Yield and Complications of Endobronchial Ultrasound Using the Expect Endobronchial Ultrasound Needle

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Abstract

Background: Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) stands as the gold standard for sampling the mediastium and possesses the capability to detect a diverse range of disease processes. The EBUS needle industry has been experiencing rapid advancement, characterized by numerous companies either enhancing existing needles or introducing innovative ones. The majority of EBUS studies to date have predominantly utilized the Olympus™ Vizishot needles, which are constructed from stainless steel. In this paper, we focus on the evaluation of a cobalt chromium needle, namely the Expect™ EBUS needle, with a specific emphasis on its diagnostic efficacy and any associated complications. It is important to note that our investigation is conducted independently, and we do not provide a comparative analysis with other needle types available in the market.

Methods: This is an institutional review board-approved retrospective analysis of all patients who have undergone an EBUS-TBNA lymph node sampling using the Expect™ needle between August 2016 and September 2017 at the IU Health University Hospital. Comparisons of clinical characteristics by complications, diagnosis, needle gauge, and lymph node size were performed using chi-square test and Fisher’s exact test.

Results: 75% of the 102 included patients had their procedures done with the 22-gauge needle which were majorly performed in the setting of suspected intrathoracic malignancy followed by sarcoidosis and lymphoma. 99% of the patients had no complications after their procedures which were almost all diagnostic with two cases of bronchoscope damage. Mutational analysis was successful with both the 22 and 25-Gauge needles.

Conclusion: In this paper, we demonstrate that the Expect™ 22 and 25-gauge needles are safe and effective when used for EBUS-TBNAs through the Olympus™ EBUS bronchoscope for the evaluation of intrathoracic lymphadenopathy.
**Introduction**

The treatment of lung cancer has been evolving rapidly over the past several years. It is of utmost importance to secure an accurate pathological diagnosis and to adequately stage lung cancer patients prior to any treatment decision. One of the primary determinants of cancer staging is lymph node tumoral involvement which makes accurate pre-operative assessment essential. The utility of endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) is now firmly established in sampling mediastinal lymph nodes and has become the gold standard method in place of mediastinoscopy in terms of cost-effectiveness, accuracy, and safety (1,2). More importantly, the use of EBUS-TBNA has been particularly important in upstaging tumors, especially in presumed N0 or N1 disease on initial imaging (3-6). Furthermore, in the era of targeted cancer treatment, it has also shown success in tissue sampling for molecular analysis, such as programmed death ligand-1 (PD-L1) analysis and other mutations (7-10).

Endobronchial ultrasound has become the gold standard for lung cancer diagnosis and staging, and its use and adoption has increased rapidly over the years. Indeed, the market share of endobronchial ultrasound needles has been growing recently with multiple companies expanding on older needles or producing new ones. Most endobronchial ultrasound studies have utilized the Olympus™ (Center Valley, PA) Vizishot needles, which are stainless steel needles (11-13). Our aim in this paper is to examine another type of needle, the Expect™ endobronchial ultrasound needle (Boston Scientific, Marlborough, MA), looking at its diagnostic yield and rate of complications when used for EBUS-TBNA. This is a cobalt chromium needle with a sharp tip that has a unique locking mechanism and method of entry into the lymph nodes. Our primary outcome is to assess the yield and specimen adequacy at different nodal stations using this specific needle. We evaluated its yield in the diagnosis and staging of lung cancer and other mediastinal diseases. The secondary objective of our study is to look at procedure-related complications pertaining to both the patients and the bronchoscope itself using the Expect™ needle.

**Materials and Methods**

**Patients**

From August 2016 to September 2017, we reviewed our database of patients older than 18 years of age with mediastinal lymphadenopathy whether associated with a suspected, or confirmed lung cancer or other causes, who were referred to the Indiana University Health University Hospital for a diagnostic workup using the Expect™ 22 and 25-gauge needles. Electronic health records were reviewed for demographic information, including age, gender, pre-procedure diagnosis, smoking status, associated comorbidities, radiographic findings with either computed tomography (CT) scan and/or Positron Emission Tomography (PET), location and size of the enlarged lymph nodes as well as their clinical course. The study was approved by the Indiana University institutional review board (study number:1610932969).

**Procedure**

All cases were performed in the operating room of Indiana University Health University Hospital under general anesthesia using an I-gel™ manufactured by Intersurgical (Berkshire, United Kingdom). The cases were performed by the same interventional pulmonologist in the presence of a pulmonary fellow. Prior to the procedure, a CT scan of the chest and reports of prior imaging (including PET scans) were available for a final review of the lymph nodes. Those lymph nodes to be sampled were selected based on appropriate lung cancer staging in cases of suspected lung...
cancer, or for diagnosis of other benign and malignant mediastinal nodal diseases. After introduction in the trachea, the bronchoscope was advanced to the main carina and the lymph nodes were examined sequentially. For all visualized lymph nodes, an EBUS image was obtained with the sizes measured prior to nodal puncture. After selection of the lymph node to be sampled, the airway mucosa was punctured under continuous ultrasound guidance using the either the 22-gauge or 25-gauge Expect™ endobronchial ultrasound needle (Boston Scientific, Marlborough, MA). The stylette is typically pulled out several centimeters prior to puncture to expose the sharp tip of the needle, then entry into the lymph node is established. Ten actuations are done and the lymph nodes are sampled on a slide in the presence of rapid onsite cytologic evaluation. Each lymph node is sampled at least 3 times. Further sampling for cell block is done based on the cytologist’s recommendations.

**Statistical Analysis**

Descriptive statistics were used to analyze clinical characteristics and outcomes. Comparisons of clinical characteristics by complications, diagnosis, needle gauge, and lymph node size were performed using chi-square test and Fisher’s exact test, when needed. In all cases, a two-tailed p-value of 0.05 or less was considered statistically significant. All data were analyzed using STATA 13.0.

**Results**

A total of 102 patients were included in the analysis. Most of the patients were older than 70 years of age (more than 70%) with almost 30% aged between 51-60 years. 40% of patients were former smokers while 35% were current smokers. More than 75% of patients had their procedure performed using the 22-gauge needle and the rest using the 25-gauge needle. A lymph node size of ≥ 8mm was selected in 78.4% of cases. The most common indications for bronchoscopy were diagnosis and staging of lung cancer with mediastinal adenopathy in 61.8% of the cases, followed by sarcoidosis and lymphoma rule out in 31%, followed by work-up of mediastinal lymphadenopathy with or without lung nodules in the setting of active extra-thoracic malignancy. The overwhelming majority of patients had no complications after their procedures (99%) which were almost all diagnostic. There were only two cases of bronchoscope damage which happened when the needle was entered without the stylette. All diagnostic procedures had no complications except one procedure complicated by a pneumomediastinum which was the only non-diagnostic case.

Table 1 explores the proportion of procedures done using the 22-gauge and 25-gauge needles by diagnosis, in which all patients (100%), had adequate tissue sample for molecular testing.

<table>
<thead>
<tr>
<th>Diagnosis (n, %)</th>
<th>22</th>
<th>25</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCLC*</td>
<td>8  (80%)</td>
<td>2  (20%)</td>
</tr>
<tr>
<td>Lung Adenocarcinoma</td>
<td>10 (80%)</td>
<td>4  (20%)</td>
</tr>
<tr>
<td>Squamous Cell Cancer</td>
<td>4  (80%)</td>
<td>1  (20%)</td>
</tr>
<tr>
<td>NSCLC**</td>
<td>6  (75%)</td>
<td>2  (25%)</td>
</tr>
<tr>
<td>Granulomatous Inflammation</td>
<td>8  (100%)</td>
<td>0  (0%)</td>
</tr>
<tr>
<td>Reactive Lymph Node</td>
<td>28 (70%)</td>
<td>12 (30%)</td>
</tr>
<tr>
<td>Metastatic Malignancy (External)</td>
<td>8 (88.9%)</td>
<td>1 (11.1%)</td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>1  (100%)</td>
<td>0  (0%)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1  (100%)</td>
<td>0  (0%)</td>
</tr>
</tbody>
</table>

*SCLC, Small cell lung cancer; **NSCLC, Non-small cell lung cancer

75-80% of lung cancer diagnoses were obtained using a 22-gauge needle, while the rest were obtained using a 25-gauge needle. 88.9% of cases with metastatic malignancy...
from outside the lungs were diagnosed using a 22-gauge needle. All cases of granulomatous disease (100%) and most cases of reactive lymphadenopathy were diagnosed with the 22-gauge needle. At Indiana University, reactive lymphadenopathy diagnosis was based on rapid on-site assessment and indicated the presence of adequate specimen with lymphocytes at our centre. Pneumomediastinum as a complication occurred in the only non-diagnostic case using the 22-gauge needle. Transvascular needle aspiration was performed successfully in two cases; one diagnosing small cell lung cancer and the second diagnosing reactive lymphadenopathy. There was no significant difference in the diagnostic yield by the two needle gauges (98.75 vs 100%); most procedures were performed using the 22-gauge needle. There was no significant difference in yield between lymph nodes less than 8 mm in size and those greater than 8 mm in size, although most lymph nodes studied were greater than 8 mm in 89% of the cases. Hence in almost all the cases, mutational analysis was adequate using both the 22 and 25-gauge needles.

Discussion
To our knowledge, this is the first study assessing the yield and complications of the Expect™ needle with EBUS. Previous studies had assessed the yield of this needle with endoscopic ultrasound (14). The results of our study show that the Expect needle demonstrated good diagnostic yield in lymph node sampling during the evaluation of mediastinal lymphadenopathy for either suspected primary thoracic, metastatic malignancy or non-malignant disease processes. As the use of the EBUS technique has become the gold standard preferred over mediastinoscopy in the management of lung cancer and evaluation of mediastinal lymphadenopathy since the end 2000s, more EBUS related techniques are being evaluated and studied to enhance their diagnostic accuracy (15-19). Indeed, overwhelming evidence has proven the lower number of complications of this technique compared to surgical mediastinoscopy while yielding very good results.

In a review of biopsy needles for mediastinal lymph node sampling, Colella et al. (20) reviewed characteristics of an ideal needle, which mostly consisted of high level of resistance, flexibility and echogenicity for better visualization under ultrasonography. There are multiple needles in the market currently trying to meet these standards. These include the Procore™ needle and the SonoTip Topgain™ needle. The Expect™ needle used in this study meets some of these characteristics, mostly attributable to the chromium-cobalt (CoCr) alloy it is made of. From a series of experimental needle trials, Keehan et al. (21) showed that the chromium-cobalt alloy was 24% harder than the tested Stainless Steel 304 (SS) indicating that these needles are more likely to conserve their sharpness and resist blunting (21). They also demonstrated greater kinking resistance and tensile properties than the SS needles. Moreover, it was shown that the needle was easily visualized on ultrasound and that upon withdrawal from the endoscope, there was less deformation of the needle itself. All of these aforementioned properties are particularly important, as several types of needle-related complications have been reported such as the release of metal particles into lymph nodes, breakage of the needles with possible migration and infectious sequelae (22-25).

As for the diagnostic properties investigated in this study, there was no significant difference between the 22 and 25-gauge needle sizes, although the 22-gauge needle was used in the majority of the cases. The overwhelming majority of prior studies have not reported significant superiority of a particular needle size though most were conducted comparing the 22 and 21 needle.
sizes (26-28). In a recent 2019 study published by Di Felice et al. (29) comparing the 22 and 25-gauge needle sizes, no significant difference was noted between their sample adequacy and diagnostic accuracy. Similarly, another 2021 study published by Sakaguchi et al. (30) showed that while the diagnostic yields of the 22 and 25-gauge sizes may be comparable in lung cancer, that of the 22-gauge is superior in the diagnosis of sarcoidosis. While no particular needle size in the evaluation of lung cancer is certainly favoured, the need for increasing tissue sampling for molecular studies, immunophenotyping and next-generation sequencing has supported the use of larger needles (31-32).

On that same note, as the treatment of advanced non-small cell lung cancer (NSCLC) has revolutionized with targeted therapies based on driver mutations positivity, more attention is drawn to maximize the yield of EBUS guided biopsies for tissue sampling (33-36). Using EBUS for this purpose is now well established especially for EGFR and ALK mutations testing (37-41). More recent studies have also supported the role of EBUS-guided TBNA samples for PDL-1 testing which draws more attention to enhance this technique as it becomes gold standard in both cancer diagnosis and management. In our study, we demonstrate that using the Expect™ needle provides adequate samples for these tests (anaplastic lymphoma kinase (ALK), receptor tyrosine kinase -1 (ROS-1), epidermal growth factor receptor (EGFR), programmed death ligand -1 (PDL-1)), particularly useful when sent for adenocarcinoma.

As for the complication rate, it was low and similar to what has been previously described in the literature (42). Indeed, the only complication (pneumomediastinum) occurred in the one non-diagnostic case. Most of the literature supports a rate of adverse events of less than 1%. In a metanalysis including more than 9000 EBUS-FNA cases, von Barthled et al. (43) found a rate of serious adverse events of 0.05%. These comprised infectious complications as sepsis and mediastinal abscess formation, pneumothorax, and hypoxemia. Another Japanese survey that also evaluated the complications related to bronchoscope damage, described a low complication rate as well. The rate of needle breakage was reported at 0.2% while the rate of bronchoscope damage at 1.33% (42). This is similar to our rate of bronchoscope damage which was 0.98%.

Our study has several limitations. It is a retrospective review, and therefore, prone to the errors associated with such reviews. It also does not provide a head-to-head comparison with other needles. The absence of a control group in this research poses a challenge in estimating the potential clinical benefits of utilizing the “expect” needle compared to various other types, including the Olympus™ needles (Vizishot and Vizishot 2). It is a single-centre study involving one interventional pulmonologist, and therefore, is operator-dependent and centre-dependent. Its strengths are that it is a rare evaluation of the needles currently on the market, and it paves the way for upcoming multi-center collaborative studies evaluating newer needles.

Conclusions
EBUS-guided biopsies have emerged as the preferred method for diagnosing and managing non-small cell lung cancer (NSCLC), prompting the exploration of various techniques for this purpose. We present evidence supporting the safety and efficacy of Expect™ 22- and 25-gauge needles when employed for EBUS-TBNA's through the Olympus™ EBUS bronchoscope in the assessment of both benign and malignant intrathoracic lymphadenopathy. This contributes to the expanding body of EBUS literature, as novel techniques and needle
options are continually being investigated and utilized. Nonetheless, the selection of the appropriate needle for EBUS entails numerous considerations. While effectiveness and the risk of complications remain paramount, factors such as the operator’s familiarity with the needle, its availability, and cost has substantial influence in decision making process.

References


