Infective Endocarditis in the Era of Intracardiac Devices: An Echocardiographic Perspective

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Although the role of echocardiography is well established in the management of native valve and prosthetic valve endocarditis, the recent introduction of intracardiac devices, including pacemakers, implantable defibrillators, closure devices, and ventricular assist devices, has expanded its utility. Echocardiography permits the direct imaging of valvular vegetations, and it allows for the identification of structural complications of endocarditis. It is useful for characterizing the hemodynamic consequences of the infection. It can also provide prognostic information concerning risk of embolization and/or need for cardiac surgery. This article reviews the roles of transthoracic echocardiography and transesophageal echocardiography in the evaluation of patients with native valve endocarditis, prosthetic valve endocarditis, and infections involving a variety of nonvalvular cardiovascular devices.

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Infective endocarditis is a clinical challenge that is associated with high patient morbidity and mortality. Since the initial description of valvular vegetations using M-mode echocardiography in 1973,[1] echocardiographic imaging and Doppler flow visualization have assumed an increasingly important role in the diagnosis, treatment, and prognosis of patients with this disease.

Echocardiography plays a number of roles in the evaluation of patients with suspected infective endocarditis.[2-8] First, echocardiography permits the direct imaging of valvular vegetations, the hallmark of endocarditis. Second, it allows for the identification of structural complications of endocarditis, such as perivalvular abscess, flail leaflet, pseudoaneurysm, or partial dehiscence of a prosthetic valve. Third, it is useful for characterizing the hemodynamic consequences of the infection, such as valvular regurgitation or fistula formation, and their effects on chamber size and function. Finally, it can provide prognostic information concerning risk of embolization and/or need for cardiac surgery. Echocardiography can be particularly useful in patients with culture-negative endocarditis, in patients with clinical signs and symptoms that are inconsistent with the severity of their infection, and in patients with bacteremia of unknown cause, to exclude endocarditis. Due to the sensitivity of the technique, echocardiographic identification of vegetations, abscesses, or partial dehiscence of a prosthetic valve has been added as one of the major Duke criteria for endocarditis (Table 1).[7]

Although the role of echocardiography is well established in the management of native valve and prosthetic valve endocarditis, the recent introduction of intracardiac devices, including pacemakers, implantable defibrillators, closure devices, and ventricular assist devices, has expanded its application.[9] In this review, we will examine the roles of transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) in the evaluation of patients with native valve endocarditis, prosthetic valve endocarditis, and infections involving a variety of nonvalvular cardiovascular devices.

Table 1
Modified Duke Criteria for Diagnosis of Infective Endocarditis

Major Criteria

Positive blood cultures for infective endocarditis

1. Typical microorganisms for infective endocarditis, including viridans streptococci, *Streptococcus bovis*, HACEK, or community-acquired *Staphylococcus aureus* or enterococcus
2. Microorganisms from persistent positive blood cultures, at least 2 positive cultures drawn > 12 hours apart

Evidence of endocardial involvement

1. New valvular regurgitation on clinical examination (worsening or changing of preexisting murmur not sufficient)
2. Echocardiographic evidence of:
   a. Oscillating intracardiac mass, on valves or supporting structures, in the path of regurgitant jets, or on implanted material, in the absence of an alternative anatomic explanation
   b. Abscess
   c. New partial dehiscence of a prosthetic valve

Minor Criteria

1. Predisposition: predisposing heart condition or intravenous drug use
2. Fever: temperature > 38°C (100.4°F) on 2 separate occasions
3. Vascular phenomenon: major arterial emboli, septic pulmonary infarcts, mycotic aneurysms, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions
4. Immunological phenomenon: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid arthritis
5. Microbiologic evidence: positive blood cultures (that do not meet the major criteria defined above)
6. Serologic evidence of active infection with organism consistent with endocarditis

HACEK, *Haemophilus* species *(H. parainfluenzae, H. aphrophilus,* and *H. paraphrophilus), Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species.

Valvular Vegetations

The principal lesion of endocarditis is the valvular vegetation. Vegetations are composed of clumps of microorganisms, platelet thrombi, fibrin, and erythrocytes attached to the surface of a valve leaflet. Their morphologic features vary, depending on the offending organism, the valve involved, and the activity of the disease. Some vegetations are discrete sessile masses closely adherent to the valve, others are pedunculated, friable clumps that prolapse freely, and still others appear as elongated fibrous strands. Fungal vegetations are commonly larger than bacterial vegetations and may partially occlude the valve orifice.[10] Fungal vegetations tend to embolize more frequently and create less leaflet destruction than bacterial vegetations.[10] As vegetations heal, infiltration by fibroblasts occurs with hyalinization or calcification of the mass. Eventually, the healing vegetation is covered with endothelium.

Vegetations generally appear on echocardiography as circumscribed, echo-producing masses that arise from the surface of leaflet tips, either as an irregular area of highly reflective leaflet thickening or as one or more discrete pedunculated or fixed masses. In acute endocarditis, the vegetations typically appear soft and friable, whereas healed vegetations become more echodense and fixed. Vegetations vary from a few millimeters to several centimeters but must be at least 3 mm to 6 mm to be reliably detected with TTE.[11] Vegetations can change size between studies due to embolization of part of the mass, continued growth of the vegetation, or intercurrent valvular disruption, so vegetation size cannot be used to determine acute response to therapy. Some vegetations, particularly those on foreign bodies, can develop a complex appearance with cystic components incorporated into or superimposed onto the mass. High-frequency motion of vegetations or a free leaflet component can be difficult to appreciate at the relatively slow frame rate of 2-dimensional imaging, and are often more apparent by M-mode or tissue Doppler imaging.[12] Because vegetations usually form on previously diseased valves, their appearance is modified by the underlying valve disorder. For example, vegetation on a densely calcified, stenotic aortic valve in an adult will appear different than one that involves an otherwise normal bicuspid valve in an adolescent. As a rule, the greater the degree of valve deformity that existed before the infection, the more difficult the superimposed vegetation is to detect. Because valve disruption is part of the natural history of endocarditis, the appearance of the vegetation is often distorted by associated components of the infected valve, such as torn chordae or flail portions of the valve leaflet. In addition to valves and prosthetic materials, intracardiac tumors such as myxomas can become secondarily infected, which further complicates diagnosis.

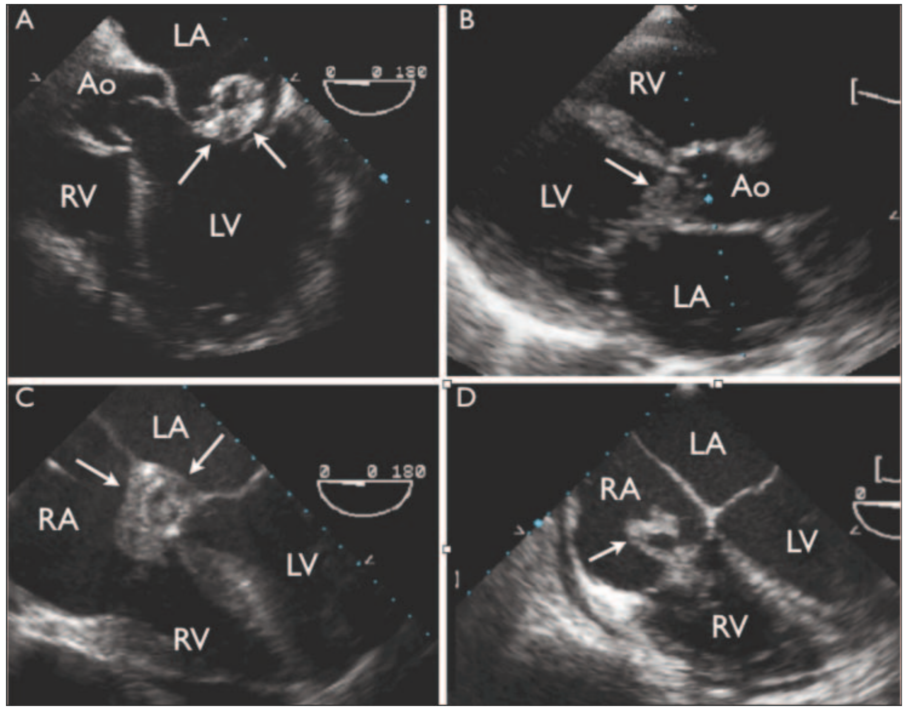

Figure 1. (A) *A large vegetation (arrows) involving the mitral leaflets on transesophageal echocardiography (midesophageal 5-chamber view).* **(B)** *A transthoracic parasternal long-axis view illustrating a vegetation (arrow) involving the aortic valve during systole.* **(C)** *An extensive abscess involving the aortic valve (arrows) on transesophageal echocardiography (midesophageal 4-chamber view).* **(D)** *A systolic frame of transesophageal 4-chamber view illustrating a large, serpiginous vegetation (arrow) attached to the tricuspid valve. LA, left atrium; Ao, aorta; RV, right ventricle; LV, left ventricle; RA, right atrium.* www.medreviews.com

Native Valve Endocarditis

Mitral Valve

The native mitral valve is the most frequently involved valve in infective endocarditis.[6] Structural abnormalities of the mitral valve, such as rheumatic deformation and myxomatous degeneration of the leaflets, may serve as a predisposing nidus for infection. Mitral vegetations can involve either the anterior or posterior leaflets, and infection of both leaflets is not uncommon. Figure 1A shows a large mitral vegetation that prolapses into the left atrium during systole, as recorded by transesophageal echocardiography. The mass is composed of both the vegetation and a portion of the disrupted anterior mitral leaflet, and it was associated with severe mitral regurgitation. On occasion, mitral vegetations may be very large and partially obstruct the orifice, simulating mitral stenosis. Other entities to consider in the differential of an echogenic mass attached to or involving the mitral valve apparatus include myxomatous degeneration of the leaflet, alone or complicated by mitral valve prolapse or partial flail leaflet, rheumatic valve, fibroelastoma, Lambl's excrescences, or a ruptured papillary muscle.[6] Mitral annular calcification can also become secondarily infected with vegetations involving the left atrial wall and/or posterior leaflet. Accompanying intramyocardial abscess is occasionally noted.

In addition to direct involvement of the mitral valve, the anterior mitral leaflet and chordae can become involved through direct extension or seeding from an infected aortic valve. Seeding of the anterior mitral leaflet can lead to mitral leaflet aneurysm and perforation of the leaflet.

The primary complications of mitral endocarditis are valve disruption with resultant mitral regurgitation, which can vary from trivial to severe, and septic embolism. Extension beyond the valve is uncommon, but myocardial abscess can occur. Progressive destruction of the mitral valve results in ruptured chordae, mitral valve prolapse, and, ultimately, flail mitral leaflet.

Aortic Valve
The aortic valve is a common site of involvement in infective endocarditis and is the most common type of endocarditis in surgical series.[6] Predisposing factors include bicuspid valve, rheumatic deformation, and senile calcification.[6] Aortic vegetations vary widely in appearance, ranging from small, discrete focal masses superimposed on the leaflet margin to larger, more diffuse sessile masses with extensive involvement of the leaflet tips, to large, mobile masses that prolapse into the left ventricular outflow tract during diastole (Figure 1B). Larger vegetations are typical of *Staphylococcus aureus* infection, and associated leaflet perforation or disruption is common. Although vegetations typically move with the valve leaflet, independent motion of large pedunculated vegetations or friable portions of fixed vegetations aids in recognition. In patients with underlying aortic regurgitation, vegetations can also occur at the site of jet lesions on the interventricular septum or anterior mitral leaflet.

Complications of aortic endocarditis include valve disruption with associated regurgitation, aortic root abscess, and mycotic aneurysm. Aortic regurgitation is virtually always seen in patients with aortic endocarditis, and some degree of valve destruction is common. Valve destruction can vary from erosion of the leaflet tips to leaflet fenestrations and, ultimately, to a partially or completely flail leaflet. Valvular perforation is a frequent complication of aortic valve endocarditis (seen in up to 50% of cases) that can lead to severe aortic insufficiency with resultant heart failure.[13] As the severity of infection and leaflet disruption increases, so does the degree of regurgitation that can be assessed with color Doppler imaging. In patients with severe regurgitation, the diastolic pressure in the left ventricle can rise rapidly and exceed left atrial pressure before the onset of systole. This process leads to premature closure of the mitral valve (closure prior to atrial contraction) that can be appreciated with M-mode echocardiography and is generally associated with the need for urgent surgical intervention.

Perivalvular abscess is generally seen with acute endocarditis, particularly when *Staphylococcus aureus* is the offending organism. Perivalvular abscesses are generally seen with more aggressive disease; therefore they are common in surgical and autopsy series and less frequent in routine practice. Aortic root abscess presents echocardiographically either as an echo-free space with the normal continuous echoes from the wall of the aorta or as an area of thickening and increased echo production of the aortic wall subjacent to an infected portion of the valve (Figure 1C). Abscesses may progress to disrupt the aortic wall, with resultant communication with adjacent chambers. The direction of shunting depends on the location of the abscess, with the most common shunts occurring between the aorta and left ventricle, left atrium, or right atrium, often in association with a ruptured sinus of Valsalva aneurysm. Periannular extension of endocarditis is associated with significant complications, including heart failure, atrioventricular block, need for surgery, and adverse prognosis, with a mortality ranging from 40% to 90%.[13]

Tricuspid Valve
Tricuspid endocarditis, although less common than disease of the mitral or aortic valve, has become more prevalent in recent years—particularly among intravenous drug users and in association with indwelling venous catheters.[14] Tricuspid endocarditis is usually acute, with *Staphylococcus aureus* as the most common infecting pathogen. Echocardiographic screening is particularly important in patients with suspected right-sided endocarditis because such patients usually lack a murmur of tricuspid regurgitation. Tricuspid vegetations are generally larger than those seen on the left-sided valves, and significant portions of the vegetation often move independently of the valve leaflet. Valve disruption with chordal rupture, partial flail leaflet, and important tricuspid regurgitation is often seen. Figure 1D is a systolic frame showing a large tricuspid vegetation attached to the tricuspid valve that prolapses into the right atrium.

The size of the vegetation in patients with right-sided endocarditis has prognostic value. In a study of patients with right-sided infective endocarditis, mortality was 33% when vegetations were > 2 cm versus 1.3% when vegetations were smaller.[14] Due to the mobility of these large vegetations, septic pulmonary emboli are a frequent complication.[15]

Pulmonic Valve
Pulmonary valve endocarditis is extremely rare in the adult population. It is most commonly seen in intravenous drug users and patients with congenital heart disease, particularly pulmonic stenosis, tetralogy of Fallot, and ventricular septal defects.[16]

Prosthetic Valve Endocarditis

Prosthetic valve endocarditis accounts for 10% to 25% of all infective endocarditis cases.[5] It is estimated to occur in approximately 1% of patients within the first year of placement, more often with aortic valve prostheses than with mitral valve prostheses.[5] Infections involving mechanical prosthetic valves usually begin in the perivalvular area at the annular insertion site. The infection can extend locally, leading to necrosis at the ring margin, and eventually disrupt the attachment of the valve with partial dehiscence of the valve or, less commonly, with pseudoaneurysm formation. When large, the vegetations can extend into the valve orifice and obstruct flow or restrict leaflet motion. In patients with bioprosthetic valves, the leaflets themselves can be involved.

Vegetations on prosthetic valves are more difficult to detect with TTE than vegetations on native valves. This difficulty occurs because the sewing ring and struts of mechanical and bioprosthetic valves are highly reflective and tend to obscure vegetations within the valve apparatus or its shadow. As a result, vegetations can only be appreciated when an uninterrupted path can be obtained between the transducer and the inflow side of the valve, where vegetations are most commonly present. For mitral prostheses, this generally requires the use of TEE; however, in the case of prosthetic aortic valves, the inflow side of the valve can generally be seen with TTE and the 2 techniques are therefore complementary. Figure 2A is a transesophageal long axis recording of a Carpentier-Edwards valve (Edwards Lifesciences, Irvine, CA) in the aortic position illustrating a large vegetation (arrow) attached to the valve leaflets and an abscess involving the posterior aortic root. Figure 2B illustrates a transesophageal midesophageal short axis view of a St. Jude Medical® aortic valve (St. Jude Medical, St. Paul, MN) with multiple nodular vegetations surrounding the valve margin.

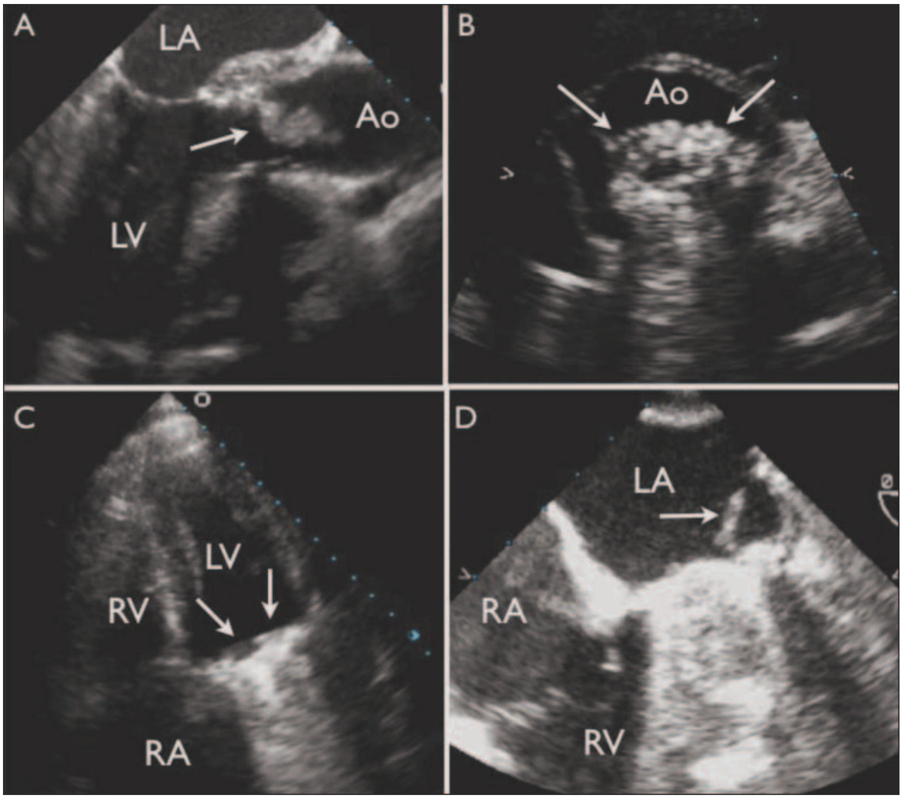

Figure 2. **(A)** *A systolic frame of transesophageal 3-chamber long-axis image illustrating a vegetation (arrow) attached to the bioprosthetic Carpentier-Edwards aortic valve, with an associated abscess.* **(B)** *A transesophageal short-axis view of a St. Jude mechanical valve in the aortic position with multiple vegetations (arrows).* **(C)** *A transthoracic apical 4-chamber view illustrating a St. Jude mechanical valve in the mitral position with shadowing of the left atrium (arrows) due to reverberations from the valve.* **(D)** *A transesophageal echo of the same patient in Figure 2C illustrating a vegetation (arrow) attached to the sewing ring of the St. Jude mechanical mitral valve. LA, left atrium; Ao, aorta; LV, left ventricle; RV, right ventricle; RA, right atrium.* www.medreviews.com

When there is a high index of suspicion of active infective endocarditis based on the Duke criteria, TTE is rarely sufficient to *exclude* the diagnosis and TEE becomes a necessity. In a large series of patients with prosthetic valve endocarditis, while TTE demonstrated a sensitivity of 36% to 69%, TEE imaging demonstrated a sensitivity of 86% to 94% and specificity of 88% to 100%.[17,18] In another study, a sensitivity of 96% was reported for TEE imaging in patients with endocarditic involvement of mechanical mitral prostheses.[19] Figures 2C and 2D compare TTE and TEE recordings of a prosthetic mitral valve in the same patient. In the TTE image recorded from the apex, the inflow side of the valve is obscured by the reverberations that arise from the highly reflective prosthetic material. However, using TEE, a mobile linear vegetation attached to the margin of the valve is clearly visible.

According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, a TTE is used initially in individuals with a clinical suspicion of native valve endocarditis, whereas TEE should be used as the primary diagnostic imaging modality in the setting of prosthetic valve endocarditis.[20] Of note, thrombus and pannus are often difficult to distinguish from vegetation on prosthetic valves; however, pannus rarely has friable or mobile components, whereas the clinical context and associated lesions (eg, paravalvular leak or abscess formation) generally permit differentiation of thrombus from vegetation.

Infective Endocarditis Related to Cardiovascular Devices

In recent years, the number of patients with intracardiac prostheses and indwelling devices, including pacemakers, implantable cardiac defibrillators, atrial septal defect closure devices, and ventricular assist devices, has increased significantly. When these patients develop unexplained fever or bacteremia, echocardiography is frequently requested to look for vegetations involving the device or adjacent structures that may be damaged or abraded by the device, creating a site for infection.

Pacemakers and Implantable Cardiac Defibrillators

Infections are reported in 0.5% to 2% of patients with pacemakers and implantable cardiac defibrillators (ICD).[21-24] In pacemaker and ICD infective endocarditis, vegetation formation can occur along the course of the electrode (Figure 3A), involve the tricuspid valve leaflets (Figure 3B), or affect the endocardium of the right atrium or right ventricle.[21,22]

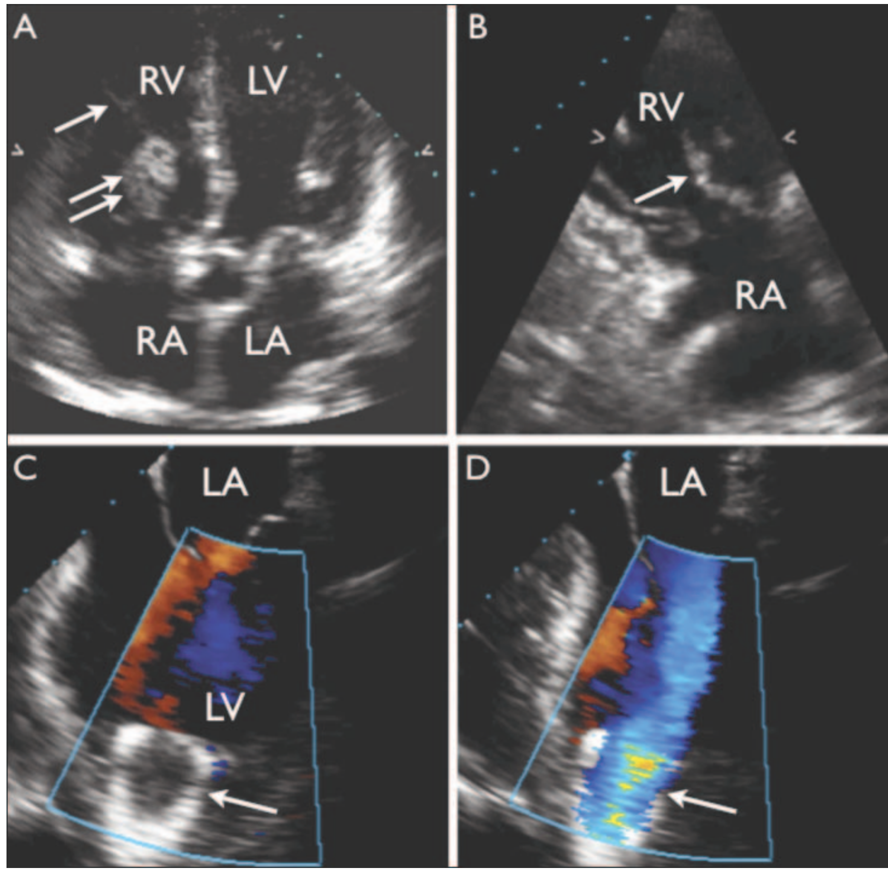

Figure 3. (A) *A transthoracic apical 4-chamber view illustrating a pacemaker wire (single arrow) with a vegetation adherent to the wire (double arrows).* **(B)** *A transthoracic echocardiographic right ventricular inflow view demonstrating a large vegetation (arrow) on the tricuspid valve.* **(C)** *A transesophageal long-axis view of the left ventricle demonstrating an inflow LVAD cannula at the left ventricular apex (arrow).* **(D)** *A transesophageal long-axis view of the left ventricle demonstrating unobstructed flow into the LVAD cannula on color Doppler (arrow). LVAD, left ventricular assist device; RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium.* www.medreviews.com

Several studies have examined the diagnostic and prognostic roles of echocardiography in the diagnosis of endocarditis involving these 2 devices.[25-27] Infective endocarditis of a pacemaker or ICD is difficult to diagnose with TTE because the leads produce reverberations and artifacts (particularly when multiple leads are present) that may mask associated vegetations. As a result, when there is a strong suspicion of lead-associated infection that is not apparent on TTE, a TEE is appropriate. In a small prospective study of 10 patients evaluating the utility of either TTE or TEE to visualize vegetations attached to pacemaker leads, vegetations were identified in only 2 patients with TTE and 7 patients with TEE. Of the 7 patients with endocarditis diagnosed by TEE, 5 underwent surgery confirming the preoperative findings.[26]

The same increase in TEE sensitivity has been demonstrated in patients with ICDs, where the sensitivity of detection of lead vegetations by TTE has ranged from 22% to 30%, compared with a sensitivity of 95% with TEE.[21-27] In addition to recording the leads in the right atrium and ventricle, TEE allows for the complete assessment of the superior vena cava and the upper part of the right atrium, areas that are difficult to depict with traditional TTE imaging.[21-27]

Atrial Septal Defect Closure Devices

Thrombus formation and infection are rare complications of atrial septal defect (ASD) closure devices, with only 5 reports of device-related infection to date.[28-31] However, with the increasing frequency of percutaneous closures of ASDs, reports of complications are likely to increase. Both thrombi and vegetations on closure devices present as shaggy masses typically with multiple mobile strands that are difficult to distinguish in the absence of an appropriate clinical history. Although the ACC/AHA guidelines for infective endocarditis prophylaxis do not recommend antibiotics for patients following the implantation of ASD closure devices, the prescription and duration of antimicrobial therapy is physician-dependent.[32]

Ventricular Assist Devices

In symptomatic patients with advanced heart failure despite optimal medical therapy, mechanical circulatory support with a left ventricular assist device (LVAD) has been used successfully. The purpose of the LVAD is to serve either as a bridge to heart transplantation or as destination therapy.[33] In a study of 68 individuals with 2.5 years of follow-up, however, one third of the left ventricular assist devices became infected within 3 months of implantation.[34]

The role of echocardiography (both TTE and TEE) in this setting is to inspect the potential sites of infection because pathogens can colonize the inner surfaces of the device or grafts. Echocardiography will ensure that the inflow from the LVAD cannula situated in the left ventricular apex and the outflow cannula in the aorta are unobstructed (Figure 3C and 3D). In a majority of infective endocarditis cases involving left ventricular assist devices diagnosed by echocardiography, prompt device debridement, removal, and replacement are required.[35]

Sensitivity and Specificity of Echocardiography in the Diagnosis of Infectious Endocarditis

Table 2 compares the relative sensitivities and specificities of TTE and TEE in detecting the vegetations that characterize endocarditis.[18,36-47] In larger series (> 100 subjects), the sensitivity of TTE has averaged roughly 60%, whereas that of TEE is > 90%. Although there is some variability of results, the specificity of both techniques appears comparable and averages roughly 95%. In analyzing these results, it is important to remember that the gold standard for the diagnosis of endocarditis is pathologic evidence of vegetations or abscess, whereas in most of these studies the diagnosis of endocarditis is based on the clinical decision to treat and the discharge diagnosis. In addition, these studies fail to distinguish between good and poor quality transthoracic echocardiograms, valve location, or degree of underlying pathology and include both

Table 2
Sensitivity and Specificity of Transthoracic Echocardiography and Transesophageal Echocardiography in Patients With Infective Endocarditis

Study (Year)	Number of Patients	Clinical Condition	Transthoracic Echocardiography		Transesophageal Echocardiography	
			Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Erbel R et al 1988[36]	124	Endocarditis	63.0	100.0	98.0	98.0
Taams MA et al 1990[37]	21	Endocarditis	28.0		86.0	
Shively BK et al 1991[38]	66	Endocarditis	44.0	98.0	94.0	100.0
Pedersen WR et al 1991[39]	24	Endocarditis	50.0		100.0	
Birmingham GD et al 1992[40]	61	Endocarditis abnormalities	30.0	100.0	88.0	97.0
Daniel WG et al 1993[18]	126	Prosthetic valve	57.0	63.0	86.0	88.0
Bayer AS et al 1994[41]	64	Endocarditis	60.0	91.0	87.0	91.0
Irani WN et al 1996[42]	134	Prosthetic valve endocarditis	68.0	100.0	100.0	96.0
Werner GS et al 1996[43]	104	Endocarditis	58.5	60.5	92.5	95.0
de Castro S et al 2000[44]	32	Endocarditis valve perforation	45.0	98.0	95.0	98.0
Bouza E et al 2001[45]	109	Endocarditis	51.4	92.0	65.2	95.0
Chang CF et al 2004[46]	24	Dialysis and clinical endocarditis	64.7	84.6	75.2	85.4
Jassal DS et al 2006[47]	74	Surgically treated endocarditis	40.0	100.0	82.0	87.0

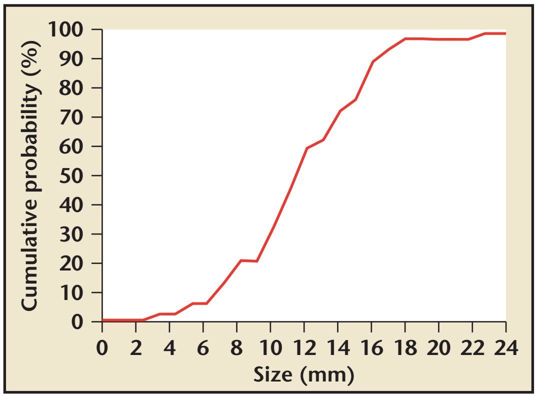

Figure 4. *The cumulative occurrence of complications relative to the maximal length of the vegetation on transthoracic echocardiography. Reprinted with permission from Sanfilippo AJ et al.*[49] www.medreviews.com

native and prosthetic valves. Clearly, the improved image quality of TEE is particularly important in patients with limited transthoracic studies and in those with prosthetic valves, particularly in the mitral position. However, in young patients with good quality studies and minimal underlying pathology (fibrosis and calcification), the incremental value of TEE is limited. For example, in a study of 48 intravenous drug users with suspected endocarditis, monoplane TEE and TTE were found to be equally sensitive in detecting vegetations.[26] This finding is presumably because the patients were young and had involvement of the tricuspid valve without prior disease.

The sensitivity and specificity of TEE (93%) for the detection of paravalvular abscess have also been reported to be higher than those of TTE (67%). However, the specificities of 98% for TEE and 100% for TTE are comparable.[48] More subtle lesions, such as valve perforation, are more easily depicted with TEE using color Doppler imaging.

Prognostic Role of Echocardiography in Infective Endocarditis

Although the identification of a vegetation is helpful in establishing the diagnosis of acute infective endocarditis, specific characteristics of the mass as shown by echocardiography are also useful in stratifying patient risk. The prognostic value of vegetation size, extension to adjacent nonvalvular structures, and degree of calcification has been extensively studied.[49-52] Sanfilippo and colleagues[49] evaluated 219 patients with vegetations and identified that both mobility and involvement of extravalvular structures were significant predictors of complications, including heart failure, cerebrovascular accident, and need for valve replacement.[49]

Figure 4 illustrates the relationship of maximal vegetation dimension and cumulative incidence of complications. Of note, 75% of complications occurred in patients with vegetations greater than 10 mm in diameter/length.[49] Di Salvo and colleagues[50] evaluated 178 patients with infective endocarditis; 66 (37%) had 1 or more embolic events as confirmed with clinical and computed tomographic findings. Embolic events occurred more frequently in patients with a vegetation length > 10 mm than in those with a vegetation length < 10 mm (60% vs 23%, respectively; $P = .001$).[50] Thuny and colleagues[51] identified 384 patients with endocarditis; 131 (34.1%) had documented embolic events. They demonstrated that a vegetation length greater than 15 mm was a strong predictor of 1-year mortality (RR = 21; 95% CI, 1.34 to 3.26; $P = .001$).[51]

Additionally, if the size of the vegetation increased appreciably during appropriate antimicrobial therapy, the patient was more likely to develop clinically significant emboli and thus might benefit from earlier surgical intervention.[52] In a series of 83 patients, Rohmann and colleagues[52] demonstrated that an increase in vegetation size was associated with an increased need for urgent valve replacement (45% vs 2%), increased rate of embolism (45% vs 17%), abscess formation (13% vs 2%), and increased mortality. Thus, the size of the vegetation is an important prognostic predictor of adverse events in individuals medically treated for infective endocarditis.

Factors other than vegetation size provide important information and may prompt early surgical intervention. These include extension of the infectious process beyond the valve leaflets leading to perivalvular abscess or mycotic aneurysm, progressive valvular destruction and regurgitation, and, more rarely, valvular or coronary obstruction by a large, critically placed mass. Although the decision to operate is generally based on the clinical status of the patient, clinical signs and symptoms may be misleading, particularly in young patients whose vital signs may remain relatively normal despite significant disease and in patients with other disorders that can modify the clinical presentation. Echocardiography, by demonstrating the various complications of endocarditis and permitting evaluation of the hemodynamic burden on the ventricle, can be particularly helpful in timing surgical intervention.

Despite appropriate prolonged antimicrobial therapy, 20% of patients will require surgical intervention for infective endocarditis.[53] The indications for surgery in infective endocarditis continue to evolve, and include intractable heart failure, abscess formation, recurrent embolic events, and the presence of prosthetic material. With increasing demands for surgery, the identification of preoperative echocardiographic findings that may identify the highest risk patient is needed. We recently identified 91 patients who underwent surgical intervention for active infective endocarditis as defined by the Duke criteria at a single center. We demonstrated that a preoperative echocardiogram demonstrating left ventricular dysfunction was an independent predictor of in-hospital death in patients undergoing surgical intervention for endocarditis. The presence of a preoperative ejection fraction < 50% had a high sensitivity of 92.3%, specificity of 95.7%, positive predictive value of 80%, and negative predictive value of 98.5% for predicting in-hospital death in this patient cohort.[53]

Preoperative echocardiogram demonstrating left ventricular dysfunction was an independent predictor of in-hospital death in patients undergoing surgical intervention for endocarditis.

Clinical Utility

With the addition of echocardiographic findings as one of the major Duke criteria, there is potential for the inappropriate use of this diagnostic imaging modality. Little data exist on the additive value of echocardiography when applied to clinical risk stratification based on the Duke risk groups (Table 1).[7] In a study of 101 patients referred for echocardiography to "rule out endocarditis," the Duke criteria was used to classify 37 patients as low risk (alternative diagnosis), 40 as intermediate risk (1 major or 3 minor), and 24 as high risk (2 major or 1 major and 3 minor Duke criteria).[54] Among patients with low or moderate risk, none were subsequently found to have endocarditis. Vegetations were identified by echocardiography in 22 of 24 patients in the high-risk group, 15 by TTE, and 7 by TEE (3 with prosthetic valves).[54]

Thus in patients with a high likelihood of infective endocarditis, the practical role of TTE for *diagnostic* purposes is low. However, both TTE and TEE, if clinically indicated, are useful for *prognostic* purposes in this setting for identifying perivalvular complications and assessing the severity of regurgitation. In patients with a transient fever and a nonregurgitant murmur, who have a low likelihood of disease, echocardiography is often requested but has a low diagnostic yield.[54]

Although not supported by the previous study,[54] others have demonstrated that echocardiography is most useful in the setting of patients with a moderate likelihood of disease.[55,56] These patients should be screened initially with TTE to confirm the diagnosis, and, if positive, treated appropriately. When the images are of good quality and the study is negative, one should entertain an alternate diagnosis. If the clinical suspicion remains moderate to high, however, or the TTE remains equivocal due to structural abnormalities or poor acoustic windows, TEE should be pursued.[55] A recent study evaluating the use of TEE as a screening tool for infective endocarditis with moderate likelihood of disease demonstrated that persistent blood cultures or a new regurgitant murmur were significant independent predictors of positive TEE results.[56]

Summary

Echocardiography is currently the only noninvasive technique that can detect vegetations and associated

Main Points

- Vegetations vary from a few millimeters to several centimeters but must be at least 3 mm to 6 mm to be reliably detected with transthoracic echocardiography (TTE).
- Other entities to consider in the differential of an echogenic mass attached to or involving the mitral valve apparatus include myxomatous degeneration of the leaflet, alone or complicated by mitral valve prolapse or partial flail leaflet, rheumatic valve, fibroelastoma, Lambl's excrescences, or a ruptured papillary muscle.
- In a large series of patients with prosthetic valve endocarditis, while TTE demonstrated a sensitivity of 36% to 69%, transesophageal echocardiography imaging demonstrated a sensitivity of 86% to 94% and specificity of 88% to 100%.
- In pacemaker and implantable cardiac defibrillator infective endocarditis, vegetation formation can occur along the course of the electrode, involve the tricuspid valve leaflets, or affect the endocardium of the right atrium or right ventricle.

complications that characterize bacterial endocarditis. It can also permit identification of a subset of patients with infective endocarditis who are at increased risk of complications, and, when integrated with clinical data, it can be helpful in timing surgical intervention. In patients with bacteriologic cure, but with residual valvular incompetence, serial echocardiographic studies can provide information about valvular integrity and ventricular function that may prove useful in timing valve replacement. ■

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