Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

Echocardiography is essential in the diagnostic evaluation of the patient with suspected endocarditis, and should be performed in all patients with a moderate or high suspicion of this condition. Recent updates in antibiotic therapy(1) and prophylaxis(1,2) for infectious endocarditis will not be discussed in this syllabus. The ACC/AHA produced guidelines for transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in patients with infectious endocarditis (IE)(3). Class I recommendations for TTE and TEE are situations in which there is evidence and/or general agreement that TTE or TEE should be performed in patients with native or prosthetic valve IE. Class IIa use suggests that the weight of evidence or opinion is in favor of the usefulness of TTE or TEE for evaluating IE. Class IIb indicates situations in which the weight of evidence or opinion is less well established for the usefulness of TTE or TEE. Class III indicates situations where there is evidence and/or general agreement that TTE is not useful in patients with native or prosthetic valve IE. The ACC/AHA recommendations for the indications for TTE and TEE in IE are summarized below(3,4):

**Class I** indications for TTE or TEE:

- TTE to detect valvular vegetations with or without positive blood cultures for the diagnosis of IE. Among patients with positive blood cultures, TEE is recommended if TTE is nondiagnostic.

- TTE to characterize the hemodynamic severity of the valve lesions in known IE. Among symptomatic patients, TEE is recommended if TTE is nondiagnostic.

- TEE as a first-line diagnostic test for prosthetic valve IE and to detect complications.
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

- TTE or TEE to assess complications of IE (such as abscesses, perforations, and shunts). TEE is recommended for preoperative evaluation of patients going to surgery unless the indication for surgery is apparent on TTE or imaging will delay urgent surgery.
- TTE for reassessment of high-risk patients, as defined by virulent organism, clinical deterioration, persistent or recurrent fever, a new murmur, or persistent bacteremia.
- Intraoperative TEE for patients undergoing valve surgery for IE.

**Class IIa** indications for TTE or TEE:

- TEE to diagnose possible IE in patients with persistent staphylococcal bacteremia who do not have a known source.
- Among patients with a prosthetic valve, TTE to diagnose IE in patients with persistent fever without bacteremia or a new murmur.

**Class IIb** indications for TTE or TEE:

- TEE to diagnose possible IE in patients with nosocomial staphylococcal bacteremia.
- Among patients with prosthetic valve IE, TTE for reevaluation during antibiotic therapy in the absence of signs of clinical deterioration.

**Class III** indications for TTE or TEE:

- TTE is not indicated to reevaluate uncomplicated IE (including no valve regurgitation at baseline) during antibiotic therapy in the absence of clinical deterioration, including new physical findings, or persistent fever.
Diagnosis of infective endocarditis (IE) is based on a combination of clinical factors such as fever, positive blood cultures, and new valvular regurgitation, as described in the modified Duke criteria (tables 1 and 2) (3-5). Definite IE is diagnosed by pathologic or clinical criteria.

Criteria confirming definite IE include:

- Pathologic criteria: when a microorganism is demonstrated by culture or histology from a vegetation or from a vegetation that has embolized, or from an intracardiac abscess, or intracardiac abscess.

- Clinical Criteria are divided into major and minor criteria (Table 1 and 2)(3-5). Definite IE by clinical criteria is defined as: 2 major, 1 major and 3 minor, or 5 minor criteria. Possible IE is defined as 1 major and 1 minor or 3 minor criterion.

The diagnosis of IE is rejected if a firm alternate diagnosis for the manifestations of endocarditis is identified or if there is resolution of the manifestations of IE with antibiotic therapy for four days or less, or if no pathologic evidence of IE is seen at surgery, autopsy, or after antibiotic therapy for four days or less.
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

Table 1: Major Criteria

1. **Positive Blood Cultures for IE:**
   - Typical organisms from 2 separate blood cultures
     - Streptococcus viridans
     - Streptococcus bovis
     - HACEK group
       - Haemophilus spp
       - Actinobacillus actinomycetemcomitans
       - Cardiobacterium hominis
       - Eikenella spp.
       - Kingella kingae
       - Staph aureus
     - Community-acquired enterococci
   - Persistently positive blood cultures

2. **Evidence of endocardial involvement**
   - Positive echocardiogram for IE
   - New valvular regurgitation

Table 2: Minor Criteria

1. Predisposition-predisposing heart conditions or iv drug use
2. Fever 38 c (100.4)
3. Positive blood cultures not meeting major criterion
   - excluding single positive coag-neg staph culture
4. Immunologic phenomena
   - Glomerulonephritis
   - Osler’s nodes
   - Roth spots
   - Rheumatoid factor
5. Vascular phenomena
   - Major arterial emboli
   - Septic pulmonary emboli infarcts
   - Mycotic aneurysm
   - Intracranial hemorrhage
   - Conjunctival hemorrhages
   - Janeway lesions
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

Echocardiography is utilized to identify, characterize and localize masses consistent with *valvular vegetation*, the pathologic trademark of IE.(4) Valvular vegetation is defined as a discrete mass of echogenic material adherent at some point to a leaflet surface which is distinct in character from the remainder of the leaflet based on the following characteristics(4):

- **Texture**: gray scale and reflectance of the myocardium
- **Location**: upstream side of the valve in the path of the jet or on prosthetic material
- **Characteristic motion**: chaotic and orbiting; independent of valve motion
- **Shape**: lobulated and amorphous
- **Accompanying abnormalities**
  - abscess and pseudoaneurysm,
  - fistulae,
  - prosthetic dehiscence,
  - paravalvular leak
  - significant preexisting or new regurgitation

Characteristically, vegetations prolapse into the upstream chamber ie. aortic vegetations into the left ventricular outflow tract during diastole and atrioventricular valve vegetations into the atrium during systole(4).

Characteristics of a mass inconsistent with a vegetation include (4):

- **Texture**: reflectance of calcium or pericardium (appears white)
- **Location**: outflow tract attachment, downstream surface of valve
- **Shape**: stringy or hair-like strands with narrow attachment
- **Lack of accompanying turbulent flow or regurgitation**
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

Masses have also been analyzed according to the following four properties (4,6):

- **Size**: established by the two largest orthogonal diameters
- **Mobility**: defined as grade 1, fixed; grade 2, fixed base free edge; grade 3, pedunculated; grade 4, prolapsing
- **Density**: defined as grade 1, calcified; grade 2, partially calcified; grade 3, denser than myocardium but not calcified; grade 4, equivalent to myocardium
- **Extent**: defined as grade 1, single; grade 2, multiple on a single leaflet; grade 3, multiple leaflets; grade 4, extending to extravalvular structures

Echocardiography has been used to determine the natural history of vegetations(4,7). Size increases suggests active disease, an ominous sign possibly indicating higher embolic risk(7). However, some vegetations persist after bacterial cure has been achieved and remain stable in size for many years (8). Unlike acute vegetations, chronic lesions are more echogenic(3,4,9).

Changes in vegetation size may depend on the causative organism, with S. aureus lesions more likely to increase in size on remain unchanged during antibiotic therapy.(7). By contrast, Streptococcus viridans is more common in vegetations that decreased in size(7).

Following identification of a vegetation, a therapeutic approach must be planned to optimize the patient’s recovery and survival. Echocardiographic and clinical analysis assist in prognostic estimations (4,7,10-12). Vegetation morphology as seen by transthoracic echocardiography (**TTE**) in 204 patients with clinical criteria for IE was evaluated in a retrospective study (6). Clinical complications included new onset congestive heart failure, embolization, drug failure requiring a change in antibiotic therapy, surgery, and death, were compared with vegetation characteristics. Findings
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

included the following:

- Complications occurred with an incidence of 55%, with equivalent rates for native and prosthetic valves and for clinical endocarditis in nonspecifically thickened valves.

- The overall complication rates were roughly equivalent for patients with mitral, aortic, tricuspid, and prosthetic valve vegetations, as well as for those with nonspecific valvular changes but no discrete vegetations.

- The most powerful predictor for complications was size.
  - Probability of sustaining a complication:
    - 10% for veg ≤ 6mm,
    - 50% for veg = 11mm
    - 100% for veg ≥ 16 mm

- Patients without discernible valvular abnormalities had significantly fewer complications (27%).

- Patients with higher grades of lesion extent and mobility tended to have more complications.

- Vegetation consistency did not predict complications, except for calcified lesions. They were associated with no complications.

Given the above variables, a risk score was proposed, and calculated as the sum of the scores (grades 1 to 4) for size, mobility and extent(4,6).

The highest possible score for any valve was 12. A high score was always present in patients with complications, but less than one-half of those with high scores developed a complication.

In multivariate analysis, these factors predicted the occurrence of complications with 70
percent sensitivity and 92 percent specificity in mitral valve endocarditis, and with 76 percent sensitivity and 62 percent specificity in aortic valve endocarditis.

**Note the above study was with TTE and observations made with TTE are not directly applicable to TEE** since a given vegetation is likely to appear larger on TEE (4). Therefore, a higher score by TEE may not signify a comparable level of risk.

Data are conflicting, but in general larger vegetations on TEE are more likely to embolize (13,14). Mugge et al, in a study of 105 patients with IE showed that a vegetation of > 10mm had a significantly higher incidence of embolic events when compared to smaller vegetations (47% vs 19%, p < 0.01)(11). This association was particularly strong in patients with mitral valve endocarditis. Vegetation size did not appear to predict other complications such as severe heart failure and death and these complications were not related to the location of endocarditis or type of organism.

Vilacosta et al, in a series of 211 patients with 28 embolic events found that vegetation size was associated with embolic risk for staphylococcus and mitral valve vegetations, but was not associated with embolic risk for streptococcus or aortic vegetations (4,14)

Regardless of size, mobility is bad (4,14).

Di Salvo et al found in a series of 178 patients with definite IE who underwent TEE, the incidence of embolism, as diagnosed by cerebral and thoracoabdominal CT scans, was higher when vegetation size was ≥15 mm (70 versus 27 percent for <15 mm) and when the vegetation was moderately or severely mobile (62 versus 20 percent for low mobility) (15).
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

83% had embolic events when vegetations were very large and mobile.

Following appropriate antibiotic therapy, observational studies suggest that embolic risk falls with time (16). Steckelberg et al found in a series of 207 patients the rate of embolization fell from 13 per 1000 patient days during the first week of antibiotic therapy to less than 1.2 per 1000 patient days after 2 weeks of therapy (4,16).

In a larger more recent series, Dickerman et al studied 1437 patients from the international collaboration of endocarditis and found that stroke rate decreased from 4.8 to 1.7 per 1000 patient years from the first to the second week of antibiotic treatment (4,17). Echocardiographic predictors of emboli still apply after the initiation of antibiotics. In the Dickerman’s study cited above, only 24 percent of observed emboli occurred after the start of antibiotic therapy, but greater vegetation length and mobility were still prognostic factors for these later embolic events(4,15).

Worse prognosis is more likely if antibiotics don’t decrease the size of the vegetation (4,7). Rohmann et al, found that an initial increase in vegetation size during appropriate antibiotic therapy or large vegetation size despite antibiotic therapy predicted a prolonged healing phase and a higher embolic risk(7). Using TEE, 83 patients were followed and the investigators found vegetations that enlarge or remain static rather than regress during 4 to 8 weeks of antibiotic therapy were associated with an increased incidence of abscess formation (13 vs 2%), embolic events (45 vs 17%), valve replacement (45 vs 2%) and mortality (10 vs 0%)(4,7).

Given this data, it is generally advisable to repeat the TEE after seven days of antibiotic therapy and compare the size of the vegetations. One week of therapy may be associated
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

with dramatic size decreases.

Echocardiography assists in diagnosis of vegetations and also in recognizing the **intracardiac complications associated with endocarditis** such as:

- Valvular regurgitation
- Valve perforation
- Abscess formation
- Fistula formation

Valve integrity can be destroyed by bacterial infiltration and proliferation leading to regurgitation. Leaflet perforation, disruption, prolapsing and flail segments, as well as mechanical prevention of coaptation of leaflets all can contribute to valvular regurgitation. Often it is difficult to distinguish between flail or prolapsing segments and mobile vegetations. Each has the same motion during the cardiac cycle, similar echocardiographic tissue characteristics, and they may both be present in the same location. Measuring a flail leaflet that has been mistaken for a vegetation may lead to miscalculation of risk level or overdiagnosis of endocarditis(4). Transesophageal echocardiography (TEE) substantially aids in distinguishing a leaflet from vegetation and this capacity contributes to its advantages as a prognostic and diagnostic tool (4).

Invasion of the infectious process beyond the valve leaflets or cavitary endocardium into the basal myocardium and tissue of the fibrous cardiac skeleton can result in perivalvular abscess or fistula formation(4). Initially the organism produces cellulits, which may be identified as echo-dense thickening of perivalvular tissue. Progressive necrosis of this infected area forms a space-occupying echo-lucent abscess cavity. S. aureus is the organism most likely to result in abscess formation. Given the
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

pressure with which the myocardial wall is subjected, disruption of the necrotic wall and communication of either ventricle or a great vessel with the abscess cavity may occur.

In the setting of such a communication, the abscess cavity may be viewed as a pseudoaneurysm, particularly if it involves the aortic wall directly (18). The distinction between an abscess and pseudoaneurysm can be made with TEE color flow Doppler, which demonstrates flow in a pseudoaneurysm but not into an abscess (4,19).

Total disruption of the wall may lead to a fistulous connection with intracardiac shunting between chambers, most commonly between the aorta and right atrium, left atrium and right ventricle, or left ventricle and right ventricle (4).

Importantantly myocardial abscess formation is associated with increased morbidity and mortality (32 to 45 percent in different series) (4,20,21). Abscess formation extending into the conduction system can result in heart block(4,22). TEE enhances the detection of an abscess cavity. In a study involving 118 patients with endocarditis, 44 (37%) of whom had an abscess documented at surgery or autopsy the sensitivity and specificity for TEE, was 87 and 95 %, respectively; and the sensitivity for TTE was much lower (28 versus 87% with TEE) although the specificity was similar (99 % vs 95%) (21). A similar wide discrepancy in sensitivity (25 versus 100 % with TEE) was noted in another report (4,23). TTE is most effective at detecting abscesses located anteriorly at the aortic septal junction, probably due to the close proximity of this area to the anterior chest wall and thus with the transducer near field (4).

TEE is more sensitive than TTE for detecting an abscess, but even TEE may miss a significant number of abscesses (4,24). This was illustrated in a report of 44 patients with
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

abscesses identified surgically (24). Only 21 (48 percent) were detected by TEE. Sixty-one percent of missed abscesses were located at the posterior mitral annulus and the majority of these were associated with a large calcification, which may have interfered with abscess detection. Leaflet perforation, true aneurysm formation, secondary infection of other valves, and vegetations on the chamber walls that are struck by jets created by blood passing through the infected valves are other complications better detected with TEE (4,25,26). In a very recent report of 89 cases involving a pseudoaneurysm in the region of the fibrous body between the mitral and aortic valve, the mitral-aortic intervalvular fibrosa (MAIVF) TEE was able to correctly identify all cases(27).

In a study looking at the ability of TTE and TEE to correctly diagnose valve perforation defined by surgical inspection found that TEE detected perforation in 21 of 22 cases compared with 10 of 22 for TTE (4,26).

**Prosthetic valve endocarditis** is best assessed with TEE and is characterized echocardiographically by the following findings(4,28):

- Vegetations (may impair leaflet or occluder motion)
- Perivalvular abscess and/or fistula and pseudoaneurysm
- Valve rocking signifying dehiscence and imminent badness
- New or worsening valvular or paravalvular regurgitation

Paravalvular regurgitation can indicate prosthetic valve endocarditis but should be compared to any prior paravalvular regurgitation (An old exam is worth gold). If prior data are lacking, moderate to severe, but not mild, paravalvular regurgitation should be considered suggestive of endocarditis (4,28).

For questions/reprints: tburch333@yahoo.com
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

Echocardiographic windows are often suboptimal because of echogenic prosthetic material obscures structures lying behind the valve. This acoustic shadowing can sometimes be avoided by imaging from atypical and/or transgastric views.

**TEE is clearly superior to TTE in assessing prosthetic valves for infection.**

Studies comparing TTE to TEE in patients with prosthetic endocarditis have found a much higher sensitivity with TEE (82 to 86 versus 36 to 43 %)(4,23,29-31).

In a prospective study comparing TTE and TEE in 114 episodes of suspected IE based on clinical findings, the following were noted(4,31):

- Two tests were concordant in 55% of cases
- TEE led to a reclassification of cases in 11% of patients with native valves and 34% of patients with prosthetic valves(4)
- TTE was usually diagnostic in cases where there was a high clinical suspicion in patients with native valves but TEE substantially aided the diagnosis in patients with intermediate probability of endocarditis on clinical grounds.
- The positive predictive value of TEE was 90% for both native and prosthetic valve endocarditis.

For some patients with native valves the negative predictive value of TEE approaches 100%. False negatives are more common in patients with prosthetic valves, thus clinical assessment is especially important in these patients. Prosthetic valve dehiscence is sometimes missed echocardiographically. In a study of 26 patients with prosthetic valve endocarditis, 14 (54%) had surgically identified valve dehiscence (4,24) four of which were missed on TEE. All 4 involved infected aortic valve prosthesis.
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

**Right sided endocarditis,** usually involving the tricuspid valve (TV), is often seen in intravenous drug users. S. aureus is the most common organism and vegetation size predicts outcome (4,32). In a series of 132 cases, mortality was much greater (33% vs 1.3%; p<0.001%) when vegetations were greater than 20mm (4). The TV is the most common right-sided valve involved, but the pulmonic valve, pacemaker leads (33) or indwelling catheters can be colonized. Most TEE publications on this condition are limited to case reports. Most reports on right-sided endocarditis utilized TTE. In a study comparing diagnostic accuracy of TTE vs TEE in 48 iv drug users suspected of IE, vegetations were seen in 22 (46%) (4,34). TTE and TEE were equally sensitive and specific. In no case did TEE find vegetation missed on TTE. It was concluded that TEE was not sufficiently more sensitive to justify its routine use.

Vegetations can sometimes have nonbacterial causes including: fungal infections, brucellosis and noninfectious lesions such as Libman-Sac’s endocarditis (35) (seen in systemic lupus erythematosus and antiphospholipid antibody syndrome), Loffler’s endocarditis (associated with eosinophilia), scleroderma and granulomatous diseases. Similar to bacterial endocarditis, these etiologies are best evaluated with transesophageal echocardiography (TEE) (3,4). Complications of nonbacterial endocarditis include: superimposed bacterial endocarditis, thromboembolic events, and severe valvular regurgitation and/or stenosis requiring surgery (35).

**Surgery in IE** — The 2006 ACC/AHA guidelines on the management of valvular heart disease included recommendations on the timing of surgery in patients with IE (3). Echocardiography is also helpful in the evaluation of potential candidates for surgery for
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

prosthetic valve and native valve IE. TTE and TEE enable identification of valve
dysfunction and TEE is particularly valuable for identification of perivalvular extension
of infection(4,24). The ACC/AHA recommendations for the timing of surgery in IE with
native and prosthetic valve endocarditis are summarized below(3,4):

**ACC/AHA guideline summary: Surgery for native valve endocarditis (NVE)**

**Class I** indications: There is evidence and/or general agreement that surgery is indicated
in patients with native valve endocarditis (NVE) with one of the following:

- Valve stenosis or regurgitation leading to heart failure.

- Aortic or mitral regurgitation with hemodynamic evidence of elevated left
  ventricular end-diastolic or atrial pressures such as premature closure of the mitral
  valve with aortic regurgitation, rapid decelerating mitral regurgitation signal by
  continuous wave Doppler (v-wave cutoff sign), or moderate to severe pulmonary
  hypertension.

- IE due to fungal or other highly resistant organisms.

- Complications such as heart block, annular or aortic abscess, or destructive
  penetrating lesions such as fistula from the sinus of valsalva to the right or left
  atrium or right ventricle, mitral leaflet perforation with IE of the aortic valve, or
  infection in annulus fibrosis.

**Class IIa** indications: The weight of evidence or opinion is in favor of the usefulness of
surgery in patients with native valve endocarditis who develop the following:

- Recurrent emboli and persistent vegetations despite appropriate antibiotic therapy.

**Class IIb** indications: The weight of evidence or opinion is less well established for the
usefulness of surgery in patients with native valve endocarditis who develop the
following:

For questions/reprints: tburch333@yahoo.com
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

- Mobile vegetations larger than 10 mm with or without emboli.

**ACC/AHA guideline summary: Surgery for prosthetic valve endocarditis (PVE)**

**Class I** indications: There is evidence and/or general agreement that surgery is indicated in patients with PVE who develop one of the following:

- Heart failure
- Dehiscence seen by cine fluoroscopy or echocardiography.
- Evidence of increasing valve obstruction or worsening regurgitation.
- Complications such as abscess formation.

**Class IIa** indications: The weight of evidence or opinion is in favor of the usefulness of surgery in patients with PVE who develop one of the following:

- Persistent bacteremia or recurrent emboli despite appropriate antibiotic therapy.
- Relapsing infection

**Class III** indications - There is evidence and/or general agreement that surgery is NOT indicated in patients with PVE in the following setting:

- Uncomplicated IE caused by a first infection with a sensitive organism.

**Synopsis:** Echocardiography is essential in the diagnostic evaluation of the patient with suspected endocarditis, and should be performed in all patients with a moderate or high suspicion of this condition. TTE and TEE are complementary for comprehensively evaluating hemodynamics and anatomy, but TEE is far superior because of its greater sensitivity in detecting native valve vegetations, prosthetic valve vegetations, perivalvular abscess and other pyogenic complications(4,29-31). A negative TEE makes native valve endocarditis unlikely, and a large vegetation that fails to shrink during therapy indicates a poor prognosis(7).
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis

In general it is recommended that all patients with suspected IE undergo TTE(4). It is the firm opinion of most experts that they should also have at least one TEE. Regardless of the echo modality chosen for initial examination, a complete Doppler examination must also be performed and clinical suspicion help guide therapy. The 2006 ACC/AHA guidelines on the management of valvular heart disease included recommendations on the role of echocardiography in IE(3,4). These include:

- Evaluation of patients in settings where endocarditis is suspected (such as persistent bacteremia without a known source or high clinical suspicion with negative cultures)
- Detection and characterization of vegetations on valves and in other sites (as in patients with congenital heart disease)
- Detection of valvular dysfunction and assessment of hemodynamic severity
- Detection of associated abnormalities such as shunts or abscesses
- Re-evaluation of patients in complex settings (such as those with virulent organisms, severe hemodynamic effects, persistent fever or bacteremia, or clinical deterioration)

References:
Echocardiography Evaluation of Endocarditis and Complications of Endocarditis


For questions/reprints: tburch333@yahoo.com


