Pathologic Correlates of Aortic Plaques, Thrombi and Mobile “Aortic Debris” Imaged In Vivo With Transesophageal Echocardiography

PERIYANAN VADUGANATHAN, MD, APRIL EWTON, MD, SHERIF F. NAGUEH, MD, DONALD G. WEILBAECHER, MD, HAZIM J. SAFI, MD, WILLIAM A. ZOGHBI, MD, FACC

Houston, Texas

Objectives. This study sought to evaluate the pathologic correlates of aortic plaques, thrombi and mobile “aortic debris” imaged in vivo by transesophageal echocardiography (TEE).

Background. Atherosclerotic plaques with various complexity, thrombi and debris are frequently identified by TEE during imaging of the aorta. However, pathologic data to characterize these lesions imaged in vivo are lacking.

Methods. Intraoperative TEE was performed prospectively in 31 patients undergoing repair of aortic aneurysm or dissection. TEE was used to guide the surgeon to mark aortic areas of interest that were sent for pathologic examination. A four-point scoring system was used for both TEE and pathologic evaluation to grade the degree of involvement of the aortic wall with atheroma. Ultrasound video intensity of the aortic wall lesions was measured and compared with quantitative measures of wall composition at pathologic examination. The presence of thrombi and mobile aortic debris by TEE was noted and compared with pathologic findings.

Results. Histologic–TEE correlations were possible in 62 aortic segments. There was 73% exact agreement between TEE and pathologic grading. Discrepancies were mostly in the inability of TEE to detect superficial ulcerations. However, separation of normal aorta and minimal intimal thickening (grades I and II) from more complex atheromas (grades III and IV) was observed in 93%. For identification of thrombus, TEE had a sensitivity of 91% (29 of 32 segments) and a specificity of 90% (27 of 30 segments). Mobile aortic debris were identified in six aortic segments and were confirmed at pathologic examination to be thrombi. Ultrasound video intensity increased with worsening complexity of atheroma and related significantly to aortic plaque composition at pathologic evaluation (r = 0.80, p < 0.0001). Ultrasound intensity of thrombi and mobile debris was similar and was lower than that of complex atheromas.

Conclusions. Thus, in the evaluation of aortic pathologic segments, TEE can assess aortic plaque complexity and identify thrombus formation, findings that may have important therapeutic implications.

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From the Section of Cardiology, Department of Medicine and Departments of Surgery and Pathology, Baylor College of Medicine, Houston, Texas. This study was presented in part at the Seventh Annual Scientific Sessions of the American Society of Echocardiography, Chicago, Illinois, June 1996.

Address for correspondence: Dr. William A. Zoghbi, Director of Echocardiography Research, Baylor College of Medicine and The Methodist Hospital, 6550 Fannin SM-677, Houston, Texas 77030. E-mail: wzoghbi@bcm.tmc.edu.

Atherosclerosis of the aorta has been demonstrated to be a marker of coronary artery disease (1,2) and is associated with a significant risk of cardiovascular mortality (3) and vascular events (4–10). Transesophageal echocardiography (TEE) has become a unique ultrasound tool that allows improved visualization of the aorta because of its proximity to the esophagus. Increased thickness and complexity of aortic plaques as visualized by TEE have been recently associated with a high incidence of vascular events (6–9). Furthermore, mobile “debris” in the aorta detected by TEE is highly associated with embolic events (10,11). However, the pathologic correlates of aortic lesions imaged by ultrasound are scant. Attenuation of ultrasound (12) or ultrasound backscatter (13) by human aortas in autopsy specimens has been related to pathologic features of atherosclerotic plaques. At present, there are no data on the pathologic correlates of aortic lesions imaged in vivo with TEE. Furthermore, pathologic characterization of mobile aortic debris seen by TEE is lacking. The purpose of the present study was therefore to evaluate prospectively the pathologic correlates of aortic plaques, thrombi and mobile aortic debris detected in vivo with TEE and to quantitate the ultrasound intensity of aortic lesions and assess its relation to quantitative pathologic findings.

Methods

Patients. The study included all consecutive patients who underwent elective aortic surgery for aortic aneurysm or dissection by one cardiovascular surgeon (H.J.S.) during 1995 at The Methodist Hospital and in whom TEE was requested for intraoperative evaluation of the aorta and cardiac monitoring. All patients provided written informed consent for participation in the study, which was approved by the institutional review board of Baylor College of Medicine and The Methodist Hospital.
**Intraoperative TEE examination.** After induction of anesthesia, preoperative TEE was performed using a biplane 5-MHz TEE probe and a Hewlett-Packard Sonos 1500 imaging system. The probe was advanced to the distal esophagus and rotated posteriorly and slowly withdrawn to scan the descending thoracic aorta and aortic arch. It was rotated and advanced again to image the ascending aorta. For every patient, gain and instrument settings were established to optimize imaging of the arterial wall. Thereafter, instrument settings were not altered. Images were recorded on videotape for subsequent analysis and interpretation.

**Identification of aortic segments.** After thoracotomy and exposure of the aorta and before aortic cross-clamping, areas of interest of the aorta within or just adjacent to the site of planned repair were imaged with TEE in short- and long-axis views and recorded on videotape while the surgeon indented the aorta at the site of interest for later identification during the TEE analysis. Silk sutures were placed on the outside of these segments as markings for later pathologic examination. One or more segments were identified per patient. After aortic clamping, the marked segments were resected, collected in separate containers filled with formalin and taken immediately for gross and histopathologic examination.

**Analysis of TEE studies.** The diameter of the aorta and thickness of the aortic wall were measured using an off-line system (TomTec Systems, Inc.). Because of the inability of the ultrasound to differentiate intima from media, the thickness measured included both inner layers and excluded the bright adventitia. The degree of aortic atherosclerosis was graded (I to IV) using a modification of the scoring system by Ribakov et al. (14), where grade I = normal; grade II = minimal intimal thickening; grade III = raised irregular plaque <5 mm in thickness; grade IV = complex protruding plaque with ≥5-mm thickness, ulceration or calcific density. Examples of grades I to IV are shown in Figures 1 to 4. Mobile protruding lesions in the aorta (aortic debris) were noted when present. Thrombus in the aorta was identified as a low density mass with homogeneous appearance and a smooth linear interface with the aortic lumen. All measurements, grading and interpretations of TEE studies were performed by an observer (P.V.) unaware of the pathologic data.

**Ultrasound video intensity of aortic pathologic features by TEE.** A computer software was used to quantitate the ultrasound video intensity of the identified aortic wall segment, thrombus or mobile lesions (TomTec Imaging Systems, Inc.). For aortic atheromas or normal aortic wall, an area ~5 mm in length in the long axis of the aorta was traced and quantitated. This area included the full thickness of the lesion just inner to the bright adventitia. For thrombus and mobile lesions, measurements were performed in the brightest area toward the middle of these lesions. Measurements represent an average of three determinations. Ultrasound video intensity was calculated for each lesion as percent of maximal intensity, corrected for background intensity, as follows:

\[ \% \text{Ultrasound video intensity} = \frac{(\text{Lesion intensity} - \text{Background intensity}) \times 100}{\text{Maximal intensity} - \text{Background intensity}} \]

where maximal video intensity was measured along the adventitia of the aortic segment and background intensity, in the lumen of the aorta, close to the aortic intima.

**Pathologic examination.** Pathologic examination was performed by experienced pathologists (A.E., D.G.W.) unaware of TEE findings. Sections were submitted for microscopic examination with hematoxylin and eosin staining as well as Verhoeff-Van Gieson staining for elastic fibers. The extent of aortic atherosclerosis was classified into four grades: I = normal; II = mild intimal thickening; III = fibrous or fibrolipid plaque, characterized by an intact fibrous cap and a fibrous or lipid core, where the thickness of the intima and media was <5 mm; IV = lipid or fibrolipid plaque, characterized by a core with abundant cholesterol crystals, areas of ulceration with an absent fibrous cap, the total intima–media thickness ≥5 mm or presence of calcification. When thrombus was present, its extent and size was described. Mobile lesions attached to the aorta were identified and characterized. Measurements were performed with a computer image analysis technique utilizing the Optima Bioscan software. For each aortic wall segment, the percent area of fibrous, lipid and calcium content of aortic plaques was calculated as a percent of the total area of intima and media.

**Statistical methods.** Results are shown as mean value ± SD. Analysis of variance (ANOVA) was used to compare echocardiographic video intensity of aortic wall lesions, thrombus and mobile debris and to compare pathologic composition of atheromatous grades by TEE. If the F value was significant, a Newman-Keuls multiple comparison test was performed. A forward stepwise regression analysis was performed to relate aortic wall composition to the ultrasound video intensity of the atheromatous grades. Sensitivity and specificity for thrombus were calculated using standard definitions. Statistical significance was set at p ≤ 0.05.

**Results**

Thirty-one patients were studied (mean age 64 years). Indications for surgical repair of the aorta were aortic aneurysm in 27 patients and aortic dissection in 4. The aortic diameter ranged between 2.5 and 8.3 cm (mean 5.2 ± 1.2). The aortic segments were identified along the descending thoracic aorta in 27 patients, the ascending aorta in 2 and the aortic arch in another 2. A total of 62 aortic segments were available for TEE–pathologic correlation: three segments from each of
Figure 1. Example of a normal aorta (Ao) (grade I) by TEE (left) and microscopy (right). This segment of the aorta is just adjacent to an aortic dissection in the distal aortic arch. The corresponding pathologic study shows an aortic wall with a media (M) of normal thickness (line) and a thin layer of intima (I [arrow]).

Figure 2. TEE (left) and pathologic features (right) of a grade II atheroma. On TEE, the area of atheroma showing minimal intimal thickening is depicted by arrow. The corresponding pathologic study shows, from top to bottom, a preserved fibrous cap (FC) followed by increased fibrosis (F) and minimal lipid core deposit (L); the dark band is the media (M). Ao = aorta.

Figure 3. TEE (left) and pathologic features (right) of a grade III atheroma (arrow [left]) (<5 mm thick). Pathologic study shows an intact fibrous cap (FC) and a rich core of lipid and cholesterol crystals (L) in the intima; the thinned media (M) is at the bottom.

Figure 4. TEE (top), gross pathologic (bottom left) and histopathologic features (bottom right) of a grade IV atheroma. The complexity of the atheroma is shown in TEE (arrows) and gross pathologic studies, with ulcerations and increased thickness >5 mm. At microscopy, there is extensive ulceration and numerous lipid (L) deposits in the intima and marked thinning of the media (arrow); the adventitia (A) is depicted at the bottom.
9 patients, two segments per patient in 13 and one segment in each of 9.

**TEE versus pathologic grades.** Examples of TEE and corresponding pathologic findings for aortic wall grades I to IV are shown in Figures 1 to 4. The distribution of TEE aortic wall grades was as follows: grade I, 8 segments; grade II, 7 segments; grade III, 26 segments; and grade IV, 21 segments. Normal segments were usually obtained from areas adjacent to aortic dissection, in an otherwise normal aorta. There was 73% (45 of 62 segments) exact agreement between TEE and pathologic grades (Table 1). The main source of disagreement was due to 11 segments with TEE grade III versus pathologic grade IV. This discrepancy was due to the inability of TEE to visualize superficial ulceration that destroyed the fibrous cap. However, agreement in differentiating normal and minimal intimal thickening (grades I and II) from more complex atheromas (grades III and IV) was observed in 93% (58 of 62) of segments (Table 1).

**TEE grades versus aortic plaque composition.** The plaque composition expressed as percent areas of lipid, fibrous and calcium content of the intima–media complex in the four TEE grades is shown in Figure 5. In normally visualized aorta (grade I), there was minimal lipid content and no calcification. Relative fibrous content increased from 18% in grade I to 41% in grade II and diminished with higher grades. A small percent of calcium was detected only in grade III and IV lesions. Percent lipid content increased progressively with increasing complexity of the atheromas by TEE and reached 49% in grade IV lesions (Fig. 5).

**Video intensity of aortic wall lesions versus TEE grades and plaque composition.** The ultrasound video intensity of the aortic wall, expressed as percent of maximal intensity, is shown in Figure 6. In normal segments, ultrasound intensity averaged 21 ± 3% and significantly increased with worsening aortic plaque grade, reaching 76 ± 8% in grade IV lesions (ANOVA, p < 0.0001). Interobserver variability of this measurement was determined in a random sample of 14 segments to be 8 ± 6%. Forward stepwise regression analysis showed that ultrasound intensity of the aortic wall related significantly to its composition at pathologic evaluation (r = 0.8, p < 0.0001; ultrasound video intensity = 25 + 0.65 [% lipid content] + 0.4 [% fibrous content] + 1.4 [% calcium content]). The strongest statistical determinant of ultrasound intensity was lipid content, followed by fibrous and calcium content: The respective standard errors and p values for the constant and slopes in the equation were 4.5, p < 0.0001; 0.07, p < 0.0001; 0.09, p < 0.0001 and 0.53, p < 0.009. All three variables were independent predictors of ultrasound intensity, with the correlation increasing from 0.67 for lipid content alone to 0.77 with the addition of fibrous content and 0.80 for all the three variables.

**Aortic thrombi and mobile aortic debris.** A total of 32 aortic lesions meeting the criteria for thrombus were identified by TEE. Compared with pathologic evaluation, TEE had a sensitivity of 91% (29 of 32 segments) and a specificity of 90% (27 of 30 segments) for detection of aortic thrombi. An

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**Table 1.** Comparison of Transesophageal Echocardiographic and Pathologic Grading of Aortic Atheroma*

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*73% exact agreement. TEE = transesophageal echocardiographic.
example of an aortic thrombus by TEE and corresponding pathologic findings are shown in Figure 7. Mobile aortic debris, associated with complex aortic plaques (grade III or IV), were observed in six segments. An example of mobile aortic debris and corresponding pathologic findings are shown in Figure 8. All mobile aortic debris in the six segments with such findings were found to be thrombi at pathologic evaluation. The ultrasound video intensity of mobile aortic debris (37 ± 6%) was similar to that of aortic thrombi (35 ± 7%). The ultrasound video intensity of aortic thrombi and mobile debris was lower than that of grade III and IV atheroma by TEE (73 ± 7%, p < 0.001) (Fig. 9).

Discussion

Atherosclerosis of thoracic aorta. In the Framingham cohort (3), the prevalence of calcified plaques on chest radiography increased steadily with advancing age, reaching >80% at age 75 to 80 years. The prevalence of atherosclerosis of the aorta with ultrasound has been reported up to 55% in intraoperative studies (15). Severe atherosclerosis on routine TEE has ranged from 7% to 17% (10,16) and is associated with a significant risk of cardiovascular mortality and vascular events (4,6–10). However, there is a paucity of data on the pathologic correlates of aortic lesions imaged with TEE. Attenuation of ultrasound (12) or ultrasound backscatter (13) by human aortas in autopsy specimens has been correlated with pathologic features of atherosclerotic plaques. To our knowledge, the present study is the first to evaluate the pathologic correlates of aortic atheromas imaged in vivo with TEE findings. Overall, TEE grading of the severity of atherosclerosis had a 73% exact agreement with pathologic grading. The main source of disagreement was superficial ulcerations that destroyed the fibrous cap and could not be visualized by TEE. Although other investigators (1) included ulcerations with grade III atheromas, we grouped these lesions with the most complex atheromas because of the potential for an ulcerated plaque to lead to thrombus formation. Importantly, despite its limitations in detecting superficial ulceration, TEE grading had good overall correlation with pathologic grading, particularly in distinguishing normal walls and those with mild intimal thickening from more severe forms of atherosclerosis, where concordance reached 93%.

TEE grading of atherosclerosis, ultrasound intensity and aortic plaque composition. With increasing grades of aortic wall atherosclerosis by TEE, significant changes in aortic plaque composition and ultrasound intensity were observed. Lipid content increased from 0.4% in grade I lesions to 49% in grade IV lesions by TEE. In contrast, percent fibrosis content was 18% in grade I, 41% in grade II and decreased relatively in the higher grades. The decrease in relative fibrous content was the result of increasing lipid content in the more complex atheromas. These findings are in concert with previous pathologic findings (12) showing similar changes in composition with increasing complexity of atheroma.

The ultrasound intensity increased with increasing complexity of aortic wall atheroma and related significantly to aortic wall composition at pathologic evaluation. The r² coefficient of 0.64 of this relation indicated that 64% of the observed variance is accounted for by the percent of lipid, fibrous and calcium content in the intima-media complex. The echogenicity of the lipid content of atherosclerotic plaques is not surprising. Although there are reports attesting to the low level of echoes detected from lipomas or subcutaneous adipose tissue, most fatty tumors and fatty infiltration of liver have shown increased echogenicity (17). Importantly, Glancy et al. (18) have shown that balloons filled with suspensions of cholesterol crystals were more echogenic than those filled with serum albumin. From these observations, it is clear that cholesterol crystals in the clefts of grade III and IV atheromas are highly echogenic and contribute significantly to the overall ultrasound intensity of the plaque. To our knowledge, quanti-
tative ultrasound video intensity of aortic plaques imaged in vivo with TEE has not been previously evaluated. Picano et al. (12) studied the attenuation characteristics of aortic wall specimens at autopsy. They found that the integrated attenuation index was lowest in normal walls and increased progressively in fibrous, fibrofatty and calcific plaques. The ultrasound video intensity quantitated in the present study is different from the attenuation index, but it is conceivable that fibrofatty and calcific plaques, which have the highest attenuation, also have the brightest video intensity.

**Thrombi and mobile aortic debris.** TEE identified thrombus formation associated with aortic aneurysm or dissection with a very high sensitivity (91%) and specificity (90%). The ultrasound intensity of thrombus was lower than grade III and IV atheromas by TEE and was similar to grade II lesions. Of interest are the pathologic findings in what has been termed mobile “aortic debris.” These lesions were first described by Karalis et al. (10) and have been associated with an increased incidence of embolization (5,10,11,19). In a preliminary report (20) involving seven patients with mobile lesions treated with Coumadin, serial TEE examinations showed that the lesions decreased in size, indirectly supporting the probability of their being thrombi. To our knowledge, the present series is the first documentation of the pathologic features of mobile aortic debris imaged in vivo with TEE that proved to be thrombus formation. Because the number of observations is small, it is important to acknowledge that although the majority of mobile debris are thrombi, some could also be ulcerated complex plaques. However, we believe that mobile ulcerated aortic plaques are highly thrombogenic and often have superimposed thrombus. In fact, all mobile aortic thrombi detected in our series were associated with grade III to IV plaques. To this end, the quantitation of ultrasound video intensity may be helpful if this distinction is needed for therapeutic decisions because the ultrasound intensity of mobile thrombi was similar to layered thrombi and lower than that of complex plaques.

**Study limitations.** In any correlative study of this nature, errors may occur in the exact matching of TEE and pathologic aortic wall segments. To minimize this error, extreme care was used in marking the exact location of the future pathologic study site during in vivo imaging with TEE. The present study included patients with aortic aneurysm or dissection, and findings in these patients may not be similar to those in the average ambulatory patient. However, these patients underwent aortic surgery, thus providing specimens for pathologic evaluation. Despite these limitations, we were able to evaluate different grades of aortic atherosclerosis. The number of mobile aortic debris examined was small, which stems from the fact that these lesions are infrequent and, importantly, do not usually constitute an indication for aortic repair.
Conclusions. TEE compares favorably with pathologic evaluation in its ability to detect significant atherosclerosis of the aorta and to assess plaque complexity. The increasing complexity of aortic plaques found by TEE is associated with increased fibrolipid content and calcification. The ultrasound intensity of aortic plaques relates significantly to plaque complexity and composition. Thrombus formation complicating aortic disease is accurately detected with TEE and has an ultrasound intensity lower than that of complex aortic plaques. Mobile aortic debris in this series were found to be thrombus at pathologic evaluation and to have an ultrasound intensity similar to that of typical thrombus. These findings, from a correlative study of the results of pathologic evaluation with those of in vivo TEE imaging, further confirm the role of TEE as a diagnostic tool in determining the severity and complexity of diseases of the aorta and may have important therapeutic implications.

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References