CLINICAL/ORIGINAL PAPERS

Transthoracic echocardiography using second harmonic imaging with Valsalva manoeuvre for the detection of right to left shunts

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Abstract

Aims To assess transthoracic echocardiography (TTE) using second harmonic imaging with Valsalva manoeuvre compared to transesophageal echocardiography (TEE) for the diagnosis of right to left cardiac and pulmonary shunts.

Methods and results One hundred and ten patients referred for TEE underwent TTE with bubble contrast. Bubbles in the left atrium within three cardiac cycles were considered diagnostic for a patent foramen ovale (PFO) and later as a pulmonary shunt. Greater than 20 bubbles in the left atrium was considered a large shunt and less than 20 a small shunt. TEE was performed immediately afterwards and read blinded to the TTE results. Pick-up rates were similar with 19 TEE positive (13 PFO) and 18 TTE positive (14 PFO) patients. There were five TEE positive/TTE negative cases who had significantly poorer TTE image quality score (2.7±0.8 vs 1.9±0.6, p<0.05). There were six TEE negative/TTE positive cases, two cases requiring Valsalva manoeuvre to become positive. The Valsalva manoeuvre significantly increased the number of bubbles shunting (10±11 vs 20±19, p<0.005).

Conclusion TTE with Valsalva manoeuvre is as good as TEE in diagnosing shunts. Valsalva manoeuvre increases the size of shunt. Both techniques produce false negative results.

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Introduction

Abnormalities in the interatrial septum and pulmonary vasculature may result in a right to left shunt. Abnormal pulmonary arteriovenous communications can lead to cerebral emboli, cerebral abscesses and unexplained hypoxaemia. Patent foramen ovale (PFO) is a common finding in the healthy population, with a prevalence of 27% in one autopsy study of 965 normal hearts and is the most common cardiac finding in young patients (<55 years of age) with an unexplained cerebrovascular event, presumably due to paradoxical emboli. Determining whether paradoxical embolism has occurred through a PFO ideally requires the ‘trip’ of the PFO, raised right atrial pressure and a venous source of thrombosis. The larger size of a PFO and greater number of microbubbles passing through a

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shunt during echocardiography has been associated with an increased incidence of cerebrovascular events. Transesophageal echocardiography (TEE) is considered the 'gold standard' technique for the diagnosis of right to left shunts, but sedation makes the performance of Valsalva manoeuvre difficult.

We investigated the ability of transthoracic echocardiography (TTE) using second harmonic imaging with Valsalva manoeuvre to detect right to left shunts compared to TEE in an unselected group of patients. We also assessed the effect of the Valsalva manoeuvre on shunt size as assessed by the number of agitated saline microbubbles crossing the left atrium.

**Methods**

**Patients**

The study population consisted of 110 consecutive patients (68 male, mean age 58.3 ± 16 years) referred for TEE. Reasons for referral were assessment of valvular heart disease (44%), embolic source (20%), aortic assessment (16%), endocarditis (15%), possible cardiac shunt (10%), pre-cardioversion (8%), intracardiac mass (4%) and pulmonary embolism (1%). All patients gave informed consent and the local ethics committee approved the protocol.

**Echocardiography**

TTE was performed immediately prior to TEE. All studies were performed using a Hewlett-Packard Sonos 5500, using a broad-band trans-thoracic transducer capable of second harmonic imaging (Hewlett-Packard S4 with 1.8/3.6 MHz). With harmonic imaging, ultrasound is transmitted at a fundamental frequency (1.8 MHz) and then echoes at the second harmonic frequency are selectively detected (3.6 MHz).

Routine images were obtained—parasternal long and short axis, apical four-chamber, apical two-chamber and subcostal views using harmonic imaging. Gain settings were adjusted to optimise visualisation of the myocardium, valvular structures and the interatrial septum. Colour flow Doppler was used to assess the interatrial septum in both subcostal and apical views. All images were recorded on S-VHS videotape for off-line analysis.

Continuous recording was obtained during bubble contrast injections with an apical four-chamber view. Following recordings during normal respiration, it was repeated during a Valsalva manoeuvre. This was produced by the patients blowing into a small calibre tube. If either testing with or without Valsalva manoeuvre was positive it was repeated a further two times to assess reproducibility. All TTE recordings were then reported retrospectively by another reader blinded to the result of the TEE.

TEE was performed using 10% topical lignocaine spray for the oropharynx and intravenous sedation (midazolam 3–10 mg). A Hewlett-Packard Sonos 5500 ultrasound machine with an omniplane 5 MHz transesophageal probe was used in all cases. Patients underwent a complete TEE study including colour flow Doppler of the interatrial septum. The TEE was performed in the left lateral decubitus position. Agitated saline contrast was injected during imaging in the four-chamber view at 0°. Additional injections with imaging in the 40°–60° plane and 110°–130° plane were performed as required in order to demonstrate clearly the interatrial septum. A Valsalva manoeuvre (abdominal straining) was performed as sedation was allowed with repeat injections. Again if during resting respiration or the Valsalva manoeuvre there was evidence of shunting, two further recordings were performed to assess reproducibility.

**Agitated saline bubble contrast**

Agitated saline contrast was produced by mixing 9 ml of saline with 1 ml of air in two 10 ml syringes connected by a three-way tap, 20 times. The mixture was injected rapidly via a cannula in the right antecubital fossa.

**Data analysis**

The TTE and TEE were analysed off-line by separate experienced observers. The observers of the TEE were blinded to the results of the TTE. An atrial shunt was diagnosed by the presence of at least three bubbles appearing in the left atrium occurring within the first three cardiac cycles following injection of the bubble contrast. Bubbles appearing after the first three cardiac cycles were classified as a pulmonary shunt.

Studies with inadequate bubble contrast were repeated during the recording of the study or excluded during reading of the study. Flow across the interatrial septum as demonstrated by colour flow Doppler was either present or absent. The number of bubbles in the left atrium were counted and categorised as either large (≥20 bubbles) or small (<20 bubbles). Large shunts have previously been shown by this categorisation to be associated with a significant risk of stroke compared to small shunts.
Image quality for both the TTE and TEE were graded semiquantitatively as:

1 = excellent: complete visualisation of interatrial septum, valves and endocardial borders;
2 = good: adequate visualisation of interatrial septum and valves but failure to detect ≤2 segments according to the segmentation of the American Society of Echocardiography;
3 = fair: hazy visualisation of the interatrial septum and valves but failure to detect >2 segments of endocardium according to the segmentation of the American Society of Echocardiography;
4 = poor: no clear visualisation of the interatrial septum, valves or endocardial borders.

Statistical analysis

All values are expressed as mean±SD. Between-group comparisons were made by Student t-test. The Wilcoxon paired test was used to compare differences in mean image quality. All tests were performed using a two-tailed distribution. Differences were considered significant at the p<0.05 level.

Results

Image quality

The distribution of TTE image quality as scored semiquantitatively was excellent 29.6%, good 51.7%, fair 16.7% and poor 5.6%, with a mean score for the 110 patients of 1.98±0.83. The TTE image quality for patients with a shunt was significantly worse than the TEE quality (2.13±0.74 vs 1.17±0.65, p<0.0005). In all positive cases reproducibility of demonstration of a shunt was 100%.

Detection of right to left shunts

An example of patients with evidence of atrial shunting is shown in Figs. 1 and 2. Of the 110 patients, 24 (21.8%) of patients showed evidence of a shunt using either imaging modality of which 16 (14.5%) showed evidence of an atrial shunting. The number of positive tests are shown in Table 1 and the breakdown of size and site in Table 2. A similar number of patients had a shunt demonstrated by TTE (n=18) as TEE (n=19). TTE and

Figure 1  TEE image at 113% showing intense contrast within the right atrium and evidence of a small PFO with four bubbles visible within the left atrium.
TEE colour flow Doppler demonstrated atrial shunts in three (all large shunts on bubble contrast) and seven (six large shunts on bubble contrast) patients, respectively.

An atrial shunt was demonstrated by TTE with bubble contrast during normal respiration in 11 and with Valsalva manoeuvre in 14 patients. Similar number of large and small shunts were detected by the two techniques (TTE: 10 large and eight small shunts; TEE: 10 large and nine small shunts). All pulmonary shunts were small with a mean number of bubbles $6.7\pm4.3$. Five cases were TEE negative/TTE positive, three at the atrial level of which two were only positive with a Valsalva manoeuvre. Six cases were TEE negative/TEE positive, two of which were at the atrial level.

When considering TEE as the ‘gold standard’, TTE with second harmonic imaging has a sensitivity of 68.4% and a specificity of 93.2% for any shunt. When considering purely for large shunts the sensitivity increased to 88.9% and specificity to 98.8%.

Shunt size increased using Valsalva in seven TTE studies, all of which were atrial shunts. There was no change in size with Valsalva manoeuvre with pulmonary shunting. The two patients who went from no shunt at rest to a small and large shunt with Valsalva manoeuvre were both negative on TEE testing. There was only one patient with a change in the TEE shunt size.

**Discussion**

Although PFO is increasingly becoming recognised as a cause for cryptogenic cerebrovascular events, there are other patients in whom documenting a right to left shunt is important. The presence of a large PFO has been associated with severe unexplained decompression sickness due to paradoxical gas embolism. Pulmonary arteriovenous malformations are frequently a manifestation of hereditary haemorrhagic telangiectasia. TTE with bubble contrast is generally considered the investigation of choice for right to left shunting and has

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been shown previously to be more sensitive than TTE.7–9 TTE with contrast has been reported to have a sensitivity of up to 80% compared to TEE.10 Recent advances in TTE including the development of second harmonic imaging have improved image quality and decreased the number of artefacts.

Unsurprisingly, the image quality was significantly better in the positive TEE studies compared to the TTE with a mean 1.17 (0.65) vs 2.13 (0.74) (p > 0.0005). However, 78.1% of TTE studies were still good or excellent. It should be noted that this was an unselected group of patients who had not been selected for the quality of their acoustic window.

We found evidence of a shunt in 21.8% and evidence of a PFO in 14.5% of patients. This is in line with the prevalence of PFO in both autopsy studies (27%)2 and TTE studies (10%).3 There were five TTE positive/TEE negative cases, three of which were PFO. Two of these three patients were negative with resting TTE but became positive with Valsalva manoeuvre. These patients may have been TEE negative due to the inability to perform a satisfactory Valsalva manoeuvre due to the necessary sedation. Six cases were TEE positive/TTE negative, one of which was a large shunt. This may be related to the quality of the images which were significantly poorer compared to those where TTE had demonstrated a shunt with mean score 2.67 (0.82) vs 1.94 (0.64) (p < 0.05). As one would expect the use of the Valsalva manoeuvre had no effect on the presence or size of pulmonary shunt.

The sensitivity and specificity for the detection of shunts with TTE compared to TEE is much better when considering large shunts only which are clinically more important. This again is probably related to image quality, with small shunts demonstrated on TEE not detected during TTE due to suboptimal acoustic windows.

Colour flow Doppler is poor at detecting atrial shunts compared to bubble contrast in both techniques but is unsurprisingly better during TEE than TTE. Although 100% specific for both techniques its sensitivity is only 21.4% for TTE and 53.8% for TEE when looking at PFOs.

The Valsalva manoeuvre increased the apparent size of shunts and can unmask PFOs not apparent with resting respiration. It is therefore vital during the assessment of cardiac shunts with bubble contrast.

### Study limitations and comparison to previous studies

For this study, agitated saline bubble contrast was injected into the antecubital vein. Femoral vein contrast injection has been shown to be more sensitive for PFO diagnosis and produce more intense left sided opacification.11 The amount of right to left contrast shunting has been shown to correlate with PFO diameter from balloon sizing, whereas by using antecubital injection there was no correlation.12 However, femoral vein cannulation is an invasive technique and was not considered for this study.

Kuhl et al.13 in their study looked at 111 patients with a cerebral event using a polygelatin contrast agent rather than agitated saline. In this selected group of patients the TTE was performed immediately following the TEE and hence the patient was still sedated, which may have limited their ability to perform a satisfactory Valsalva manoeuvre. Despite this they had similar results to ours with similar positive TTE and TEE for PFOs. Camp et al. in their study of 109 consecutive patients detected 24 patients (22%) with a shunt by both TTE and TEE, compared to 26% in our study. Again in this study the TEE was performed first which potentially could result in an unsatisfactory Valsalva manoeuvre. Ha et al.14 in their study of 136 consecutive stroke patients detected 40 patients with PFO. Interestingly they found the sensitivity and specificity of TTE with harmonic imaging to be 62.5 and 100%, respectively, when compared to TEE as the ‘gold standard’, with no TTE positive/TEE negative patients.
Conclusion

Both TEE and TTE have a similar yield for the detection of right to left shunts. False negatives occur with both techniques due to poor acoustic windows leading to poor transthoracic images, and a poor Valsalva manoeuvre due to sedation during TEE. Therefore these techniques are in fact complimentary. As well as unmasking a PFO, the Valsalva manoeuvre can increase the size of shunt across a PFO as categorised by the number of microbubbles passing into the left atrium. The Valsalva manoeuvre is therefore vital during the echocardiogram when assessing for a cardiac shunt. Colour flow Doppler, although if present is specific for the presence of a PFO has a low sensitivity, albeit better with TEE.

References
