THE ROLE OF ECHOCARDIOGRAPHY IN THE DIAGNOSIS AND MANAGEMENT OF INFECTIVE ENDOCARDITIS AND ITS COMPLICATIONS

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INFECTIVE ENDOCARDITIS (IE) continues to be a major challenge to the diagnostic and management skills of the clinician. Significant advances in antibiotic therapy and cardiac surgical techniques necessitate accurate diagnosis and well-timed surgical intervention which have a favorable impact on both morbidity and mortality. Although the therapeutic options have improved due to the progress in the discovery of new potent and efficacious antibiotics as well as advanced surgical techniques, there is, however, a price to pay for these new developments. Greater availability and technical progress in cardiac surgery have conceived more prosthetic valve replacements and longer survival of patients with congenital heart defects, both of which are at higher susceptibility of acquiring infective endocarditis. The low threshold for using antibiotics due to their availability, for mere suspicion of unconfirmed infection, has clouded the clinical presentation and dwindled the chances of obtaining positive blood cultures.

The discovery of M-mode echocardiography and the later development and advances that took place with the introduction of two-dimensional echocardiography and Doppler, and the latest crowning of the technology by the state-of-the-art transesophageal echocardiography, have undoubtedly made a great impact and played a major role in the diagnosis and management of infective endocarditis and its complications.

Echocardiography provides a direct noninvasive visualization of valvular vegetations. The echo reflectant properties of vegetations, their mobility, their shaggy appearance and their location and spatial relation to the valve leaflets are important tell-tale signs for their identification.

M-mode Echocardiography

Dillon et al. were the first to report the value of M-mode echocardiography in the detection of vegetations in patients with the clinical diagnosis of infective echo (IE). The M-mode characteristics of vegetations are shaggy echo-dense masses attached to the valve leaflets or intimately related to them without limiting their motion, but sticking to the leaflets during their mobility throughout the cardiac cycle (Figure I). M-mode echocardiography has its limitations in the detection of valvular vegetations due to its ice-pick view of the heart. It lacks the ability to define vegetation size, mobility, area of attachment, involvement of other valves, and detection of complications such as valve ring abscesses, valve perforation or destruction and myocardial abscesses.

Two-Dimensional Echocardiography

Two-dimensional echocardiography (2DE), which was introduced with the discovery of the mechanical and phased array sector scanners in 1974, soon complemented the utilization of M-mode echocardiography in the diagnosis and management of IE and its complications. The powerful spatial resolution of 2DE has overcome all the limitations of M-mode echocardiography. 2DE allows full assessment of the size and extent of vegetations, their site of attachment, involvement of other valves and presence of complications such as valvular ring abscess, flail or perforated leaflets, aneurysm.
Figure 1. M-mode of the aortic valve depicting shaggy echodense vegetation attached to the aortic leaflets throughout the cardiac cycle without restriction to leaflet mobility. Note RV dilatation as the patient was in congestive heart failure and had severe tricuspid regurgitation. RV = right ventricle.

Table I. Complications of IE detectable by two-dimensional echocardiography.
Valve destruction.
Myocardial and ring abscesses.
Aneurysm and fistula formation.
Pericardial effusion (especially purulent pericarditis). Myocardial infarction due to:
(i). Coronary embolization.
(ii) Main coronary ostial obstruction by an aortic vegetation.

Table 2. Causes of reduced sensitivity of transthoracic 2DE.
Non-vegetative endocarditis or small vegetations of 1 mm to 2 mm which are below the resolution of the technique.
Pre-existing bad valvular pathomorphology: calcific valvular deposits, myxomatous valve tissue and ruptured chordae with or without flail leaflets.

Technical Factors: machine-related (resolution of the machine) or patient related (poor acoustic windows).

formation and pericardial effusion (Table I) (Figures 2 and 3). These complications are common in IE and moreover, they have strong adverse impact on the prognosis. The recognition of these complications is important, not only in aiding the diagnosis of IE in patients without visible vegetations, but also in making the appropriate decisions regarding management, especially when considering the optimum timing of surgical intervention. Moreover, 2DE is an excellent tool in evaluating left ventricular systolic function both regionally and globally, which is another important factor that is utilized in the timing of surgery in patients with IE.

The reported sensitivities for visualizing vegetations with transthoracic 2DE ranges from 30% to 80%.4,11 Multiple factors play some role in the limitations of the sensitivity of transthoracic 2DE in detecting vegetations (Table 2). Many of the vegetations seen on gross inspection are 1 mm to 2 mm in size,12 thus being below the resolving capabilities of the presently available 2DE machines. Also, many cases of endocarditis occur on pre-existing fibrotic echo-dense, calcified or myxomatous valves, which make identification of vegetations difficult or indeed impossible. Additionally, 10% to 15% of the adult population...
cannot be adequately or optimally examined by transthoracic 2DE due to poor acoustic windows. Initial reports and observations suggested that patients with echocardiographically demonstrable vegetations were at a very high risk for complications, and most required early surgical intervention as a treatment of congestive heart failure and for the improvement of survival. However, subsequent reports have demonstrated that while patients with echo-detected vegetations are still at a greater risk for complications such as congestive heart failure, emboli and the need for surgical intervention, as high as 70% of patients in this group do well with medical treatment alone.

13.14 Mugge et al. reported that patients with vegetations larger than 1 cm in diameter were at higher risk for clinical embolic events than patients with smaller vegetations. This increased risk applied only to patients with native mitral valve infection.

The pooled data support the increased risk of patients with echocardiographically detected vegetations and identify a group of patients without vegetations who have considerably lower risk of developing complications. It is prudent that closer observation, continued assessment and serial echocardiographic studies should be adopted in patients with echocardiographically demonstrable vegetations to identify changes that may require surgical intervention.

The identification of vegetations by 2DE, therefore, should not in itself be considered as an indication for surgery. An exception to this rule may be fungal endocarditis, in which large vegetations are frequently seen on echocardiography and urgent surgery may be warranted, as fungal endocarditis is rarely cured with medical therapy alone.

2DE can increase the likelihood of the correct diagnosis of IE when vegetations are detected in patients with culture-negative endocarditis, or in those with less than clear or atypical clinical picture.

Doppler Echocardiography

With advances in echocardiographic technology and the introduction of spectral and color Doppler in 1974 and 1985, respectively, Doppler echocardiography was soon utilized in IE for the detection of valvular insufficiency which frequently precedes and predisposes to IE, or occurs as a common complication of the disease. Doppler echocardiography provides considerable help in the assessment of the hemodynamic consequences of the valvular regurgitation and the need for surgical intervention. It also detects some of the complications of IE, such as fistula formation and leaflets perforation.

Transthoracic Echocardiography (TEE)

The identification of vegetations has greatly improved since the introduction of transthoracic echocardiography. The transthoracic window facilitates a closer approximation of the transducers to the heart, allowing the use of high-frequency, high-resolution transducers that provide superior image quality when compared to those obtainable with transthoracic echocardiography. Erbel et al. compared the transthoracic and transesophageal approaches for detection of vegetations in a prospective series and found sensitivity of 63% and 100%, specificity of 98% and 98%, positive predictive accuracy of 91% and 100%, respectively, in a subgroup of patients undergoing surgery. Mugge et al. reported that 82% of patients with clinical IE had vegetations on TEE, as compared with 69% on transthoracic echocardiography. Transthoracic echocardiography identified only 25% of the vegetations smaller than 5 mm in size, 69% of those 6 mm to 10 mm, and all of those larger than 11 mm that were detected by TEE. Several other studies have also documented the superiority of TEE.
over transthoracic echocardiography in diagnosing valvular vegetations. Furthermore, TEE is up to eight times more sensitive than transthoracic echocardiography for the detection of intracardiac abscesses associated with IE. TEE has been reported to have a sensitivity of 93%, specificity of 94%, and positive and negative predictive values of 86% and 93%, respectively, for the detection of abscesses associated with endocarditis. Homograft aortic root replacement may be necessary in cases of complicated aortic annular abscess formation.

Myocardial abscess formation is most common in patients with aortic valve and prosthetic valve IE, especially when the infective organism is Staphylococcus aureus. Intramyocardial abscess may rarely rupture into the pericardial space causing pyogenic pericarditis. In general, patients with intramyocardial abscess formation have 1.5-fold to 2-fold increase in overall mortality, compared to those without abscess formation.

In patients with a valve ring abscess, the cardiac rhythm should be monitored for evidence of conduction abnormalities. All centers caring for patients with IE should, therefore, have facilities for temporary pacemaker insertion. On rare occasions, however, heart block may develop in patients with IE in the absence of a valve ring abscess due to embolization to the atrioventricular nodal artery.

In summary, TEE enhances the detection of valvular vegetations, especially small vegetations on native valves or vegetations on metallic prostheses. TEE also improves the recognition of complications of IF such as abscesses, fistulae or aneurysm formation, valve destruction (perforation or chordal rupture), and valvular regurgitation, especially when the leak is associated with metallic prosthetic infection.

Indications of TEE in IE are, therefore, numerous and include poor transthoracic imaging quality, hemodynamic compromise, clinical suspicion of complications, especially abscess formation, prosthetic valve infection due to the increased risk of abscess formation and prosthetic malfunction (both of which constitute a diagnostic dilemma).
Table 3. Indications of trans esophageal examination in infective endocarditis.

- Poor transthoracic imaging quality. Hemodynamic compromise.
- Suspected complications (especially abscesses).
- Prosthetic valve endocarditis (especially metallic prostheses).
- Preoperative evaluation of mitral valve infection in aortic valve endocarditis and culture-negative or unexplained bacteremia when the transthoracic echocardiogram is non-informative or of poor technical quality (Table 3).

Prophylactic Valve Endocarditis (PVE)

Prosthetic valve endocarditis is estimated to occur in 1% to 4% of prosthetic valves over the lifetime of the valve, and has a mortality rate estimated at between 25% to 64%. The advances in surgical techniques and the availability of a wide variety of prosthetic valves have led to a rise in the prevalence of patients with prosthetic valve replacements. As a consequence, the incidence of PVE continues to increase as more valves are inserted. PVE can be divided into early PVE and late PVE. Early PVE usually occurs within the first six months postoperatively, and constitutes an aggressive infection with a high mortality and requires surgical intervention. Late PVE occurs later than six months after valve replacement, and tends to have a less aggressive clinical course.

Prosthetic valves provide a formidable challenge to transthoracic echocardiographic and Doppler examination. From the echocardiographic point of view it is important to differentiate between mechanical and bioprosthetic valves. Mechanical valves are made of a variety of metallic, sialistic, cloth and other nonbiologic materials that cause reverberating echoes and also obstruct the ultrasound beam. Despite these limitations, echocardiography is helpful in detecting large vegetations, ring abscesses and the hemodynamic effects of prosthetic dysfunction. The evaluation of the bioprosthesis, on the other hand, is more likely to be helpful. However, differentiation between bioprosthetic degeneration and IE is often difficult, and great consideration should be given to the clinical presentation. Large masses are also more likely to be vegetations, and associated valve ring abscess is a tell-tale sign for the correct diagnosis of IE. Ring abscess frequently leads to valve dehiscence, resulting in rocking motion of the prosthesis and peri prosthetic leak, both of which can be detected by echocardiography and Doppler (Figure 8). Recent studies have indicated that TEE is superior to transthoracic echocardiography in prosthetic valve endocarditis (Figure 9). Daniel et al. in a small number of 22 patients with prosthetic valves have reported that TEE can correctly predict the presence of vegetations in 77% of the cases versus only 27% when the transthoracic

Figure 8. Transverse 4-chamber TEE with color Doppler showing metallic mitral peri prosthetic (paravalvular) leak in a patient with prosthetic valve endocarditis.

Figure 9. Transverse 4-chamber TEE view eliciting a small vegetation on a mitral metallic prosthesis. This vegetation has been missed on transthoracic examination. Veg = Vegetation, Pros = prosthesis.
approach is utilized. This superiority of the transesophageal window is due to the fact that the transducer in the esophagus is close to the left heart and the ultrasound beam is not blocked by the prosthesis, especially when it is situated in the mitral position.

Echocardiography and Timing of Surgery in IE

The timing of cardiac surgery in IE is a clinical decision based on a multitude of factors. These comprise infection by virulent or antibiotic-resistant organisms and the development of a major cardiac or extracardiac complication of IE. The hemodynamic state of the patient is the most important consideration in deciding when to operate.32 The likelihood of death is directly proportional to the severity of heart failure at the time of cardiac surgery.32-34 Inadequately controlled or invasive infection is an indication in itself for early surgery. 17,35 Uncontrolled or persistent bacteremia after 7 to 14 days of maximal antimicrobial therapy is also an indication for operation. Despite the stress on the above clinical parameters or indicators that are important for the timing of operative intervention, certain echocardiographic features of IE are associated with higher rates of complications and, therefore, have more need for cardiac surgery (Table 4). These comprise large vegetations which are associated with higher rates of systemic embolization and congestive heart failure,6 abscesses, especially ring abscesses, purulent pericardial effusion, which is usually due to Staphylococcus aureus, or outward rupture of intramyocardial abscess, and severe acute valvular regurgitation resulting from valvular or subvalvular damage that is caused by the infective process.

Table 4. Echocardiographic features that are associated with a higher rate of complications and therefore more need for surgery.

Large vegetations (higher rate of systemic embolization and heart failure).
Abscesses, especially ring or periprosthetic abscesses.
Pyogenic pericardial effusion (usually associated with Staphylococcus aureus or ruptured intramyocardial abscess).
Severe acute valvular regurgitation.

Conclusions

Echocardiography provides considerable information in patients with suspected IE. The technique can provide adequate supportive information for establishing the diagnosis, prediction of prognosis by detecting the risk of congestive heart failure, systemic embolization and the expected clinical course, identification of the anatomic complications that influence the need for and approach of operative intervention, and more important, the accurate timing of such surgical therapy.

Although transthoracic imaging will allow a complete evaluation in many patients with IE, the transesophageal approach is superior for the detection of various complications of IE, especially intramyocardial and ring abscesses and the evaluation of prosthetic valve infection, especially those of metallic prostheses.

The echo cardiographic findings must always be interpreted in the context of the clinical findings and should not be considered in isolation. In culture-negative endocarditis, detection of a vegetation is a solid support for the diagnosis of IE, however, it must be emphasized that when there is a strong clinical suspicion of IE, echocardiographic absence of a vegetation should not exclude the diagnosis. The timing of surgical intervention in IE should always be based on the overall clinical evaluation of the patient, however, strong consideration should also be given to the echocardiographic features that are usually associated with high risk of complications and bad prognosis.

References