Assessment of Value of Three Dimensional Transesophageal Echocardiography versus Conventional Two Dimensional Transesophageal Echocardiography in Guiding Transcatheter Closure of Atrial Septal Defects and Patent Foramen Ovale
Assessment of Value of Three Dimensional Transesophageal Echocardiography versus Conventional Two Dimensional Transesophageal Echocardiography in Guiding Transcatheter Closure of Atrial Septal Defects and Patent Foramen Ovale

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Abstract

**Objective:** To evaluate the benefit of using three-dimensional transesophageal echocardiography (3DTEE) over conventional two-dimensional transesophageal echocardiography (2DTEE) in evaluation of various morphological features of atrial septal defect (ASD) and patent foramen ovale (PFO) during transcatheter closure.

**Methods:** This is an observational cross sectional study including 115 patients (45 PFO and 70 ASD patients) who underwent 2D/3DTEE guided transcatheter closure from April 2019 to October 2021 in cardiology department, Tanta university hospital.

**Results:** 70 ASD patients were divided into two groups; the pediatric age group (18 patients, mean age 9.05 ± 3.51 years) and the adult group (52 patients, mean age 39.3 ± 10.15 years). ASD morphology was simple in 12.9% and complex in 87.1% of patients, where 3DTEE was superior in the evaluation of posterior, infero posterior rims, fenestrated flimsy rims, aneurysm shape, orientation, and quality of its tissue. Procedural success was defined as complete defect closure with no complications. The procedure was successful in 68 and failed in 2 patients.

45 PFO patients were divided into two groups; the pediatric age group (14 patients, mean age 13.5 ± 3.25 years) and the adult group (31 patients, mean age 35.2 ± 4.5 years). PFO morphology was simple in 22.2% and complex in 77.8% of patients, where 3DTEE was superior in the evaluation of the exact PFO opening from the left atrium, additional fenestration, aneurysm shape, orientation, and quality of its tissue. The procedure was successful in all patients.

**Conclusion:** 3DTEE guided transcatheter ASD/PFO closure provides an additional value over conventional 2DTEE in assessment of complex ASD/PFO morphology.

**Keywords:** Atrial septal defect, Patent foramen ovale, Real-time 3-dimensional transesophageal echocardiography

1. Introduction

Meticulous morphological evaluation of atrial septal defect (ASD) and patent foramen ovale (PFO) is the cornerstone for appropriate device selection. Two-dimensional transesophageal echocardiography (2DTEE) has traditionally been used for dynamic evaluation of the interatrial septum (IAS); however, it requires multiple views due to complex septal three-dimensional structure [1,2].

Real-time three-dimensional transesophageal echocardiography (RT-3DTEE) demonstrates ASD/PFO morphology and their relationship to the surrounding structures in a single enface view without the need for mental reconstruction. It also clarifies the dynamic change in defect size during the cardiac
cycle and directly visualizes bubbles crossing PFO tunnel to exclude extracardiac shunts [2–4].

RT3DTEE facilitates monitoring of the position of wires, catheters, as well as, the occluder device, and its relation to the surrounding structures. RT3DTEE has enhanced both pre-procedural planning and intra-procedural guidance [1].

The aim of this study was to evaluate the additional benefit of 3DTEE over conventional 2DTEE during ASD/PFO transcatheter closure.

2. Methods

This is an observational cross-sectional study including 115 patients (45 PFO and 70 ASD patients) who underwent 2D/3DTEE guided transcatheter closure from April 2019 to October 2021 in cardiology department, Tanta University Hospital.

2.1. Inclusion criteria

1. ASD secundum defects (amenable for device closure with evidence of either haemodynamic significance or embolic complications) [5].

2. PFO inducing cryptogenic cortical events together with high Risk Of Paradoxical Embolism (ROPE) score ≥7 (in patients ≥18 years) after confirmation of right to left shunt by transcranial Doppler [TCD] and TEE.

2.2. Exclusion criteria

1. Irreversible pulmonary vascular disease

2. Other causes of stroke e.g atherosclerotic cerebrovascular disease, thrombophilia and atrial fibrillation [6–12].

After approval from the ethical committee of Faculty of Medicine, Tanta University, an informed consent was obtained from all participants by themselves or their parents after a full explanation of the benefits and risks of the study.

Pre-procedural planning was made using trans-thoracic echocardiography (TTE), 2DTEE and 3DTEE to confirm the suitability for device closure.

The procedure was done under general anaesthesia guided by fluoroscopy and 2DTEE/3DTEE using matrix-array 3DTEE probe (GE 6VT-D), and (Vivid E9, General Electric Corporation, USA) machine.

2.3. 2DTEE

Multiple 2DTEE views; Mid-esophageal four-chamber, mid-esophageal aortic valve short-axis and bicalve views were used to evaluate ASD/PFO morphology [13–15].

1- ASD morphology: was simple in 9 patients (12.9%) and complex in 61 patients (87.1%).

Complex ASDs included: large defects in 20 patients (large for body surface area in pediatric age group or more than 30 mm in adults), deficient rims in 50 patients (less than 5 mm), small left atrium size for body surface area in 10 patients, and flimsy (thin floppy) rims in 15 patients [16].

ASD was associated with: PFO (hybrid defects) in 10 patients (14.3%), atrial septal aneurysm (ASA) (denoting excessive mobility of IAS with an excursion more than 10 mm in either direction from septal plane or more than 15 mm total excursion between both atria) in 30 patients (42.9%) [17,18]. ASA was multi-fenestrated in 6 patients. Prominent Eustachian valve (EV) was present in 11 patients (15.7%).

2- PFO morphology: was simple in 10 patients (22.2%) and complex in 35 patients (77.8%). Complex PFO included: ASA in 15 patients, thick secondary septum (more than 10 mm) in 10 patients and long tunnel (more than or equal to 12 mm) in 14 patients. Prominent EV was present in 16 patients and dilated aortic root in 2 patients [17–19].
Agitated saline was injected to confirm right to left shunt in cases of PFO, ASD associated with PFO (hybrid defects), ASA and in presence of large Eustachian valve. The test was considered positive when a large number of bubbles passed across the PFO to the left atrium (LA) within the first 3 cardiac cycles [17].

2.4. 3DTEE

Using the same Vivid E9 machine, evaluation included; Live 3D and 3D zoom of the IAS using TUPLE (tilt up then left) plus ROLZ (rotate left in z-axis) maneuver. The area of interatrial septum was selected in bical view to obtain a 3D zoom image that was tilted up to view the septum from the right atrial perspective with superior vena cava (SVC) located at the right side of the screen. Then, the image was rotated to the left by 90° in the z-axis. After that, it was tilted to the left around its vertical axis to obtain the view of the IAS from LA perspective [20].

Cropping was performed to remove the surrounding structures, image gain was adjusted and, enface view of IAS was obtained [20,21].

Mid-esophageal aortic short axis view was used for procedural guidance using Zoom and 3D live modes.

Volume rendered data was analyzed to visualize ASD/PFO, relation to the surrounding structures, dimensions (measured in end-systolic frame of the cardiac cycle, Flexi-slice software), defect shape, rims, position, other fenestrations, and associated ASA [1–4,22–25] (Figs. 1–4).

During 3DTEE examination, bubble study was repeated in patients with positive 2DTEE study while looking from LA enface view, to confirm shunting through PFO itself.

2.5. Transcranial Doppler (TCD)

TCD was performed in all patients with right to left shunt by TEE, TCD is graded as: (grade 1): no occurrence of micro-bubbles (MB); (grade 2): 1–10 MB; (grade 3) > 10 MB, but no curtain, and (grade 4): curtain, where a single MB cannot be discriminated [26]. Grades 3 and 4 were considered as significant right to left shunt.

2.6. Transcatheter closure

It was performed under general anaesthesia. Right femoral venous access was obtained using Sildenger technique, heparin (100 IU/Kg) keeping activated clotting time (ACT) > 200 s and antibiotics were administered. In case of mobile Eustachian valve, it was held against right atrial wall using a steerable ablation catheter (Boston Scientific/Vascular, Quincy, MA) introduced through another venous access on the opposite side [27–29].

Both fluoroscopic and 2D/3DTEE guidance were used to visualize passage of catheters, wires and delivery sheath across the defect into the LA. The device was prepared in heparinized saline, then advanced through the long sheath to LA. 3D data set was rotated during device deployment to provide simultaneous views from both atria using 3D zoom and live 3D modes (Fig. 5).

In ASD patients with significant pulmonary hypertension (10 patients with systolic pulmonary artery pressure >50 mmHg), calculation of pulmonary vascular resistance (PVR) was done, all patients were candidate for closure (pulmonary vascular resistance was less than 5 WU and final PVR: SVR ratio was <0.33). After closure, the device wasn’t immediately released but kept connected to the cable with close haemodynamic monitoring; they didn’t develop any heart failure signs or hemodynamic compromise.

Choice of the device

ASD patients; Atrial septal occluder (ASO) was chosen according to the maximum TEE diameter (1–4 mm larger than defect size), considering the total IAS length. Cribriform device was used in case of multi-fenestrated ASDs with appreciable tissue thickness. Tissue thickness, rims and associated fenestrations could be assessed in single view using 3DTEE [30].

Regarding PFO Patients; Larger PFO occluders were used in the presence of a long tunnel or floppy primum septum [30–32].

Immediate post deployment and release, 2DTEE/3DTEE evaluation was done to assess residual leaks, device embolization or malposition. After that, patients joined regular TTE follow-up schedule (before discharge, after 1 week, 1 month, 6 months and yearly).

Procedural success was defined as complete defect closure with no complications. Procedural failure was defined as abortion of the procedure or device embolization.

Medications

A) Aspirin 3–5 mg/kg/day for 6 months and clopidogrel for 1–3 months (in patients with PFO, large ASDs or in the presence of large EV).

B) Endocarditis prophylaxis for 6 months after closure
Fig. 1. ASD assessment by both TEE modalities; (a-b, Patient No.15) a) 3DTEE: RA enface view, flimsy fenestrated posterior and IVC rims (arrow), b) 3DTEE; Defect measurement using Flexi-slice software. (c-f, Patient No. 20) c) 2DTEE: Absent aortic rim, deficient posterior rim, d) 2DTEE: Deficient IVC rim, e) 3DTEE: RA enface view, absent aortic rim, short just efficient posterior and IVC rims. f) 3DTEE: dynamic change of ASD size with cardiac cycle. (g-h, Patient No. 23) g) 2DTEE: Small centralized ASD secundum with turbulent left to right shunt. h) 3DTEE: Enface view from RA, small centralized circular defect with long Eustachian valve (arrow). (IVC: inferior vena cava, RA: right atrium)
2.7. Statistical analysis

Data were analyzed using the IBM® SPSS statistical software, version 21. Numerical data were presented as mean and standard deviation and categorical data were presented as number and percentage.

Chi-square test was used for comparing the qualitative data. Paired t test was used to compare the two means between 2DTEE & 3DTEE in the same groups. The level of significance was adopted at $p < 0.05$.

Logistic Linear regression was used to detect the predictor variables most affected by using 3DTEE.

3. Results

3.1. ASD group

A- Pediatric age group: included 18 patients with age ranged from (5–18) years; the mean age was $9.05 \pm 3.51$ years, and the mean weight was $43.3 \pm 16.45$ Kg. They presented with dyspnea
(NYHA class II) in 12 patients (66.7%), palpitation (with no documented arrhythmia) in 11 patients (61.1%), and repeated chest infections in 8 patients (44.4%).

B- Adult group: included 52 patients with age ranged from (22–55) years; the mean age was 39.3 ± 10.15 years and the mean weight was 86.3 ± 9.85 kg. 33 patients (63.5%) presented with palpitation (with no documented arrhythmia), 29 patients (55.8%) with dyspnea (NYHA class II-III), 5 patients (9.6%) with transient ischemic attack (TIA) and 2 patients (3.8%) with cryptogenic stroke.

2DTEE was compared to 3DTEE in both pediatric and adult ASD groups

1- ASD Measurements: There was no significant difference between ASD measurement by both modalities, the mean minimum ASD diameter measured by 2DTEE was 16.41 ± 5.25 mm and by 3DTEE was 16.71 ± 5.36 mm (P value 0.27). The mean maximum ASD diameter measured by 2DTEE was 23.32 ± 6.67 mm and by 3DTEE was 23.54 ± 7.26 mm (P value 0.38).

2- ASD Shape: Both modalities were significantly different (Table 1). Multiple 2DTEE views were needed to assume ASD shape. ASD was considered circular if the difference between its diameters was <1–2 mm, mental reconstruction was needed for assumption of its shape. However, with a single 3DTEE enface view of IAS, we could appreciate ASD shape.

3DTEE demonstrated the complex shape in (patient number 3) who had double atrial septae enclosing an interatrial chamber (Fig. 2 e-j).

3- ASD Position: There was no significant difference between both modalities. Multiple 2DTEE views were needed to evaluate ASD rims to assume whether the defect was central or eccentric. A single 3DTEE enface view of IAS could instantly demonstrate ASD position (Table 1).

4- ASD Rims: were much easily evaluated in a single enface view from both RA and LA perspectives using 3DTEE. 3DTEE was beneficial in 11 patients with deficient posterior and inferior vena cava (IVC) rims by 2DTEE, using 3DTEE, they looked just efficient with appreciable tissue deserving trial of device closure. Regarding other rims, there was no significant difference between both modalities (Table 1).

Flimsy (thin floppy) rims were present in 15 patients (21.4%), 3DTEE was more superior in detection of fenestrations within these rims (8 patients with 3DTEE; 2 patients with 2DTEE) with significant P-value (0.03). This has also affected our decision making in device sizing as these defects needed oversizing of the occluder device to cover these weak fenestrated rims.
5- **Aneurysmal ASDs**: 30 patients had associated ASA. 3DTEE was beneficial in the assessment of (Table 2):

- **Aneurysm shape**: oval or circular.
- **Orientation**: vertical, horizontal, or oblique according to ASA long axis.
- **Tissue thickness**: that was beneficial in determining the device size and type with no need for balloon sizing. In the case of soft aneurysmal tissue, we oversized the device. Tough thick multi-fenestrated ASA was detected in patient number 47 (Fig. 2 a-d).

**Devices used**: Atrial septal occluders were used in 66 patients with sizes ranging from 6 to 40 mm, and mean $27.71 \pm 9.36$ mm. Cribriform device was used in 4 patients with aneurysmal multi-fenestrated ASDs and appreciable aneurysmal tissue; the device size ranged from 25 to 35 mm, and mean $28.75 \pm 1.25$ mm.

**Procedural Success**: procedure was aborted in 2 patients

- Patient number 47 had a cone shaped, multi-fenestrated ASA; its tissue looked thick and tough during evaluation with 3DTEE. After cribriform...
device deployment, it couldn’t include such tough ASA tissue in between its two discs with significant residual shunt; the device was removed, procedure was aborted, and patient was referred for surgery Fig. 2 (a-d).

- Patient number 3 presented with cryptogenic stroke and double atrial septum due to accessory septal tissue forming an interatrial chamber. Several trials of crossing this chamber failed due to its restrictive right atrial orifice resulting in procedural failure, and patient was kept on anticoagulation Fig. 2 (e-j).

3DTEE was beneficial in the demonstration of such complex atrial septal morphology

Logistic linear regression analysis was done to determine ASD parameters having the most benefit from using 3DTEE. It was significant in evaluation of posterior rim, IVC rim, ASDs with associated certain morphological features e.g. ASA and PFO, and in presence of additional fenestrations within the flimsy rims (Table 3).

3.2. PFO group

A- Pediatric age group: included 14 patients with age ranged from (6–18) years; the mean age was 13.5 ± 3.25 years and mean weight was 57.9 ± 15.65 Kg. They presented clinically with TIA in 5 patients (35.7%), cryptogenic stroke in 4 patients (28.6%) and TIA associated with migraine in 5 patients (35.7%). TCD results were Grade 3 in 6 patients (42.9%) and Grade 4 in 8 patients (57.1%).

B- Adult group: included 31 patients with age ranged from (23–49) years; the mean age was 35.2 ± 4.5 years and the mean weight was 74.5 ± 9.85 kg. They presented clinically with TIA in 13 patients (41.9%), cryptogenic stroke in 5 patients (16.1%), TIA associated with migraine in 7 patients (22.6%) and cryptogenic stroke associated with migraine in 6 patients (19.4%). ROPE score ranged from (7–10), with a mean 8.44 ± 1.71. TCD results were Grade 3 in 12 patients (38.7%) and Grade 4 in 19 patients (61.3%).
2DTEE was compared to 3DTEE in both pediatric and adult PFO groups

1- **PFO tunnel measurements**: there was no significant difference between both modalities as regards tunnel length, but PFO width measurement was significantly larger by 3DTEE (Table 4)

2- **PFO rims**: both modalities showed no significant difference (Table 4)

3- **Aneurysmal PFOs**: ASA was present in 15 patients (33.3%). 3DTEE was beneficial in assessment of (Table 2):

- Aneurysm shape.
- Orientation.
- Tissue thickness.
- Additional fossa ovalis fenestrations: 3DTEE was more superior in their detection (1 patient with 2DTEE, 7 patients with 3DTEE) with significant p-value. (0.03)
- Evaluation of tissue thickness and other fenestrations was beneficial in device sizing; larger devices were needed in case of floppy thin
aneurismal tissue and in the presence of other fenestrations to be covered by the occluder.

**Procedural Success:** Procedure was successful in all patients with no complications.

3DTEE was helpful in the exclusion of a patient with left atrial pouch with fused PFO tunnel (Fig. 4).

Logistic Linear regression analysis was significant for evaluation of additional fossa ovalis fenestrations (Table 5).

### 3.3 Role of 3DTEE in procedural guidance

3DTEE provided optimum monitoring of all procedural steps through visualization of catheters and guide wires passing through the defect into the left atrium up to the pulmonary vein, followed by the delivery sheath, and device deployment. 3DTEE also confirms good device position and its spatial orientation in relation to the surrounding structures to exclude encroachment on any of them (Fig. 5).
4. Discussion

RT-3DTEE guidance offers the potential for shorter and safer interventional procedures [33]. 3DTEE images can be obtained in different modes: biplane, full-volume, live 3D, and 3D zoom imaging, which is the most beneficial because it provides instantaneous images of the entire IAS [20].

This study aimed to evaluate the benefit of using 3DTEE over conventional 2DTEE during ASD/PFO transcatheter closure.

3DTEE uses volume datasets that can be sliced into different planes after acquisition. The multiplanar reconstruction (MPR) technique (known as Flexi-slice in GE system) providing all the needed information in a single view [34–39].

4.1. ASD group

1- ASD measurement: There was no significant difference between both modalities. Hascoet S., et al. and Contreras A.E., et al. also reported non-significant difference of ASD size between both modalities, and both correlated well with balloon sizing [37,38].

2- ASD Shape and position: 3DTEE demonstrated ASD shape and position in a single 3D ‘enface’ view. Roberson D.A., et al. reported concordance between 3DTEE with surgical inspection regarding ASD shape [35].

ASD patient number 3 presented with cryptogenic stroke and double atrial septum, further clarified by 3DTEE. Robaei et al., Alobaidan et al., Vijaykumar Reddy et al., described such anatomy and its relation to cryptogenic stroke [40–42].

Manabu Taniguchi et al. reported that 3DTEE is superior to 2DTEE in ASD position assessment [43].

3-Rims: were easily evaluated in single enface view from both RA and LA using 3DTEE without the need for mental reconstruction. Deficient posterior and IVC rims by 2DTEE actually looked just sufficient by 3DTEE with appreciable tissue in 11 patients. So, the decision changed from surgery to trial of device closure and procedure was successful in all of them. Vinay K Sharma et al. reported that 3DTEE is better in the evaluation of ASD rims than 2DTEE [15].

4- Evaluation of tissue thickness of ASA in aneurysmal ASDs: 3DTEE was useful in evaluation of ASA tissue thickness. This is in agreement with Taha. F and ElShedoudy. S [20]. In the case of soft aneurysmal tissue, we had to oversize the device. ASD patient number 47 had thick ASA that couldn’t be included in between the device discs.

4.2. PFO group

3DTEE provided accurate PFO diagnosis through direct visualization of the bubbles coming out from PFO opening differentiating intracardiac from extracardiac shunts [3].Tanaka J et al. also reported that 3DTEE PFO width measurement was larger than 2DTEE, and there was no significant difference between tunnel length measured by both modalities [32].

Table 2. Description of ASA Shape, Orientation, and Tissue thickness in ASD/PFO patients using 3DTEE.

| Shape          | ASD patients (n = 30) | PFO patients (n = 15) |
|----------------|----------------------|-----------------------|
|                | No. %                | No. %                 |
| Shape          |                      |                       |
| Oval           | 24 80%               | 9 60%                 |
| Circular       |                      |                       |
| cone shaped    | 5 16.7%              | 6 40%                 |
| Tissue         |                      |                       |
| Soft           | 21 70%               | 5 33.3%               |
| Appreciated    | 8 26.7%              | 10 66.7%              |
| Tough          | 1 3.3%               | 0 0%                  |
| Orientation    |                      |                       |
| Vertical       | 11 36.7%             | 4 26.7%               |
| Horizontal     | 4 13.3%              | 3 20.0%               |
| Oblique        | 9 30%                | 2 13.3%               |
3DTEE helped us in the exclusion of a patient with left atrial pouch presenting clinically with cryptogenic stroke, left atrial pouch is a blind pouch that results from incomplete fusion between primum and secundum septae allowing no shunt across IAS, this patient had also a left atrial ridge representing a thickened tissue on the left atrial aspect of IAS, the patient was kept on anti-coagulation. Subramaniam C. et al. reported left atrial pouch in anatomical specimens due to tunnel fusion only at its most caudal part [44]. Zisa et al. reported a case series of patients with abnormal septal fusion patterns including the left atrial pouch and ridge [45].

4.3. Procedural Guidance

3DTEE was used for monitoring of all procedural steps; this is in agreement with Bushra S. Rana and Balzer J. et al. who concluded that RT- 3DTEE was of additional value while guiding the procedure over 2DTEE [46,47].

| Predictor variables | standard coefficients Beta | T | P value | R square (effect) |
|---------------------|----------------------------|---|---------|------------------|
| Tunnel dimensions length | -0.19- | -0.64- | 0.15 | 4.2% |
| Tunnel dimensions width | 0.25 | 0.21 | 0.37 | 2.4% |
| Total aneurysmal minimum dimensions | 0.47 | 0.12 | 0.32 | 4.6% |
| Total aneurysmal maximum dimensions | -0.14- | -0.34- | 0.41 | 3.3% |
| Aortic Rim (mm) | 0.36 | 0.45 | 0.32 | 2.7% |
| Aortic Rim (mm) | 0.21 | 0.82 | 0.98 | 1.2% |
| ASA | -0.14- | -0.54- | 0.45 | 1.3% |
| EV | 0.18 | 0.65 | 0.97 | 1.7% |
| Dilated Aortic root | 0.23 | 0.32 | 0.98 | 1.2% |
| Additional fenestrations in flimsy rims | 0.36 | 12.7 | 0.03* | 10.2% |

Table 3. Linear Regression Analysis to determine ASD parameters most affected by using 3D TEE.

Table 4. Comparison between Tunnel Length, Width, and Rims by 2DTEE and 3DTEE in PFO patients.

Table 5. Linear Regression Analysis of PFO parameters most affected by using 3DTEE.
The study has some limitations as it was confined to a single center and was restricted to patients more than 15 kg as appropriate to the adult 3DTEE probe.

5. Conclusion

Due to complex 3D anatomy of IAS, 3DTEE provides incremental value to ASD/PFO assessment and the surrounding fossa. 3DTEE enhances pre-procedural planning and guidance through visualization of the position of catheters and devices relative to surrounding structures. This has improved both safety and efficacy of these procedures.

Author contribution

Conception and design of Study: EHED, MMEM; Literature review: EHED, MMEM, HKK, AMES, SAES; Acquisition of data: EHED, MMEM, HKK, AMES, SAES; Analysis and interpretation of data: EHED, MMEM, HKK; Research investigation and analysis: EHED, MMEM, HKK, AMES, SAES; Data collection: EHED, MMEM, HKK; Drafting of manuscript: EHED, MMEM, AMES, SAES; Revising and editing the manuscript critically for important intellectual contents: EHED, MMEM, HKK, AMES, SAES; Data preparation and presentation: EHED, MMEM, HKK, SAES; Supervision of the research: EHED, MMEM, AMES, SAES; Research coordination and management: HKK, AMES, SAES; Funding for the research: EHED, MMEM, HKK, SAES

Disclosure of funding

None.

Conflict of interest

None.

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