Diagnosing a Patent Foramen Ovale in Children
Is Transesophageal Echocardiography Necessary?

Zakariya Hubail, MD; Matthew Lemler, MD; Claudio Ramaciotti, MD; Jay Moore, RDCS; Catherine Ikemba, MD

Background and Purpose—Transesophageal echocardiography (TEE) is the gold standard for the diagnosis of a patent foramen ovale in adults. In children, acoustic windows on transthoracic echocardiography (TTE) are better than in adults; thus, an invasive TEE may not be necessary. Our goal was to assess the validity of TTE with agitated saline injection for the diagnosis of a patent foramen ovale in children using TEE as the gold standard.

Methods—Fifty consecutive pediatric patients >1 year of age referred for TEE were prospectively enrolled. Imaging included 2-dimensional, color Doppler, and agitated saline contrast injections with and without Valsalva by TTE followed by TEE. Interpreters of the TTE were blinded to TEE results. Studies were categorized as “inconclusive” if the TTE images were inadequate for definitive diagnosis by the blinded interpreter.

Results—TTE results were considered conclusive in 43 of 50 (86%) patients. Among the 43 conclusive studies, the 2 modalities disagreed in 1 patient. TTE had a positive predictive value of 100%, negative predictive value 97%, sensitivity of 88%, and specificity of 100% for detecting a patent foramen ovale.

Conclusions—TTE with agitated saline injection is diagnostic for the assessment of atrial septal integrity in the majority of children. (Stroke. 2011;42:98-101.)

Key Words: contrast ■ echocardiography ■ foramen ovale ■ patent ■ pediatrics

A probe patent foramen ovale (PFO), often considered a normal variant, is present in at least 1 in 4 patients on autopsy studies.1–3 The prevalence of detectible PFO in children, however, is unknown and likely decreases with age.3,4 Recently PFOs have been implicated in the pathogenesis of both cryptogenic stroke and migraine headache.5–14 Younger adult patients with cryptogenic stroke are more likely to have a PFO than patients with other types of stroke.5,10,15–18 PFOs are associated with migraine headaches and migraine headaches appear to be an independent risk factor for stroke.2,8,19–21 Closure of PFO is associated with improvement or resolution of migraine symptoms in many patients.22,23 Recent population-based studies, however, report that PFO does not seem to be an independent risk factor for stroke in the general population nor do PFOs appear to be associated with migraine headache in a multiethnic, elderly, population-based cohort.24–26 In children with sickle cell disease, an intracardiac shunt is likely a risk factor for stroke.27 The contribution of an isolated PFO to the risk of paradoxical embolus in children, however, remains controversial.14,28,29 To clarify the role of a PFO in pediatric cases of stroke and migraine, it becomes imperative to develop a strategy to diagnose a PFO in pediatric patients. A retrospective study of 18 pediatric patients with an unexplained ischemic cerebrovascular event suggests that the noninvasive transcranial Doppler should be used; however, transcranial Doppler offers only indirect proof of an intracardiac shunt and does not distinguish from other shunts such as intrapulmonary.14 In adults, transesophageal echocardiography (TEE) is considered the gold standard for diagnosing a PFO.1,30–40 Published guidelines recommend echocardiography to identify the presence of a potential right to left shunt in children but does not specify transesophageal versus transthoracic (TEE).35,41 Transthoracic acoustic windows in adult patients often lead to images of such poor quality that studies are considered to be inconclusive. Transthoracic acoustic windows in children, however, are typically better than in adults. Furthermore, using a contrast medium such as agitated saline, an adequate Valsalva maneuver as well as harmonic imaging improves the ability to diagnose intra- and extracardiac shunting.30,33,38,39,40,42,43 Injecting agitated saline into a systemic vein creates microcavitations that appear echobright on the right side of the heart but are filtered by the lung capillary bed. Thus, the echobright contrast does not reach the left side of the heart unless a right to left shunt is present (Figure 1). It is our hypothesis that a TEE is not always necessary in the pediatric population when a transthoracic study is complemented with agitated saline injection and a Valsalva maneuver. The objective of this study was to determine the sensitivity, specificity, and positive and negative predictive

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values of TTE with agitated saline injection for the diagnosis of a PFO in pediatric patients using TEE as the gold standard.

**Methods**

From August 2005 to September 2006, we prospectively evaluated 50 consecutive pediatric patients referred for TEE regardless of the reason for referral. Patients with a known atrial septal defect, single ventricle physiology, or age <1 year were excluded. The study protocol was reviewed and approved by the Institutional Review Board. After informed consent, TTE was performed before TEE. Studies were performed using commercially available echocardiography machines (Acuson Sequoia C512; Siemens Medical Solutions). Transducer type was chosen to obtain the optimal balance between spatial resolution (higher frequency) and penetration (lower frequency) using anywhere from 3- to 8-MHz transthoracic probes. Harmonics were used if the quality of the images was improved by this modality. Two-dimensional and color Doppler images were obtained from subcostal, apical, and parasternal views on TTE. If no interatrial communication was detected, a contrast study was performed with a 5-mL agitated saline injection in patients >20 kg and 10 mL in larger patients. If no shunt was detected, the agitated saline injection was repeated with a Valsalva maneuver in cooperative patients. In anesthetized patients, a Valsalva maneuver was simulated with a positive pressure ventilation breath hold. Studies were categorized as positive, negative, or inconclusive. A positive study was defined as shunting noted by color Doppler across the foramen ovale or the presence of echobright microcavitations in the left atrium within 3 heartbeats after agitated saline reached the right atrium as shown in Figure 1. A negative study was defined as no shunting across the atrial level by color Doppler and no echobright microcavitations on the left side of the heart after agitated saline injections. Studies were defined as inconclusive if (1) the TTE and color Doppler images were of such poor quality that any question could be raised and an irrefutable, definitive diagnosis could not be reached by the blinded interpreter; or (2) if complete opacification of the right atrium could not be achieved with agitated saline injection. TEE was subsequently performed obtaining 2-dimensional, color Doppler, and, if required, agitated saline injections with and without Valsalva using the TE-V7M probe in patients less than 20 kg and the TE-V5Ms probe in larger patients. The nonparametric, Wilcoxon/Kruskal-Wallis test was used to assess for significant differences between means.

**Results**

Characteristics of the study population are detailed in Table 1. The prevalence of PFO in our nonrandom study population referred for TEE was 20%. None of the study patients demonstrated an atrial septal aneurysm.

TEE was ordered in 40 patients as part of their intraoperative evaluation during cardiac surgery. Two studies were ordered due to suspicion of endocarditis. One study was performed before electric cardioversion in a patient with atrial flutter. One was performed due to a history of stroke. The remaining 6 TEE studies were ordered due to poor acoustic windows on transthoracic studies in the following patients: an obese patient with chest pain; an obese patient with pulmonary valve stenosis and obstructive sleep apnea; a patient with a ventricular septal defect in which intracardiac thrombus was suspected; a patient with a mechanical aortic valve to rule out thrombosis; a patient with a history of syncope and a family history of cardiac tumor; and a patient suspected to have an atrial septal defect.

Studies were considered “conclusive” for the diagnosis of an interatrial communication in 43 of 50 (86%) patients (Figure 2). Comparing the 7 “inconclusive studies” with the 43 conclusive studies, the median body mass index of the “inconclusive studies” was larger than the conclusive studies; however, the age and weight were not significantly different (Table 2). Among the 43 conclusive studies, the 2 modalities disagreed in 1 patient (Figure 2). The 1 false-negative TTE occurred in a 16-year-old, 67-kg boy. PFO was noted by TEE by both color and contrast imaging and confirmed on surgical inspection. Among the 8 conclusive studies with a PFO, 4 were noted by color Doppler and 4 required agitated saline for detection on the TTE. Overall, TTE with agitated saline as a contrast agent has a positive predictive value of 100%, negative predictive value of 97%, sensitivity of 88%, and specificity of 100% for detecting a PFO.

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>34 male, 16 female</td>
</tr>
<tr>
<td>Age</td>
<td>9.5 years (1.2–18.6)</td>
</tr>
<tr>
<td>Weight</td>
<td>33.5 kg (8–150)</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.12 m² (0.39–2.62)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>18 kg/m² (13–55)</td>
</tr>
</tbody>
</table>

Patient characteristics are reported as medians with (ranges).

![Figure 1. Positive bubble study. Subcostal long-axis view with echobright agitated saline noted in the left atrium and left ventricle.](Image)

![Figure 2. Echocardiographic results. Among the 43 conclusive TTE studies, there was 1 false-negative using TEE as the gold standard.](Image)
Table 2. Characteristics of Inconclusive Versus Conclusive Studies

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight</th>
<th>Body Mass Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inconclusive</td>
<td>10.5 years</td>
<td>56 kg</td>
</tr>
<tr>
<td>(6.8–16.7)</td>
<td>(23–150)</td>
<td>(14–55)</td>
</tr>
<tr>
<td>Conclusive</td>
<td>9.4 years</td>
<td>40 kg</td>
</tr>
<tr>
<td>(1.2–18.6)</td>
<td>(8–109)</td>
<td>(13–27)</td>
</tr>
</tbody>
</table>

Patient characteristics are reported as medians with (ranges).

Interobserver variability was performed in 10 randomly selected patients. Three had a PFO confirmed by TEE. Five did not have an interatrial communication. Two TTEs were considered “inconclusive” by both observers. There was 100% agreement in the overall conclusion of the TTE. There was 100% agreement on the transesophageal interpretations.

There were no adverse events related to the use of agitated saline, Valsalva maneuver, nor TEE.

Discussion

Due to the recent interest and awareness of the importance of PFO in young patients with stroke and migraine, and the ability to close interatrial communications with less invasive catheter-based technology, it has become critical to define the presence of a shunt at the atrial level. Our results indicate that in many children, unlike adults, a TTE with contrast may confirm or exclude the presence of an interatrial communication without the need for a TEE. A reliable diagnosis of a PFO by TTE offers significant advantages in pediatric patients, because it is less expensive, less invasive, and can often be performed without sedation. In addition, avoidance of a TEE in pediatric patients and the related general anesthesia allows more reliable clinical observation of a patient with stroke, whose neurological examination is important to follow.

TEE is considered the gold standard for diagnosis of PFO in adults. However, recent publications have called for more judicious use of TEE in adult patients with stroke and, similar to our conclusions, suggest that TTE with contrast should be used as a screening test before TEE.31,44 Furthermore, 1 study involving only adult patients suggests that TTE with agitated saline is superior to TEE except in patients with an unfavorable body habitus.33

At our institution, all TTEs are performed with the assistance of an anesthesiologist. The charge for a typical TTE at our institution at the time of this study was $3251. The charge for TEE was $6829 with an additional $1200 for anesthesia. Using TEE as the first study in 50 patients, including anesthesia, the charge would be $401 450. Using our recommendations, performing the transthoracic study in these 50 patients, followed by 7 TTEs in the inconclusive patients, the charge would be $218 750, which is a savings of $182 700. Using TEE as the first study in 50 patients, including anesthesia, the charge would be $401 450. Using our recommendation without the need for a TEE. A reliable diagnosis of a PFO offers significant advantages in pediatric patients, because it is less expensive, less invasive, and can often be performed without sedation. In addition, avoidance of a TEE in pediatric patients and the related general anesthesia allows more reliable clinical observation of a patient with stroke, whose neurological examination is important to follow.

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The addition of agitated saline to the TTE improved detection of PFO by 50% in our pediatric study population, which is similar to the addition of agitated saline to adult TEE studies.33 There are a variety of techniques that can be used to detect a PFO. A routine echocardiogram is likely to miss a probe patent PFO diagnosed on autopsy or surgical inspection leading to a discrepancy in the prevalence of PFO depending on diagnostic modality and technique.3,11,14,33,40,45 Furthermore, many adult echocardiographic studies do not use subcostal views that provide a better angle for assessing atrial septal integrity, particularly with color Doppler. Using subcostal views, agitated saline contrast, and a Valsalva maneuver is imperative to maximize detection of PFO with TTE in children.

There was considerable overlap between the conclusive and inconclusive studies in our cohort in terms of age and size; thus, a particular “cutoff” above which TEE is necessary could not be elucidated. It appears that the individual quality of acoustic windows is more important that a particular size or age. Thus, we advocate the use of TTE with agitated saline before TEE in the pediatric patient. If the TTE is not conclusive, one should proceed to TEE. According to our study, >85% of TTEs can be avoided.

Our study was limited by the fact that it was not a random sample population. The majority of studies was performed before cardiac surgery. The remainder of the studies was in patients for whom the transthoracic studies were unable to answer a particular question. Thus, our study population potentially contained children with more difficult acoustic windows than the general population. We would expect a smaller number of TEEs to be required if this approach is applied to a general pediatric patient population. In addition, due to the small size of population studied, a weight or body mass index that could be defined as having lower specificity and sensitivity to detect a PFO could not be determined. Further studies are needed to better characterize this issue.

Our study indicates that in many pediatric patients, TTE with agitated saline is adequate to detect the presence of an interatrial communication (88% sensitivity) as well as to define atrial septal integrity (97% negative predictive value for PFO detection). We propose that a less invasive TTE should be the first step in the evaluation of the atrial septum in pediatric patients and agitated saline is an important component of this study.

Disclosures

None.

References


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