more sensitive method than necropsy examination for documenting the presence of disproportionate septal thickening. The implication of our findings is that in certain patients with genetically transmitted ASH the diagnosis will not be established at necropsy by simple measurement of the relative thicknesses of ventricular septum and left ventricular free wall. In such patients, the correct diagnosis will rely on ancillary observations, including the typical clinical, hemodynamic and echocardiographic features of ASH during life and the presence of a documented family history of ASH. Other necropsy findings suggestive of ASH would include an endocardial contact lesion on the ventricular septum associated with thickening of the anterior mitral leaflet and, more definitively, the presence of numerous hypertrophied, disorganized cardiac muscle cells in the ventricular septum.

References


Two-dimensional Echocardiographic Assessment of Vegetative Endocarditis

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SUMMARY Real-time, two-dimensional echocardiography was used to document the presence and assess the size and location of vegetative lesions of the cardiac valves and chambers in seven patients with bacterial endocarditis. Anatomic correlation (surgical or autopsy) was accurate in all patients. Two-dimensional echocardiography was shown to be of particular value in determining morphologic characteristics of the lesions since this technique provides spatial information concerning moving cardiac structures. The results of two-dimensional echocardiography were most helpful in determining suspected. Clinicians have emphasized the difficulty in diagnosing vegetative endocarditis, since as many as ten percent of cases report negative cultures. For the last few years, standard time-motion echocardiography has proven to be of value for the noninvasive detection of the presence of vegetative lesions. Dillon, Martinez, Wray, and others have demonstrated the ability of M-mode echocardiography to find vegetative lesions on valvular structures. Real-time, two-dimensional, or cross-sectional, echocardiography, because of its unique ability to provide spatial information and anatomical resemblance of cardiac structures, might provide further helpful information for the noninvasive diagnosis and management of patients with vegetative en-

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docarditis. The purpose of this study was to examine the ability of this new echocardiographic technique to detect the presence, locate the position, and estimate the size of vegetations in patients with endocarditis.

Methods

Patients

Seven consecutive patients examined at the Duke University Medical Center in whom morphologic (surgical or autopsy) documentation was available, were included in this study. All patients had a clinical suspicion of endocarditis as manifested by one or all of the following: fever, embolic phenomena, the presence of a new murmur, or the presence of congestive heart failure. There was a pre-existing history of congenital or valvular heart disease or illicit drug use in all seven. All patients underwent clinical and laboratory investigation for endocarditis including multiple serial blood cultures. Although vegetative endocarditis was a presumed problem in all patients, an absolute diagnosis of endocarditis was made in only three prior to either time-motion or two-dimensional echocardiographic examination. The pertinent clinical data are summarized in table 1.

Echocardiographic Examination

Standard time-motion echocardiography was performed by previously described techniques in all patients using a commercially available M-mode ultrasonoscope. The patients were then examined by a previously described real-time, phased-array, two-dimensional imaging system. This prototype system uses a hand-held, 24-element, 2.25 MHz transducer that measures 14 × 24 mm at the site of skin contact and relies upon phased-array principles that electronically steer and focus the sound beam through the structures under investigation. Real-time, cross-sectional images of cardiac structures are presented in the circular sector format, 50, 60, or 90 degrees in azimuth. Images are permanently recorded on videotape for later playback and analysis. The stop-frame images presented in this article are 35 mm photographs of single-frame images from the videotape. As such, there is a loss of visual integration of motion normally seen with real-time recordings. Moreover, there is a severe degradation in image quality caused by the videotape recording process. An individual field from the television tape represents only 1/60th of a second. When operating in the 160-line format, therefore, each single-frame visual field represents only one-half (or 80 lines) the information provided on the actual scan on a real-time playback.

With the patient in the supine or left lateral position, the transducer was placed along the left sternal border and the heart was examined. The planes of view are shown schematically in figure 1. Slight medial angulation of the transducer in Position I usually reveals an anterior aortic cusp (right cusp) and a posterior aortic cusp (noncoronary cusp). Slight lateral angulation of the transducer in the same position retains the right cusp in the anterior position but places the left cusp in the posterior position. Position IV (short axis through the mitral valve leaflets) is not pictured because scans through this plane are not pictured in this manuscript. The method of examination and the numerical identification of the various views corresponds to data previously published from this laboratory. In addition, the ostia of the right and left coronary arteries were examined using the approach described by Weyman.

Results

Time-Motion Echocardiography

The standard time-motion echocardiograms revealed thickened, abnormal, rapidly vibrating echoes on the aortic valve of four patients (C.C., W.B., H.W., and C.P.), the mitral valve of one patient (E.S.), and the tricuspid valve of one patient (J.M.).

In one patient (M.N.) time-motion echocardiography failed to reveal the tricuspid valve vegetation due to inaccessibility of the tricuspid valve. The time-motion echocardiograms of patient C.P. are shown in figure 2. Premature mitral valve closure (fig. 2, panel a) and high-frequency oscillations on the anterior mitral leaflet were seen in this patient and in three others with aortic valve vegetations. The left ventricle was dilated in five patients (C.C., W.B., H.W., and E.S.), the right ventricle in one patient (M.N.), and the left atrium in one patient (E.S.). A pericardial effusion was present in one patient (J.M.).

Two-dimensional Echocardiography

Two-dimensional echocardiography demonstrated the presence of large mobile masses in the four patients with aortic valve, one patient with mitral valve, and one patient

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Underlying cardiac disease</th>
<th>Organism</th>
<th>Valvular involvement</th>
<th>Cardiac cath</th>
<th>Therapy</th>
<th>Documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.C.</td>
<td>60</td>
<td>M</td>
<td>None</td>
<td>Staphylococcus coagulase</td>
<td>Aortic</td>
<td>No</td>
<td>Medical, valve replacement</td>
<td>Surgery</td>
</tr>
<tr>
<td>W.B.</td>
<td>38</td>
<td>M</td>
<td>None (drug addict)</td>
<td>Negative blood cultures</td>
<td>Aortic</td>
<td>No</td>
<td>Medical, valve replacement</td>
<td>Surgery</td>
</tr>
<tr>
<td>H.W.</td>
<td>54</td>
<td>M</td>
<td>None</td>
<td>Microaerophilic streptococcus</td>
<td>Aortic</td>
<td>No</td>
<td>Medical, valve replacement</td>
<td>Surgery</td>
</tr>
<tr>
<td>C.P.</td>
<td>17</td>
<td>F</td>
<td>Murmur of aortic stenosis</td>
<td>Staphylococcus coagulase</td>
<td>Mitral</td>
<td>No</td>
<td>Medical, died at surgery</td>
<td>Surgical and autopsy</td>
</tr>
<tr>
<td>E.S.</td>
<td>62</td>
<td>F</td>
<td>Systolic murmur</td>
<td>Microaerophilic streptococcus</td>
<td></td>
<td></td>
<td>Medical, died at surgery</td>
<td>Medical, died at surgery</td>
</tr>
<tr>
<td>J.M.</td>
<td>17</td>
<td>M</td>
<td>Ventricular septal defect</td>
<td>Streptococcus viridans</td>
<td>Tricuspid</td>
<td>Yes</td>
<td>Medical, valve replacement</td>
<td>Surgery</td>
</tr>
<tr>
<td>M.N.</td>
<td>26</td>
<td>M</td>
<td>(drug addict)</td>
<td>Pseudomonas aeruginosa</td>
<td>Tricuspid</td>
<td>No</td>
<td>Medical, valve replacement</td>
<td>Surgery</td>
</tr>
</tbody>
</table>
with tricuspid valve involvement as detected by time-motion echocardiography. In addition, the tricuspid valve was visualized in patient M.N. and a large vegetation was seen.

Similarly, in patient W.B. a vegetation was found in the left ventricular cavity that was not suspected previously.

The masses could be localized to a specific cusp or leaflet, and the size of the lesions could be estimated using two-dimensional echocardiography. All valvular vegetative lesions appeared on two-dimensional echocardiography as rapidly oscillating masses that either were attached to, or replaced, normal valvular tissue. The morphology of the lesions ranged from large, relatively immobile masses, to smaller or pedunculated mobile lesions.

Two-dimensional Echocardiographic-Morphologic Correlations

In all cases, morphologic inspection of diseased valve tissues corroborated the two-dimensional echocardiographic findings. Figure 3 demonstrates the systolic (panel A), early diastolic (panel C), and late diastolic (panel E) stop-frame images of a long axis of the aortic root in patient C.C. A long, thin vegetation attached to the right coronary cusp is seen moving into the aortic root in systole and back into the left ventricular outflow tract in diastole. Also, the posterior noncoronary cusp is abnormally thickened. In other views a small vegetative mass was seen on the third cusp. Figure 4 demonstrates the pathological correlation of the two-dimensional echocardiographic findings of this patient obtained at surgery. All three cusps were involved. A long, thin fragile vegetation was attached to the right cusp.

Figure 5 shows the sequential systolic (panel A) and diastolic (panels C and E) stop-frame images of the aortic root in patient H.W. Large vegetations are seen replacing the right and left coronary cusps in panels A and C. Slight medial angling of the transducer revealed the large vegetation on the noncoronary cusp. Figure 6 shows the pathological specimen obtained at surgery in this patient. As seen on the two-dimensional echocardiographic examination, all three cusps were involved with the largest lesion found on the noncoronary cusp.

Figures 7, 8 and 9 demonstrate vegetations in patients W.B., C.P., and M.N., respectively.
The findings of two-dimensional echocardiography were confirmed by surgery or autopsy in all seven patients. In addition, in one patient (E.S.) small vegetations (1 mm or less) were found in the left atrium and on the aortic valve that were not seen by two-dimensional echocardiography, and in another patient (W.B.) a small vegetation (1 × 2 mm) was seen on the anterior mitral leaflet that was not noted by two-dimensional echocardiography.

**Clinical Course**

In all patients, the results of two-dimensional echocardiography in combination with the clinical status, guided patient management. For fear of potential embolic phenomena from the large lesions seen with two-dimensional echocardiography, in association with severe aortic regurgitation, patients C.C., H.W., and W.B. underwent successful aortic valve replacements without prior cardiac catheterization. In patient C.P., the detection of vegetative lesions on the aortic valve occluding the orifice of a left main coronary artery in diastole explained the cause of a recent anterior wall myocardial infarction detected by electrocardiography. Right heart catheterization and supravalvular aortography were performed immediately following two-dimensional echocardiography in the patient because physical examination also suggested the presence of a ventricular septal defect. No left-to-right shunt was found at catheterization and the patient died during aortic valve replacement.

The results of two-dimensional echocardiography in patient E.S. showed a large, dilated, poorly contracting left ventricle in addition to the vegetative lesions on the mitral valve. The patient's course was complicated by massive mitral regurgitation and severe congestive heart failure. Because of these findings, no surgery was attempted, and the patient rapidly deteriorated and died.

Patient M.N. presented with recurrent fever and blood cultures positive for pseudomonas aeruginosa. There were, however, no physical findings to suggest the presence of spe-
specific cardiac valvular involvement. Two-dimensional echocardiography revealed the presence of a large vegetative lesion on the tricuspid valve. This finding caused an adjustment in the antibiotic regimen appropriate for the treatment of bacterial endocarditis. Despite two weeks of intensive antibiotic therapy, the patient's blood cultures remained positive. At the end of the second week, the patient suffered severe chest pain and hemoptysis suggestive of a pulmonary embolus. Repeat two-dimensional echocardiography, at that time, failed to detect the large vegetative mass noted on the initial two-dimensional echocardiographic examination. Because of these findings, the patient underwent immediate,
successful, tricuspid valve replacement.

Serial two-dimensional echocardiographic examination in patient J.M. revealed a progression of tricuspid valve destruction from severe prolapse to frank flail of the anterior tricuspid leaflet. After a several week course of antibiotics, he underwent a cardiac catheterization and subsequent successful tricuspid valve replacement.

Discussion
Vegetative endocarditis often presents as a difficult diagnostic problem. With its increasing incidence and serious prognosis, clinicians have emphasized the need for a noninvasive technique that could document the presence and localize the specific valvular involvement in patients with this entity.

Figure 8. Systolic (panel A), early diastolic (panel C), and late diastolic (panel E) stop-frame images through the short axis of the aortic root in patient C.P. Vegetations are seen on all three cusps. Note a mobile mass in the area of the left coronary cusp seen moving adjacent to (panels C and D) and then into the orifice of the left main coronary artery in late diastole (panels E and F). LCA = left coronary artery; IAS = interatrial septum.

Figure 9. Stop-frame systolic (panel A), early diastolic (panel C), and late diastolic (panel E) images through the tricuspid valve in patient M.N. Panels B, D, and F are the respective schematic diagrams. A large vegetative mass attached to the posterior tricuspid valve leaflet can be seen moving from the right atrium (panel A) through the tricuspid orifice (panel C) into the right ventricular cavity (panel E). ATL = anterior tricuspid leaflet; PTL = posterior tricuspid leaflet; TV = tricuspid vegetation; RA = right atrium.
Standard, time-motion echocardiography has already been shown to be of value in the diagnosis of vegetative endocarditis. Feigenbaum,11 Lee,12 Gramiak,13 and others14,15 have demonstrated the unique advantage of time-motion echocardiography in that it is capable of recording dynamic motion of structures in a continuing time fashion. The rapid, high-frequency oscillations of vegetative lesions and/or destruction of leaflet integrity can often be documented using this technique. M-mode echocardiography also allows for exact timing of cardiac events, such as premature diastolic closure of the mitral leaflet (fig. 2, panel a). In six patients in this study, vegetations were seen on various cardiac valves by time-motion echocardiography, but estimation of lesion size, morphology, and localization to specific leaflet involvement was not possible. Figure 2b reveals abnormal echoes within the aortic root in patient C.C., but it is most difficult to say which cusps are actually involved. Also, in one patient, J.M., adequate visualization of the tricuspid valve by M-mode echocardiography could not be obtained due to an abnormal chest wall configuration.

Real-time, two-dimensional echocardiography has the unique characteristic of providing spatial information concerning cardiac structures.7 This ability should allow for estimation of lesion size, morphology, and specific leaflet involvement. The wide sector arc (90 degrees) also allows for visualization of subternal structures such as the tricuspid valve and the right atrium.9 There is no reason to believe, however, that two-dimensional echocardiography is able to detect the presence of vegetative lesions in all patients with clinically manifest bacterial endocarditis.

It is apparent from this study that the estimation of vegetation size correlated well with that seen in the gross anatomic specimens. For example, the largest of the aortic valve vegetations in H.W. was seen by two-dimensional echocardiography on the noncoronary cusp, and this was verified at surgery. Accurate measurement of vegetation size, however, was difficult even at gross anatomic examination since most lesions were so varied in anatomic configurations. Recognizing this limitation, measurement of lesion sizes from echo closely approximated (within 3 mm in any dimension) similar measurements from the gross specimen. Nevertheless, two-dimensional echocardiography was able to assess the morphology of the specific vegetations which varied in a spectrum from the pedunculated lesion seen on the right coronary cusp of patient C.C. (fig. 3) to the massive sessile lesions found in patient H.W. (fig. 5). All vegetations noted on specific valve structures were validated at surgery or autopsy. It is also of interest that the technique visualized a left ventricular endocardial lesion in patient W.B. (fig. 7).

The results of this study also point out that real-time, two-dimensional echocardiographic information can be most useful in understanding the symptoms associated with bacterial endocarditis. The intermittent severe angina and anterior myocardial infarction noted in patient C.P. could be explained by the observation that the vegetative lesions occluded the orifice of a left main coronary artery in diastole (fig. 8). The sudden pleuritic chest pain in patient M.N. was explained by embolization of the large vegetative lesion from the posterior leaflet of the tricuspid valve (fig. 9) to the lungs. In another patient (J.M.), serial two-dimensional echocardiographic scans showed progressive destruction of the anterior tricuspid leaflet which explained his clinical deterioration. Details of this particular case have been previously reported.19

The information provided by this new technique can be most helpful in patient management. Four of the six patients who went to surgery did not require cardiac catheterization since echocardiography provided sufficient information to make catheterization unwarranted. In patient E.S., the detection by two-dimensional echocardiography of a large, dilated, uniformly poorly contractile left ventricle in combination with rapid clinical deterioration precluded surgical intervention. In three patients in whom the clinical evidence of endocarditis was tenuous, the detection of valvular vegetations by two-dimensional echocardiography aided in adjustment of the appropriate dose of antibiotic therapy.

Until now, there has been no acceptable method for observing the size and morphology of vegetative lesions. The ability of two-dimensional echocardiography to accomplish this raises certain important questions concerning the time for surgical intervention. Although the visualization of large mobile masses raises the fear of embolization, there are no data available that would indicate that one type of lesion (sessile vs pedunculated) is prone to embolize. Our laboratory has examined six other patients with vegetative endocarditis suspected by time-motion and two-dimensional echocardiography that were not included in this study because the diagnosis was not verified by surgery or autopsy. One patient has since died and an autopsy was not available. After successful medical therapy, another patient had no evidence of vegetative lesions on the involved cardiac valves. The remaining four patients were successfully treated with medical therapy and repeat echocardiographic information is not available. The fact that two-dimensional echocardiography has the ability to estimate lesion size is of interest. By continued experience with this technique, it may be possible to measure more accurately the dimensions and follow the potential changes that might occur as a result of antibiotic therapy.

Although two-dimensional echocardiography proved helpful in these seven patients, the limitations of this technique should be emphasized. This study did not attempt to test the sensitivity of this imaging method for the diagnosis of vegetative endocarditis. Two-dimensional echocardiography, like all pulsed ultrasonic techniques, is somewhat limited in its applicability to all patients due to poor sound transmission characteristics induced by abnormal chest wall configuration, the presence of interposed lung and other, as yet undefined, reasons. Despite the fact that all seven patients in this study had adequate ultrasound scans, clinical experience with this technique would indicate that totally unsatisfactory two-dimensional echocardiograms are obtained in approximately ten percent of examinations. Furthermore, a potential for false positive diagnosis exists in improper gain settings that result in artifactually large echoes appearing on normal valve structures. Similarly, in our experience, echoes from fibrotic, calcified, or redundant valves (as occasionally seen in mitral prolapse) could also lead to a false positive interpretation. The lack of mobility and gross oscillations, however, serve to differentiate these abnormalities from vegetations. This laboratory has had no
experience with nonbacterial verrucous endocarditis. Lastly, small vegetations may be missed with two-dimensional echocardiography. There is no information at the present time to indicate the size of lesion necessary for echocardiographic visualization. Several small vegetations (2-3 mm in size) found at surgery or autopsy were not detected in this study using echocardiography.

In this study, two-dimensional echocardiography and time-motion echocardiography, in combination with the clinical condition of the patient, all proved useful in the diagnosis and management of bacterial endocarditis. The additional information provided by real-time, two-dimensional echocardiography demonstrate the unique ability of this ultrasonic imaging method to provide important new diagnostic information in this disease entity.

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Six Year Review of the Results of Freehand Aortic Valve Replacement Using an Antibiotic Sterilized Homograft Valve


SUMMARY The long-term behavior of an antibiotic-treated homograft aortic valve inserted in a freehand fashion was assessed in 121 patients operated upon for aortic valve disease and followed from four to six and one-half years. There were seven hospital deaths (5.7%) and 30 late deaths, only one of which was related to the homograft valve. The six year survival was 69% (77% for single valve and 52% for multiple valve surgery). At six years 9% had important homograft aortic valve incompetence (HAVI) and most of these re-
quired reoperation. Important HAVI occurred in only 5% of patients
with an aortic root diameter < 24 mm and in 38% of those with a markedly dilated or distorted proximal aorta (P < 0.01). The free-
hand aortic homograft was considered superior to prosthetic devices
because of the absence of chronic anticoagulation, thrombo-
embolism, sudden death from valve failure and significant obstruction in a small aortic root. With slightly restricted patient selection the valve failure rate is expected to fall to less than 1% per year.

OUR EXPERIENCE WITH HOMOGRAFT VALVE SURGERY began in August 19621 with the subcoronary placement in a freehand fashion of an aortic valve collected using sterile techniques from a 23-year-old donor. The valve had been stored for 16 days in Hanks' balanced salt solution which contained no antibiotics and the recipient was a 14-year-old girl in severe heart failure from aortic in-
competence. Thirteen years later she is well and active

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without anticoagulant or other drugs and has had three normal pregnancies. Her electrocardiogram and chest X-ray are normal, her blood pressure is 110/70 mm Hg and an unimpressive aortic diastolic murmur has not changed since hospital discharge. A similarly pleasing long-term result has been achieved in 10 of the 16 patients in whom similar, un-
treated, aortic homografts were inserted in 1962 or 1963. Unfortunately, because such valves were difficult to collect, unsterile collection and chemical sterilization using beta-
propiolactone2 and later ethylen oxide were substituted. With this method the early results were good but longer follow-up revealed an unacceptable incidence of cusp rup-
ture. Accordingly, in August 1968, a technique of antibiotic sterilization,3 which produced a sterile valve in 92% of cases, was substituted.
Two-dimensional echocardiographic assessment of vegetative endocarditis.
B W Gilbert, R S Haney, F Crawford, J McClellan, H A Gallis, M L Johnson and J A Kisslo

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