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# Enhanced detection of patent foramen ovale by systematic transthoracic saline contrast echocardiography

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ABSTRACT

*Objective:* We aimed to evaluate the effectiveness of transthoracic saline contrast echocardiography (TSCE) in detecting patent foramen ovale (PFO).
*Background:* Transesophageal echocardiography (TEE) is semi-invasive and not ideal for PFO screening.
*Methods:* 112 patients (48 males, 46 ± 14 years) with suspected PFO received intravenous agitated-saline contrast at rest and stress (strain and release phases of Valsalva maneuver and coughing). The presence of interatrial shunting was defined as >5 bubbles appearing in the left heart within 3 cardiac cycles. The stage of the maneuver at which interatrial shunting occurred was recorded. The TSCE findings were validated by TEE.
*Results:* TEE identified PFO in 45% of patients. The sensitivities of TSCE in detecting PFO at rest, during strain and release of Valsalva maneuver, and coughing were 12.0%, 38.0%, 80.0% and 94.0% respectively (each $p<0.05$ when compared to previous stage). Specificities were similar and >95% for all stages. Moreover, the release phase of the maneuver improved the diagnostic accuracy [defined as (number of true positives + true negatives) divided by total in sample] with incremental value over the preceding strain phase (89.2 vs. 70.5%, $p<0.001$).
*Conclusions:* Patent foramen ovale can be identified confidently with proper conduct of the Valsalva maneuver during the transthoracic saline contrast echocardiography.



## 1. Introduction

Patent foramen ovale (PFO), which is present in 25% of the normal population, refers to the persistence of the flap-like opening at interatrial septum (IAS) after birth [1]. This lesion allows right-to-left shunting (RLS) during the crossover of pressure that occurs in the respiratory cycle, often at end-diastole or in situations when right atrial pressure increases (i.e. Valsalva maneuver, coughing). Presence of PFO is associated with cryptogenic stroke and transcatheter closure may be warranted in selected patients [2]. While transesophageal echocardiography (TEE) remains the reference standard [3,4] in diagnosing PFO, it is semi-invasive and not ideal for screening. TEE also fails to detect PFO in sedated subjects due to ineffective or inadequate Valsalva maneuver [5,6]. Use of second harmonic imaging [7–9], agitated saline or contrast medium injection [10,11] with or without repetitive Valsalva maneuver [3,4,12–14] can all improve the sensitivity of PFO detection by transthoracic echocardiography. However, there is a lack of studies to address the phase of the maneuver to be imaged and the value of additional cough test in demonstrating RLS that occurs in PFO patients. We, therefore, sought to evaluate the diagnostic utility of different phases of Valsalva maneuver and the cough test during transthoracic saline contrast echocardiography (TSCE).

## 2. Methods

A consecutive of 112 patients suspected to have PFO prospectively received TSCE and TEE at the Prince of Wales Hospital between 2005 and 2009. They were suspected to have PFO because of: 1) presence of suspicious 2-dimensional color Doppler flow at interatrial septum (Fig. 1) or 2) previous history of cryptogenic stroke. Patients with suboptimal echocardiographic windows, contra-indications for TEE, secundum atrial septal defects, intrapulmonary shunting and significantly raised left atrial pressure (restrictive LV filling pattern or severe mitral regurgitation or stenosis) were excluded from the study. Informed consent was obtained from all participants and the study was approved by local ethical committee.

### 2.1. Contrast administration protocol

Standard 2-dimensional and Doppler echocardiography was performed using a 3.5-MHz probe on Vivid 5 system (General Electric Medical Systems, Milwaukee, WI, USA) with second harmonic imaging, followed by multiplanar TEE on the same day using either Vivid 5 or iE33 system (Philips Medical System, Andovor, MA, USA). Patients were taught to perform standard Valsalva maneuver and a post-maneuver cough test before their echocardiographic examination: First, sustained straining against a closed epiglottis causing abdominal distension for 10 seconds before sudden release of the strain by deep inspiration, followed by forceful coughing for 5 seconds. Adequate performance of Valsalva maneuver was checked quantitatively by a ≥10% reduction of early Doppler mitral inflow velocity [15,16], and qualitatively by a decrease in the left atrial and ventricular sizes with IAS bulging to the left atrium.

An 18 French angiocatheter was inserted at the right antecubital vein, which was connected by an extension tube to a 3-way stopcock with two 10 ml Luer Lock syringes. One ml of patient's blood was drawn from the angiocatheter into a syringe containing

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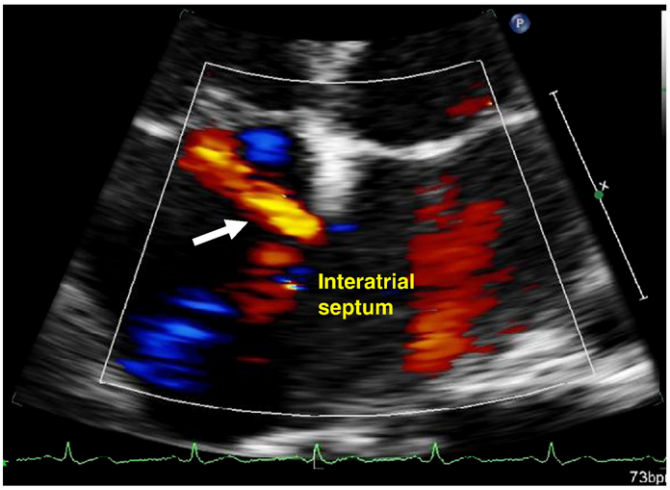


**Fig. 1.** An example of a patient with 2-dimensional color Doppler flow (white arrow) at interatrial septum which is suspicious of patent foramen ovale.

**Table 1**
Baseline Patient Characteristics.

| Variables | Patients (n = 112) |
|---|---|
| Age (yrs) | 46 ± 14 |
| Men | 48 (43%) |
| Co-morbidities | |
| Diabetes Mellitus | 8 (7%) |
| Hypertension | 11 (10%) |
| Coronary artery disease | 2 (2%) |
| Clinical indications: | |
| 1. 2D Color Doppler flow detected at interatrial septum | 66 (59%) |
| 2. Follow-up for suspected paradoxical embolism Cryptogenic stroke | 46 (41%) |
| Transesophageal echocardiogram diagnoses | |
| Absence of interatrial shunt | 62 (55%) |
| Patent foramen ovale | 50 (45%) |

2D = two-dimensional.

8 ml of sterile normal saline solution and 1 ml of air [11]. The content was forcefully injected back and forth for few times between the two syringes to become a cloudy and foamy pink emulsion. It was then rapidly administered intravenously to the patient at baseline, before the Valsalva maneuver on transthoracic and subsequent TEE examinations (Fig. 2).

Presence of RLS was defined as the appearance of >5 bubbles in left heart within 3 cardiac cycles [8,17] when the contrast first appeared in the right atrium. Gain settings were individually adjusted to enhance the visualization of IAS and bubble contrast in apical 4-chamber view. The stage of the maneuver at which RLS occurred was recorded.

For the TEE examination, subjects were only given topical pharyngeal anesthesia to allow adequate performance of Valsalva maneuver. The diagnosis of PFO was confirmed on TEE by both visualization of the defect and demonstration of interatrial shunting either by saline contrast or color Doppler imaging. Those patients with bubble contrast appeared in left heart after 3 cardiac cycles would receive additional contrast administration for further examination of all pulmonary veins. Any contrast emergence from pulmonary veins confirmed presence of intrapulmonary shunting. All images were digitally stored as cine-loops and recorded on videotapes for off-line analysis. The TSCE findings were later interpreted by 2 independent cardiologists who were unaware of the TEE results. Disagreement results would be discussed among them to reach final conclusions.

### 2.2. Statistical analysis

Continuous and categorical variables were expressed as mean ± SD and percentage respectively. Sensitivity, specificity, and accuracy of various phases of the maneuver for detecting RLS on transthoracic echocardiography were calculated using TEE as the "reference standard". Diagnostic accuracy was defined as:

$$\frac{(\text{true positives}) + (\text{true negatives})}{\text{total in sample}}$$

Comparisons for dichotomous variables were performed using Chi-square or Fisher's Exact test as appropriate. A significant difference was defined as $p<0.05$. Statistical analysis was performed by dedicated software (SPSS 13.0, Chicago, Illinois, USA).

## 3. Results

One hundred and fourteen patients were recruited initially. Two patients were excluded from analysis because of evidence of

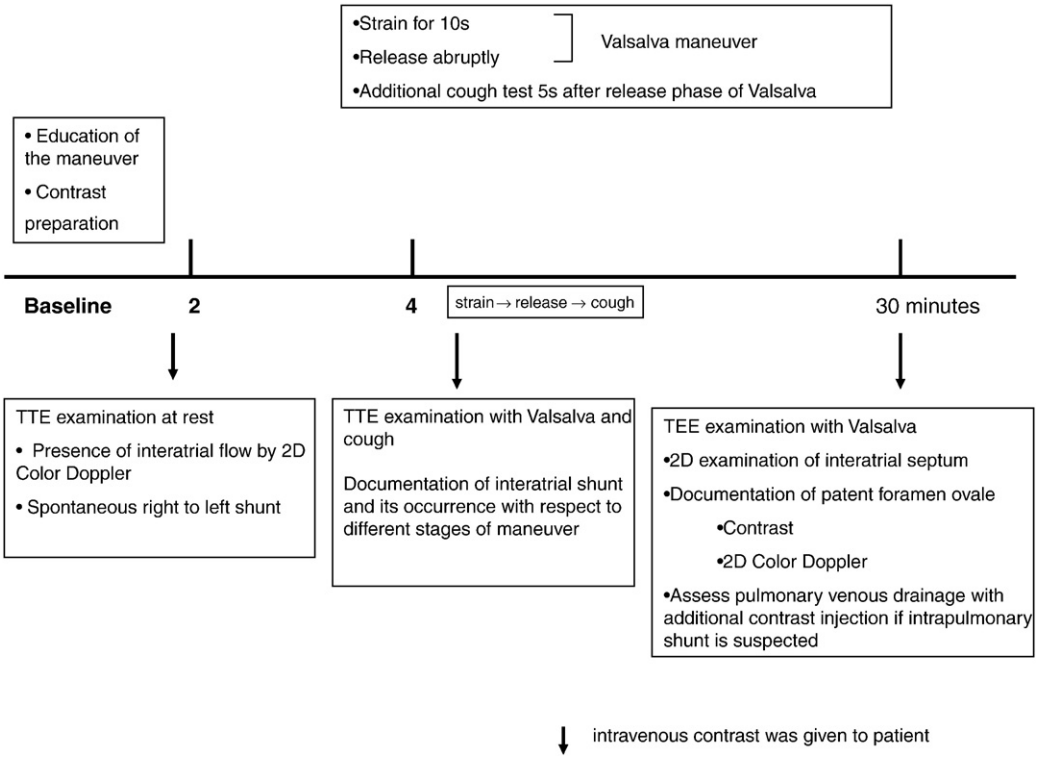


**Fig. 2.** Flow Chart of the Design of the Study.