Pericardial Thickness Measured With Transesophageal Echocardiography: Feasibility and Potential Clinical Usefulness

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Objectives. **This study assessed the reliability of transesophageal echocardiographic measurements of pericardial thickness and the potential diagnostic usefulness of this technique.**

Background. **Transthoracic echocardiography cannot reliably detect thickened pericardium. The superior resolution achieved with transesophageal echocardiography should allow better pericardial definition.**

Methods. **Pericardial thickness measured at 26 locations in 11 patients with constrictive pericarditis who underwent intraoperative transesophageal echocardiography was compared with pericardial thickness measured with electron beam computed tomography. Intraobserver and interobserver variabilities were determined. Pericardial thickness was then measured in 21 normal subjects. With these values as a guide, two observers reviewed 37 transesophageal echocardiographic studies to determine whether echocardiographic measurement of pericardial thickness could be used to distinguish diseased from normal pericardium.**

Results. **The correlation between echocardiographic and computed tomographic measurements ($r \geq 0.95$, $SE \leq 0.06$ mm, $p < 0.0001$) was excellent. The ±2 SD limits of agreement were ±1.0 mm or less for pericardial thickness <5.5 mm and ±2.0 mm or less for the entire range of thicknesses. Intraobserver and interobserver agreements were good. Mean normal pericardial thickness was 1.2 ± 0.8 mm (±2 SD) and did not exceed 2.5 mm. Pericardial thickness ≥3 mm on transesophageal echocardiography was 95% sensitive and 86% specific for the detection of thickened pericardium.**

Conclusions. **Measurement of pericardial thickness with transesophageal echocardiography is reproducible and should be a valuable adjunct in assessing constrictive pericarditis.**

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The use of transthoracic echocardiography to determine pericardial thickness is reportedly unreliable (1). For this reason, the echocardiographic diagnosis of constrictive pericarditis has been based predominantly on hemodynamic rather than anatomic abnormalities. Hatle et al. (2) described respirophasic Doppler velocity changes indicating interventricular "coupling" (3) and the dissociation between intrathoracic and intracardiac pressures (2), which are the pathophysiologic hallmarks of pericardial constriction. However, Doppler echocardiography may not always conclusively confirm or exclude disease (4,5). In these situations, pericardial imaging with either computed tomography (6–8) or magnetic resonance imaging (9–11) is helpful in clarifying the diagnosis. It has been suggested that transesophageal echocardiography, with its superior image resolution, may be used to reliably visualize the pericardium (12). The objectives of this study were 1) to compare the accuracy of transesophageal echocardiographically measured pericardial thickness with that of electron beam computed tomography; and 2) to determine whether a pericardial thickness >2 SD above normal identified surgically confirmed thickened pericardium in a blinded retrospective review of intraoperative transesophageal echocardiographic examinations.

Methods

Phase I: accuracy of transesophageal echocardiography. The study group for phase I of the study consisted of 11 consecutive patients with constrictive pericarditis confirmed surgically and pathologically and in whom both preoperative cardiac electron beam computed tomography and intraoperative transesophageal echocardiography had been performed. All computed tomographic and transesophageal echocardiographic studies were performed within 2 months of one another (median 11 days).

Intraoperative transesophageal echocardiographic examinations were performed with 5.0- or 7.0-MHz biplane or multiplane transducers and commercially available ultrasound instruments. Standard imaging planes (13) were recorded on 0.75-in. (1.9 cm) tape before pericardiectomy. The primary

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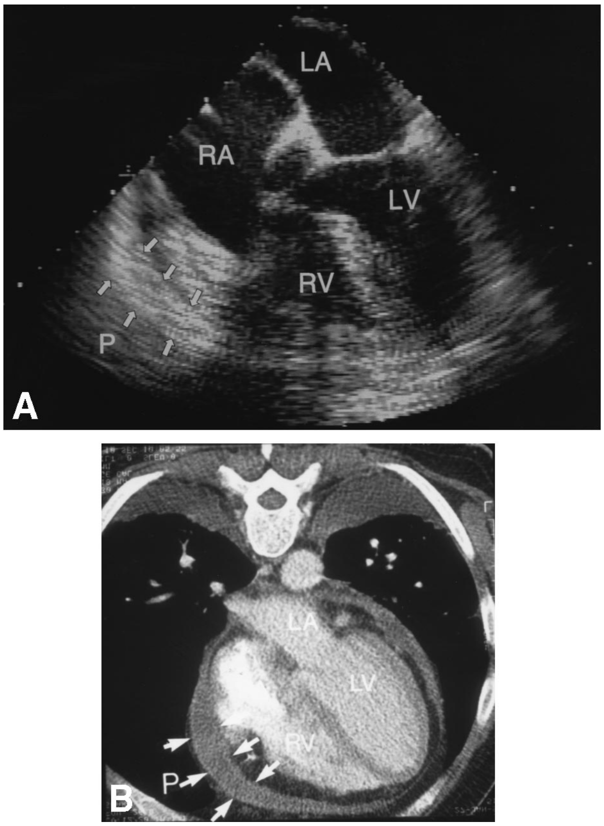

Figure 1. A, Transesophageal echocardiogram (four-chamber transverse plane view) and **(B)** corresponding transaxial electron beam computed tomographic scan from Patient 8 (see Table 1) showing grossly thickened (up to 18 mm) **(arrows)**, "fleshy" parietal pericardium (P) over the right side of the heart. This patient had a 3-month history of dyspnea and progressive heart failure. LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle.

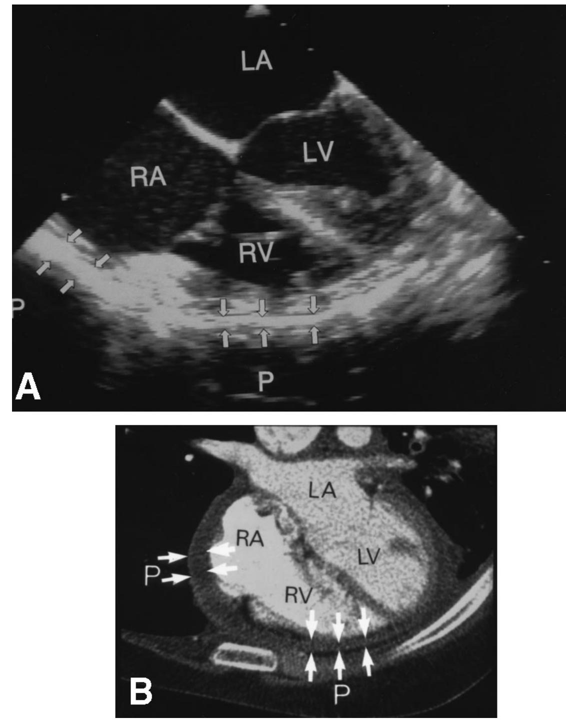

Figure 2. A, Transesophageal echocardiogram from Patient 1 (see Table 1) showing thickened parietal pericardium (P, **arrows**) overlying right ventricle (RV) and right atrium (RA) in four-chamber transverse plane view. Pericardium appears as a highly echo-dense, "fibrotic" structure. Right atrial wall is tethered to adjacent thickened pericardium. **B,** The corresponding transaxial electron beam computed tomographic scan showing findings similar to those in **A**. LA = left atrium; LV = left ventricle.

purpose of these echocardiographic studies was to assess the effect of pericardiectomy on cardiac filling.

The Imatron C-100 computed tomographic scanner (14) was used for all studies. Electron beam technology permits image acquisition in 100 ms and allows excellent definition of cardiac borders and structure without blurring due to motion. Scanning was electrocardiographically triggered in mid to late diastole while multiple transaxial images 6 mm apart were acquired. Acquisition time was 100 ms per scan. Nonionic contrast medium (80 to 100 ml of iopamidol) was injected intravenously in all patients to define the cardiac chambers.

Transesophageal echocardiographic measurement of pericardial thickness. The pericardium was identified as an echodense linear structure, often separated from the myocardium by a lucent space denoting either fluid or epicardial fat (Fig. 1). Measurement of pericardial thickness was performed independently by two experienced echocardiographers (observers 1 and 2) after digitization of selected images in mid to late diastole from 0.75-in. videotape on a Dextra D-200 analyzer (Dextra Medical Inc.). The specific region of interest (for instance, over the right ventricle 3 cm from the atrioventricular groove) was magnified by a factor of two, and three measurements were made per location over a pericardial span of 10 to 15 mm and averaged for a mean thickness. Measurements were repeated 2 weeks later to assess intraobserver variability. Measurements were not made in areas where the pericardium was inadequately visualized or grossly irregular. If an echo-free space (either subepicardial fat or fluid) existed between the pericardial layers, only the thickness of the parietal pericardium was measured (Fig. 1A). Otherwise, the thickness of the pericardium was measured from the outer myocardial border to the outer edge of the pericardium (Fig. 2A). For consistency with electron beam computed tomography, pericardial thickness was measured in only four-chamber and basal short-axis sections.

Electron beam computed tomographic measurements were made independently (at the same locations as with transesophageal echocardiography) by a cardiac radiologist using either electronic or manual calipers. Three measurements taken over a 10- to 15-mm segment were averaged for a mean computed tomographic pericardial thickness.

Phase II: blinded review of intraoperative transesophageal echocardiography. To determine the reliability of transesophageal echocardiography in differentiating thickened from normal pericardium, normal pericardial thickness was first established in subjects who had a normal transesophageal

Table 1. Clinical Profile, Diagnostic Investigations and Sites of Measurement of Pericardial Thickness in 11 Patients With Constrictive Pericarditis

Pt No.	Age (yr)/Gender	Etiology	Main Presentation	Pericardial Calcification*	Typical Catheterization Findings†	Doppler Physiology‡	Pericardial Regions Measured on TEE and EBCT
1	17/M	Irradiation	CHF	No	Yes	Constriction	RA, RVFW
2	32/M	Idiopathic	Arrhythmia	Yes	Not done	Constriction	RA, RAVG, LVFW
3	49/M	Irradiation	CHF	No	Not done	Mixed	RVFW, RVOT
4	52/M	Idiopathic	CHF	No	Not done	Constriction	RVFW, RVOT, LVFW
5	56/M	Post-CABG	CHF	No	Not done	Constriction	RVFW, RVOT, LVFW
6	58/M	Post-CABG	CHF	No	Not done	Constriction	RAVG, RVFW
7	59/M	Idiopathic	CHF	No	Yes	Constriction	RVFW, LVFW
8	60/M	MDS	CHF	No	Not done	Constriction	RA, RAVG, RVFW
9	63/M	Idiopathic	Syncope	Yes	Yes	Constriction	RAVG, RVFW, LVFW
10	63/M	Post-CABG	CHF	Yes	Yes	Restriction	RVFW
11	67/M	Post-CABG	CHF	No	Yes	Constriction	RVFW, RVOT

*Present either on chest X-ray film or computed tomogram. †Defined as elevation and end-diastolic equalization of right and left ventricular pressures. ‡Changes in right and left filling velocities consistent with constriction, restriction or mixed constriction–restriction physiology, as described by Oh et al. (4). CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; EBCT = electron beam computed tomography; F = female; LVFW = left ventricular free wall; M = male; MDS = myelodysplastic syndrome; Pt = patient; RA = right atrium; RAVG = right atrioventricular groove; RVFW = right ventricular free wall; RVOT = right ventricular outflow tract.

echocardiogram and no history of cardiovascular disease. Pericardial thickness was measured as described earlier.

Two experienced echocardiographers (observers 3 and 4) independently reviewed a videotape compiled from intraoperative transesophageal echocardiographic examinations of patients who had cardiac surgery and, on surgical inspection, had either normal or thickened pericardium. Care was taken to ensure that the type of surgical procedure performed was not evident. Using electronic calipers, observers 3 and 4 attempted to distinguish normal from abnormal pericardial thickness semiquantitatively, with >2 SD of normality, as previously established, being the limit. All studies were approved by the Institutional Review Board of the Mayo Foundation.

Statistical analysis. Continuous variables are described as mean value ± SD unless otherwise stated. Categoric variables are expressed as the percentages and differences tested by the chi-square method. The strength of the association between transesophageal echocardiographically and electron beam computed tomographically measured pericardial thickness was analyzed by simple linear regression, and the agreement between these variables was quantified by the method of Bland and Altman (15). Intraobserver and interobserver variability of the transesophageal echocardiographic measurements was assessed using the method of Bland and Altman. Sensitivities, specificities and predictive accuracies of a predefined threshold pericardial thickness for the diagnosis of pericardial disease were calculated in the usual manner. A p value <0.05 was considered significant.

Results

Phase I: accuracy of transesophageal echocardiography. *Clinical characteristics.* The clinical features of the 11 patients (mean age 53 ± 15 years, range 17 to 67) with constrictive pericarditis are shown in Table 1. All patients had thickened pericardium, as seen on electron beam computed tomography. Histologic examination of the resected pericardium revealed either chronic calcific or fibrotic pericarditis in all cases.

Transesophageal echocardiographic measurements. Pericardial thickness was measured with transesophageal echocardiography at 26 locations in the 11 patients (mean 2.5 sites per patient). The range of these measurements for observers 1 and 2 was 2.5 to 14.8 mm (mean 5.7 ± 3.0) and 2.2 to 14.5 mm (mean 5.5 ± 3.0), respectively. In the eight patients with noncalcified fibrotic pericardium, 19 measurements were made (mean 2.4 per patient), whereas in the three patients with calcific constrictive pericarditis, seven measurements were possible (mean 2.3 per patient). Pericardial thickness could be measured over the right ventricular free wall in 10 patients (91%), left ventricular free wall in 5 patients (45%), right atrioventricular groove in 4 patients (36%), right ventricular outflow in 4 patients (36%) and right atrium in 3 patients (27%) (Table 1).

Relation between transesophageal echocardiographic and electron beam computed tomographic measurements. As measured with computed tomography, pericardial thickness ranged from 2.7 to 16.0 mm (mean 5.7 ± 3.1). Figures 1 and 2 show thickened pericardium imaged with transesophageal echocardiography and the corresponding computed tomographic section. Figure 3 shows the regression plots between these two methods. For both observers, the correlation between measurements obtained with the two methods was excellent, with small residual standard errors. In plotting the mean pericardial thicknesses measured by both methods versus the difference between the two measures, the 95% confidence limits of agreement between the measurements was ±1.6 mm or less for observer 1 and ±2.0 mm or less for observer 2 (Fig. 4). For pericardial thickness <5.5 mm, the ±2 SD limits of agreement were ±0.8 and ±1.0 mm for observers 1 and 2, respectively. Intraobserver and interobserver variability by the Bland and Altman method was ±1.4 mm or less and ±0.9 mm or less (±2 SD limits of agreement), respectively.

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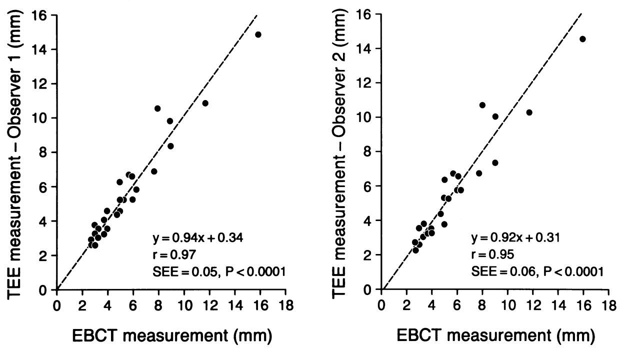


Figure 3. Scattergrams of relation between pericardial thickness measured with electron beam computed tomography (EBCT) and transesophageal echocardiography (TEE), the latter made independently by Observers 1 (**left**) and 2 (**right**).

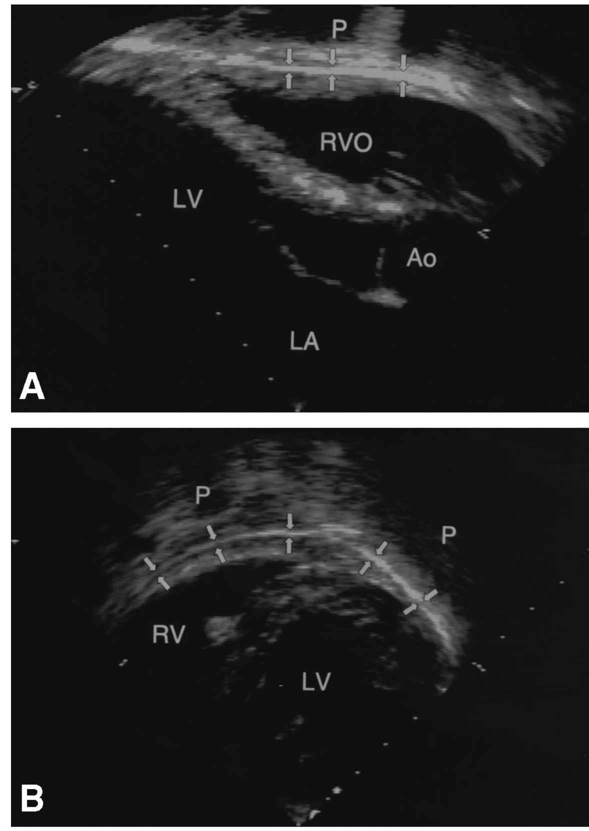
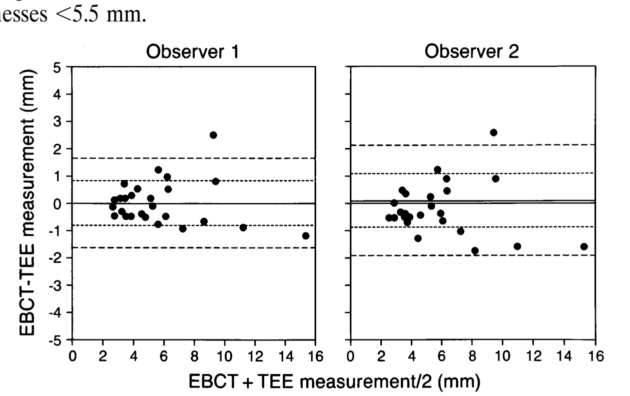


Figure 5. Transesophageal echocardiograms showing (**A**) thin, normal pericardium (P, **arrows**) overlying the right ventricular outflow tract (RVO) in the midesophageal long-axis view and (**B**) over the right ventricle (RV) and left ventricle (LV) in the transgastric short-axis view. Ao = aorta; LA = left atrium.

Phase II: blinded review of intraoperative transesophageal echocardiography. *Normal transesophageal echocardiographic values for pericardial thickness.* In 21 normal subjects (8 men and 13 women, mean age 58 ± 7 years [range 47 to 75]), 59 measurements of pericardial thickness (mean 2.8 measurements per subject) were made. Mean normal pericardial thickness was 1.2 ± 0.8 mm (mean ± 2 SD); no value exceeded 2.5 mm. Extensive segments of the pericardium were visualized clearly in all the subjects, particularly over both ventricles and the right ventricular outflow tract (Fig. 5). On the basis of these findings, pericardial thickness ≥3 mm was deemed abnormal.

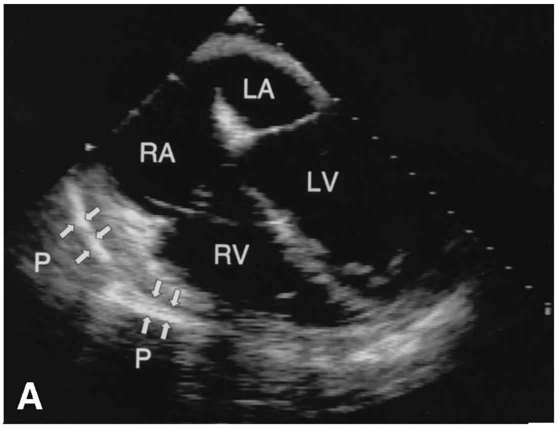
Correlation between pericardial thickness measured with transesophageal echocardiography and that at surgical inspection. After establishing the feasibility of transesophageal echocardiography and normal pericardial thickness, observers 3 and 4 reviewed a random series of transesophageal echocardiograms taken intraoperatively in 37 patients. Of these 37 patients, 18 had normal pericardium on surgical inspection. None of these control subjects previously had cardiac surgery, significant valvular disease, left ventricular hypertrophy or obvious abnormality of regional wall motion. The other 19 patients had thickened pericardium, and all of them had constrictive pericarditis, except for one patient who had chronic relapsing pericarditis. Pericardial thickness ≥3 mm on transesophageal echocardiography (Fig. 6) had a high sensitivity and negative predictive accuracy and moderate specificity and positive predictive accuracy for identifying thickened pericardium intraoperatively (Table 2).

Figure 4. Bland-Altman plots comparing mean and difference of electron beam computed tomographic (EBCT) measurements of pericardial thicknesses and those made by Observers 1 (**left**) and 2 (**right**) from transesophageal echocardiographic (TEE) images. **Dashed lines** indicate ±2 SD limits of agreement for the entire range of pericardial thicknesses; **dotted lines** indicate these limits for thicknesses <5.5 mm.



Discussion

Evaluation of thickened pericardium with transthoracic echocardiography. The pericardial signal, as assessed with transthoracic echocardiography, is influenced by transducer position, gain and gray-scale settings and ultrasound reverberation (16). Of 57 patients with constrictive pericarditis pooled from six M-mode echocardiographic studies, thickened pericardium could be identified reliably in only 26 (46%) (1). This "low" incidence of thickened pericardium in patients with constrictive pericarditis may be attributed to the technical limitations of transthoracic echocardiography and to nonuniform pericardial thickening (17–19). With two-dimensional imaging, an echogenic pericardial "rind" may be visualized in



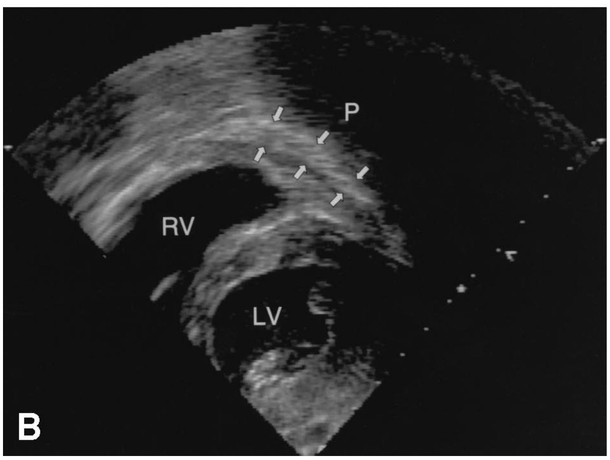


Figure 6. A and B, Intraoperative transesophageal echocardiographic studies typical of the cases reviewed in blinded manner to determine the correlation with surgically determined pericardial thickening (**arrows**). LA = left atrium; LV = left ventricle; P = pericardium; RA = right atrium; RV = right ventricle.

patients with constrictive pericarditis (20). Hinds et al. (21), however, found two-dimensional echocardiography to have a sensitivity of only 63% for detecting pericardial thickness >2 mm. In contrast, Pandian et al. (22) measured pericardial thickness in dogs with experimentally induced constrictive pericarditis and found a systematic overestimation of true thickness due to side-lobing artifact.

Related studies using transesophageal echocardiography. In the only published series on the usefulness of transesophageal echocardiography, Hutchison et al. (23) found thickened pericardium on transesophageal echocardiography in nine patients with suspected constrictive pericarditis (the diagnosis was confirmed surgically or pathologically in eight of these patients), whereas transthoracic echocardiography identified thickened pericardium in only four of the nine patients. Because the distinction between normal subjects and patients with constriction was semiquantitative, measurement bias from a priori knowledge of the diagnosis is a potential limitation of their study (23). In a preliminary communication, Klein et al. (24) found excellent concordance between transesophageal echocardiography and magnetic resonance imaging in assessing the distribution of thickened pericardium. The results of the current study suggest that in adequately visualized pericardial segments, transesophageal echocardiography can quantitate thickness to within ±1 mm of a comparison standard.

In the present study, the pericardium in normal subjects and in patients with constrictive pericarditis was most easily visualized anteriorly, consistent with the conclusions of previous radiologic studies (9,25–27). Although the right ventricular free wall in transverse plane midesophageal imaging is not a near-field structure, the overlying pericardium is often well imaged because 1) the abundance of epicardial fat in this location (26) enhances definition of the anterior pericardium; 2) the esophageal transducer is oriented perpendicularly to this segment of pericardium, thus optimizing axial resolution; and 3) the most exuberant pericardial thickening in constrictive pericarditis usually occurs anteriorly (9,10,28).

Potential role of transesophageal echocardiography in constrictive pericarditis. Most patients presenting with symptoms of constriction are evaluated initially with transthoracic echocardiography. When the transthoracic Doppler echocardiographic study is diagnostic for constriction, no further imaging may be necessary before considering pericardiectomy. In equivocal cases, further evaluation with transesophageal echocardiography or other diagnostic modalities may be helpful (5). Transesophageal echocardiography readily permits sampling of pulmonary venous and transmitral flow (13), facilitating confirmation of constrictive Doppler hemodynamic data (29,30). Useful two-dimensional information such as myocardial tethering (31) may also be appreciated better during transesophageal echocardiography. Also, the feasibility of pericardial imaging, described in the present study, provides a means of defining the anatomic substrate responsible for constriction physiology, thereby addressing these dual concerns in the evaluation of constrictive pericarditis.

The mean normal pericardial thickness of 1.2 mm obtained in our study is identical to that reported in anatomic studies (32) and is comparable to the results of previous computed

Table 2. Sensitivity, Specificity and Predictive Accuracy of Using Pericardial Thickness ≥3 mm Measured With Transesophageal Echocardiography in Predicting Pericardial Thickening Found Intraoperatively

	Sensitivity (%)	Specificity (%)	Positive Predictive Accuracy (%)	Negative Predictive Accuracy (%)
Observer 3	100 (19/19)	89 (16/18)	90 (19/21)	100 (16/16)
Observer 4	89 (17/19)	83 (15/18)	85 (17/20)	88 (15/17)
Mean	95	86	88	94

tomographic (26) and magnetic resonance imaging (27) series. The threshold of 3 mm used in the present study is in agreement with the values for pericardial thickness, ranging from 4 to 20 mm, obtained previously with computed tomography in patients with constriction (33). More important, the 3-mm value was a useful guide in a simulated clinical situation.

Study limitations. The use of electron beam computed tomography as a comparison standard has its limitations. Although this technique clearly distinguishes mediastinal or epicardial fat from pericardium, small serous or purulent effusions with high attenuation may be indistinguishable from thickened pericardium (8), leading to overestimation of pericardial thickness. However, none of our patients had significant pericardial effusion.

Anatomic loci defined on transesophageal echocardiography cannot be matched exactly with those defined on computed tomography (and conversely). However, the present study attempted to avoid major discrepancies in sampling site by using comparable tomographic planes, avoiding measurements of sites where pericardial thickness was grossly irregular and averaging multiple measurements over a segment of pericardium. The excellent correlation between measurements made with the two techniques suggests that selected sampling sites were closely approximated.

Despite the absence of a prospective protocol for gain settings, the reasonably good agreement between these measurements also suggests that instrument factors did not significantly affect the echocardiographic measurements. However, the reliability of measurements depends critically on attention to image quality in ultrasound studies, and it is important to optimize the transesophageal examination with appropriate gain and other settings.

The retrospective nature of the study introduced a potential for measurement bias. However, the purpose of the study was not to differentiate normal from thickened pericardium but to ascertain the accuracy of transesophageal echocardiographic measurements. Also, pericardial thickening in constrictive pericarditis is not homogeneous, as reflected by wide dispersion in measurement values. Of importance, all observers had no knowledge of the measurements obtained with electron beam computed tomography.

Important caveats. As with any diagnostic application, the recognition of pericardial thickening with transesophageal echocardiography involves a learning curve. It is important, for instance, to appreciate that subacutely inflamed and edematous pericardium (Fig. 1A) may have different ultrasound tissue characteristics in comparison with chronic pericardial fibrosis or calcification (Fig. 2A). However, increased pericardial thickness can be diagnosed with greater confidence using transesophageal echocardiography rather than transthoracic echocardiography because of superior image resolution and clearer definition of the interface between the pericardium and fat or fluid.

The inability to visualize the entire pericardium is a limitation of echocardiography, but it is not exclusive to this technique (25,34). Nevertheless, if thickened pericardium is the only information required in the clinical setting, electron beam computed tomography or magnetic resonance imaging is the diagnostic modality of choice because of the superior circumferential resolution of the pericardium (25,27). However, electron beam computed tomography is available in only about 60 medical centers worldwide. Conventional computed tomographic scanners typically require at least 1 s to obtain an image, resulting in increased blurring artifact. Magnetic resonance imaging is a good alternative to electron beam computed tomography (9–11), but because of dependence on electrocardiographic gating, imaging may be impossible in patients with atrial fibrillation and low voltage electrocardiograms.

Although nearly all the study patients with thickened pericardium had constrictive pericarditis, the two conditions are not uniformly associated. Thickened pericardium may be present in adhesive pericarditis, and a relatively normal pericardium may be found in some cases of constriction after cardiac surgery or visceral epicarditis (35). Although a thickened pericardium is not a sine qua non for constriction, its presence in the setting of a compatible clinical picture and physiologic profile is compelling evidence for this diagnosis (9,28,36,37). In contrast, demonstration of normal-thickness pericardium usually excludes constriction.

Conclusions. Transesophageal echocardiographic measurement of pericardial thickness is feasible, reproducible and sufficiently accurate for clinical purposes. Determination of pericardial thickness complements the comprehensive hemodynamic data provided by Doppler echocardiography and should be attempted whenever transesophageal echocardiography is indicated in patients with suspected pericardial disease.

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