart disease with New York Heart Association (NYHA) classification of III / IV, or any severe co-morbid disease underwent EBUS-TBNA using GA.

STATISTICAL ANALYSIS

To demonstrate a 20% difference in the diagnostic yield between sedation types, ensure a statistical power of at least 80%, and allow for a level of confidence of 5%, a sample group of 200 subjects was calculated: 100 subjects for each sedation type. Comparison between the two study groups was conducted using *t*-test, Mann-Whitney test, Fisher's exact test, or Pearson chi-square test according to the scale measured variables. Sensitivity was calculated as the rate of true-positive vs. all participants. Linear or logistic regression, as appropriate, was used to neutralize confounders such as gender, disease of referral and stage, number of lymph nodes sampled, pathological imaging prior to procedure, complications related to procedure, etc. $P < 0.05$ was considered significant. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 23 (SPSS, IBM Corp, Armonk, NY, USA).

ETHICS APPROVAL

The study was approved by the local institutional review board in accordance with the Declaration of Helsinki and with good clinical practice guidelines (0124-17-MMC).

RESULTS

PATIENT CHARACTERISTICS

During the study period, 191 patients underwent EBUS-TBNA; 91 procedures were performed under MS and 100 under GA. Demographically, the groups were similar except for a slightly higher mean age among the MS group ($P = 0.01$) [Table 1]. All other parameters, excluding severe respiratory co-morbidity, such as sex, smoking history, and non-respiratory co-morbidities

were comparable between the groups [Table 1]. Extremely severe co-morbid respiratory illnesses were represented by worse lung function test results (i.e., lower DLCO% and FEV1%) and elevated PCO_2 levels were significantly more prevalent among the GA group ($P < 0.001$) [Table 1].

Table 1. Patient characteristics

Parameter	General anesthesia N=100	Moderate sedation N=91	P value
Age (mean ± SD)	61.3 ± 13.9	66.4 ± 13	**0.01**
Sex (% male)	59	63.7	0.50
Smokers (%)	53 (53%)	56 (61.5%)	0.28
Pack years (mean ± SD)	43.2 ± 28.5	54.9 ± 35.3	0.19
Co-morbidities			
IHD (%)	14 (14%)	22 (24%)	0.08
CHF (%)	6 (6%)	5(5.5%)	0.88
Renal failure (%)	7 (7.1%)	8(8.8%)	0.66
DM Type II (%)	35 (35%)	24 (26.4%)	0.12
Hypertension (%)	39 (39.4%)	31 (34.1%)	0.45
COPD (%)	16 (16%)	20 (22%)	0.29
Asthma (%)	2 (2%)	2 (2.2%)	0.93
Mental/ Psychiatric condition (%)	18 (18.2%)	15 (16.5%)	0.76
Obesity (%)	23 (23.2%)	18 (19.8%)	0.56
Other significant co-morbidity (%)	62 (62.6%)	58 (63.7%)	0.87
Known malignancy (%)	32 (31%)	23 (25.3%)	0.38
Lung function tests			
FEV1 (% ± SD)	58.3 ± 21.9	79.5 ± 21.7	< 0.001
FVC (% ± SD)	87.6 ± 24.1	84.3 ± 18	0.48
FEV1/FVC ± SD	74.1 ± 15	74.7 ± 16.96	0.86
TLC (% ± SD)	90.4 ± 20.8	94.1 ± 10.4	0.52
DLCO (% ± SD)	51.1 ± 25.1	75.2 ± 25.17	< 0.001
Oxygen saturation at rest (± SD)	87 ± 4	94 ± 5	< 0.001
Transcutaneous PCO2 (± SD)	54 ± 4	38 ± 6	< 0.001

CHF = congestive heart failure, dm = diabetes mellitus,
COPD = chronic obstructive pulmonary disease, IHD = ischemic heart disease, SD = standard deviation

Pulmonary functions
DLCO = diffusing lung capacity for carbon monoxide (CO), FEV1 = forced expired volume in the first second, FVC = forced vital capacity, TLC = total lung capacity

A SIMILAR DIAGNOSTIC YIELD IS ACHIEVED IN SEVERE RESPIRATORY COMPROMISED PATIENTS

Our primary outcome was the diagnostic yield, which was defined by attaining a specific diagnosis made by the EBUS-TB-NA biopsy. As expected, the procedure provided a high diagnostic yield, with no significant difference between the groups (89% in GA group and 78% in the MS group; $P = 0.11$). Approximately half (54%) of the subjects were eventually diagnosed with cancer. Malignancy was diagnosed in 60 subjects in the MS group (65.9%) vs. 40 in the GA group (40%) ($P < 0.01$) [Figure 1] and the sensitivity rate for detection of malignancy was similar between the groups (74% vs. 78%, respectively).

There were no major complications or escalation of care in either group. The overall complication rate was 13% and 20.9% in the GA vs. the MS groups, respectively ($P = 0.14$). The most frequent complication was minor bleeding (11% vs. 12.1%, respectively, $P = 0.81$). Other complications included transient hypoxemia (O_2 saturation < 90%), hypotension (systolic blood pressure < 90 mmHg) and bronchospasm episodes (1% in both groups, $P = 0.94$), which resolved completely following bronchodilator administration. Same day discharge rate was significantly higher among the MS group as compared with that of the GA group ($P < 0.01$).

GA ENABLES FURTHER INVESTIGATIONAL MODALITIES DURING THE SAME PROCEDURE

The number of additional diagnostic procedures performed for each patient, in addition to the EBUS-TBNA, was compared. Interestingly, while the number of brushings, bronchoalveolar lavage, and endobronchial biopsy was similar in both groups, the percent of subjects that underwent transbronchial biopsy (TBB) was significantly higher in the GA group (49% vs. 24.2%, $P < 0.01$).

Another parameter examined was the number of lymph nodes examined per procedure in those with suspected lung cancer. In general, the number of total samples obtained per procedure was also significantly higher in the GA vs. the MS group (4.1 ± 2.1 vs. 2.1 ± 1.33, $P < 0.01$).

In fact, when comparing the final diagnoses, other than cancer, between the two types of sedation we found that sarcoidosis (n=39, of which 31 were in the GA group) and silicosis (n=5) were mostly found using GA ($P < 0.01$) [Figure 1]. Notably, the diagnostic accuracy of EBUS-TBNA alone for these conditions was lower (i.e., 66% for sarcoidosis and only 40% for silicosis), thus requiring additional tests such as TBB or cryobiopsy to reach a final diagnosis. Thus, by using GA, a diagnosis could be achieved in severe patients during one procedure that often included the TBB as well.

DISCUSSION

EBUS-TBNA is recommended as a first line diagnostic modality for histological sampling by the ACCP [9] in managing sub-

Figure 1. Final diagnoses per sedation type

Final diagnoses are shown for the general anesthesia and moderate sedation groups.
*Other includes Still's disease, non-specific interstitial pneumonia, interstitial bronchiolitis, desquamative interstitial pneumonia, and bronchiolitis obliterans with organizing pneumonia (BOOP)

NSCLC = non-small-cell lung carcinoma, SCLC = small-cell lung carcinoma

[A] General anesthesia

[B] Moderate sedation
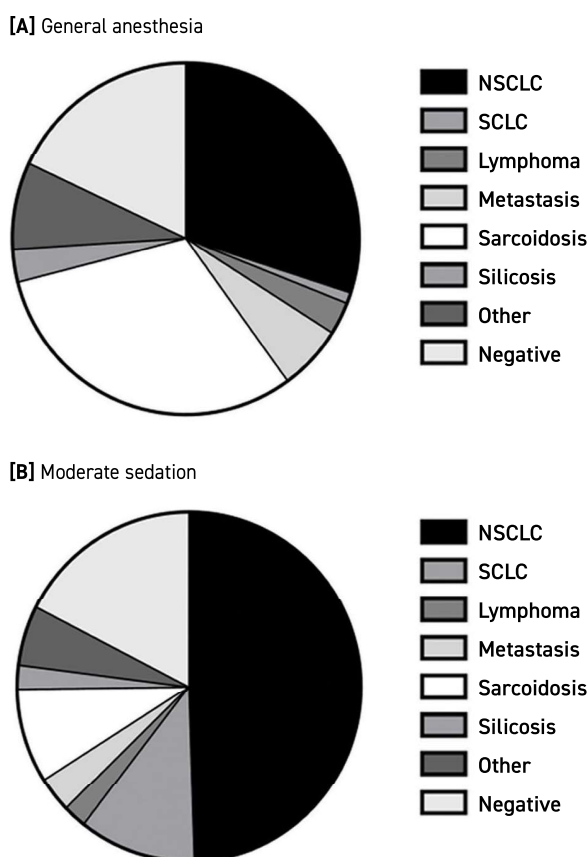
jects with suspected lung cancer, as well as for the investigation of other causes of mediastinal lymphadenopathy. In the present study, we assessed the diagnostic yield and complications rate of EBUS-TBNA in respiratory compromised patients. We found that the GA mode for EBUS-TBNA in this population could lead to high diagnostic yield without increased rate of complications. Our diagnostic yield for malignancy was high, as previously reported by others [17].

While previous studies [11,18,19] have shown that safety of EBUS-TBNA is unaffected by anesthesia type [17], our study is unique in its focus on patients with severe respiratory co-morbidities and compromised respiratory status. Therefore, when allocated to GA, EBUS-TBNA can be performed with a low rate of complications among severely compromised patients with respiratory co-morbidity.

It should be noted that the total number of lymph nodes sampled was higher in the GA group. Similar findings were previously noted by Yarmus et al. [13] and Casal and colleagues [12]. Interestingly in our study, the increased number of nodal stations sampled did not result in an increased yield, similar to the data published by Casal's group [12]. In contrast to the use of rapid on-site evaluation (ROSE) in the two previously mentioned studies, these data were not available in our study. Therefore, with no immediate feedback as to tissue adequacy on the one hand, and the controlled environment of GA on the other, it is possible that the pulmonologist performing the EBUS-TBNA felt more comfortable to proceed with additional node samplings as compared with the situation of EBUS-TBNA under MS.

In addition, subjects in the GA group underwent more accessory procedures, specifically TBB. This finding could be explained by the differential disease with a substantial proportion of sarcoidosis and silicosis patients allocated to the GA group. In these subjects, beside nodal enlargement, there was also parenchymal lung involvement, which probably prompted the pulmonologist to perform the TBB sampling as well. The option to perform TBB was probably increased due to the GA mode.

More subjects in the MS group were diagnosed with malignancy compared to a majority of sarcoidosis in the GA group. This difference may reflect the issue that sarcoidosis is also a disease that can seriously complicate the patient's status and lead to a respiratory compromised state [20]. In addition, systemic sarcoidosis can also lead to cardiac involvement, which might further deteriorate the subjects' status [21].

LIMITATIONS

This retrospective data cohort had a relative small number of patients. Second, there was an absence of ROSE during the EBUS-TBNA procedures. However, as previously described in most of the studies in the literature [22], the addition of ROSE does not necessarily lead to an increase in the diagnostic yield.

CONCLUSIONS

EBUS-TBNA is a relatively minimally invasive diagnostic technique with excellent performance and safety. Nevertheless, it is frequently avoided in respiratory compromised individuals due concern for increased risk of complications. We showed that by using GA, EBUS-TBNA can be done safely and accurately in this group of patients.

ACKNOWLEDGEMENTS

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