Diagnosis of Malignancy of Adult Mediastinal Tumors by Conventional and Transesophageal Echocardiography

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Abstract

Background: Transesophageal echocardiography (TEE) is a well-established method for detecting and diagnosing heart tumors. In contrast, its role in assessing the presence, growth and evidence of malignant tumors originating from mediastinal sites remains unclear. The aim of this study was to compare the diagnostic impact of TEE and transthoracic echocardiography (TTE) for determining the localization, growth and malignancy of adult mediastinal tumors (MTs).

Methods: In a prospective and investigator-blinded study, we evaluated 144 consecutive patients with MT lesions to assess the diagnostic impact of TEE and TTE for detecting the presence of tumors spreading both inside and outside of the heart and for determining infiltration and invasion using pathological examination results as a reference.

Results: All tumor lesions were diagnosed and carefully evaluated by biopsy. Biopsy revealed malignant tumors in 79 patients and benign tumors in 65 patients. When compared to histological findings, TEE predicted malignancy from the presence of tumors spreading both inside and outside of the heart and from infiltration and invasion in 49/79 patients (62.0%). TTE predicted malignancy in only 8/79 patients (10.1%, $P < 0.005$). TEE visualized tumor lesions in 130 patients (90.3%) while the TTE visualized tumor lesions in 110 patients (76.4%) and was less effective at detecting MT lesions ($P < 0.001$). TTE and TEE could detect anterior MTs and adequately verified MTs ($P > 0.05$); TEE detected medium MTs better than TTE ($P < 0.001$).

Conclusions: TEE is effective and superior to TTE for predicting the localization and growth of MTs as well as for accessing evidence of tumor malignancy. TTE and TEE were able to detect anterior MTs; TEE was able to detect medium MT better than TTE.

Key words: Adult; Mediastinal Tumors; Transesophageal Echocardiography; Transthoracic Echocardiography

Introduction

Most adult mediastinal tumors (MTs) are asymptomatic or are associated with vague complaints, such as chest pain, dyspnea, and cough. Symptoms predominantly affect the cardiovascular, respiratory, and gastrointestinal systems, with nerve involvement (phrenic and recurrent laryngeal) resulting in specific symptoms as well. Thus, early diagnosis is vital for improving management and prognosis. Among imaging techniques, echocardiography has the potential to provide a complete anatomic and functional characterization of mediastinal mass with the advantage that it can be rapidly performed at the patient's bedside, without ionizing radiation or a nephrotoxic contrast agent. Transesophageal echocardiography (TEE) is well established for detecting and diagnosing heart tumors. In contrast, its role in assessing the presence, growth and evidence of malignant tumors originating from mediastinal sites remains widely uncertain. In this study, we aim to investigate the potential use of TEE for the diagnosis and anatomic and functional characterization of mediastinal masses; these results will be compared to those obtained employing transthoracic echocardiography (TTE), using a straightforward protocol that includes pathological examination results as a reference standard.

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Methods

Study population

From December 2010 to December 2013, we evaluated 144 patients admitted to General Hospital of Shenyang Military Area Command of People's Liberation Army who presented with MT that was confirmed by biopsy. All enrolled patients gave written informed consent for TEE and TTE. The study was approved by the appropriate ethics committee and was performed in accordance with the ethical standards adopted in the 1964 *Declaration of Helsinki* and its later amendments.

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Echocardiographic study

Transthoracic and TEE were performed in all patients as described. An echocardiograph equipped with a 2.5 or 3.5 MHz transducer for transthoracic examination (Acuson 128XP10 and Diasonics equipment) or a 5 MHz transducer for transesophageal examination (HP 1000 and Aloka SSD-650) was used. Imaging from the transthoracic view included multiple approaches, including the right and left parasternal, apical, subcostal, and suprasternal views. The echocardiographic evaluation included the localization and growth of the tumor lesions, involvement of the great vessels and the presence of malignancy criteria (Localization: Intracardiac, extracardiac, intra- and extra-cardiac; Growth: Invasion, infiltration, compression; Surface/border: Smooth, filiform, rough).[1]

Tumors spreading both inside and outside of the heart, infiltration, invasion, rough surfaces, uneven echo or hypoecho were taken as echographic evidence of malignant growth. The transthoracic and transesophageal data were transferred onto a CD. For each imaging approach, all tumor lesions were graded independently by two experienced investigators blinded to each other and to the patient's clinical and histological diagnosis. In the study, we evaluated patients with MT lesions to assess the diagnostic impact of TEE and TTE on the presence of tumors spreading both inside and outside of the heart and on infiltration and invasion using the pathological examination results as a reference regardless of whether the biopsy was acquired with a fine or coarse needle or by surgery resection. The collected specimens were of high quality, and the expertise of the pathologist led to very accurate pathological diagnoses. There were two separate groups of echocardiographers, one group performed and analyzed TEE, and the other group performed and analyzed TTE. Each group was blinded to the echocardiography results from the other group. The sequence of analysis of the transthoracic and transesophageal examinations was randomized. In each group, a consensus was reached by a third investigator in case of discrepant results.

Statistical analysis

Data were expressed as the mean ± standard deviation or as a percentage. Group comparisons were performed using Student's *t*-test. The significance of differences in the frequency ratio of the two imaging methods was assessed by the McNemar test. A $P < 0.05$ was considered as statistically significant. SPSS 15.0 (SPSS Inc., USA) was used for the statistical analysis.

Results

During the study period, 144 patients who presented with MT confirmed by biopsy were admitted to our hospital, which included 84 men and 60 women; the mean age was 49.7 ± 17.4 years (range, 19–77 years) [Table 1]. Histological evaluations of the tumor lesions were available for all patients from tissue sampling during resection surgery ($n = 96$; 66.7%) or biopsy ($n = 48$; 33.3%); the samples were obtained using a thoracoscope ($n = 18$), bronchoscopy ($n = 15$) or transthoracic needle puncture ($n = 15$). None of the 144 patients in this study presented any difficulties in having TEE and TTE; the TEE and TTE results are summarized in Table 1. Eighty-seven asymptomatic patients (60.4%) were diagnosed with MT through a regular physical examination. Fifty-seven patients (39.6%) presented with clinical symptoms, of which the most common was dyspnea followed by chest/back pain, cough and fever or fatigue. Sixty-five patients (45.1%) had a benign tumor; malignant tumor lesions were present in 79 patients (54.9%). Typical cases are illustrated in Figures 1–5.

Marked differences were observed in patients with MTs. TEE visualized tumor lesions in 130 patients (90.3%) while TTE visualized tumor lesions in 110 patients (76.4%) and was significantly less effective at detecting MT lesions ($P < 0.001$). TTE and TEE both visualized anterior MTs well and adequately verified MTs ($P > 0.05$); TEE visualized medium MTs better than TTE ($P < 0.001$) [Table 2]. When compared to histological findings, TEE predicted malignancy from the presence of tumors spreading both inside and outside of the heart and from infiltration and invasion in 49/79 patients (62.0%) with histologically proven malignancies (sensitivity 43%); a false positive result was obtained in only 2/65 patients (3.1%) with a benign tumor (specificity 96.9%). TTE predicted malignancy in only 8/79 patients (10.1%, $P < 0.001$) [Table 3]. When compared to histological findings, TEE predicted malignancy from the presence of tumors spreading both inside and outside of the heart and from infiltration and invasion in 62.0% patients with histologically proven malignancies. TTE predicted malignancy in only 10.1% of patients. We also observed malignant MTs with intra- and extra-cardiac localization in 25.3% patients and infiltrative and/or invasive growth in 40.5% patients, much higher than the rate for benign

Table 1: Clinical characteristics of the patients

Clinical characteristics	Value
Age, years	49.7 ± 17.4
Male/female	84/60
Dyspnea, *n* (%)	48 (33.3)
Chest/back pain, *n* (%)	27 (18.8)
Cough, *n* (%)	27 (18.8)
Fever or fatigue, *n* (%)	12 (8.3)
History of smoking, *n* (%)	21 (14.6)
History of drinking, *n* (%)	15 (10.4)

Table 2: Localization in 144 patients with MT using TEE and TTE (*n*)

Diagnosis	Anterior MT	Medium MT	Posterior MT	Total
TTE	76	24	10	110
TEE	78	52	4	130
P	>0.05	<0.01	>0.05	<0.01

MT: Mediastinal tumors; TEE: Transesophageal echocardiography; TTE: Transthoracic echocardiography.

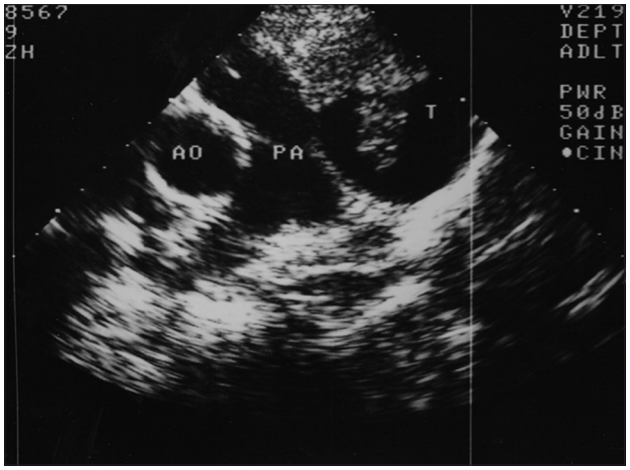

Figure 1: Two-dimensional ultrasonography showing the sites of the tumors (T: Tumor; PA: Pulmonary artery; AO: Aorta).

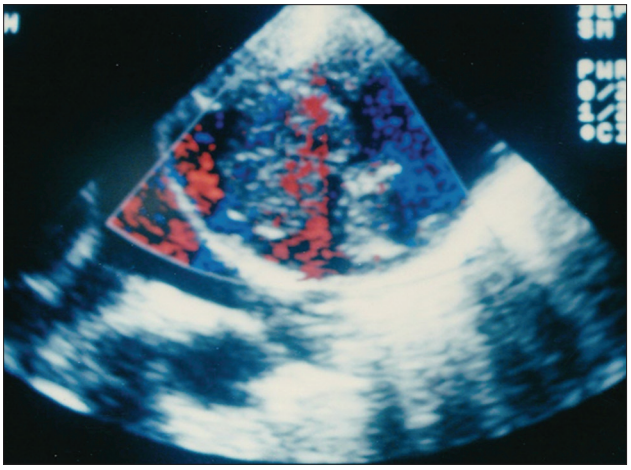

Figure 2: Color Doppler flow imaging showing the internal blood flow signal of the tumor.

Table 3: Localization, evaluation of tumor growth and border zone characterization in 144 patients with MT using TEE and TTE, *n* (%)

Diagnosis	Localization intra- and extra-cardiac	Infiltrative and/or invasive growth	Tumor compression	Border zone characterization
Benign ($n = 65$)				
TTE	0 (0)	0 (0)	54 (83.1)	33 (50.8)
TEE	0 (0)	0 (0)	58 (89.2)	60 (92.3)
Malignant ($n = 79$)				
TTE	0 (0)	8 (10.1)	19 (24.1)	20 (25.3)
TEE	20 (25.3)	32 (40.5)	35 (44.3)	40 (50.6)

MT: Mediastinal tumors; TEE: Transesophageal echocardiography; TTE: Transthoracic echocardiography.

tumors ($P < 0.05$) through TEE examination. Malignant MTs displayed infiltrative and/or invasive growth in 10.1% of patients, a much higher rate than the benign tumors ($P < 0.05$) through TTE examination. Three techniques were used to treat MTs in the patients: Open resection in three patients, video-assisted thoracoscopic surgery (VATS) in 18 patients and robot (Da Vinci surgical robot)-assisted minimally invasive resection surgery in 75 patients [Table 4].

Table 4: Treatment of mediastinal tumors

Resection technique	Operation time (min)	Intraoperative bleeding (ml)	Hospital stay (days)
Open ($n = 3$)	128.7 ± 18.5	133.3 ± 28.9	17.3 ± 2.1
VATS ($n = 18$)	208.3 ± 19.2	82.5 ± 43.8	11.5 ± 5.3
Robot-MIS ($n = 75$)	111.5 ± 58.1	20.9 ± 21.4	11.6 ± 2.2

Open: Thoracotomy; VATS: Video-assisted thoracoscopic surgery; Robot-MIS: Robot (Da Vinci surgical robot) assisted minimally invasive surgery.

Discussion

Most adult MTs are asymptomatic or are associated with vague complaints such as chest pain, dyspnea, and cough. In the current study, 87 asymptomatic patients (60.4%) were diagnosed with MTs through a regular physical examination. Fifty-seven patients (39.6%) presented with clinical symptoms, of which the most common was dyspnea followed by chest/back pain, cough and fever or fatigue. Furthermore, operating on a patient with a MT can be a risky and challenging endeavor. There are multiple reports of life-threatening perioperative complications, including death, in both adults and children.[2] Despite these risks, however, overall mortality remains low regarding all MT resection procedures (VATS resection, robot and open resection).[3-6] Thus, early diagnosis is vital for improving management and prognosis. Recognition of the mass and proper planning by the surgical teams seem to be at the forefront of successful and uncomplicated MT resections. Among imaging techniques, echocardiography has the potential to provide a complete anatomic and functional characterization of mediastinal masses with the advantage that it can be rapidly performed at the patient's bedside, without ionizing radiation and nephrotoxic contrast agent.

Although preoperative TTE has frequently been used in the past, TEE has recently been accepted as allowing for a more detailed evaluation of the mediastinum for masses and secondary compression of vascular structures.[7] Although computed tomography/magnetic resonance imaging (CT/MRI) is often adequate to assist with preoperative planning for resection, the dynamic nature of many MTs often requires a real-time imaging modality for maximum intraoperative benefit to the patient.[8] It may even be sensible to perform a preoperative TEE if the patient can tolerate

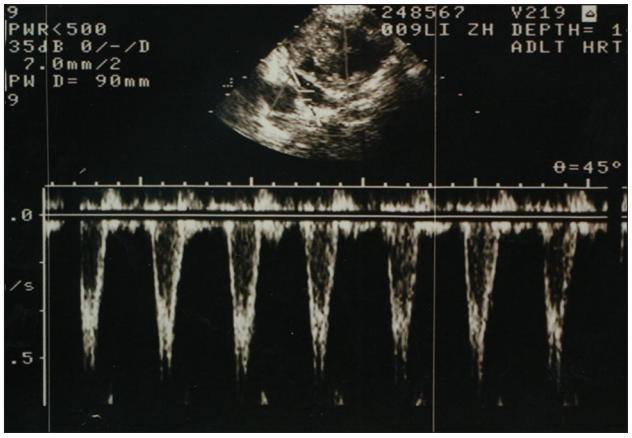

Figure 3: Pulse Doppler imaging the flow velocity of the pulmonary artery that was compressed by the tumor.

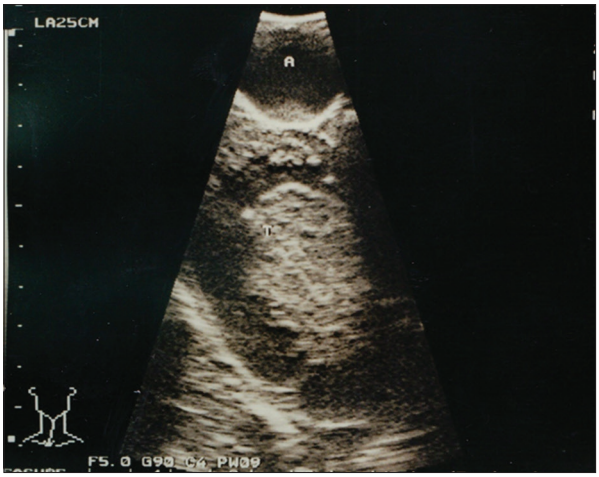

Figure 4: Transesophageal echocardiography showing a mediastinal teratoma.

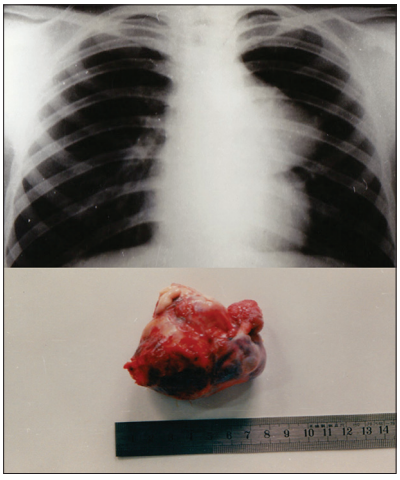

Figure 5: Chest X-ray, gross anatomy of a mediastinal teratoma.

the procedure because this may guide surgical planning more accurately compared to CT/MRI alone. Because the transducer travels posterior to mediastinal structures, a unique ultrasonic window is available for the detection of masses.[9] TEE is useful for the evaluation of mass size, composition, associated lymph nodes and the anatomic relation of the mass to other structures. In addition, TEE also assesses hemodynamic consequences of compression, possible obstruction of the great vessels, the site of tumor implantation, wall infiltration, and the involvement of heart cavities. TEE can aid in the distinction between benign and malignant masses on the basis of echogenicity, tumor spreading, infiltration, and invasion.[9] When compared to histological findings, TEE predicted malignancy from the presence of tumors spreading both inside and outside of the heart and from infiltration and invasion at a much higher rate than TTE in patients with histologically proven malignancies. Furthermore, malignant MTs exhibited both intra- and extra-cardiac localization in 25.3% of patients and displayed infiltrative and/or invasive growth in 40.5% of patients, results that are much higher rates than for benign tumors examined by TEE. Malignant MTs exhibited infiltrative and/or invasive growth in 10.1% of patients, a result that was much higher than the rate for benign tumors examined by TTE. Therefore, tumors that spread both inside and outside of the heart and that are infiltrative and/or invasive should be considered echographic evidence of malignant growth.

Transesophageal echocardiography was clearly superior to the transthoracic approach for assessing the diagnosis, localization and evidence of malignant tumor lesions originating from the mediastinal site. Marked differences were observed in patients with MTs. TEE visualized the tumor lesions in 90.3% of patients while TTE visualized tumor lesions in 76.4% of patients and was less effective at detecting MT lesions. TEE was of particular diagnostic importance when the tumor was located above the atrial level in the vicinity of the great vessels and in the medium part of the mediastinum.

Due to recent advancements in contrast-enhanced ultrasound, liver and pancreatic lesions can be diagnosed more effectively, showing good diagnostic performance in differentiating benign from malignant pancreatic tumors and focal liver lesions.[10-15] Fan *et al*.[11] noted that contrast-enhanced ultrasound has an obvious superiority over conventional ultrasound in the general diagnostic accuracy of solid pancreatic lesions and in the diagnostic consistency among doctors. Contrast-enhanced ultrasound represents a useful method in clinical practice for differentiating between malignant and benign focal liver lesions detected on standard ultrasonography.[12] In the near future, we will investigate the diagnostic values of contrast-enhanced ultrasound in the differential diagnosis of malignant from benign MTs, and we believe that contrast-enhanced ultrasound may play an important role in the differential diagnosis of malignant from benign MTs.

In conclusion, transesophageal echocardiography use is increasing and is widely used to assess patients with suspected MTs. The early and correct assessment of localization, growth and malignancy can be a great help in guiding further diagnostic and surgical treatments.

TEE typically produces clearer images compared to those generated by TTE, especially when viewing structures that are difficult to see transthoracically. In the present study, TEE was superior to conventional TTE in reliably assessing the diagnosis, localization, growth and malignancy of tumors originating from the mediastinum. Tumors that spread both inside and outside of the heart and that were infiltrative and/or invasive were taken as echographic evidence of malignant growth. TTE and TEE both showed anterior MTs; TEE showed medium mediastinal tumors better than TTE.

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