

Exploration under the dome: Esophageal ultrasound with the ultrasound bronchoscope is indispensable

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ABSTRACT

Background: Effective use of the convex curvilinear ultrasound bronchoscope in the esophagus (EUS-B) for fine needle aspiration biopsy of mediastinal structures is now well described. In contrast, there is little to no reporting, depending on the site of EUS-B for access to sub-diaphragmatic structures. Our practice has been accessing sub-diaphragmatic sites for years. This review documents our experience with EUS-B to biopsy liver, left adrenal glands, and coeliac lymph nodes. **Methods:** After Institutional Review Board’s approval, all endosonographic procedures performed by interventional pulmonary between July 2013 and June 2015 were reviewed. Those including biopsy of sub-diaphragmatic sites were then selected for analysis. **Results:** Over the study interval, 45 sub-diaphragmatic biopsy procedures (25 left adrenal glands, 7 liver, and 13 celiac node) were performed with EUS-B. In all cases, cellular adequacy was present, and samples were large enough for immunohistochemistry and any relevant ancillary studies. Metastatic malignancy was documented in 58% of cases, 16% of cases contained benign diagnostic findings, and in 27% of cases, normal organ tissue was documented. There were no complications. **Conclusions:** Operators comfortable with the endobronchial ultrasound scope in both the airway and the esophagus can actively seek and successfully perform biopsy of sub-diaphragmatic abnormalities when present and can thereby add to the diagnostic value of the procedure.

Key words: Adenopathy, adrenal masses, endobronchial ultrasound, esophageal ultrasound, liver masses, lung cancer, sarcoidosis

INTRODUCTION

Endobronchial ultrasound (EBUS) was initially developed for improved access to hilar and mediastinal nodes in the diagnosis and staging of lung cancer. After the technology matured and the convex curvilinear EBUS bronchoscope had been developed, its range of utility was broadened to include the diagnosis of thoracic masses, lymphoma, and benign conditions with mediastinal involvement.^[1-5]

Multiple recent studies have cemented the validity of use of the EBUS scope both for EBUS and for esophageal ultrasound with the ultrasound bronchoscope (EUS-B). This dual use of the EBUS scope gives the pulmonologist broader access to the mediastinum, alternative access to some nodes, and a greater safety margin for tenuous patients for whom diagnostic material is available from

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para-esophageal sites.^[6-12] We have previously demonstrated the feasibility of the left adrenal access with EUS-B.^[13,14] In this retrospective review, we have collected serial biopsies of all sub-diaphragmatic structures – left adrenal glands, liver, and coeliac nodes performed over a 2-year period. We evaluated for adequacy of yield and for complications.

METHODS

After Institutional Review Board's approval for the study, we retrospectively reviewed all ultrasound-assisted endoscopic procedures performed by interventional pulmonary at one institution from July 1, 2013 to June 30, 2015. The study group consisted of all cases of EUS-B in which sub-diaphragmatic structures were sampled.

All EUS-B procedures were performed in the endoscopy suite with an Olympus EBUS scope (BC-UC180F, Olympus Medical Supply Corporation, Tokyo, Japan). Conscious sedation in all cases consisted of physician-administered propofol. Patients were positioned in the supine position for both EBUS and EUS, with the head of the bed elevated to approximately 30°. The patient's position was not changed when transitioning from EUS-B to EBUS or vice versa. Procedures were performed orally through a bite block. Neither esophageal insufflation nor the saline-filled EBUS balloon was used for any EUS-B biopsy. All fine needle aspirations (FNAs) were performed using the Olympus 21-gauge needle designed for use with the EBUS scope. The liver was visualized through the esophageal wall anterolaterally below the left atrium, while the left adrenal glands and coeliac nodes were accessed through the gastric wall with a posteromedial ultrasound orientation. Rapid on-site cytologic examination was available for all procedures.

The following data were collected; age, gender, height, type of procedure (EUS-B, EBUS, and EUS-B + EBUS), diagnosis, specific sites sampled, pathology, and final diagnoses.

RESULTS

During the study, we performed 868 endosonography-assisted procedures. Out of this population, 42 patients underwent EUS-B FNA of 45 sub-diaphragmatic structures. These 42 patients

had an age of 58 ± 12 years. Racial distribution was as follows; 25 Caucasians, 17 African-Americans, 2 Hispanics, and 1 patient of Middle Eastern origin. Men comprised the majority at 28 (67% of the patients). The mean height of the subjects was 168 cm, with a range of 154 cm to 199 cm. The left adrenal gland was the most commonly sampled sub-diaphragmatic structure (25 of 45 cases, 56%), followed by coeliac nodes, 13 (28%), and liver 7 (16%). Whenever appropriate, both thoracic and extra-thoracic sites were sampled with EUS-B. Twelve patients (26%) underwent EBUS after EUS-B to access thoracic abnormalities not accessible from the esophagus. No complications were noted during or subsequent to any of the procedures.

All sub-diaphragmatic biopsies yielded adequate cellularity, with 58% of the patients proven to have Stage IV malignant disease. The breakdown of results by site and category is listed in Table 1. Out of the 25 left adrenal glands that were sampled, eight samples were cytologically benign (4 benign adrenals and 4 benign cortical adenomas). The remaining 17 demonstrated malignant metastases. There were 12 lung adenocarcinomas, 3 small cell cancers, 1 squamous cell cancer, and 1 high-grade urothelial cell tumor. Adrenals that were cytologically benign were smaller (10 ± 8 mm) than those that contained metastases (23 ± 15 mm, $P < 0.001$).

The majority of coeliac node biopsies (7 of 13, 53%) contained benign lymphoid tissue. The remaining 6 demonstrated metastatic disease, 5 (38%) with staining consistent with a gastrointestinal primary, and 1 (14%) staining for adenocarcinoma of lung origin.

Of the seven liver biopsies, four were part of an endoscopic evaluation for sarcoidosis. Three of the four demonstrated granulomas and one demonstrated benign hepatocytes. Three liver biopsies were performed for possible liver metastases, and all the three were positive (1 lung adenocarcinoma, 1 gastrointestinal adenocarcinoma, and 1 tumor of genitourinary tract origin).

Table 1. Diagnostic results by site

	Malignant	Benign abnormal*	Benign normal	Total
Left adrenal	17	4	4	25
Coeliac	6		7	13
Liver	3	3	1	7
Total	26	7	12	45
Percentage	58	15	27	100

*Adenoma for adrenal; granulomas for liver

DISCUSSION

This review of 45 consecutive applications of EUS-B below the diaphragm demonstrates that adequate sampling and clinically relevant diagnostic material can be obtained consistently and with minimal risk. In all cases in our series, adequate malignant or normal tissue was obtained, and in all cases of malignancy, the cell block was large enough for any indicated additional immunohistochemistry and molecular studies. This series extends the literature on the left adrenal biopsy and is the first report of the use of EUS-B to sample coeliac nodes and the liver. The implication is clear; with a combination of EUS-B and EBUS the pulmonologist skilled in EUS-B can effectively reach and biopsy all of the endosonographic sites that may contribute to the diagnosis of thoracic diseases, in one setting.

The EBUS scope is in some ways inferior to the dedicated EUS scope. The EUS scope has a broader field of view, a greater depth of view, and can be angulated more easily than the EBUS scope.^[15] The EUS scope is also more rigid, a factor that may facilitate visualization of abdominal structures from the stomach. The EUS scope is longer, and it has been presumed by some that the EBUS scope is incapable of reaching the very sub-diaphragmatic structures that are the topic of this report.^[15] The range of patients' height was documented for this series specifically because of the issue of scope length with EUS-B; we were able to sample the left adrenal glands of a very tall gentleman (199 cm, 7'6"), underscoring the fact that the length of the scope is more than likely to be adequate for the vast majority of patients. This sequential series demonstrates that in most cases, despite theoretical disadvantages, an experienced operator can reach with EUS-B the same sub-diaphragmatic structures most commonly accessed with conventional EUS.

The left adrenal gland was the sub-diaphragmatic site most commonly biopsied (We had previously reported 6 cases of the left adrenal biopsy with EUS-B; this extended series subsequent to that initial series extends the validity of our initial conclusions). The adrenal glands represent the fourth most common site of metastasis for lung cancer,^[15,16] and had the highest percentage of malignant involvement in our series. Benign adrenal adenomas are also common; adrenal masses are seen in 4%–10% of patients with nonsmall cell lung cancer undergoing evaluation, and the majority of those masses are proven to be benign.^[17-19] There

are pitfalls to all the available noninvasive diagnostic modalities, even when used in conjunction with each other.^[19-21] Cytologic material is thus often needed before the question of adrenal metastasis can be adequately addressed. Several studies, including our prior report, have looked at the use of EUS-FNA for the diagnosis of the left adrenal lesions.^[13,21-23] These studies have demonstrated tissue adequacy in the 94%–100% range and a safety profile superior to that of either computed tomography-guided biopsy or transcutaneous ultrasound-guided biopsy.^[21]

Gastroenterologists have demonstrated the efficacy and safety of EUS for liver and coeliac lymph node sampling with the dedicated EUS scope,^[24-27] but as noted, this is the first series to document the successful serial biopsy of both coeliac nodes and liver with EUS-B. The coeliac nodes lie in the same field as the adrenal, and morphologically appear similar to adrenal when both are involved by tumor; the approach to each is identical, and background cellularity documents the tissue of origin. Singh *et al.* documented the importance of coeliac nodes, which were involved in 11% of their lung cancer cases.^[27]

Seven cases of liver biopsy were performed over the study interval. FNA biopsy of the liver for cytology is distinctly different from biopsy for liver architecture in the diagnosis and staging of cirrhosis; EUS-B FNA of the liver involves small needle aspiration of a magnified image on which vascular structures can be easily avoided. We performed EUS-B FNA of the liver for two indications (1) the diagnosis of sarcoidosis and (2) the diagnosis of liver metastases. The diagnosis of sarcoidosis can at times be problematic; negative nodes do not rule out the diagnosis, and diseases such as fungal infection can present with granulomatous adenopathy. The liver is involved in extrapulmonary sarcoidosis at 60%–90% of the time when there are co-existing pulmonary findings and is involved in isolation in 10%–15% of cases.^[28,29] FNA of the liver can increase sensitivity for a diagnosis of sarcoidosis if there is granulomatous liver involvement, when other biopsies are negative, and can increase specificity if granulomas are present in both mediastinal nodal tissue and liver. This study supports the use of liver FNA, as three-fourths of the patients had evidence of granulomas. The liver also tends to be a frequent site of lung cancer metastasis, especially small cell (a third of noted metastasis), and is associated with the poorest survival when compared to other sites of metastasis.^[30]

CONCLUSION

Our data demonstrate that operators comfortable with the EBUS scope in both the airway and the esophagus can actively seek and successfully perform biopsy of sub-diaphragmatic abnormalities when present and can thereby add to the diagnostic value of the procedure. While the EUS scope may be superior for sub-diaphragmatic structures, this does not negate the fact that experienced pulmonologists can combine EUS-B and EBUS for a single comprehensive staging procedure. We submit that all interventional pulmonology training programs should include EUS-B in their curricula.

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Conflicts of interest

There are no conflicts of interest.

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