Yield of ultrasound-guided biopsy in anterior mediastinal lesions

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Background Mediastinal masses span a wide histopathological and radiological spectrum. Anterior mediastinal tumors account for 50% of all mediastinal masses, including thymoma, teratoma, thyroid disease, and lymphoma. Ultrasound guidance can be used for biopsy of anterior mediastinal lesions that extend to the anterior parasternal chest wall with the advantage of being a real-time procedure and its ability to perform the biopsy at the bedside of critically ill or dyspneic patients.

Aim of the study The aim of this study was to evaluate the efficacy and safety of using ultrasonography as a guiding modality during percutaneous biopsies for anterior mediastinal lesions.

Patients and methods This prospective study for diagnostic accuracy was conducted on 22 patients with anterior mediastinal masses. In total, lesions in 19 patients were approached through parasternal approach under local anesthesia using lidocaine 2% and in two patients the lesions were approached through suprasternal approach. Lesion in one patient failed to be approached by either parasternal or suprasternal approach because of its deep location.

Results Conclusive results were obtained in 18 patients (81.8%), nonconclusive results in three patients (13.6%), and biopsy was not performed for one patient (4.6%) because of technical difficulty. Malignant lymphoma was the most encountered pathological diagnosis. Two patients developed vasovagal attacks at the beginning of the procedure. No procedure-related mortality was encountered in this study.

Conclusion Ultrasound-guided biopsy is a useful technique for anterior mediastinal lesions with a good diagnostic yield (81.8%) and minimal complications.
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Introduction

Mediastinal masses span a wide histopathological and radiological spectrum. The most frequent lesions encountered in the mediastinum are thymoma, neurogenic tumors, and benign cysts, altogether representing 60% of patients with mediastinal masses. Neurogenic tumors, germ cell neoplasms, and foregut cysts represent 80% of childhood lesions, whereas primary thymic neoplasms, thyroid masses, and lymphomas are the most common lesions in adults [1].

Anterior mediastinal tumors account for 50% of all mediastinal masses, including thymoma, teratoma, thyroid disease, and lymphoma [2].

Many mediastinal reflections can be appreciated at conventional radiography, and their presence or distortion is the key to the interpretation of mediastinal abnormalities [3].

Computed tomography (CT) is the most important tool in the evaluation of a mediastinal mass [4]. Characterization on CT is based on specific attenuation of air, fat, water, and calcium. High-resolution multiplanar reformation images display the detailed anatomical relationship of the tumor with the adjacent structures [5].

MRI is largely used as an adjunct to CT scanning in the evaluation of mediastinal abnormalities; it often provides additional information about the nature, location, and extent of the disease [6].

The vast majority of transthoracic image-guided biopsies for mediastinal lesions are performed percutaneously using CT guidance. Complications may include bleeding and pneumothorax. Up to 10% of patients require the placement of a catheter after biopsy for the evacuation of pneumothorax [7].

Ultrasound (US) guidance can be used for biopsy of anterior mediastinal lesions, which extend to the anterior parasternal chest wall [8]. The advantages of US guidance include the real-time, continuous

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monitoring of the needle during advancement and sampling; the availability of oblique needle paths; and the ability to perform the biopsy at the bedside in critically ill patients or in patients with dyspnea who cannot tolerate a supine position in semi-sitting positions during the biopsy [9].

Aim of the study

The aim of this study was to evaluate the efficacy and safety of using ultrasonography as a guiding modality during percutaneous biopsies for anterior mediastinal lesions.

Patients and methods

Patients

This prospective study for diagnostic accuracy was performed on 22 patients with anterior mediastina masses and it was conducted at Kasr Al Ainy Teaching Hospital during the period from August 2011 to April 2014.

Inclusion criteria

Patients included in this study were patients with symptomatic and asymptomatic anterior mediastinal masses.

Exclusion criteria

(1) Patients with vascular lesions.
(2) Patients with bleeding tendency.

Methodology

Each patient was assessed for epidemiological features (age, sex), risk factors (smoking, environmental, occupational exposure, radiation exposure), clinical presentation (asymptomatic, pain, hemoptysis, compression symptoms, fever), the technique used during intervention (access, used window, histological accuracy), and associated complications.

(1) All patients were prepared preoperatively by checking their coagulation profile.
(2) Technical success was assessed by accurate localization of the lesion with adequate accessibility and histological confirmation.
(3) All patients underwent plain chest radiograph after the procedure together with histopathological confirmation of the biopsied specimen.

Procedural data

Preprocedural preparation

(1) All patients were subjected to routine laboratory assessment.
(2) Preprocedural prothrombin time and concentration (PT, PC, and international normalized ratio) were checked to avoid possible postprocedural puncture site hematoma or bleeding and to correct any bleeding diathesis.
(3) All patients underwent chest radiography and CT chest (as shown in Fig. 1) with contrast to gain proper delineation of the target lesion and the surrounding anatomy.
(4) All patients signed an informed consent after the main steps of the procedure with all possible complications were explained to them.

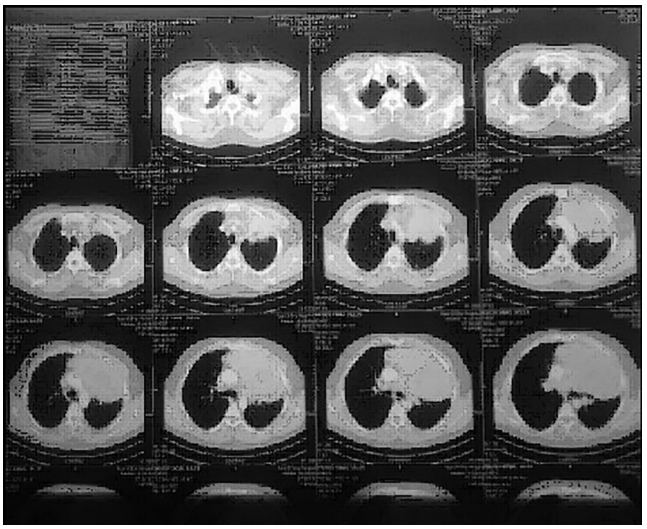
Patient position

(1) All patients underwent a preliminary diagnostic US study of the chest to localize the lesion, identify a safe path for needle placement, and consequently choose the optimal patient position.
(2) A color-coded Doppler imaging was performed to identify surrounding major vessels.
(3) Sonographic views of the anterior mediastinum were obtained through suprasternal or parasternal approaches. This is performed while the patient is sitting or lying supine with shoulders supported with a pillow and head extended backwards.

Approach

(1) In the current study, lesions in 19 patients were approached through parasternal approach under local anesthesia using lidocaine 2%, and in two patients lesions were approached through suprasternal approach. Anterior mediastinal mass in one patient failed to be approached by either parasternal or suprasternal approach because of its deep location. No lesions were approached through subxiphoid approach.

Fig. 1



44-year-old male patient presented with cough, expectoration, and dyspnea. Computed tomography (CT) chest demonstrated a large anterior mediastinal mass.

(2) Sedation in the form of intravenous midazolam together with intramuscular atropine were required in patients who had needle phobia and for prophylaxis against vasovagal attacks at the beginning of the procedure.
(3) Patients with hypoxaemia were kept on oxygen mask or nasal pronge during the procedure.

Ultrasound setting

(1) US equipment suitable for thoracic imaging includes 3.5, 5, 7.5, and 10 MHz linear, convex, and sector transducers.
(2) Patients were examined in supine or prone position using intercostal approach.
(3) A water-soluble transmission gel was applied to the skin as a coupling medium.
(4) The lesion was visualized in grey scale, real-time US imaging.
(5) A high frequency (i.e. 5 or 7.5 MHz) linear or convex transducer was used to examine lesions in anterior mediastinum.
(6) A sector transducer was used for lesions with small US window (as shown in Fig. 2).

Needle

All US-guided biopsies were performed using 16-G Tru-cut biopsy needles. No biopsies were performed using fine needle aspiration cytology (FNAC).

Technical success

(1) Assessment of technical success was achieved by accurate visualization and localization of the lesion with good accessibility.
(2) Multiple biopsies were usually required to exclude superficially performed biopsies, which mostly revealed nonspecific chronic inflammatory cells on histopathological examination.

Postprocedural monitoring

(1) All patients were subjected to routine assessment of vital signs as some patients develop vasovagal attacks during the procedure or develop tachypnea during or after the procedure.
(2) All patients were observed for occurrence of puncture site hematoma or bleeding, which may cause hemodynamic instablility.
(3) Routine chest radiography was carried out for all patients 30 min after the procedure to exclude hemothorax and/or pneumothorax.

Statistical analysis

All data were collected, summarized, presented, and analyzed by using an appropriate statistical package program (SPSS version 10).

Quantitative data were summarized by mean and SD. Qualitative data were summarized by number and percentage [10].

Results

This study included 22 patients who presented to Kasr Al Ainy Teaching Hospitals during the period from August 2011 to April 2014. 12 males (54.5%) and 10 females (45.5%) were included in the current study.

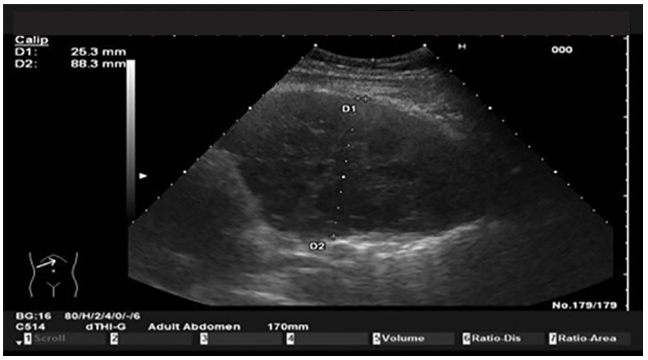
The most encountered histopathological result for patients with anterior mediastinal masses included in our study proved to be malignant lymphoma (45.5%).

Patients' presentations were variable and sometimes more than one presentation was found in the same patient. Dyspnea was the most common presenting symptom in our patients (81.8%) (Table 1).

In our study, lesions in 21 patients were successfully approached while in one case it failed to be approached. Overall, lesions in 19 out of the 21 patients were approached through parasternal approach, and in two patients lesions were approached through suprasternal approach. Lesions in none of the patients were approached through subxiphoid approach.

US-guided biopsy technique revealed conclusive results in 18 patients (81.8%), nonconclusive results in three patients (13.6%), and in one of our studied patients (4.6%) there was a technical difficulty to reach

Fig. 2



Ultrasound-guided biopsy was taken and sent for histopathological examination, which revealed Hodgkin's lymphoma.

Table 1 Anatomical distribution

Lesion position	*n* (%)
Anterior mediastinal	20 (90.9)
Middle mediastinal	0 (0)
Posterior mediastinal	0 (0)
Extra-mediastinal	2[a] (9.1)

[a]For patients with mediastinal extension of extramediastinal lesion (retrosternal extension of goiter into anterior mediastinum).

the mass because of its deep location leading to failure in taking a biopsy from the lesion.

Morbidity

Two patients developed vasovagal attacks at the beginning of the procedure. No patients developed pneumothorax, hemothorax, hemopneumothorax, or chylothorax. Infection (cutaneous or empyema) was not encountered in our patients and no cases developed bronchial perforation.

Mortality

No procedure-related mortality was encountered in this study.

Discussion

Mediastinal masses represent a wide diversity of disease states. The location and composition of a mass is critical to narrow the differential diagnosis [11].

In the current study, the most frequently affected age group was between 40 and 70 years (54.2%) – especially the fifth decade of life (Table 2). This coincides with studies conducted by Vaziri *et al*. (2009) [12] and Nasit *et al*. (2013) [13], who also documented, regarding the management of mediastinal lesion, that the most involved age group was between 30 and 70 years.

In a study conducted by Nasit *et al*. (2013) [13] on 50 patients with anterior mediastinal masses, there were 36 men and 14 women with a mean age of 38.6 years (range=1–76 years). The male to female ratio was 2.5 : 1.

In the current study, male to female ratio was 1 : 1.2 as 12 males (45.5%) and 10 females were included (54.5%).

Patients with anterior mediastinal masses had variable presentations in our study (Table 3). Most of the patients presented with dyspnea (81.8%), cough and expectoration (36.4%), and pain (36.4%). However, more than one symptom could coexist in the same patient.

In our study, five patients (22.7%) presented with associated complications in the form of mediastinal compression (e.g. superior vena cava compression) but no associated diseases were recorded (e.g. myasthenia gravis).

In a study conducted by Beau *et al*. (2005) [11], the most common clinical presentation was cough (60%), chest pain (30%), fever and chills (20%), and dyspnea (16%). Most symptoms can be categorized into the following two groups: localizing symptoms and systemic symptoms. Localizing symptoms are secondary to tumor invasion. Common localizing symptoms include respiratory compromise; dysphagia; paralysis of the limbs, diaphragm, or vocal cords; Horner syndrome; and superior vena cava syndrome. Systemic symptoms are typically due to the release of excess hormones, antibodies, or cytokines. A classic example is hypercalcemia, which is caused by a parathyroid adenoma.

Table 2 Age of the patients at presentation

Age (years)	Number of patients [*n* (%)]
<10	2 (9.1)
11–20	2 (9.1)
21–30	3 (13.6)
31–40	1 (4.6)
41–50	5 (22.7)
51–60	3 (13.6)
61–70	4 (18.2)
>70	2 (9.1)

Table 3 Clinical presentation

Clinical presentation	Number of patients [*n* (%)]
Dyspnea	18 (81.8)
Cough and expectoration	8 (36.4)
Pain	8 (36.4)
Fever	5 (22.7)
Mediastinal compression	5 (22.7)
Hemoptysis	2 (9.1)

Nasit *et al*. (2013) [13], found that out of 50 patients, 47 (94%) were symptomatic, presenting clinical features of dyspnea, cough, chest pain, hoarseness of voice, weight loss, and features suggestive of myasthenia gravis, whereas other three patients (6%) were detected on routine physical examination.

Vaziri *et al*. (2009) [12] reported that nonspecific symptoms as dyspnea (41%) and cough (40%) constituted the most common presenting complaint followed by pain (28%), weight loss (20%), fever (14%), and pleural effusion (12%).

This is quite relevant to what have been concluded in our study, where dyspnea (81.8%) and cough (36.4%) were the most common presenting symptoms followed by chest pain and fever.

Vaziri *et al*. (2009) [12] encountered a number of interesting associated diseases with some mediastinal masses, including sternal osteochondroma with Schwannoma, nasopharyngeal carcinoma with intrathoracic goiter, and neurofibromatosis with ganglioneuroma.

The most encountered histopathological result for patients with anterior mediastinal masses included in our study proved to be malignant lymphoma (45.5%) (Table 4).

Davis *et al*. (1987) [14], studied 400 patients with mediastinal masses; malignancy was seen in 59, 29, and 16% of anterior, middle, and posterior mediastinal masses, respectively. Age was an important predictor of malignancy with many lymphomas and germ cell tumors presenting between the second and fourth decades of life.

Beau *et al*. (2005) [11] noticed that thymomas represented about 20% of anterior mediastinal neoplasms in adults. For lymphomas, they found that primary mediastinal lymphoma is a rare entity comprising only 10% of the lymphomas in the mediastinum. It occurs usually in the anterior mediastinum. Hodgkin's disease represented ~50–70% of mediastinal lymphomas whereas non-Hodgkin lymphomas comprised 15–25%.

In a study conducted by Laurent *et al*. (1998) [1], the most frequently encountered lesions in the mediastinum were thymomas, neurogenic tumors, and benign cysts, altogether representing about 60% of patients with mediastinal masses. However, significant differences existed between adult and children. Neurogenic tumors, germ cell neoplasms, and foregut cysts represented 80% of childhood lesions, whereas primary thymic neoplasms, thyroid masses, and lymphomas were the most frequently encountered lesions in adults.

According to Engels and Pfeiffer (2003) [15], thymomas are the most common neoplasm of the anterior mediastinum with an incidence of 0.15 cases per 100 000. Although rare in children, thymomas represent 20% of anterior mediastinal masses in adults.

Strollo *et al*. (1997) [16] reported that the anterior mediastinal lesions account for about 50% of all mediastinal masses with thymomas being the most common pathology.

Table 4 Histopathological results

Pathology	Number of patients [*n* (%)]
Malignant lymphoma	10 (45.5)
Sarcoidosis	1 (4.5)
Retrosternal malignant goiter	2 (9.1)
Thymic carcinoma	2 (9.1)
Sclerosing mediastinitis	1 (4.5)
Germ cell tumor	1 (4.5)
Metestatic adenocarcinoma	1 (4.5)
Nonconclusive	3 (13.6)
Failure to reach the mass	1 (4.5)

In agreement with our study, Vaziri *et al*. (2009) [12] studied 105 patients with mediastinal lesions. Most of the lesions were found within the anterior mediastinum (65%), with lymphomas being the most predominant pathology (31.5%), followed by Schwannoma (10%), teratomas (7.5%), thymomas (7.5%), and intrathoracic goiter (3.7%).

Nasit *et al*. (2013) [13] included 49 cases with anterior mediastinal lesions in their study and they were divided into carcinoma (22 cases) and noncarcinoma groups (27 cases). In agreement with our study, most of the lesions in the carcinoma group were found to have lymphomas as the predominant pathology (18 cases) whereas thymomas were found in six cases only.

Otani *et al*. (1996) [17] found that the most common location for mediastinal lesions is the anterior mediastinum (89%), followed by posterior mediastinum (11%) with no reported cases with middle mediastinal lesions.

In addition, Tscheikuna and Suttinont (2009) [18], Shrivastava *et al*. (2006) [19], and Karki and Chalise (2011) [20] reported that most mediastinal lesions were found within the anterior mediastinum.

Prasnath *et al*. (2007) [21] assumed variations in the presentation in mediastinal masses on the basis of the anatomic site with age. Anterior mediastinal masses were detected in adults in 54% of cases and in children in 46%.

In the study conducted by Davis *et al*. (1987) [14], out of 400 patients with mediastinal masses malignancy was detected in 59, 29, and 16% of anterior, middle, and posterior mediastinum, respectively.

In the current study, malignancy was detected in 68.2% of cases of anterior mediastinal lesions.

Tissue diagnosis of mediastinal lesions can be performed by a variety of techniques ranging from core-needle biopsy (CNB) to surgical procedure allowing biopsy as well as resection [18].

Open biopsy can certainly assure a definite histological diagnostic rate, which might be as high as 100%; it is associated with significant morbidity, increased chance for pleural dissemination, and poor long-term results. For this reason, the surgically oriented strategies are no longer considered suitable for anterior mediastinal neoplasms [22].

Percutaneous FNAC and CNB under US guidance have a major role in the diagnosis of anterior mediastinal masses and have several advantages over

open biopsies. This can be performed safely with shorter hospital stay [23].

US can be used to guide biopsy of mediastinal masses and lymph nodes located in the anterior mediastinum. These can be visualized through suprasternal, parasternal, or subxiphoid approaches. Color Doppler imaging helps in the identification and avoidance of the major vessels injury within the mediastinum [24].

In our study, lesions in 19 patients were approached through parasternal approach, and in two patients they were approached through suprasternal approach. Lesions in none of the patients were approached through subxiphoid approach (Table 5). There was a technical difficulty in reaching the mass in one of our studied patients because of its deep location leading to failure in conducting a biopsy of the lesion.

Suprasternal approach allows adequate assessment in 90–95% of cases [25]. A major advantage of suprasternal approach is its multiplanner capability, allowing the use of combined angled approaches for needle placement in the craniocaudal and mediolateral planes (which would not be possible with CT guidance), and the ability to continuously monitor the needle tip relative to the lesion and the major vessels [26].

The advantages of US guidance through parasternal approach include the real-time, continuous monitoring of the needle during advancement and sampling; the availability of oblique needle paths; the ability to perform the biopsy at the bedside of critically ill patients; or to have patients with dyspnea who cannot tolerate a supine position in a semi-sitting position during the biopsy [26].

Of the previously mentioned 22 patients in the current study, conclusive results were obtained in 18 cases (81.8%) (Table 6 and Fig. 3). Four patients required further evaluation [three nonconclusive results (13.6%) and one patient with failure to reach the mass by US (4.6%)].

Reintervention was carried out in the form of CT-guided biopsy (two patients), excisional biopsy (one patient), and open-lung biopsy (one patient).

In their study for the efficacy of CNB and FNAC in anterior mediastinal lesions under guidance of US or CT scan, Nasit et al. (2013) [13] obtained conclusive results by FNAC in 35 out of 50 patients with a diagnostic yield of 71.42% compared with a diagnostic yield of 97.95% by CNB. In comparison with our study, FNAC was not performed in our patients whereas the diagnostic yield of CNB was 81.8%.

Saha and Deb (2015) [27] studied mediastinal lesions in 50 patients. They obtained a diagnostic yield of 75% for transthoracic US-guided Tru-cut biopsies as compared with a yield of 81.8% in our study.

Hsu *et al.* (1995) [28] obtained a diagnostic rate of 52% using US-guided FNAC for sampling mediastinal lesions. In concordance with our results, Rubens *et al.* (1997) [8] achieved a sensitivity rate of 77% using needle biopsy as a diagnostic technique. Another study in Springfield, USA, on diagnostic accuracy of image-guided percutaneous fine needle biopsy of the mediastinum, also showed a high proportion of agreement (78%) between needle biopsy and subsequent histological diagnoses for mediastinal lesions [29].

Despite being a minimally invasive procedure in nature, US-guided biopsy may result in some complications. Pneumothorax is the most frequently mentioned complication in the literature [18].

In a series study conducted by Nasit *et al.* (2013) [13], only single case required an intercostal tube insertion for moderate pneumothorax. They claimed that in most cases the mediastinal lesion would have been in direct contact with the chest wall and accessible without

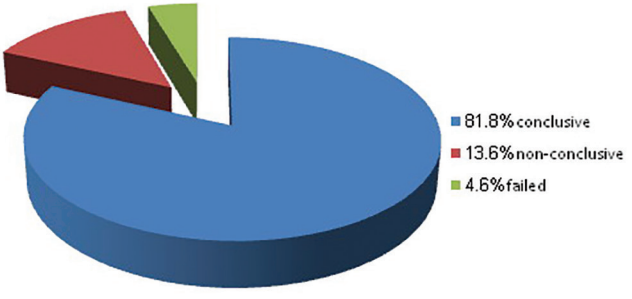
Table 5 Approach used in this study

Approach	Number of patients [*n* (%)]
Parasternal	19 (90.5)
Suprasternal	2 (9.5)
Subxiphoid	0 (0)
Total number of successfully approached patients	21 (100)

Table 6 Yield of ultrasound-guided biopsies in the study

Yield	Number of patients [*n* (%)]
Conclusive	18 (81.8)
Nonconclusive	3 (13.6)
Failure	1 (4.6)

Fig. 3



Diagnosic yield in the study.

traversing the lung or pleura. This explanation supports the low incidence of pneumothorax in their study. In addition, this low incidence of complication might be due to real-time observing of the needle by US during the biopsy procedure.

Vaziri *et al*. (2009) [12] mentioned a significant and previously unreported complication when a massive spontaneous hemothorax occurred because of ruptured ganglioneuroma in a young woman with neurofibromatosis.

In the current study, two patients developed mild vasovagal attacks at the beginning of the procedure. No patient developed pneumothorax, hemothorax, hemopneumothorax, chylothorax, infection (cutaneous or empyema), and no patients developed bronchial perforation. No procedure-related mortality occurred in the study.

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Conflicts of interest
There are no conflicts of interest.

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