STANDARDISATION OF ECHOCARDIOGRAPHIC PROCEDURE

Applicable to: All echocardiograms performed during the course of the trial where contrast valsalva bubble trial is required.

Background: Patent foramen ovale (PFO) may vary in both anatomical and functional size, and as such the clinical impact of a PFO may differ. Quantification of the volume of right to left shunting through a patent foramen ovale (PFO) has been attempted in prior studies, in part using a bubble counting mechanism, with classification schemes based on the absolute number of microbubbles seen in the left atrium after complete opacification of the right atrium. This technique, has not been completely validated with correlation to large anatomical studies, with 2-dimensional measurements on transesophageal echocardiography, or balloon sizing techniques of PFO size; and as such is not uniformly accepted as a “gold standard” for PFO sizing in the echocardiography community. Part of the differences in detection and sizing of PFO are due to inherent limitations in the technique.

Most literature reports on PFO closure, while often utilizing classification schemes that attempt to quantify the number of microbubbles crossing into the left atrium, have not utilized a core echocardiography lab to validate the method or its accuracy, leaving the validity of bubble counting as an accurate, reproducible, and correlative method potentially suspect. As such, significant differences can exist with regard to the exact frame and moment used for interpretation at a trial site versus at the core laboratory, potentially resulting in significant inter-observer variability.

The most recent example of this comes from a report published by Mas et al. In this trial of PFO and atrial septal aneurysm and the risk of cerebrovascular events, contrast echocardiograms were reviewed by multiple observers to validate microbubble count and thus presence of a PFO. In that trial there was significant intra-observer variability, with disagreement in PFO in 13.9% of patients, and in shunt quantification in 26.6%.

The central hypothesis of our trial is based on three premises:

• The patient has echo demonstration of a PFO.
• The patient has a documented history of refractory migraine.
• The patient does or does not experience ongoing migraines during the trial period.
Based on these premises, and the potential weaknesses of hard counting methods, our trial proposes to use a practical, clinical hybrid method that describes the shunt capacity based on count and visual appearance of the shunt (bubbles).

**Recommended Supplies/Preparation**

- 20 gauge Venflon needle.
- Three way stopcock connected to Venflon with a 6-inch extension tubing, primed with saline (stopcock connected to end away from patient).
- One empty 10 cc syringe.
- Three 10 cc syringes filled with 8-9cc saline plus 0.3-0.5ml of air in each syringe. (Three syringes are for three separate injections-manoeuvres.)

**Recommended Procedure**

1. Note that echo equipment preparations, including probe insertion and equipment settings are not listed in the following steps. The TTE probe should be well prepared or inserted prior to the bubble trial being performed. Optimal PFO viewing windows and ultrasound unit parameters should be optimised prior to performing the bubble trial.
2. Explain the procedure to the patient, and have patient perform practice valsalva.
3. Start IV in right antecubital vein. (Note: Post implant bubble trial may be performed using a catheter inserted via the groin access site provided the catheter is placed in the SVC such that contrast injectate enters the right atrium from the SVC.). Insure good patency. Secure with adhesives.
4. Connect the empty syringe to one port of the stopcock and draw 0.5cc of blood into syringe.
5. Connect saline-filled syringe to the “straight thru” port of the stopcock.
6. Turn the stopcock off to the patient, create the bubbles in solution by pushing the saline back and forth between the two syringes a minimum of 10 exchanges to insure proper agitation of media.
7. When the sonographer is ready, turn the stopcock off to the empty syringe, inject the agitated saline into the patient, injecting through the “straight flow” pathway of the syringe and stopcock. Raise the patient’s right arm.
8. On appearance and filling of right atrium with bubble solution, have the patient perform valsalva pressure and hold until instructed to release (5-7 seconds).
9. Repeat the process for a minimum of three manoeuvres or as needed to achieve adequate evaluation of shunt.
10. If patient is not able to perform valsalva manoeuvre, they will be asked to cough or to take deep respiration.

Presence of Shunt

- **Yes**: Based on appearance of bubbles in the left heart either spontaneously or after provocative manoeuvre within 5 cardiac cycles after opacification of the right atrium.
- **No**: Based on no bubbles in left heart either spontaneously or after provocative manoeuvre within 5 cardiac cycles after opacification of the right atrium.

Assessment of Flow

The appearance of contrast in the left heart will be characterised as occurring before or during Valsalva strain or with/after release and will be graded according to the scale below. Classifications are based on bubbles appearing in left heart either spontaneously or after provocative manoeuvre within 5 cardiac cycles after opacification of the right atrium.

- **Grade 0**: None

No bubbles appearing in the left heart on valsalva.

- **Grade 1**: Trace

The distinct appearance of between one and approximately ten bubble(s) in the left heart during the manoeuvre, but at no time does the appearance of the bubbles constitute a concentration that could be circumscribed as a section within the left atrial cavity.

- **Grade 2**: Moderate

The distinct appearance of a moderate quantity (approximately ten to twenty five) of bubbles in the left heart such that a distinct circumscribable section of the LA cavity can be described as filled.

- **Grade 3**: Substantial

The distinct appearance of a significant quantity (approximately 25 or more) of bubbles in the left heart, some of said bubbles reaching the contralateral left atrial wall, such that complete filling of LA chamber can be described.


