Transmitral Doppler: A New Transthoracic Contrast Method for Patent Foramen Ovale Detection and Quantification

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OBJECTIVES
This study compared a new transthoracic echocardiographic (TTE) method for detection of right to left bubble passage, transmitral Doppler (TMD), against two-dimensional (2D) TTE contrast study and the gold standard, of transesophageal echocardiography (TEE), and assessed its utility in quantitative assessment of patent foramen ovales (PFO).

BACKGROUND
Current TTE methods are relatively insensitive in PFO detection and do not allow quantitative assessment of right to left shunt.

METHODS
In 44 patients (59 years, range 34 to 76 years) saline contrast and color Doppler studies were performed in three conditions—TTE TMD, TTE 2D and TEE. Bubble transit on the TMD was measured semiquantitatively by a visual bubble score and objectively by integrating the acoustic power within the mitral velocity envelope.

RESULTS
By TEE it was determined that 17 patients (39%) had PFOs; 16 had right to left contrast passage, and only 1 had left to right flow by color Doppler. Against TEE contrast study, the sensitivity of TMD and 2D contrast studies were 100% and 75%, respectively, with specificity of 96% and 100%. Greater than 10 bubbles on a single beat of the resting contrast TMD identified patients with a maximum resting TEE PFO opening diameter >2 mm with 78% sensitivity and 100% specificity. There was a strong correlation (r² = 0.72, p < 0.01) between the TMD acoustic power and PFO opening diameter.

CONCLUSIONS
Transmitral Doppler is a sensitive and specific method for TTE PFO detection that allows quantification of right to left bubble passage and may obviate the need for TEE in many patients after stroke. (J Am Coll Cardiol 2000;36:1959–66) © 2000 by the American College of Cardiology

Paradoxical embolism from right to left passage of material through a patent foramen ovale (PFO) is a potentially correctable cause of stroke. Several studies have demonstrated that a PFO is a risk factor for stroke (1–4), and recent studies have found that transesophageal echocardiography (TEE) measures of PFO opening diameter and right to left bubble passage with saline contrast study are positively correlated with stroke risk (5–8), potentially allowing better risk stratification of patients with PFO. Currently, the echocardiographic assessment of PFOs often requires TEE because of the reported poor sensitivity of two-dimensional (2D) transthoracic echocardiography (TTE) for detection of PFO (9–11) and the lack of any validated TTE echocardiographic method for quantifying right to left bubble passage through the PFO.

Detection of bubble signals from the transmitral Doppler (TMD) velocity profile is a new and potentially superior approach for detecting right to left bubble passage by TTE. Doppler is specific for moving objects, and, because bubbles are much brighter than the blood cells they travel with, they can easily be detected as high intensity transient signals in the Doppler flow profile. This approach, analogous to the well-validated transcranial Doppler (TCD) method for bubble detection (12–17), may facilitate both detection and quantification of bubble passage.

The first aim of this study was to compare the sensitivity and specificity of PFO detection by transthoracic TMD saline contrast study and standard 2D TTE contrast study against TEE as a gold standard. The second aim was to assess the utility of transthoracic TMD to quantitate right to left bubble passage across PFOs.

METHODS

Study population. In a predetermined random fashion, consecutive patients referred for elective TEE on one day of each week over a seven month period were screened for study inclusion. Patients were excluded if they had a known atrial septal defect or if they were unable or unwilling to provide informed consent. The study was approved by the hospital’s institutional review board.

Design. Each patient underwent transthoracic TMD and 2D agitated saline contrast studies followed within 30 min by TEE 2D, color Doppler and saline contrast studies. In each condition the saline contrast study was performed first without (rest study) and then with a maneuver (Valsalva for TTE studies and release of abdominal compression for TEE) to provoke right to left shunt.
TTE. Patients were studied supine in the partial left lateral position using one echocardiographic machine (Agilent Technology Sonos 5500, S4 transducer, Andover, Massachusetts). For all saline contrast studies 10 ml of saline was agitated with 0.2 ml of air between two 10 ml syringes mounted on a three-way stopcock and injected rapidly through a 20G cannula in the right antecubital vein. The patients were tutored in the performance of the Valsalva maneuver and had several trial performances to maximize maneuver intensity and timing. The maneuver was continued for 5 s, and release was coordinated with opacification of the right atrium (RA).

TMD. The TMD recording is obtained in the apical four-chamber view insonating at 1.8 MHz. The pulsed-wave sample width was 5.2 mm at 10 cm based on the half-maximum power. The sample volume was positioned at the mitral leaflet tips. Sweep speed was set at 100 cm/s. The Doppler gain and transmit power were reduced to very low levels until there were no bright signals in the baseline mitral inflow velocity profile to facilitate detection of superimposed high intensity bubble signals. To facilitate detection of bubble appearance in the RA and, therefore, maneuver timing, a screen format was used allowing visualization and update of a 2D image on every beat. The TMD waveform was taped continuously during each saline contrast study. A preinjection baseline and the first five beats after appearance of contrast in the RA (resting study) or after Valsalva release were captured digitally to optical disc and also recorded on videotape.

2D transthoracic study. Two-dimensional imaging was performed with gains and dynamic range optimized for bubble detection. In 65% harmonic, fusion imaging was used. The apical (typically the apical four-chamber view) or subcostal window, which best visualized the left ventricular cavity, was used for the contrast study. The interatrial septum was also interrogated using color Doppler with the color scale reduced to maximize detection of low velocity flow across the interatrial septum. Where a PFO was seen, the plane in which the separation of septum primum and septum secundum was best seen was imaged for at least 10 cardiac cycles, and the maximum separation of the limiting orifice was measured (Fig. 1) (7). Two saline contrast studies were performed—the first at rest and the second with release of 5 s of abdominal compression upon complete RA opacification.

ANALYSIS

PFO detection. The 2D TTE and TMD studies for each patient were transferred to separate videotapes and scored independently as positive or negative for early contrast passage by a reader blinded to the TEE results. The same procedure was repeated by a second reader.

A 2D TTE or TEE contrast study was considered positive for a PFO if at least 1 microbubble was seen in the left atrium (LA) or left ventricle within three beats of RA opacification (rest study) or maneuver release (Valsalva or abdominal compression). A TMD study was considered positive if at least one high intensity transient signal was observed on the velocity envelope of the mitral inflow signal within three beats of RA opacification or maneuver release. Signals occurring in the first half of the E or A wave up slopes were not considered positive because it is common to observe baseline high intensity signals related to rapid valve movement within the sample volume. These potential sources of false positive results could be readily identified by comparison with the patient’s preinjection profiles. Color Doppler studies were considered positive if color flow was identified traversing the region of the interatrial septum at the level of the foramen ovale.

The aggregate of TEE saline contrast study and color
Doppler study was considered the gold standard for PFO detection.

**Correlation of TMD bubble passage recording with PFO opening diameter by TEE.** To examine the correlation between TMD bubble passage and TEE PFO diameter in the patients with TEE proven PFOs, the TMD profiles for the first five beats after RA opacification on the resting study were examined. The beat with greatest contrast-related signal augmentation was used for analysis. Where there was no obvious amplification, the third beat was used. Data were analyzed in two ways. First by a visual semiquantitative scale similar to that reported for TCD analysis (8) and, second, by measuring the returned Doppler signal power for each condition. One reader blinded to the TEE results performed both analyses. A second reader, also blinded to TEE results, analyzed 20 randomly selected profiles to assess interobserver variability.

**TMD bubble score.** The maximal mitral inflow Doppler profile was scored on a 0 to 4 scale: 0 = no bubbles, 1 = 1–5 bubbles, 2 = 6–10 bubbles, 3 = >10 bubbles but less than envelope saturation and 4 = envelope saturation. Representative examples of each score are shown in Figure 2.

**Integrated signal power (Fig. 3).** Digitally recorded Doppler video display intensities, nonlinearly compressed, were reconverted to their original uncompressed acoustic amplitudes and power (amplitude squared) based on the acquisition compress and reject settings (18,19). For laminar flows the power of the Doppler signal is linearly proportional to the number of backscatterers passing through the sample volume (20). The strength of the power signal is proportional to the backscattering coefficient relating backscattered power to the volume of scatterers returning signals. Since this is far higher for microbubbles than it is for blood, the power within the mitral signal will be dominated by the backscatterer from microbubbles passing through the mitral valve and, therefore, has the potential to provide a rough measure of their number. To achieve this the velocity envelope of the mitral inflow was defined by tracing around the profile. This allowed signals outside the velocity envelope to be excluded. We also excluded signals arising from the valve, opening and closing transients identified from baseline beats before contrast injection. The power was then integrated over time to give the power-time integral (PTI) per beat using MATLAB software (Version 5.1, Mathworks, Natick, Massachusetts). To correct for variation in absolute signal strength between patients, the data were normalized by calculating the ratio of PTI with bubble passage to the

![Figure 2. Representative examples of transmitral Doppler bubble scores from 1 to 4 are shown.](image)
Figure 3. The method of transmitral Doppler (TMD) signal power analysis. Two TMD velocity profiles are shown. (Left panel): Immediately before contrast injection (baseline), (right panel): three beats after RA opacification. Individual bubble signals are indicated by the arrows in the postcontrast profile. An envelope was traced around each TMD profile (illustrated for the baseline profile) allowing exclusion of the valve opening signal present at baseline. The distribution of signal power within the envelope for each profile is plotted in the lower panels. Note that single bubbles in the TMD envelopes correspond to spikes in the power display. The signal power within each envelope was then integrated to give the power time integral (PTI). The postcontrast PTI is normalized by dividing by the baseline power. In this patient the normalized power is 6.
preinjection baseline PTI for the same patient. This provides an empirical adjustment for ultrasound attenuation, which equally affects sound travelling and returns from both blood and bubbles at the same sample volume.

**Interobserver variability.** A second observer blinded to TEE or 2D results independently scored all TMD studies for presence or absence of early bubble passage and scored 20 randomly chosen positive TMD profiles using the visual bubble score and signal power analysis.

**Biostatistical analysis.** Continuous data were presented as the mean value ± standard deviation. Comparisons between the two groups were made in qualitative data using Fisher exact test. Sensitivity and specificity were calculated for the test performance. Percentage agreement was used to assess the interobserver variability for PFO detection and visual bubble scores. For PTI interobserver variability the mean percentage difference score ± standard deviation are reported. Simple regression analysis was used to assess the correlation between continuous data and Kendall rank correlation for ordinal data. A p value <0.05 was considered significant. Statistical analysis was performed with GB-Stat (Mac version 6.5 (Dynamics Microsystems, Silver Springs, Maryland).

**RESULTS**

Forty-four patients were studied—27 men and 17 women of mean age 59 (range 34 years to 76 years). The reason for referral for TEE was to assess for a cardiac source of embolism (n = 23) and, in patient 21, for other reasons.

**PFO detection.** A PFO was detected by TEE in 17 patients (39%) (Table 1). In 16 patients this was positive by contrast study and in 1 patient it was positive by only color Doppler, which demonstrated left to right shunt. Transthoracic TMD contrast study was concordant with TEE in all but two patients, with a sensitivity of 94% and a specificity of 96%. One patient with severe left ventricular hypertrophy was negative on TEE but positive on TMD. In this patient the TMD study was negative at rest and positive after Valsalva, while the 2D image quality was poor, precluding bubble detection by 2D TTE. The other discordant patient had negative TEE and TTE contrast studies with left to right shunt by TEE and TTE color Doppler. The sensitivity of TMD for the detection of right to left shunt, which is evidence of a potential pathway for paradoxical embolism, was 100% with specificity of 96%.

Transsthoracic 2D contrast study alone was positive in 12 of the 17 (71%) patients positive on TEE, with a specificity of 100%. For the detection of right to left shunt, the sensitivity of TEE 2D contrast was 75% (12 of 16 patients). **Transsthoracic TMD versus TTE.** Transmitral Doppler detected four PFOs not detected by 2D TTE and was also positive for one patient who was negative on both TEE (discussed earlier) and 2D TTE. These five patients all had poor quality 2D TTE images. Even in these patients good quality mitral inflow profiles were obtained, and individual bubble signals were readily detected with contrast study. Transmitral Doppler also detected right to left bubble passage at rest more frequently than 2D TTE (13 and 9, respectively). All 13 patients positive at rest on TMD had resting positive contrast studies on TEE.

**Role of maneuvers to increase RA pressure.** As seen in Table 1, the Valsalva maneuver (for TTE) and abdominal compression (for TEE) resulted in improved detection of PFO by contrast for all modalities. Compared with the TEE gold standard, for 2D TTE, the addition of the Valsalva maneuver increased the sensitivity from 53% for resting contrast study to 71%. Likewise, the sensitivity of transthoracic TMD increased from 76% to 94%, and for TEE contrast, it increased from 82% to 94%.

**Relationship between measures of bubble passage and PFO opening diameter by TEE.** The mean maximum resting PFO opening diameter at TEE in 17 patients was 2.2 mm (range 0 to 4.3 mm). There was a significant positive correlation between this opening diameter and both resting TMD bubble score (Kendall’s tau = 0.71, p < 0.01; Fig. 4) and normalized power ($r^2 = 0.72$, p < 0.01) (Fig 5).

A TMD bubble score $>2$ was a good predictor of an opening diameter $>2$ mm ($p < 0.01$; Table 2). A PFO diameter cutoff of 2 mm has previously been reported to dichotomize PFOs into those that are small and larger ones that confer increased risk for embolic stroke (7). In this small group of patients, all seven patients with bubble scores of 3 or 4 had PFO diameters $>2$ mm. A TMD bubble score

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**Table 1.** PFO Detection by Three Echocardiographic Methods

<table>
<thead>
<tr>
<th></th>
<th>n = 44</th>
<th>TTE</th>
<th>TMD</th>
<th>TEE</th>
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<tr>
<td>Color Doppler*</td>
<td>6</td>
<td>6</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Contrast*</td>
<td>9</td>
<td>13</td>
<td>14</td>
<td></td>
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<tr>
<td>Maneuver</td>
<td>12</td>
<td>17</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Contrast or Doppler*</td>
<td>13</td>
<td>18</td>
<td>17</td>
<td></td>
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</table>

TTE = transesophageal echocardiography; TMD = transmitral Doppler; TEE = transthoracic echocardiography.

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**Figure 4.** The relationship between resting transthoracic transmitral Doppler bubble score and transesophageal echocardiography (TEE) measured maximum resting patent foramen ovale (PFO) opening diameter. A good correlation is noted (Kendall’s tau = 0.71). TTE = transthoracic echocardiography.
Transthoracic TMD versus transthoracic 2D contrast. The sensitivity of TMD contrast study for PFO detection was 94% compared with 71% by TTE 2D contrast study. This improved sensitivity occurred due to improved bubble detection for patients with suboptimal 2D windows. In these cases, despite significant acoustic speckling and image dropout that precluded bubble detection, it was possible to obtain good quality mitral inflow Doppler signals in which individual bubble signals could readily be distinguished. Recently, incremental value of second harmonic imaging has been shown over standard fundamental frequency for TTE 2D detection of bubbles in the left heart (21). In this study second harmonic fusion imaging was used in 65% of the 2D studies. Specifically, it was not used in two of the four patients who were negative on 2D TTE and positive on TEE, raising the possibility that a small increase in sensitivity might occur if it were used routinely.

Transthoracic TMD contrast versus TEE detection. The one patient missed by TMD study was also negative on TEE contrast study. The patient had severe mitral regurgitation with left to right flow across a PFO by color Doppler on both TEE and TTE imaging. Of course, the reason for doing a contrast study is not to identify left to right shunt but rather to look for right to left shunt as a potential pathway for paradoxical embolus. For this the sensitivity of TMD was 100%.

The specificity of TMD contrast compared with TEE was 96%. One patient was negative on TEE but positive on TMD after the Valsalva maneuver, but not at rest. This patient had severe left ventricular hypertrophy suggestive of high LA pressure, which would tend to keep the PFO closed at rest. It is likely that only the strong Valsalva maneuver possible in an alert patient could reverse the atrial pressure gradient sufficiently to allow right to left bubble passage. The failure to detect bubble passage by TEE may reflect the less vigorous maneuvers possible in a sedated patient.

These results were obtained in a group with a wide range of transthoracic image quality. Interobserver concordance on the presence or absence of early saline contrast passage was 100%, indicating that this is a very reliable test for the detection of saline contrast passage.

Transthoracic quantification of bubble passage. There are no currently accepted methods of quantifying bubble passage by TTE because of the wide range of 2D image quality that precludes accurate bubble counting in many patients. The ability to reliably detect bubble signals by TMD provides an opportunity to objectively quantify bubble passage with TTE and, thus, indirectly assess the size of the right to left shunt across a PFO. In this study we observed significant correlations between two TMD measures of bubble passage (visual bubble score \( r^2 = 0.71 \) and normalized power-time integral \( r^2 = 0.72 \)) and PFO opening diameter measured at TEE. Both TMD measures of bubble passage were useful in categorizing patients according to PFO size. In this study a simple visual

**Transthoracic TMD versus transthoracic 2D contrast.**

<table>
<thead>
<tr>
<th>Bubble Score</th>
<th>≤2 mm</th>
<th>&gt;2 mm</th>
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<tbody>
<tr>
<td>TMD bubble score</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>&gt;2 mm</td>
<td>0</td>
<td>7</td>
</tr>
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</table>

**Table 2.** Prediction of PFO Opening Diameter by TMD

**DISCUSSION**

In this study we found that a new TTE method for detecting right to left bubble passage across a PFO, TMD contrast study, was superior to the standard TTE 2D contrast technique and at least as sensitive as TEE for detecting the right to left shunt that may predispose a patient to paradoxical embolism. In addition, measures of bubble passage by TMD correlated well with PFO opening diameter measured at TEE. These results indicate that TMD may be a viable transthoracic alternative to TEE assessment of PFOs.

**Figure 5.** The relationship between resting transthoracic transmitral Doppler (TMD) normalized power and transthoracic echocardiography (TEE) measured maximum resting patent foramen ovale (PFO) opening diameter. A good correlation is observed \( r^2 = 0.72 \) after log10 transformation.

>2 was 78% sensitive in identifying patients with an opening diameter >2 mm.

The relationship between opening diameter and normalized signal power demonstrated that, at PFO diameters >2 mm, a wide scatter exists in bubble passage as measured by normalized power (Fig. 5). Empirically plotting PFO opening diameter versus log (normalized power) gave a linear relationship \( r^2 = 0.72, p < 0.001 \).

**Interobserver variability.** There was 100% agreement between the two observers for presence or absence of bubble passage by TMD. There was 95% agreement for bubble scores with one discordant reading. This patient was allocated a score of 2 by one observer and a score of 3 by the second. A third independent reader gave this case a score of 3. For PTI measurement the mean percentage difference and standard deviation between the two observers was 2% ± 3.6%.

**Table 2.** Prediction of PFO Opening Diameter by TMD

<table>
<thead>
<tr>
<th>Bubble Score</th>
<th>n = 17</th>
<th>TEE PFO Size</th>
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<tr>
<td></td>
<td></td>
<td>≤2 mm</td>
</tr>
<tr>
<td>TMD bubble score</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>&gt;2 mm</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

PFO = patent foramen ovale; TEE = transesophageal echocardiography; TMD = transmitral Doppler.

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The specificity of TMD contrast compared with TEE was 96%. One patient was negative on TEE but positive on TMD after the Valsalva maneuver, but not at rest. This patient had severe left ventricular hypertrophy suggestive of high LA pressure, which would tend to keep the PFO closed at rest. It is likely that only the strong Valsalva maneuver possible in an alert patient could reverse the atrial pressure gradient sufficiently to allow right to left bubble passage. The failure to detect bubble passage by TEE may reflect the less vigorous maneuvers possible in a sedated patient.

These results were obtained in a group with a wide range of transthoracic image quality. Interobserver concordance on the presence or absence of early saline contrast passage was 100%, indicating that this is a very reliable test for the detection of saline contrast passage.

Transthoracic quantification of bubble passage. There are no currently accepted methods of quantifying bubble passage by TTE because of the wide range of 2D image quality that precludes accurate bubble counting in many patients. The ability to reliably detect bubble signals by TMD provides an opportunity to objectively quantify bubble passage with TTE and, thus, indirectly assess the size of the right to left shunt across a PFO. In this study we observed significant correlations between two TMD measures of bubble passage (visual bubble score \( r^2 = 0.71 \) and normalized power-time integral \( r^2 = 0.72 \)) and PFO opening diameter measured at TEE. Both TMD measures of bubble passage were useful in categorizing patients according to PFO size. In this study a simple visual
assessment of bubble score yielded similar results to the more time consuming quantitative method (integration of signal power). In routine clinical practice the more quantitative method may, therefore, offer little advantage. It would, however, lend itself better to automated echocardiographic machine bubble quantitation.

Patients with larger PFO opening diameters (≥2 mm) have been reported to be more likely to have embolic infarcts than those with small PFOs (7). In our patient sample a resting bubble score >2 was 78% sensitive and 100% specific for a resting PFO opening diameter >2 mm. The relationship between opening diameter and normalized signal power demonstrated that, at PFO diameters >2 mm, a wide scatter exists in bubble passage as measured by normalized power. This observation stresses that PFO diameter is not the only determinant of shunt. The volume of right to left shunt through a PFO depends on: 1) the shape and area of the orifice (incompletely captured by the diameter), 2) how this shape and area change over the cardiac cycle and 3) the instantaneous pressure difference between the left and right atria while the PFO is open. The observed shape of our normalized power versus PFO diameter curve may be explained if, as is likely, larger opening diameters are correlated with longer opening times and higher transatrial pressure gradients. Assuming roughly comparable bubble concentrations between patients, an estimate of bubble passage, because it is correlated with flow, may be superior to using the size of the PFO opening as a measure of right to left shunt size for stroke risk stratification. Quantitative correlation between transmural bubble score and TEE PFO diameter was studied at rest rather than with Valsalva maneuver because many patients were sedated for the TEE and were unable to reproduce a Valsalva maneuver equivalent to that while awake for the transthoracic study.

Other investigators have reported TEE methods of measuring bubble passage. They have either counted the number of bubbles seen in the LA (6) or the percentage area of the LA filled by bubbles (5). In these studies larger PFO size inferred from magnitude of bubble passage was a risk factor for cryptogenic stroke (5) and recurrent neurological events (6). An important limitation of TEE assessment of bubble passage is that the burst of bubbles traversing the PFO may be eccentrically directed and partly out of the imaging plane, leading to potential underestimation of shunt size. Furthermore, the patient must undergo TEE to obtain this information. Using TMD a measure of bubble passage can be obtained transthoracically, and, because the sample volume at the mitral leaflet tips is constant across patients, the bubble counts obtained may correlate better with absolute bubble passage.

Transcranial Doppler has been found in several studies to be a sensitive and specific noninvasive method for diagnosis of PFOs. Serena et al. (8) used TCD to semiquantitatively score degree of bubble passage in a similar way to the bubble score we used for TMD. In their study patients with cryptogenic cerebral vascular accident were more likely to have TCD evidence of larger shunts across a PFO than patients with stroke of recognized cause. The TMD method we used required only 0.2 ml of air to be agitated with 10 ml of saline, whereas studies reporting good sensitivity for PFO detection by TCD used 1 ml of air, potentially exposing patients to a greater risk of cerebral air embolism, especially when multiple injections are performed. It follows that a smaller bubble concentration would be required for PFO detection by TMD as sampling is closer to the PFO, allowing less time for bubble collapse, and the TMD sample volume width (5.2 mm) within which bubbles are detected is greater than that of an intracerebral artery. Because contrast is directly visualized entering the RA, release of the Valsalva can be optimally timed. This also allows ready differentiation between early (cardiac) and late (typically transpulmonary) shunts. Finally, TMD can be integrated into the standard echocardiographic examination for cardiac source of embolus, and information from the saline contrast study can be integrated with 2D and color Doppler examination of the interatrial septum to provide a more complete assessment than is possible by TCD.

Study limitations. The patients recruited for this study included a high percentage of patients in a tertiary referral hospital after CVA or transient ischemic attack whose physician suspected a possible cardiac source of embolus. This may explain the slightly higher than expected prevalence of PFO found in this study population compared with that expected in the general population (25% in older adults) (22). Further studies of TMD in a more general population would be desirable to confirm its sensitivity and specificity as a more general screening tool.

The primary purpose of this study was to assess the TMD contrast study for the transthoracic detection of right to left shunt. A secondary aim was to assess it as a method to obtain an improved transthoracic estimate of right to left bubble passage that can be applied routinely. It was not our purpose to measure shunt flow per se. A limitation of saline contrast that may limit its use in quantification of shunt size is that the backscattered signal power is dependent on bubble size, which, for agitated saline contrast, varies widely (24 to 144 μm) (12). There is, therefore, no simple relationship between returned signal power and bubble number.

This study was performed using a single echocardiographic machine, and the method has not been optimized using other systems. The estimates of bubble passage in this study are dependent on machine characteristics (sample volume size) and the saline contrast protocol used. Variation in these parameters would alter, respectively, the sample volume within which bubbles are detected and the RA bubble concentration with a resultant scaling of the number of bubbles detected. Use of this technique for bubble detection is dependent on optimal Doppler settings. In particular it is important to reduce the Doppler gain and transmit power to very low levels until there are no bright signals in the
baseline mitral inflow velocity profile to facilitate detection of superimposed higher intensity bubble signals.

We have reported a correlation between TMD measures and PFO diameter at rest. Given the dynamic opening of PFO with maneuvers that increase RA pressure and volume, it would be useful to study the same correlation with a maneuver. In this study this was not possible because many patients were well sedated for the TEE, and it was not possible to match maneuver intensity between the two tests.

Conclusions. Transmitial Doppler is a sensitive and specific method for transthoracic detection of PFOs that also allows quantitation of right to left bubble passage. The method is simple to perform and potentially easy to implement in routine clinical practice. It avoids the uncertainty of scrutinizing the 2D echocardiographic image for faint bubble passage among acoustic speckle and gains sensitivity because it is specifically looking for moving objects that are much brighter reflectors than the accompanying blood cells in the velocity flow stream. It, therefore, has potential as a useful adjunct to clinical echocardiographic practice as well as a technique for noninvasive population-based studies to better assess the prognostic significance of PFO shunts of variable size.

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REFERENCES