The Relative Roles of Transthoracic Compared With Transesophageal Echocardiography in Children With Suspected Infective Endocarditis

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OBJECTIVES
The study evaluated the additional benefit of transesophageal echocardiography (TEE) versus transthoracic echocardiography (TTE) in pediatric cases with suspected bacterial endocarditis.

BACKGROUND
In adult patients, TTE has a lower sensitivity and specificity than TEE for the detection of vegetations or aortic root abscess formation. Few data are available about the relative benefits of TEE over TTE in the pediatric age group.

METHODS
Patients were included if they had positive blood cultures for typical microorganisms and had a TTE and TEE within 14 days of each other. The patients had to meet the Duke criteria for a positive diagnosis of bacterial endocarditis. The TTE and TEE data were analyzed using the McNemar test for the significance of change.

RESULTS
Twenty-one patients fulfilled the criteria, at a median age of 9.5 years. Congenital heart disease was present in 13 patients; 4 patients were previously healthy and 4 patients had other medical problems. Nine patients had surgical confirmation of bacterial endocarditis. Fifteen patients had a positive cardiac finding, with 12 vegetations, 2 vegetations plus aortic root abscess, and 1 isolated abscess. There was excellent agreement between TTE and TEE in those cases with positive cardiac findings, with a p = 0.32, kappa 0.89. Using positive TEE cardiac findings as the gold standard, the sensitivity for TTE was 86% for all 15 events and 93% for the detection of a vegetation.

CONCLUSIONS
In pediatric cases, TTE has a high degree of sensitivity for the detection of supportive evidence of endocarditis, and TEE should be reserved for patients with a poor transthoracic window. (J Am Coll Cardiol 2003;41:2068–71) © 2003 by the American College of Cardiology Foundation

Although infective endocarditis (IE) in pediatric patients is a relatively rare disease with a prevalence of 0.8 to 3.3/1,000 hospital admissions, it is associated with a high morbidity and mortality (1–4). Under certain circumstances (e.g., presence of shunts and conduits) this is a difficult diagnosis to establish (1). Positive blood cultures and other supporting laboratory investigations in conjunction with the clinical status are the gold standards for classification.

Ever since its advent in the late 1970s (5), echocardiography has become an important adjunctive technique for the evaluation of patients with suspected bacterial endocarditis. Results from echocardiographic studies in adults have demonstrated a sensitivity of approximately 70% in detecting vegetations by transthoracic echocardiography (TTE) (6). Similarly, the positive predictive value of transesophageal echocardiography (TEE) for the correct diagnosis of IE was close to 90% both in patients with prosthetic and native valves (7), with a negative TEE having a negative predictive power of >90% (8).

Optimal use of echocardiography in the diagnostic evaluation of endocarditis in pediatric patients is still a topic of considerable debate, and few data are available to clarify the situation. Two published studies showed a sensitivity of 46% and 67% for TTE using the Duke criteria, with no comparison for TEE (9,10).

We reviewed our clinical experience and evaluated the relative roles of TTE and TEE for the detection of supportive evidence of bacterial endocarditis.

METHODS
A search was performed within the hospital and Division of Cardiology database at the Hospital for Sick Children, Toronto, to identify all patients with the diagnosis “infective endocarditis”, along with their specific treatment, between January 1988 and March 2000. To be included in the study the patients had to meet the Duke criteria for IE (11,12). They had to have typical microorganisms for IE from at least two separate blood cultures, or persistently positive blood cultures, a fever >38.0°C, and vascular and immunologic phenomena supportive of the diagnosis or evidence of endocardial involvement. By definition they were Duke positive if they had either: 1) two major criteria, 2) one major plus three minor criteria, or 3) five minor criteria.

The patients had to have at least one TEE and TTE study as part of a diagnostic evaluation within the same admission or within 14 days at our institution. Two-dimensional transthoracic and color Doppler echocardiograms were performed using either a Hewlett-Packard (models HP 1000, HP 2500, and HP 5500, Andover, Massachusetts), Advanced Technology Laboratories (models ATL HDI Ultramark 9, ATL HDI 5000, Advanced
Technology Laboratories, Bothell, Washington), Acuson 128 xp, and Aloka ultrasound systems with transducer frequencies appropriate for patient size. Transesophageal echocardiograms were performed with either a monoplane, biplane, or omniplane probe.

The patient’s age, gender, and weight at diagnosis of endocarditis were recorded. The previous history, physical examination, laboratory and microbiology results, underlying disease, heart defects, previous cardiac or other surgical and dental interventions, treatment, and outcome were reviewed.

Echocardiographic studies on super VHS tapes were reviewed randomized and blinded by one of the investigators (J.F.S.). Data collected included the presence or absence of vegetations, size, attachment, shape, involvement of valves and chordae, abscess formation, and the detection of the mass in multiple planes.

**Statistical analysis.** Data are described as frequencies, medians with ranges, and means with SDs as appropriate. All analyses were performed using SAS statistical software Version 8 (SAS Institute, Cary, North Carolina) employing default settings. To compare findings on TTE versus TEE, the McNemar test and the kappa statistic were used. Kappa (κ) is a measurement of agreement that is corrected for agreement that would be expected to occur simply by chance. A κ value of ≥0.75 represents excellent agreement beyond chance, whereas values of <0.4 indicate poor agreement beyond chance, and values between 0.4 and 0.75 indicate fair-to-good agreement beyond chance.

### RESULTS

A total of 96 patients (age range, 10 days to 17.5 years) were identified with the discharge diagnosis of “infective endocarditis.” From this group, 21 fulfilled the requirements of positive Duke criteria and the prerequisite of having both a TEE and TTE echocardiogram within the defined time period.

There were 13 male and 8 female patients, with a median age of 9.5 years (range, 0.3 to 17.5 years) and a median weight of 28.8 kg (range, 4.5 to 59 kg). The underlying abnormality was congenital heart disease in 13, one case each of post-bone marrow transplant, chronic otitis media, mycotic aneurysm, and liver transplant, with 4 children being otherwise healthy.

Congenital heart disease or variants included bicuspid aortic valve (n = 1), aortic stenosis (n = 1), uncomplicated ventricular septal defect (n = 4), atrioventricular septal defect (n = 2), tetralogy of Fallot or pulmonary atresia (n = 2), and complex forms of congenital heart disease (n = 3). Pulmonary artery banding had been performed in two patients, with one case having patch closure of a ventricular septal defect, two an arterial-to-pulmonary artery shunt, and one patient a cavopulmonary anastomosis. Seven patients with congenital heart disease had no prior cardiac surgery. One patient had a dental procedure within a time frame that was close to the onset of the symptoms of endocarditis.

Organisms found in two to five blood cultures included *Streptococcus viridans* (n = 6), *Staphylococcus aureus* (n = 6), coagulase-negative staphylococcus (n = 4), *Staphylococcus pyogenes* (n = 1), *Staphylococcus hominis* (n = 1), alpha-hemolytic streptococcus (n = 1), and *Staphylococcus epidermidis* (n = 1). In one patient, the cultures remained negative (had positive echocardiographic findings as well as peripheral emboli and other criteria to be Duke positive). All patients were treated with antibiotics appropriate to their organism. Nine patients underwent a surgical procedure, providing confirmation of the echocardiographic findings (debridement, valve repair, drainage of an abscess, conduit replacement.

Fifteen patients had positive echocardiographic findings to support a diagnosis of endocarditis, which included vegetations in 12, vegetations plus an abscess in 2, and isolated abscess formation in 1 patient. Using these 15 positive cardiac findings to compare the two techniques, there was an excellent agreement between TEE and TTE with regard to the identification of evidence supportive of cardiac involvement (p = 0.32, κ 0.89). If TEE was used as the gold standard for recognition of cardiac involvement supportive of the diagnosis of bacterial endocarditis, then the sensitivity of TTE was 86% for all cardiac involvement and 93% for the recognition of a vegetation. A vegetation was not identified in one case by TTE. This was in a 12-year-old patient postanatomical repair of corrected transposition, with a difficult TTE window and a vegetation situated in the tunnel from the morphologic left ventricle to aorta. One other patient with a vegetation that was seen by both TTE and TEE had an early aortic root abscess, which was confirmed at surgery and seen only by TEE. In all nine patients who underwent surgery for their endocarditis, the TEE findings corresponded with the intraoperative observations. In the same group by TTE, one vegetation and one abscess were not identified.

### Additional benefits of TEE over TTE

In general, apart from the missed vegetation by TTE there was very little benefit of TEE over TTE (Table 1). Subjectively, the image quality was better by TEE; however, this did not impact on management or outcome. Mitral valve regurgitation was better assessed by TEE, with four cases having none on TTE (p = 0.04). However, for aortic, tricuspid, and pulmonary regurgitation, the two were comparable (aortic regurgitation, p = 0.32; tricuspid regurgitation, p = 0.18; with complete agreement for pulmonary regurgitation). Transthoracic echocardiography was adequate at defining the shape of the vegetation, with disagreement in only four

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**Abbreviations and Acronyms**

- IE = infective endocarditis
- TEE = transesophageal echocardiography
- TTE = transthoracic echocardiography
patients (p = 0.32). Abscess formation was seen both by TTE and TEE in two patients whereas in the third patient it was not identified on the TTE study.

**DISCUSSION**

Both the widespread availability and the low invasiveness of echocardiography have resulted in an increasing use of this technology in patients with a fever, positive blood cultures, and a possible diagnosis of endocarditis. This is even more relevant in patient groups at a higher risk for IE—for example, those with congenital or acquired heart disease, before and after cardiac surgery, immunocompromised patients, or patients with indwelling catheters.

The increasing importance of echocardiography has been demonstrated in its role as a major element in the revised Duke criteria (12). To avoid abuse of echocardiography as a screening tool, it is necessary to employ rigorous diagnostic criteria to determine which cases might benefit from this technology. This includes a skilled clinical evaluation and a diagnostic algorithm that incorporates a history and microbiological results (9).

In adult patients there is a definite advantage of TEE to provide better visualization of the shape and size of a vegetation, as well as the surrounding tissues, severity of valvar regurgitation, and associated hemodynamics (13,14). One group (15) studied 113 adult patients with 115 episodes of IE with the initial classification being based on TTE findings. The patients were subsequently reclassified by use of their TEE results. Five patients went from “rejected” to “possible” IE and 21 cases from a “possible” to “definite” diagnosis of IE. In consideration of these findings, the investigators (15) suggested TEE as the initial diagnostic test only for patients with “possible infective endocarditis,” suspected complicated IE (i.e., paravalvular abscess), and those with suspected prosthetic valve involvement. All other patients were believed to need only a TTE as the initial diagnostic test.

However, applying these criteria to infants, toddlers, and even adolescents is more difficult, as TEE usually requires general anesthesia with endotracheal intubation and ventilation of the patient. The essential question therefore is: “what is the difference between TTE and TEE as a diagnostic aid in the pediatric patient?”

Timing of the procedure is also of considerable consequence. Small vegetations might not be detected during the first (e.g., transthoracic) study. Serial investigations, even transesophageal, should be performed if there is any doubt. Our data indicate a very good agreement in the diagnosis or exclusion of vegetations for both TTE compared to TEE in children. The disagreement in vegetation detection in the one case was clearly due to a poor ultrasound window in an older patient who had a complex intracardiac tunnel.

Abscess formation, especially in the area of the aortic root, might be difficult to assess, which was evident in one case with root involvement. Although a recent case report by Shah et al. (16) reported detection of abscess formation in a 14-year-old, it is clear that not enough data are available in the pediatric age group to draw any conclusions. Although this was not studied in our series, limitations for prosthetic valves in pediatrics are most likely similar to adults, with a higher positive yield from TEE (17–19).

It has been suggested that a more extensive use of echocardiography as a diagnostic tool may be indicated, particularly as patients are frequently pretreated with antibiotics, resulting in negative blood cultures (20).

De Castro et al. (21) recently reported a low diagnostic sensitivity in the detection of valvular perforations (aortic and mitral valve) in adults with TTE. To improve the quality of TTE, tissue Doppler imaging might be another option in detecting small masses, as shown recently in adult patients (22). Besides the potential side effects of anesthesia, TEE has additional risk factors, even when performed in a controlled setting. The potential risk of airway compression in the very small infant (23), vascular compression, damage of the teeth and oral cavity, as well as esophageal and gastric mucosa have been reported (23,24).

**Study limitations.** This was not a population-based study, and it remains unclear whether the preselection of the patients had an influence on the actual results. The sample size was relatively small, and the study was retrospective in nature. This study was performed over several years, so is also prone to the limitations of changing transducer technology. As there were only nine cases with surgical confirmation of the echocardiographic observations, this may artificially inflate the sensitivity of TEE in the detection of cardiac findings supportive of endocarditis. Because of this it was not possible in this study to determine the specificity of either TTE or TEE in the detection of cardiac involvement.

**Conclusions.** This study demonstrates that TTE in conjunction with the Duke criteria is a valuable tool in pediatric cases for confirming or excluding supportive evidence of bacterial endocarditis. If a vegetation was identified on TTE, then little additional benefit was seen from a TEE study. Transesophageal echocardiography should be reserved for those cases in whom an adequate transthoracic study cannot be performed, or with a microorganism that has a high association with aortic root abscess.

**Table 1. Additional Benefits of TEE Over TTE**

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<th>TTE</th>
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AI = aortic regurgitation; MR = mitral regurgitation; PI = pulmonary regurgitation; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.
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REFERENCES