

3D ECHOCARDIOGRAPHIC GUIDANCE FOR TRANSCATHETER ASD DEVICE CLOSURE – A COMPARATIVE STUDY

***Project submitted for the degree of
PDF (Adult Cardiac Interventions)***



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CERTIFICATE

I, **Dr. Avinash Mani**, hereby declare that the project in this book, titled “**3D Echocardiographic guidance for transcatheter ASD device closure – a comparative study**” was undertaken by me under the supervision of the faculty, Department of Cardiology, Sree Chitra Tirunal Institute for Medical Sciences and Technology.

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DECLARATION BY CANDIDATE

I, **Dr Avinash Mani**, hereby declare that I have done my project entitled **“3D echocardiographic guidance for transcatheter ASD device closure – a comparative study”** under my allotted guides in the department of Cardiology , SCTIMST.

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3D Echocardiographic guidance for transcatheter ASD device closure – a comparative study

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Introduction

Atrial septal defects (ASD) are one of the most common congenital heart diseases noted in the adult population. Females constitute majority of patients with ostium secundum ASD (1). These patients are predominantly asymptomatic or may present with symptoms of atypical chest pain, dyspnea, palpitations or syncope. Transcatheter closure of ASD is considered as treatment of choice in patients with significant left to right shunt (2). Percutaneous ASD device closure was initially guided by fluoroscopy and 2D transthoracic echocardiography. However, both these modalities have their inherent limitations. The routine use of transesophageal echocardiography (TEE) has led to a better understanding of anatomy of ASD and plays a vital role in planning and guiding percutaneous device closure. Use of TEE helps in assessment of defect rims as well as device sizing (3). However, two-dimensional (2D) TEE does not provide very robust information about shape of the defect and its location in relation to other cardiac structures.

The advent of three-dimensional (3D) echocardiography has improved our understanding of cardiac anatomy and associated abnormalities. Real time 3D gives a better idea of the relationship of cardiac structures as compared with 2D echocardiography (4). 3D TEE can be used to obtain enface view of ASD which can help to understand the spatial orientation of ASD as well as help in assessment of rims. Different 3D software can be used to obtain an anatomical view of ASD which helps in planning for device sizing. However, routine use of 3D echocardiography is limited due to limited resources and lack of generalized expertise in the field. Ideally, 3D echocardiography gives better guidance for percutaneous device closure of ASD when compared to 2D echocardiography. However, there is lack of robust data comparing both imaging modalities for procedural guidance. 3D echocardiography can also play a role in determining device size based on defect shape and orientation, something which may not be clear on 2D imaging. However, there is no definite evidence which shows superiority of 3D imaging over the existing gold standard of 2D imaging. Comparative analysis of both modalities will give a better idea about the ideal modality for guiding intervention.

Review of Literature

Atrial septal defects are one of the most common congenital heart anomalies noted in daily clinical practice. These defects usually come to light due to a systolic murmur elicited during routine physical examination during infancy. In many instances, they remain undetected till adulthood. Patients with ASD are usually asymptomatic till late in life. The most common symptoms noted in ASD patients are chest pain, dyspnea, palpitations and rarely syncope. As ASD causes predominant L-R shunting of blood, symptoms are usually dictated by the level of shunt. In patients with significant L-R shunt, patients can develop features of right heart failure and pulmonary hypertension. The magnitude of shunting primarily depends on the relative compliance of the ventricles and arterial bed. Conditions which lead to reduction in left ventricular compliance or left ventricular inflow obstruction will increase the magnitude of shunt across ASD. On the other hand, reduction in right ventricular compliance, due to ventricular dysfunction or pulmonary hypertension, can lead to R-L shunting across ASD, causing arterial desaturation. Any L-R shunt $>1.5:1$ is considered as significant.

Significant L-R shunt associated with ASD causes dilatation of right sided cardiac chambers. This can predispose to development of atrial arrhythmias. Onset of atrial arrhythmias is usually accompanied by onset of symptoms in these patients. Patients with significant shunting can also present with decompensated right heart failure, related to tricuspid regurgitation and varying degrees of pulmonary hypertension. Heart failure in ASD is usually noted in elderly population, contributed by age related reduction in ventricular compliance and development of pulmonary hypertension(1). Patients with ASD are prone to develop stroke or transient ischemic attack resulting from a paradoxical embolism.

A vast majority of ASD patients reach adulthood without detection as they are asymptomatic. As a result, more number of adult patients are undergoing ASD closure worldwide(5). Surgical closure was the initial preferred strategy for patients with ASD. Surgical closure done early in life was associated with good long-term outcomes. However, in patients above 40 years age, the results of surgical closure were mixed. Actuarial survival rates were lower in patients undergoing ASD closure above 40 years age as compared to

those below 40 years of age (6). This led to a debate whether adult ASD patients, above 40 years of age, should undergo ASD closure.

The advent of device closure revolutionized the management of ASD. It is safer and relatively simpler to perform as compared to surgical closure. Complication rates are also lower with device closure and they are associated with better long term outcomes(7). Device closure for ASD has been proven to be beneficial in both young and adult patients. In a study of 236 ASD patients undergoing transcatheter device closure, Humenberger et al. showed that there was significant reduction in pulmonary artery(PA) pressures and right ventricular(RV) size in all age groups after transcatheter device closure (8). Patients above age of 60 years had higher PA pressures and RV size at baseline as compared to the rest of the cohort. Patients with higher PA pressures and RV size at baseline had lesser reduction after device closure as compared to their counterparts. Thus, device closure for ASD is beneficial in all age groups. Majunke et al. also demonstrated the feasibility and safety of transcatheter device closure in patients above 60 years of age (9). Another study by Swan et al. showed the efficacy of transcatheter device closure with reduction in PA pressures and RV size noted in elderly patients (10).

Incidence of arrhythmias is lowered in patients after transcatheter device closure. Patients with paroxysmal arrhythmias have a reduced likelihood of recurrence. However, the favorable effect of device closure on arrhythmia incidence decreases with increasing age (11). Transcatheter device closure is also associated with improvement in functional class amongst all patients. Elderly patients, who have higher symptoms at baseline, also achieve significant improvement in functional status after transcatheter device closure (8). Transcatheter device closure of ASD has a favorable effect on PA pressures. Elderly patients usually have higher PA pressures at baseline. Post device closure, significant reduction in PA pressures have been noted in all age groups. However, the PA pressures may not return to baseline in some patients. Elevated PA pressures in ASD patients is mainly attributed to L-R shunting causing increased pulmonary blood flow. Long standing ASD with L-R shunt can induce pulmonary vascular bed changes leading to elevation of pulmonary vascular resistance. These changes are more commonly seen in elderly patients with ASD who develop significant changes in pulmonary vasculature. This subset of patients has comparatively lower reduction in PA pressures after transcatheter device closure. Yong et al. demonstrated that patients with advanced pulmonary hypertension had significant

decrease in PA pressures after device closure. However, they were less likely to reach normal levels and become totally asymptomatic (12). ASD device closure is also associated with significant reduction of RV and LV volumes. RV volume reduction is noted immediately after device closure with continued reduction noted upto 3-6 months (13).

Transcatheter ASD device closure were initially guided by fluoroscopy, which has its inherent limitations and problems. The routine use of echocardiography has revolutionized the field of transcatheter interventions including device closure for ASD. The advancements in cardiac imaging have made structural interventions easier with improvement in success rates. The basic premise of cardiac imaging during structural interventions is for :-

- Understanding the morphology of structure of interest
- Identification of key anatomical landmarks, which can be used during the procedure.
- Device sizing
- Identifying specific imaging views needed during procedure
- Intra-procedural guidance
- Post procedural evaluation for procedural success

The introduction of transesophageal echocardiography has simplified the assessment of atrial septal defects and has helped immensely in planning for device closure of ASD. Owing to the superior resolution and image quality provided by TEE over TTE, assessment of defect rims can be done with great accuracy and efficacy. TEE assessment of ASD usually begins with localization of the defect within the atrial septum followed by characterisation of the defect rims. The rims analysed for purpose of suitability for device closure are pulmonary vein(PV) rim, AV valve/mitral rim, posterior rim, aortic rim, SVC rim, IVC rim and coronary sinus rim. TEE also helps in determining relation of defect with neighboring structures like mitral valve, aortic valve and pulmonary veins(14).

TEE assessment of atrial septal defects starts in conventional 0° view where the defect can be fully profiled. The rims noted in 0° view are PV rim and mitral rim. The TEE probe is usually placed in mid-esophageal position to visualize the defect, but depending on the anatomy, push or pull on the probe is required to optimize the image.

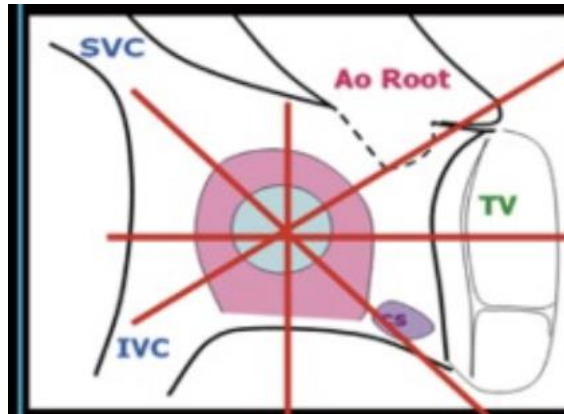


Figure 1. Schematic diagram showing presence of atrial septal defect in relation with surrounding structures.

After evaluation in 0° view, the probe angle is changed to 45° while maintain it at the mid-esophageal position. This view highlights the posterior and aortic rim. A good posterior rim is very important for planning device closure. Aortic rim is commonly deficient or absent in majority of cases. However, absence of aortic rim is not a contraindication for device closure. The probe is then rotated to bicaval 90° view which profiles the SVC and IVC rim along with the defect. Lastly, in 120° view, the coronary sinus rim is profiled along with SVC. All the rims need to be assessed for their length and thickness. Minimum rim of 7mm is required for device closure. Floppy rims have a higher chance of having device embolization. Thus, device sizing needs to be done accordingly in such cases. In some cases, the defects can be mal-aligned which can affect the device sizing and placement.

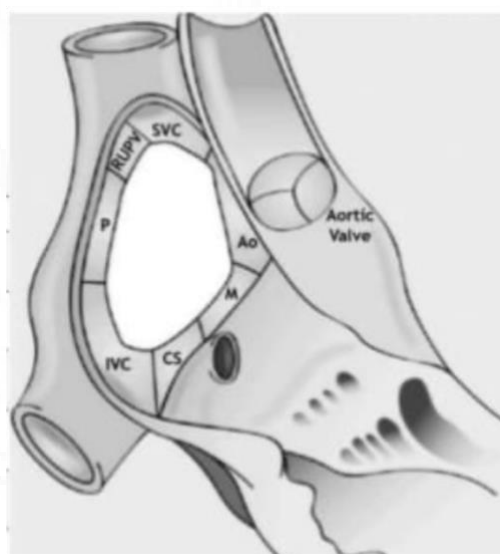


Figure 2. Schematic representation of different ASD rims

Along with assessment of ASD, pulmonary venous drainage also needs to be assessed. In the event of anomalous PV drainage, the patient is better suited for surgical closure of defect along with re-routing of pulmonary venous drainage to left atrium(LA). Presence of atrial septal aneurysm should be recorded as it can cause difficulty during device anchoring. Device sizing needs to be altered accordingly. Mitral valve needs to be assessed prior to device closure to rule out any associated mitral valve pathology which can cause elevated LA pressure after closure of ASD. Using a large device can sometimes encroach on the mitral valve, causing valve damage and mitral regurgitation. Hence, adequate mitral rim is important for planning device closure. Mitral valve also needs to be assessed before deploying the device to rule out any device impingement. In many cases, eustachian valve is very prominent and can be mistaken for IVC rim. A prominent eustachian valve may also cause obstruction to placement of device across the ASD.

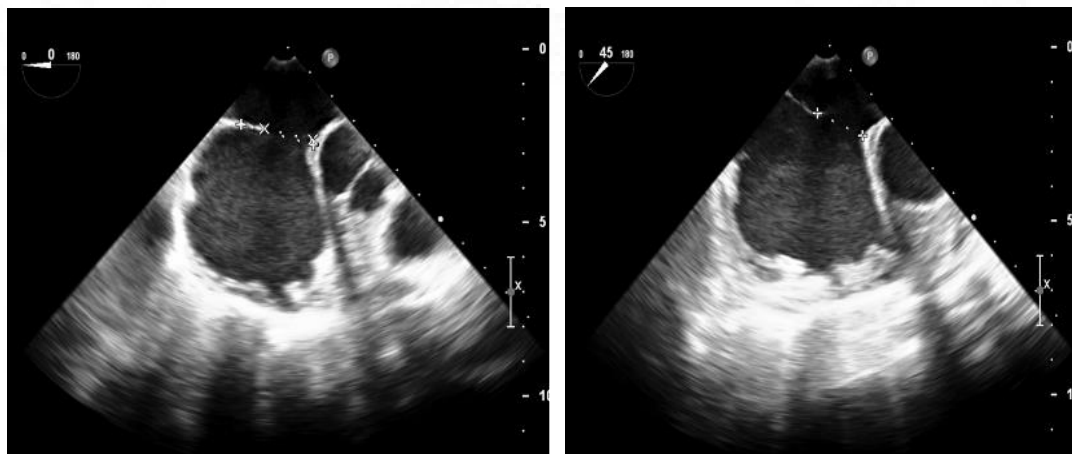


Figure 3. TEE in mid-esophageal position at 0° and 45° showing a mal-aligned ASD with adequate PV rim and posterior rim. Aortic rim is deficient.

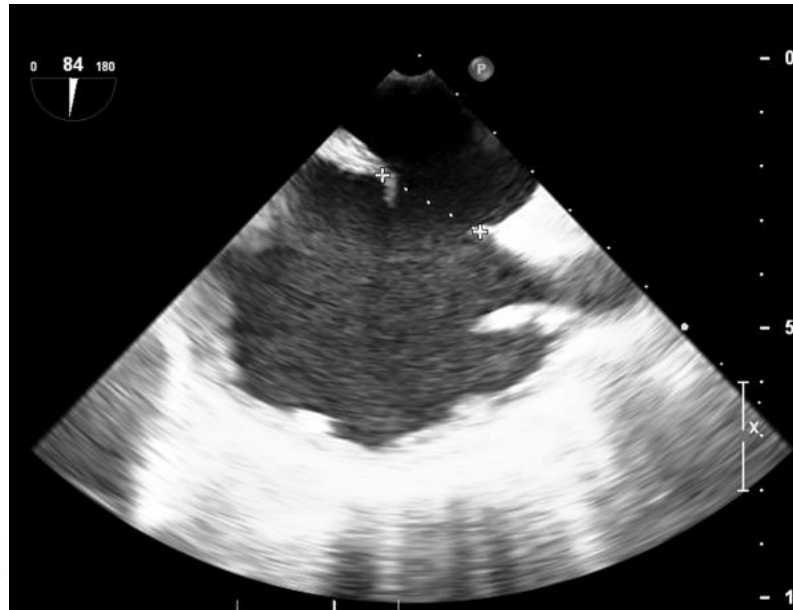


Figure 4. TEE in mid-esophageal position at 90° shows IVC and SVC rim with atrial septal defect. IVC rim is long and thick, which makes the defect suitable for device closure.

Presence of additional ASD also needs to be ruled out by careful examination of the entire atrial septum. In case of additional ASD, the size of ASD as well as distance from the other defect needs to be noted. If the secondary defect is close to the primary defect ($<7\text{mm}$), both defects can be closed using a single device, if rims are adequate.

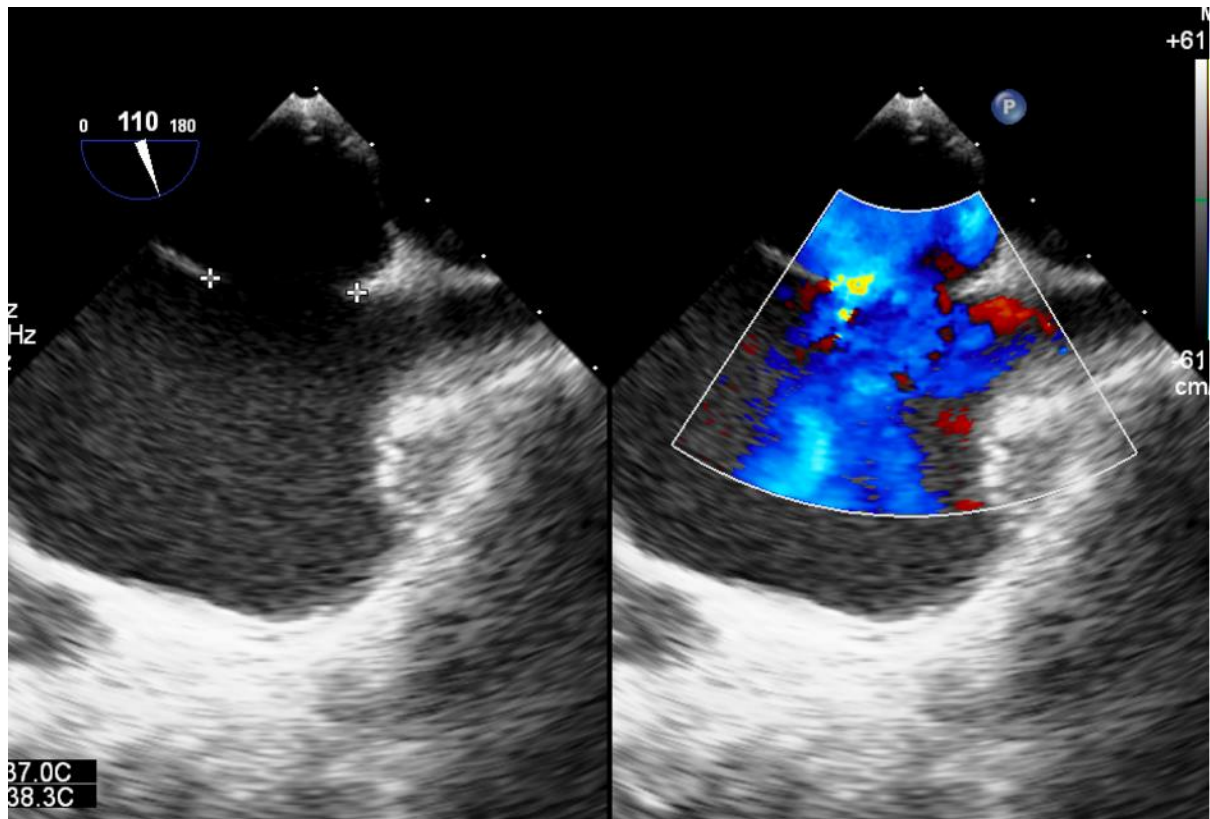


Figure 5. TEE 120° view at mid-esophageal location shows presence of adequate coronary sinus rim and SVC rim. Color doppler shows presence of single atrial septal defect shunting L-R.

During device deployment, TEE gives intraprocedural guidance as individual discs can be released while visualizing it on TEE. After initial placement of device across the defect, TEE helps in assessment of device stability and position of device in relation to various rims. A stable device position warrants that all rims should be well caught. Color flow doppler reveals any residual flow through the defect. If position is stable and all rims have been captured by the device, final deployment of the device can be done. Thus, 2D TEE helps in pre-procedural assessment of ASD as well as intraprocedural guidance during device closure.

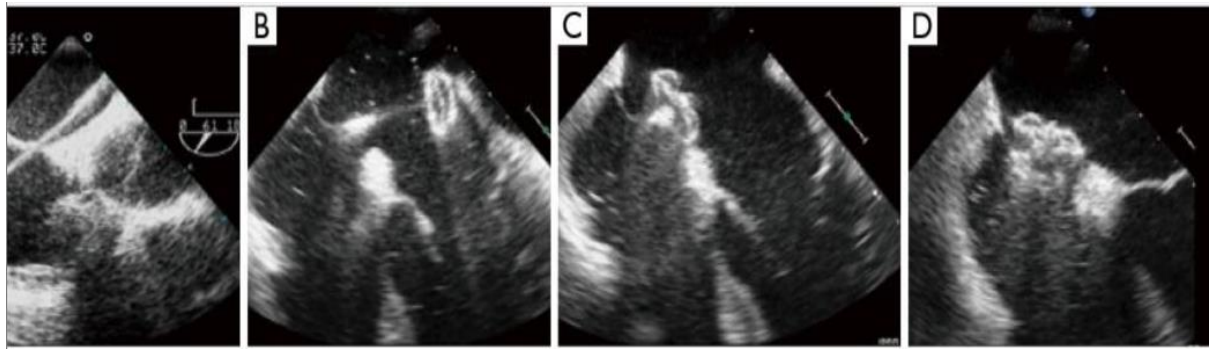


Figure 6. TEE guidance during ASD device closure. The sheath with the device can be seen across the defect. Initially, the LA disc is unsheathed which can be seen fully opening on TEE. Then, the system is pulled back towards the atrial septum till a tug is felt. The RA disc is slowly released from the sheath to deploy the device across the septum.

2D TEE is the most common modality used for ASD assessment. However, the major drawback is that we can only do a two-dimensional assessment of the defect which prevents analysis of important characteristics. The advent and regular use of 3D echocardiography has revolutionized the space of transcatheter structural heart interventions. It gives an opportunity to visualize the structure in 3D as it exists in its anatomical location and thus helps in proper evaluation and planning (15). The use of 3D TEE has been shown to be safe and feasible in transcatheter closure of ASD (16). Use of 3D imaging gives a better understanding of the defect characteristics including its spatial orientation, shape and relation to surrounding structures.

3D echocardiography provides multiple modalities which can be used for ASD assessment. The 3 main modes for 3D imaging are 3D zoom mode, Live 3D mode and full volume mode with iCrop. Each modality has its own strengths and weaknesses while delineating the ASD characteristics. 3D zoom mode utilizes a user-defined pyramid-shaped sample volume which can be adjusted in size and position. This imaging modality has the slowest volume rates amongst all 3D modalities. 3D zoom gives a clear en-face view of ASD with excellent image quality.

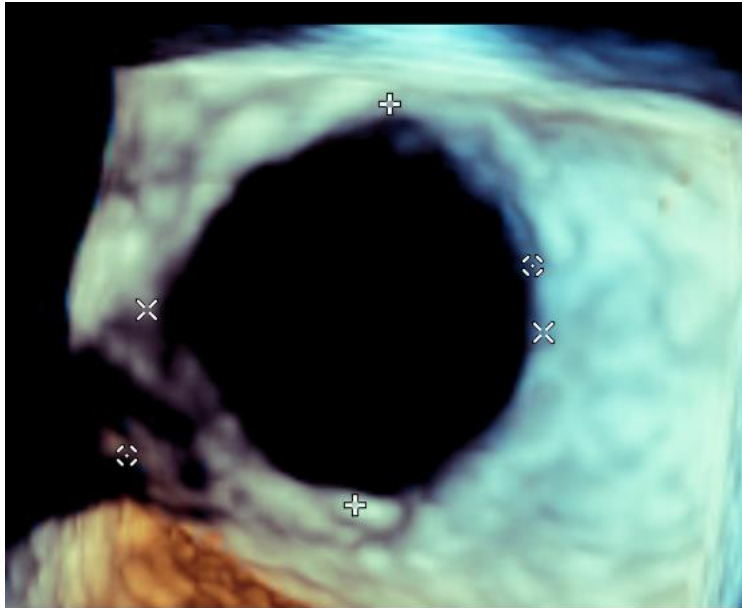


Figure 7. 3D zoom showing en-face view of ASD with surrounding rims.

Live 3D mode is another modality which can be used for 3-dimensional assessment of ASD. This modality has faster volume rates and better resolution. Good live 3D views can be obtained from the transgastric position. Full volume mode is the third modality which can be used for obtaining en-face 3D views. This modality stitches multiple beats in virtual real time to produce the image. The iCrop tool can be further utilized to trim and adjust the image as required.

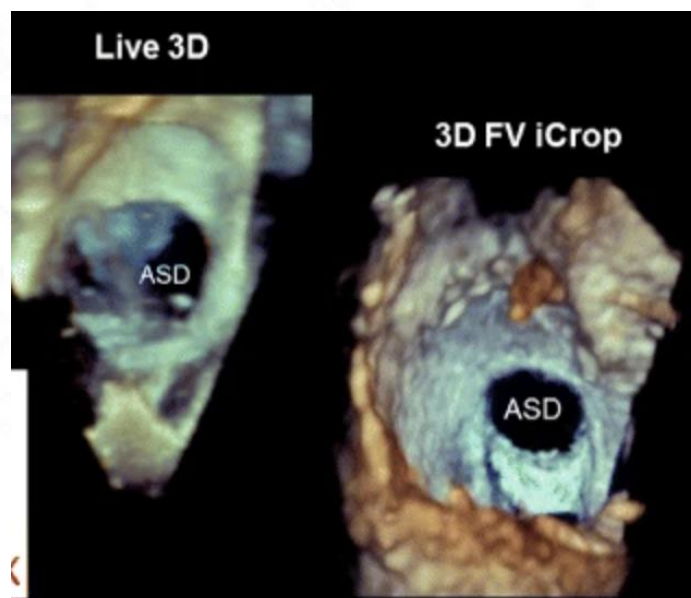


Figure 8. Live 3D and 3D full volume modalities showing en-face projection of ASD.

There are inherent advantages as well as limitations of 3D imaging for ASD assessment. 3D imaging helps to delineate the size, shape, orientation and rims status in a single image with excellent detail. Device related hardware can be easily seen on 3D imaging. The spatial relation of the device related hardware with surrounding structures can be easily made out when using 3D imaging, thus helping in intra-procedural guidance. Limitation of 3D imaging are mainly related to failure to obtain good 2D images on TEE in some patients. 3D zoom has low volume rates which can be overcome by using high volume rate settings. Similarly, full volume mode can have stitch artifacts which can hamper imaging. Overall, obtaining good quality 2D images with TEE is central to the process of 3D imaging.

Aims and Objectives

Hypothesis :

3D TEE has comparable efficacy for assessment and intraprocedural guidance for transcatheter ASD device closure as compared to 2D TEE.

Aim :

To evaluate the efficacy of 3D TEE for assessment of ASD and guidance for ASD device closure.

Objectives :

- Compare morphological characteristics of ASD using 3D TEE and 2D TEE
- Feasibility of using 3D imaging data for device sizing for transcatheter ASD closure

Methodology

Study design :

This was a prospective, single center observational study, conducted over a period of 1 year.

Sample size :

30 patients, who were planned to undergo transcatheter ASD closure, were recruited over a period of one year.

Inclusion criteria :

All patients, above 18 years of age, who were eligible for transcatheter ASD closure were included in the study.

Exclusion criteria :

Patients who have deficient rims, very large size ASD and poor TEE window were excluded from the study.

Study protocol :

All patients underwent a pre-procedure evaluation and their baseline demographics were recorded using a structured questionnaire. 2D TTE was done to determine the location and type of ASD as well its hemodynamic burden, including assessment of right cardiac chamber volume and function. Any other cardiac abnormality involving cardiac valves or ventricular function was sought for. Pulmonary hypertension was assessed in each case using tricuspid regurgitation jet. Right ventricular systolic pressure (RVSP) was used to calculate the pulmonary artery mean pressure using the formula [Pulmonary artery mean pressure = $(0.6 \times \text{RVSP}) + 2$]. Pulmonary artery mean pressure > 20mmHg was considered to be elevated. TAPSE (tricuspid annular plane systolic excursion) was used as a marker for right ventricular systolic function. TAPSE > 16mm was considered to be normal.

All patients underwent TEE using a Phillips EPIQ 7C ultrasound machine and 5MHz TEE probe. ASD assessment was done in the recommended echocardiographic views at 0°, 45°, 90° and 120°. In each view, ASD rims were assessed for length, thickness and stability. The maximum and minimum ASD diameter was recorded after assessment of different 2D TEE views. Presence of floppy rims were also recorded. ASD was also evaluated for any malalignment. After 2D TEE images were obtained, 3D imaging was performed using the same ultrasound machine. 3D zoom modality was used for generating high resolution en-face views of the ASD. Using the 3D image, other defect characteristics like defect shape, defect area and defect circumference were recorded. 3D imaging also gave an idea about the relation of defect with the surrounding structures. Using 3D imaging characteristics like defect area and circumference, a formula was devised to predict the appropriate device size for each defect.

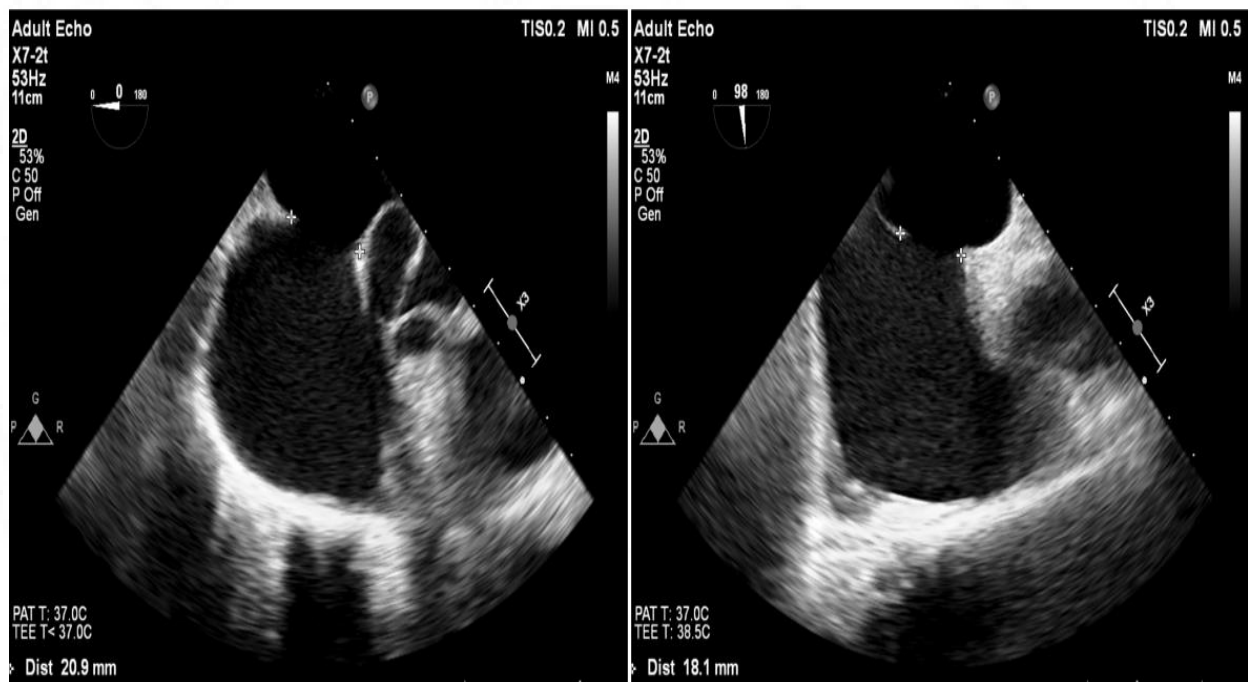


Figure 9. ASD measurement in different views on 2D TEE.

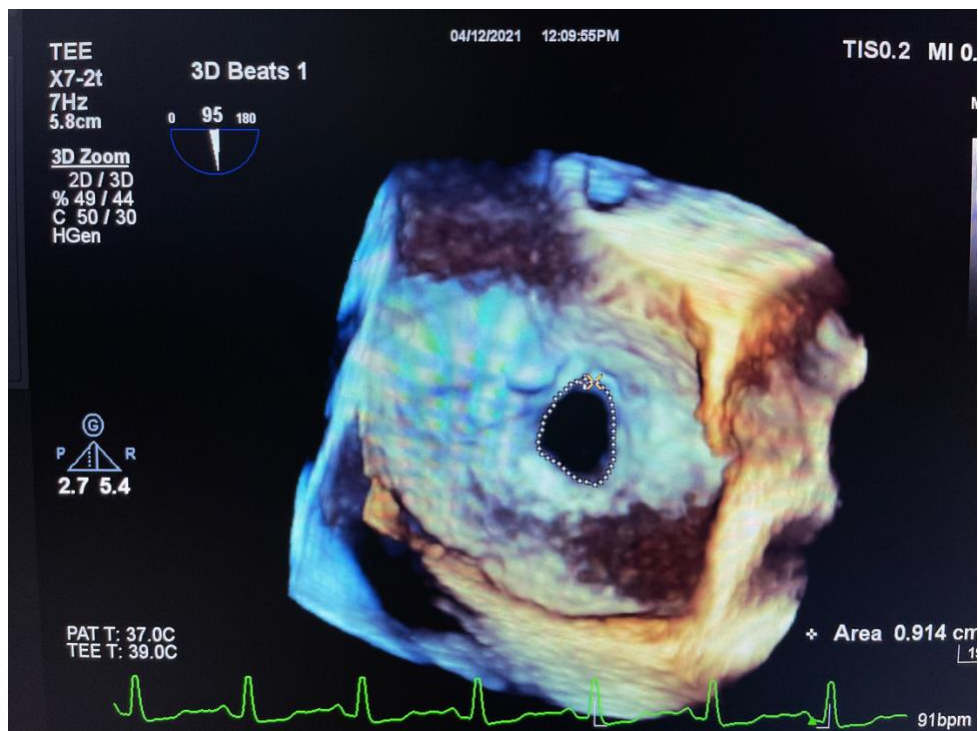


Figure 10 . 3D imaging showing presence of circular ASD with 3D area measuring 91.4 mm².

All patients, who were deemed suitable for transcatheter ASD closure, were taken up for device closure under both fluoroscopy and TEE guidance. Fluoroscopy was used intermittently during the procedure to check hardware position. Device sizing was done based on measurements obtained from 2D TEE imaging. The largest defect diameter was taken for the purpose of device sizing. An oversizing of 20% was considered while selecting the device size. We no longer use balloon sizing, for determining device size, at our institute. The hardware and device placement were guided by both fluoroscopy and 2D TEE. After deployment, 2D TEE was used to check for device stability and sealing of all ASD rims. Any residual flow was evaluated using color doppler. Mitral valve assessment was done to rule out any device impingement. Once satisfied, the device was released from the delivery cable.

Procedural time, defined as the time period from start of the procedure (after obtaining vascular access) to final deployment and release of device, was noted for each case. Any intraprocedural events like rhythm disturbances, hemodynamic instability was noted. Procedural complications like vascular access issues, cardiac perforation/tamponade, device embolization was recorded. All patients underwent 2D TTE prior to discharge for evaluating device stability , residual ASD flow and ventricular function.

Statistical analysis :

All data obtained using a structured questionnaire was recorded in a tabular format. Categorical variables were expressed as proportions and continuous variables were expressed as mean and standard deviations. Independent T test was used to compare the ASD rim sizes between the two diagnostic modalities. Correlation analysis was used to determine degree of correlation between ASD size measured on 2D vs 3D TEE. Device size used for defect closure was correlated with 3D characteristics of the defect. Regression analysis was used to derive an equation for predicting device size based on 3D defect characteristics. A p-value of <0.05 was considered as statistically significant. All analysis was done using SPSS v25.

RESULTS

30 patients were studied over the period of one year. The average age of the study population was 40.5 ± 12.05 years. Majority of patients were in the age group between 22-36 years.

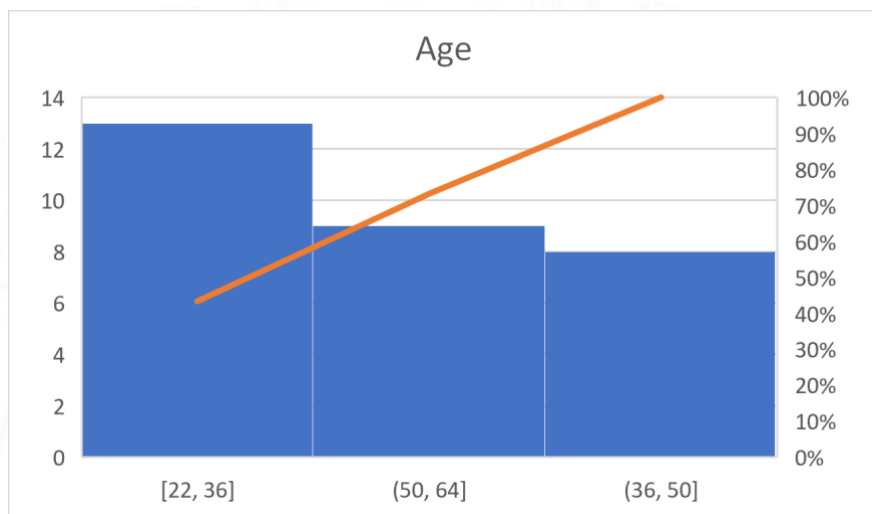


Figure 11. Age distribution of study population.

Majority of patients in the study cohort were females (83.3%).

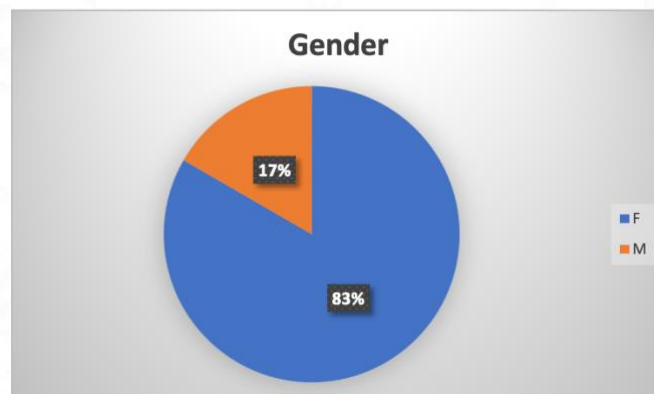


Figure 12. Gender distribution in study population

ASD patients have a variety of clinical presentation amongst which dyspnea was the most common in the current study (56.6%). The other clinical symptoms were chest pain (30%), palpitations (40%) and syncope (3.3%).

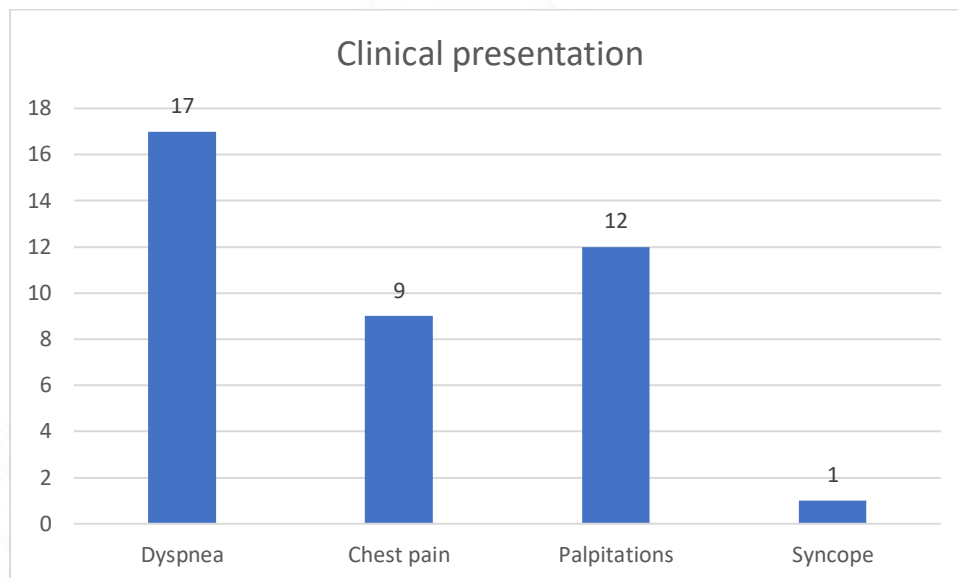


Figure 13. Clinical presentation in the study population

Amongst the study population, 16.6% patients were diabetic, 10% were hypertensive whereas 3.3% were dyslipidemic. Hypothyroidism was noted in 13.3% of the study population.

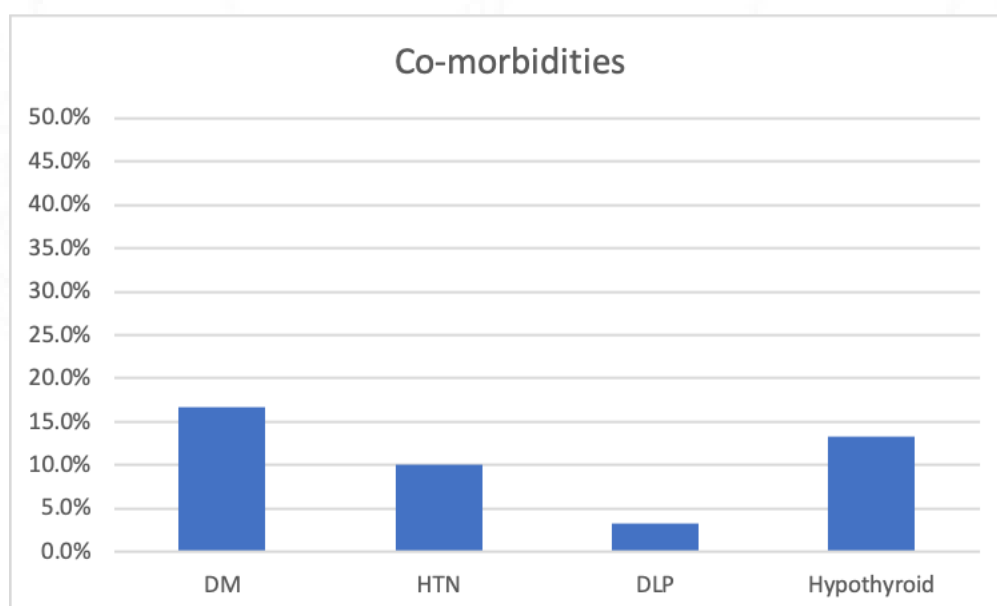


Figure 14. Co-morbidities within the study population

None of the patients in the study cohort had known coronary artery disease or history of right heart failure.

ECG analysis revealed that majority of patients were in sinus rhythm (96.7%). Only one patient in the study cohort was in atrial fibrillation at the time of presentation. Right bundle branch block pattern was noted in 63.3% patients. The mean QRS axis in the patient cohort was 61 ± 32.6 degrees. Chest x-ray did not reveal significant cardiomegaly in any of the study participants with mean cardiothoracic ratio (CTR) being 0.52 ± 0.06 .

Transthoracic echocardiography (TTE) revealed normal LV function in all study participants. The mean LV ejection fraction in the study group was $65.9 \pm 6.8\%$. Mitral regurgitation was noted in 10% of the patients. Tricuspid regurgitation (TR) was mild in majority of the patients (96.7%) whereas moderate TR was noted in one patient. Mean right ventricular systolic pressure noted in the study population was 31.9 ± 11.5 mmHg signifying mild pulmonary hypertension. The mean ASD diameter noted on TTE was 19.8 ± 5.3 mm.

2D transesophageal echocardiography (TEE) was performed for all study participants. The average maximum ASD diameter noted on 2D TEE was 20.9 ± 4.87 mm whereas the average minimum diameter was 17.1 ± 4.6 mm. ASD rim assessment was done on 2D TEE for the purpose of assessing suitability for device closure. Adequate rims were noted in all patients in the study cohort.

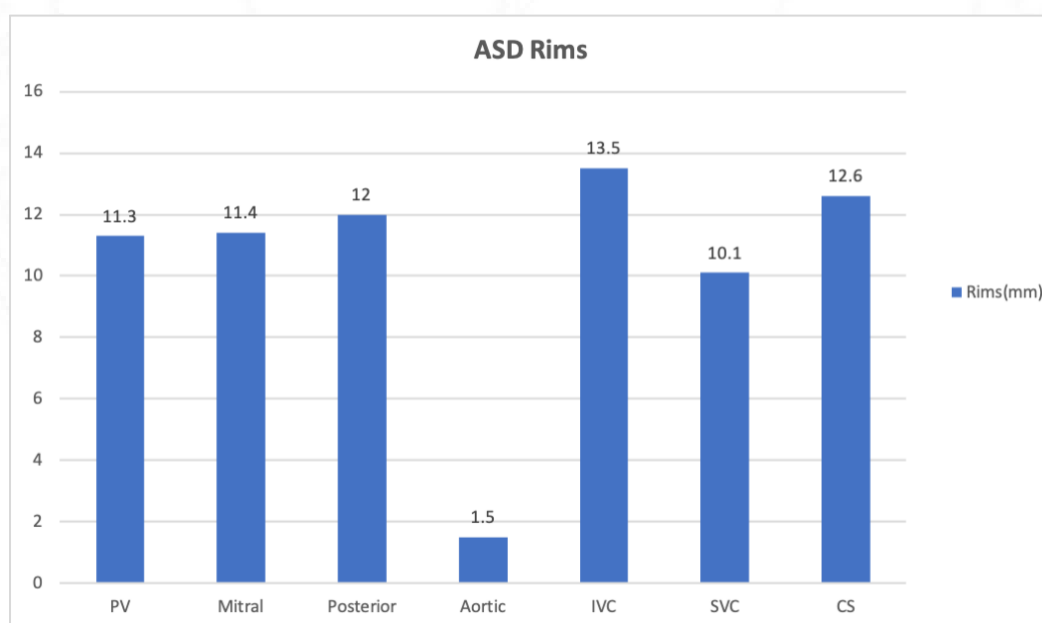


Figure 15. ASD rims on 2D TEE.

Aortic rim was deficient in all cases whereas all other rims were good sized. A significant proportion of defects noted in the study population were malaligned (63%) whereas one or more rims were mildly floppy in half of the study population.

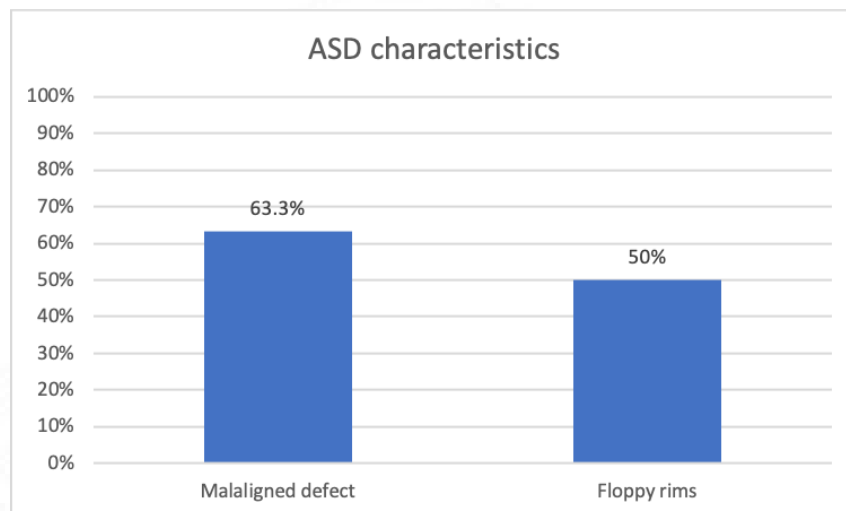


Figure 16. Characteristics of ASD on 2D TEE

3D imaging was performed in 25 patients in the study cohort. 3D rendering could not be done in the remaining five patients predominantly due to floppy rims and poor 2D image quality. The average maximum ASD diameter on 3D imaging was 19.04 ± 4.6 mm whereas the average minimum ASD diameter on 3D was 15.3 ± 4.3 mm. 3D imaging of ASD was used to determine area and circumference of ASD. The average ASD area derived on 3D imaging was 214.3 ± 104 mm² whereas average ASD circumference was 50.4 ± 13.2 mm. 3D imaging also helped to determine the shape of the defects, with majority (60%) of them being circular in shape.

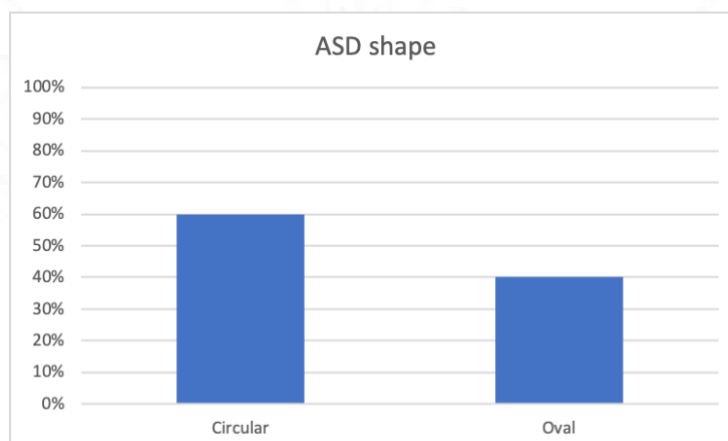


Figure 17. ASD shape on 3D imaging

ASD device closure was done in all patients under TEE guidance. The average device size used in study cohort was 25.8 ± 4.9 mm. The average surface area of device used was 549.9 ± 202.7 mm² whereas device circumference was 81 ± 15.4 mm. The average procedural time in the study cohort was 25.4 ± 8.9 min. 3 patients had arrhythmia during device closure. 2 patients had atrial arrhythmias which subsided spontaneously at the end of the procedure whereas the other patient had accelerated junctional rhythm during the procedure which spontaneously reverted to sinus rhythm. None of the patients had any access site complications or device related complications like cardiac tamponade or device embolization.

Post procedure, all patients had stable device position with no residual flow on transthoracic echocardiography. The average post-implant LVEF was $64.2 \pm 5.3\%$. None of the patients had RV dysfunction on pre-discharge TTE.

On analysis of baseline characteristics, no difference was noted in defect size between male and female patients ($p=0.230$). There was poor correlation between defect size and age of the study population ($R=0.245$, $p=0.237$). Similarly, there was no correlation between QRS axis on ECG and defect size ($R=0.1036$, $p=0.585$). A high degree of correlation was noted between maximum ASD diameters as measured on 2D and 3D TEE ($R=0.9101$, $p<0.0001$). Similarly, high degree of correlation was also noted for minimum ASD diameter as measured on 2D and 3D TEE ($R=0.8815$, $p<0.0001$).

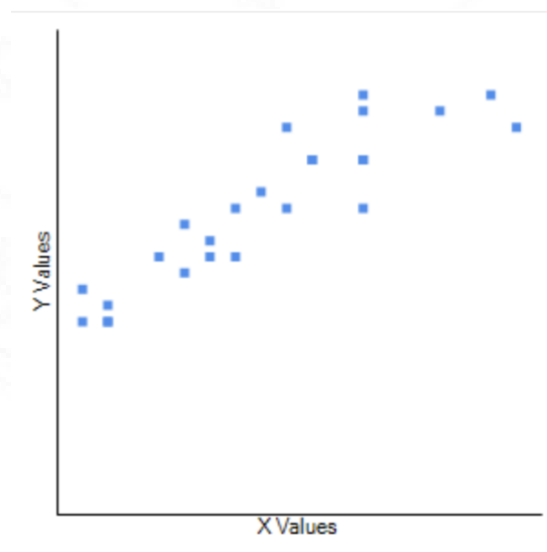


Figure 18. Correlation between maximum ASD diameters as measured on 2D and 3D TEE. X axis – 2D TEE diameter, Y axis – 3D TEE diameter.

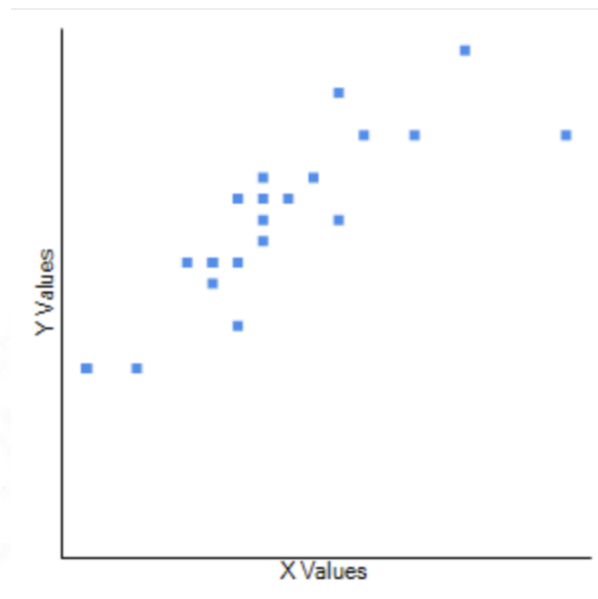


Figure 19. Correlation between minimum ASD diameters as measured on 2D and 3D TEE. X axis – 2D TEE diameter, Y axis – 3D TEE diameter.

3D imaging characteristics for different defects were also analysed. There was a significant difference noted in 3D defect area between oval and circular defects, with oval defects having significantly larger area than circular defects (270.5 ± 108.3 vs 176.8 ± 104.1 mm², respectively; $p=0.011$). Device area was significantly larger than measured 3D defect area (512.6 ± 202.7 vs 214.3 ± 104.1 mm², respectively; $p<0.0001$). Similarly, device circumference was also larger than 3D defect circumference (78.1 ± 15.4 vs 50.4 ± 13.2 mm, respectively; $p<0.0001$). Device size was significantly larger for oval defects as compared to circular defects (27 ± 4.9 vs 23.4 ± 4.9 mm, respectively; $p=0.02$). A significant proportion of patients had defects which were malaligned or had floppy rims. No significant difference in 3D defect area was noted between malaligned and non-malaligned defects (219.8 ± 104 vs 206.1 ± 107.2 mm², respectively; $p=0.377$). Similarly, 3D defect area was similar amongst ASD with floppy and sturdy rims (193.4 ± 107.2 vs 228.2 ± 104.1 mm², respectively; $p=0.211$).

There was very good correlation noted between 3D defect area and device size ($R=0.756$, $p<0.0001$) as well as 3D defect area and device area ($R=0.746$, $p<0.0001$).

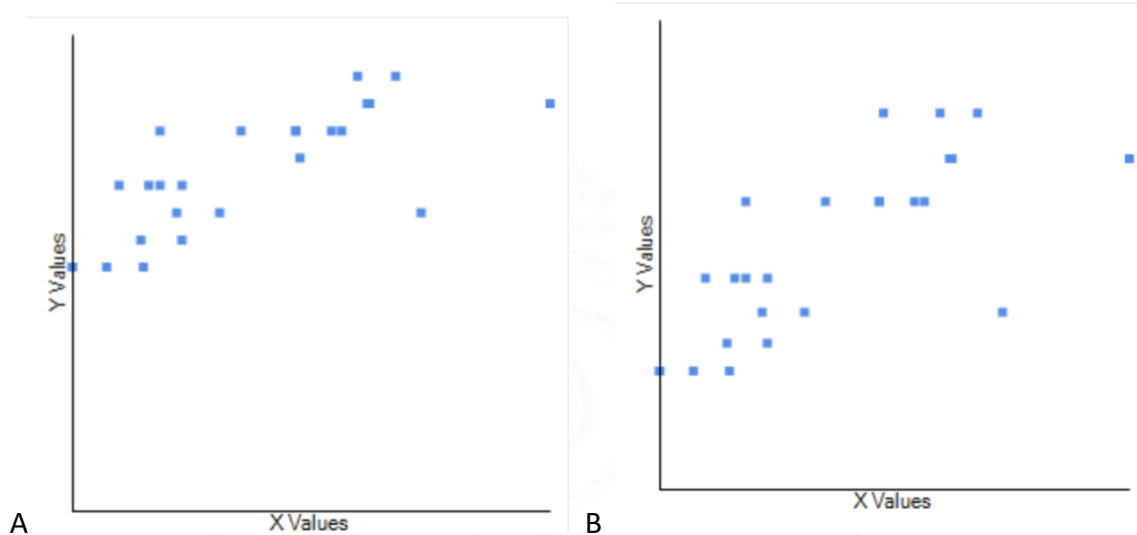


Figure 20.A. Correlation analysis between 3D defect area and device size (x-3D defect area, y-device size). B. Correlation analysis between 3D defect area and device waist area (x-3D defect area, y-device waist area)

Similarly, there was high correlation between 3D defect circumference and device size ($R=0.662$, $p=0.003$) as well as device circumference ($R=0.663$, $p=0.0003$).

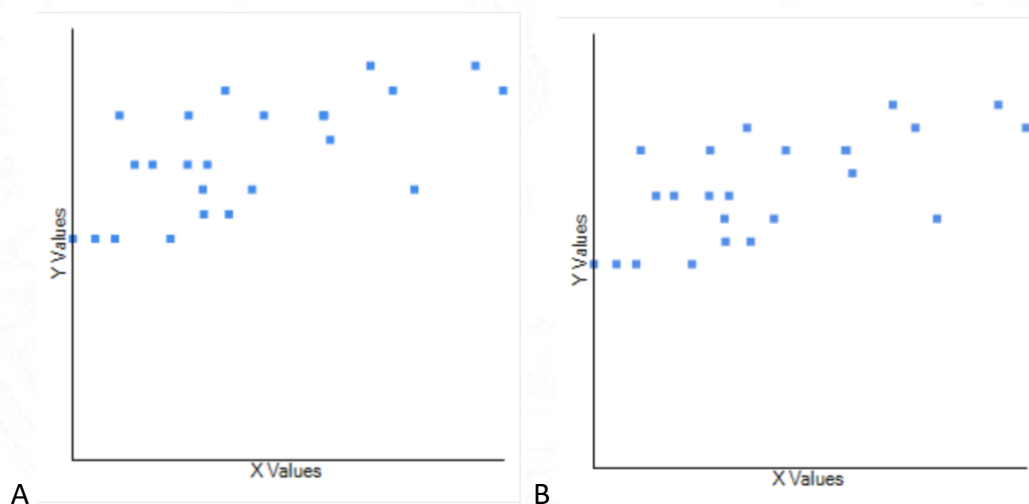


Figure 21. A. Correlation analysis between 3D defect circumference and device size (x-3D defect circumference, y-device size). B. Correlation analysis between 3D defect circumference and device circumference (x- 3D defect circumference, y-device circumference).

Based on the regression analysis, we aimed to calculate the predicted device size using 3D imaging characteristics of device area and device circumference. In order to do so, a regression equation was derived as follows :

$$\hat{y} = 0.03199X_1 + 0.01238X_2 + 17.39961$$

where x1 – area, x2 – circumference, y – predicted device size

Based on the above regression equation, predicted device size was calculated for each patient based on 3D defect area and circumference. There was no difference noted between predicted device size, calculated from the regression equation, and actual device size used in the procedure (24.88 ± 4.9 vs 24.32 ± 3.2 mm, respectively; $p=0.31$).

Discussion

The unique ability of 3D echocardiography to provide high resolution en-face view of ASD helps in proper assessment of defect size and rim adequacy, as well as evaluation for any additional ASD. It is these characteristics of 3D imaging which was utilized in the current study, to determine its feasibility for use in transcatheter ASD closure. The current study included 30 adult patients, deemed suitable for transcatheter ASD closure, who were recruited over a period of one year. The study population was middle aged with mean age being 40.5 ± 12.05 years. Majority of the patients in the study cohort were females. This highlights the fact that ostium secundum ASD has a female preponderance of almost 2:1 and majority of cases are diagnosed in adulthood(17). Dyspnea, palpitations and chest pain were the most common presenting complaints in the current study cohort. The symptomatology usually depends on the defect size. Small defects are usually asymptomatic and go undetected. Larger defects usually present with symptoms in the third decade of life with main symptoms of dyspnea, exercise intolerance, fatigue and palpitations(18). Overt right heart failure is uncommon with ASD, as was seen in the current study. Patients who develop significant pulmonary hypertension may get predisposed to developing right heart failure on long term follow up. ECG analysis showed that majority of study patients were in sinus rhythm. Patients with ASD are predisposed to develop atrial arrhythmias like atrial flutter or fibrillation, secondary to atrial dilatation. It can be noted in one-fifth of ASD patients pre-operatively (19). The typical rsR pattern in lead V1 on ECG was seen in 63% of the study population, which is a marker of right heart overload (1).

2D TTE revealed normal ventricular function in all study participants. None of the patient in the study had more than mild pulmonary hypertension. Majority of the patients had only mild tricuspid regurgitation whereas mitral regurgitation was noted in 10%. The ASD diameter measured on 2D TTE was consistently smaller than that measured on 3D TEE. This is expected as TEE provides better resolution images which helps to image the entire length of atrial septum. The best window for ASD evaluation in 2D TTE is the subxiphoid view, which is usually sub-optimal in adult patients.

2D TEE is the main modality used for ASD assessment and intraprocedural guidance. 3D imaging was also used in cases where good 3D datasets were acquired. There was no significant difference between ASD dimensions measured on 2D vs 3D TEE. A high degree of correlation was noted between 2D and 3D imaging for maximum and minimum ASD diameters. Hascoet et al. evaluated 30 ASD patients using 2D and 3D TEE and compared the ASD dimensions with balloon sizing diameters. There was a high correlation noted between 2D and 3D TEE for maximal ASD diameters in both round and oval ASD(20). Another study by Seo et al. enrolled 107 consecutive patients who underwent transcatheter ASD closure. They also showed that there was very good correlation between maximal ASD diameters as measured on 2D and 3D TEE (21).

3D imaging helps in determining the shape and orientation of the defect, which ultimately affects the device size. The device area was significantly larger than the defect area for both oval and circular defects in the current study. Similar findings were also noted in the study by Roushdy et al. This can be attributed to the fact that device sizing is currently based on maximal diameters obtained on 2D TEE. Device oversizing by 2-4mm is recommended on the basis of maximal ASD diameter. A significant proportion of these defects are oval, which can only be deciphered on 3D imaging. Hence, larger devices are commonly used to ensure complete coverage of defects. In spite of significant differences, there was good correlation between 3D defect area and circumference with device area and circumference. Roushdy et al. also showed good correlation between defect and device measurements.

Oval defects had larger defect area and circumference than round defects on 3D imaging. Consequently, the device area and circumference for oval defects were also larger than those for round defects. Presence of malalignment or floppy rims did not significantly device sizing as 3D defect area was similar amongst these patients.

A very good correlation was noted between 3D defect area and device size as well as 3D defect circumference and device size in our study. Owing to good correlation between the two modalities, we were able to derive an equation to predict device size using 3D imaging characteristics involving defect area and circumference. This will help to incorporate the 3D characteristics of the defect when planning for device closure and help in better device sizing. To our knowledge, this is the first study which has incorporated both defect area and circumference into a single equation to predict optimal device size. There

are limited studies in the literature which have used regression equations to derive device sizes. However, majority of them were complex equations which were difficult to use in routine clinical practice and did not take into account all the 3D characteristics of the defect.

One of the first studies which attempted to derive an equation for predicting device size was by Seo and colleagues who prospectively enrolled 107 consecutive patients who underwent transcatheter ASD closure(21). They evaluated the relationship between balloon stretched ASD diameter and diameters measured using 2D and 3D TEE. They devised an equation as follows –

$$\text{Device size} = (0.964 \times 3D \text{ max}) - (2.622 \times \text{circular index}) + 7.084$$

Where 3D max refers to maximal ASD diameter on 2D TEE whereas circular index refers to ratio of maximal and minimal ASD diameters. This study did not take into account the other 3D defect characteristics like defect area and defect circumference like the current study, which can provide a lot more information. Moreover, it is difficult to use complex equations in everyday clinical practice.

Another study which attempted to derive an equation for device size was by Hascoet et al., who enrolled 30 consecutive ASD patients undergoing transcatheter ASD closure and derived an equation using multivariate linear regression analysis. All the equations were based on predicting the balloon stretched diameter of the ASD. Hascoet and colleagues derived 2 separate models. The 1st model was :

$$BS = (1.07 \times 3D \text{ max}) - (3.1 \times \text{ASD shape}) + 3$$

Where BS refers to balloon stretched diameter and 3D max refers to maximum ASD diameter measured on TEE. Oval defects were assigned a value of 1 whereas circular defects were assigned a value of 0.

The 2nd model was :

$$BS = (4.5 \times \text{ASD area}) + 11.5$$

Both the models mentioned above were based on predicting the balloon stretched diameter of ASD and not the actual device size. There can be considerable differences between balloon sized diameter and the actual device size used, based on multiple variables. Hence, these models are not very feasible for routine clinical practice.

Balloon sizing of ASD is commonly used in many centers for purpose of deciding on device size for ASD closure. The stretched diameter of the balloon, measured either on fluoroscopy or TEE, which fully occludes the defect is used for the purpose of device

selection. However, this method is fraught with disadvantages and its use has likely come down with routine use of TEE. Balloon sizing can be associated with tear in the flap valve of the septum primum which can lead to enlargement of the defect (22). Prolonged balloon inflation across the defect can be associated with bradycardia and hypotension, due to reduced diastolic filling (23). There also underlies a small risk of damage to the interatrial septum. Moreover, the diameter obtained from balloon stretching the ASD may not be appropriate if the defect is not profiled correctly. Comparative analysis has been done between balloon sizing of ASD and using TEE alone for determining device size for ASD closure. In a cohort of 128 consecutive patients who underwent transcatheter ASD closure, Gupta et al. compared patients who underwent device closure based on balloon sizing (group 1) as compared to those who underwent device closure based on TEE measurements (group 2) (24). They found that device success was higher in group 2 as compared to group 1 (89.6% vs 67.2%, respectively; $p = 0.002$). Upsizing of ASD device was also comparatively lower in group 2 ($p < 0.001$). This shows that balloon sizing is not necessary for transcatheter ASD closure and TEE gives comparable and better results.

Similar to the current study, Roushdy et al. aimed to devise a novel 3D echocardiographic method for transcatheter device closure (25). They prospectively recruited 50 patients undergoing ASD device closure on the basis of 2D and 3D TEE measurements. Their study showed a high degree of correlation between ASD diameters measured on 2D and 3D TEE whereas similar correlation was noted between 3D defect area and device size. This was similar to what was noted in the current study. Based on correlation analysis, they used regression analysis to develop models for device size prediction.

$$\text{Device size} = 10.8 + (3.95 \times 3\text{D ASD area})$$

$$\text{Device size} = (3.85 \times 3\text{D ASD circumference}) - 1.02$$

Both these models were used to predict device size, which was not significantly different from the actual device size used for defect closure ($p=0.94$). Although both models have been shown to have similar predictive value, there can be instances where the results may be discordant. Thus, it is easier to use a single model which has all the different variables incorporated together. It will improve the ease of use and will reduce the problems arising from discordant results.

The current study helps to incorporate different 3D imaging variables into a single model which can help predict device size. The predicted device size in the current study was similar to the actual device size used. This makes the model accurate and a relatively simpler one to use in daily clinical practice. The use of 3D defect characteristics will likely help us improve our device sizing as 2D TEE gives only an incomplete idea about a 3-dimensional structure. Device sizing needs to be accurate as larger devices can be associated with mushrooming deformity, impingement of neighboring cardiac structures and cardiac erosion (26). Another utility of using 3D imaging is that helps in determining shape of the defect. The defect area varies with the shape of the defect, as shown in the current study. Thus, a single sized device may not be suitable for different shaped defects having same diameter. Currently, we do not have custom made devices available in the market for different ASD shapes. However, this may be useful in certain circumstances where significant device oversizing carries the risk of cardiac erosion. Custom made devices can help mitigate the risk in these situations. Thus, new innovations in the field of device technology needs to be explored and encouraged.

Limitations

The current study has its inherent limitations. 3D echocardiography is associated with its own set of challenges and limitations. Optimal 2D images are required to generate high resolution 3D images, which may not be possible in each case. In the current study, we could not generate 3D datasets for 5 patients due to similar reasons. Secondly, proper optimization of 3D image plays a big role in correct assessment of defect. Improper gain settings, presence of artifacts like stitch artifacts can hamper proper interpretation of defect characteristics. Thirdly, the device prediction equation generated in the study needs to be validated in another large cohort of patients. After proper validation only, the equation can be used on a wider basis. If the model is validated in larger studies, automated 3D software can be devised which can automatically generate predicted device size based on the recorded 3D images. This artificial intelligence(AI) based software can make the procedure easier and faster.

Conclusion

3D TEE guidance for transcatheter ASD closure is equally efficacious when compared to 2D TEE guidance. A high degree of correlation is noted between the defect characteristics measured on 2D and 3D imaging. 3D imaging helps to provide additional information about the defect which can help in device sizing. Prediction models for device sizing, which incorporate 3D defect characteristics, have been shown to be accurate. The use of 3D imaging-based models provides a simple and novel technique that increases the safety and accuracy of transcatheter ASD closure.

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APPENDIX

Study Proforma

Patient ID -

Name -

Age -

Gender –

Chief complaints – Dyspnea/palpitations/syncope/angina/others

Comorbidities – DM/HTN/DLP/Thyroid disease/CAD

Medications –

Age at diagnosis –

Clinical examination

PR = , Distal pulses palpable Y/N

BP =

JVP -

Pedal Edema -

Cardiovascular examination –

Chest –

Any other relevant findings –

Investigations -

ECG –

Chest X-Ray –

2D echo –

LV dimensions/LVEF

RV dimension/RV function

Pulmonary artery flow velocity

ASD size

MR/TR

2D Trans-esophageal echocardiography –

ASD maximum diameter –

ASD minimum diameter -

Rims – SVC/IVC/Aortic/Pulmonary vein/coronary sinus

Malaligned defect – Y/N

Floppy rims – Y/N

3D TEE –

ASD maximum diameter –

ASD minimum diameter –

ASD shape – circular /oval

3D ASD area –

3D ASD circumference -

Size of occluder device –

Fluoroscopy time –

Total procedure time –

Procedural complications – Arrhythmias/access related complications/tamponade/device embolization

Post procedure

TTE findings –

Device stability

Residual flow – Y/N

RV dimensions/RV function

LV dimensions/ LV function

CONSENT FORM

Title of the study:

3D echocardiographic guidance for transcatheter ASD device closure : a comparative study

Participant's name:

Age (in years):

I _____, son/daughter/husband/wife of
_____ declare that (Please tick boxes)

- I have read the above information provided to me regarding the study. []
- I have clarified any doubts that I had. []
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal Rights []
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. []
- I understand that my identity will not be revealed in any information released to third parties or in publication of study results. []
- I voluntarily agree to take part in this study []
- I understand that participation in the study means that I am willing to undergo the said procedure as already explained and my health records shall be accessed by the investigators for the purpose of the study. []
- I understand that I do not have to bear any extra expense for the purpose of this study. No financial support will be provided to me for participation in the study. []
- I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [].
- I have received a copy of this signed consent form []

Name:

Signature:

Name of witness:

Signature:

Relation to participant:

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her
, in nontechnical terms, all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I

further certify that I encouraged the participant to ask questions and all questions asked were answered.

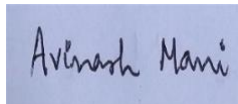
Name:

Signature:

Date:

Place:SCTIMST, Thiruvananthapuram

Principal investigator

A small rectangular box containing a handwritten signature in blue ink. The signature appears to read "Avinash Mani".

Dr. Avinash Mani

SreeChitra Quarters, Kumarapuram

Trivandrum

Mobile. 08820311853

Study Independent Contact Person

Dr. Srinivas G

0471-2344689

MASTER CHART

[illegible]

ASD max(30 TE)	ASD min	ASD area(mm ²)	ASD circumference(mm)	ASD shape	ASD device size	Device area(mm ²)	Device circumference	Procedure time	Fluo time	Arrhythmias	Access site complica	Temperature	device embolisation	UV function	RV dysfunction	device stable	residual flow	Device size based o
18	14	156	45 CIRCULAR		22	379.94	69.08	25	5 N	N	N	N	N	66 N		Y	N	22.52
26	22	316	66.2 OVAL		30	706.5	94.2	25	6 N	N	N	N	N	68 N		Y	N	27.532
26	24	340	75.4 OVAL		32	803.84	100.48	60	19 Y	N	N	N	N	55 N		Y	N	28.344
					34	907.46	106.76	30	1.5 N	N	N	N	N	75 N		Y	N	
12	9	128	41.4 CIRCULAR		18	254.34	56.52	15	3.5 N	N	N	N	N	72 N		Y	N	21.644
16	9	126	47.9 OVAL		20	314	62.8	30	10 N	N	N	N	N	65 N		Y	N	21.649
13	9	68.4	30.5 OVAL		18	254.34	56.52	35	9 Y	N	N	N	N	60 N		Y	N	19.747
20	17	192.2	50.5 CIRCULAR		22	379.94	69.08	20	7 N	N	N	N	N	60 N		Y	N	23.661
19	17	210.2	51.8 CIRCULAR		28	615.44	87.9	20	5 N	N	N	N	N	65 N		Y	N	24.214
25	17	294.6	35.7 OVAL		28	615.44	87.9	30	6 N	N	N	N	N	62 N		Y	N	26.885
					34	907.46	106.76	25	5 N	N	N	N	N	70 N		Y	Y	
					24	452.16	75.36	20	4 N	N	N	N	N	77 N		Y	N	
19	15	361.5	68.6 CIRCULAR		22	379.94	69.08	25	5 N	N	N	N	N	65 N		Y	N	28.921
24	18	469.9	78.5 OVAL		30	706.5	94.2	25	4 N	N	N	N	N	65 N		Y	N	32.272
25	20	318.4	47.5 OVAL		30	706.5	94.2	20	4 N	N	N	N	N	62 N		Y	N	27.417
17	14	160.4	45.1 CIRCULAR		20	314	62.8	20	3.5 N	N	N	N	N	61 N		Y	N	22.653
24	20	308.1	63.7 CIRCULAR		32	803.84	100.48	22	4 N	N	N	N	N	64 N		Y	N	27.27
					30	706.5	94.2	20	3.5 N	N	N	N	N	60 N		Y	N	
					30	706.5	94.2	25	4 N	N	N	N	N	60 N		Y	N	
22	20	286.1	58.4 CIRCULAR		28	615.44	87.9	18	4.5 N	N	N	N	N	58 N		Y	N	26.557
22	17	259.7	59.2 OVAL		26	803.84	81.64	18	3 N	N	N	N	N	60 N		Y	N	25.773
14	9	68.3	33 CIRCULAR		18	254.34	56.52	18	3.5 N	N	N	N	N	62 N		Y	N	19.769
22	16	256.1	58.5 OVAL		28	615.44	87.9	20	3.5 N	N	N	N	N	58 N		Y	N	25.658
15	13	132.6	39.4 CIRCULAR		24	452.16	75.36	18	4 N	N	N	N	N	60 N		Y	N	21.762
16	14	142.1	43.4 CIRCULAR		28	615.44	87.9	45	10 N	N	N	N	N	65 N		Y	N	22.087
12	11	107.6	37.4 CIRCULAR		24	452.16	75.36	30	4.5 N	N	N	N	N	66 N		Y	N	20.992
12	9	97.1	35.2 CIRCULAR		18	254.34	56.5	25	4 N	N	N	N	N	74 N		Y	N	20.655
22	16	256.1	58.5 OVAL		28	615.44	87.9	28	4.5 Y	N	N	N	N	66 N		Y	N	25.658
16	14	142.1	43.3 CIRCULAR		24	452.16	75.36	25	4 N	N	N	N	N	66 N		Y	N	22.086
19	18	160.6	45.5 CIRCULAR		24	452.16	75.36	25	4 N	N	N	N	N	60 N		Y	N	22.663



Technical Advisory Committee (Clinical Studies)
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM - 695011, INDIA



TAC Registration No: SCT-/S/2021/1247

Date: 05.05.2021

Project title: COMPARISON OF INTRACARDIAC ECHOCARDIOGRAPHY VS. TRANS-ESOPHAGEAL ECHOCARDIOGRAPHY GUIDANCE FOR PERCUTANEOUS ATRIAL SEPTAL DEFECT CLOSURE

Principal Investigator:	
Dr. Avinash Mani, PDF, Adult Interventions, Department of Cardiology, SCTIMST Degree MBBS, MD (Med), DM (Cardiology)	
Co-Principal Investigator(s):	
Dr. Harikrishnan S, Professor, Department of Cardiology, SCTIMST	Degree MBBS, MD (Med), DM (Cardiology)
Dr. Bijulal S, Professor, Department of Cardiology, SCTIMST	Degree MBBS, MD (Med), DM (Cardiology)
Dr. Ajit Kumar V.K., Professor Senior Grade, Department of Cardiology, SCTIMST	Degree MBBS, MD, DM

Members who participated in the TAC meeting on 23.03.2021 and 24.03.2021

Dr. Harikrishnan S (Chairman)
Dr. Manikandan S
Dr. Sylaja P N
Dr. Sanjeev G
Dr. Ramshekhar N Menon
Dr. Jayanand Sudhir B
Dr. Jayadevan E R
Dr. Syam K
Dr. Sabarinath Menon
Dr. Deepti A N
Dr. Madhusoodanan U K
Dr. Srinivas G (Member Secretary)

Dr. Sylaja P N, Dr. Ramshekhar N Menon, Dr. Jayanand Sudhir B, Dr. Manikandan S, Dr. Jayadevan E R, Dr. Syam K, Dr. Deepti A N, Dr. Madhusoodanan U K and Dr. Harikrishnan S stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#1218, 1219, 1225, 1226, 1227, 1229, 1232, 1233, 1235, 1238, 1240, 1245, 1247)

Risk Classification of the project (Minimum/ Moderate/ High): Minimum

Requirement of DSMB: No

Recommended members of DSMB: Not applicable

Recommendations of TAC:

Recommended for consideration of IEC in the light of the responses received from the investigator

The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

Dr. Harikrishnan S
Chairman, TAC (Clinical Studies)

Note for IEC

Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

Appendix-1

1. Since ICE is already known to be a standard technique for percutaneous ASD closure, please check the objective #2: safety.

Answer: As has been mentioned, ICE is a standard technique for ASD closures but it is not very routinely used. In the current study, we also aim to evaluate the safety of ICE use so that routine use can be encouraged. However, evaluation of safety is not one of the primary objectives of the study.

2. Check the Malayalam translation of title

Answer: Appropriate changes have been made.

3. How many times can an ICE probe be used / reused and would it lead to an additional procedural charge?

Answer: According to the instruction for use from the manufacturer, ICE probes should not be sterilised and reused. However, owing to increased procedure costs, ICE probes are routinely re-used after sterilisation, which has been documented to be both safe and efficacious. Some reports state that the ICE probes can be reused even up to 10 times if resterilised with care.

4. What is the current level of expertise in the use of ICE and is there a learning curve involved? Are the views for image acquisition in ICE standardized?

Answer: ICE usage is similar to use of trans-oesophageal echocardiography (TEE), except for the probe being inside the cardiac chamber. The learning curve is very small. The views in ICE are also standardised like TEE. Operators who are proficient in TEE are very likely to perform ICE with ease.

5. Comparison of procedural time is one of the objectives of the study. The investigator needs to define procedural time.

Answer: Procedural time is defined as the time period from start of the procedure (after obtaining vascular access) to final deployment and release of device.

6. Comparison of fluoroscopic time has been mentioned as one of the objectives. As fluoroscopy is not regularly used for ASD device closure across many centers in the country and the investigator himself mentions that the use of fluoroscopy for ASD device closure is limited due to the risk of radiation exposure and poor resolution of soft tissue, it would be better if the investigator describes the current practice in SCTIMST. If fluoroscopy is not regularly used for ASD device closure in the institute this objective may be deleted.

Answer: The current practice in our hospital is predominantly imaging guided device closure. Fluoroscopy is only used for initial device placement and final device release. The entire procedure is guided by TEE. Measurement of fluoroscopic time is not a primary objective of the study.

7. The review expertise can be in more detail with respect to the use of ICE.

Answer: Appropriate changes have been made.

8. In the IEC form the investigator mentions "In case of minors, the consent would be obtained from the Guardian". This can be deleted as all patients in this study would be > than 18 years.

Answer: Appropriate changes have been made.



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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-21)

SCT/IEC/1726/SEPTEMBER/ 2021

13.12.2021

Dr. Avinash Mani
Resident
Department of Cardiology
SCTIMST, Thiruvananthapuram

Dear Dr. Avinash Mani,

The Institutional Ethics Committee held on 24th September, 2021, reviewed and discussed your application to conduct the study titled "COMPARISON OF INTRACARDIAC ECHOCARDIOGRAPHY VS. TRANS-ESOPHAGEAL ECHOCARDIOGRAPHY GUIDANCE FOR PERCUTANEOUS ATRIAL SEPTAL DEFECT CLOSURE (IEC/1726)".

The following members of the Ethics Committee were present at the meeting held on 24th September, 2021 at Residences and Offices of IEC Members via Video Conference

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Prof. C.C. Kartha	MBBS,MD	Male	Basic Medical Scientist (Chairman)	No
2.	Dr. Kala Kesavan P	MBBS,MD	Female	Basic Medical Scientist	No
3.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
4.	Dr. Pradeep S	MBBS, MD	Male	Basic Medical Scientist	No
5.	Adv. N Anand	BAL, LLB	Male	Legal Expert	No
6.	Adv. Priya Kaimai	LLM, MBL	Female	Legal Expert	No
7.	Dr. Harkrishna Varma P. R	Ph.D (Materials Sciences)	Male	Medical Technology	Yes
8.	Dr. Narayanan Namboodiri, K.K	MBBS,MD,DM	Male	Clinician	Yes
9.	Dr. Ashalatha R	MBBS, MD,DM	Female	Clinician	Yes
10.	Dr. Biju Soman	MBBS,MD, DPH, MSc, DLSHTM	Male	Basic Medical Scientist	Yes
11.	Dr. Srinivas G	PhD	Male	Basic Medical Scientist (Member Secretary)	Yes

The following documents were reviewed:

Original submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 16.07.2021
2. IEC Application Form
3. CV of PI and Co-PIs
4. Proforma
5. Consent Form in English and Malayalam Patient Information Sheet in English and Malayalam
6. TAC Approval Letter
7. Checklist form
8. Proposal
9. Declaration Form

Revised submission

1. Covering letter addressed to the Chairperson, IEC, SCTIMST dated 01.11.2021
2. Clarifications/Queries
3. Checklist form
4. IEC Application Form
5. Project Proposal
6. CV of PI and Co-PIs
7. Proforma
8. Consent Form in English and Malayalam
9. Patient Information Sheet in English and Malayalam
10. Declaration Form
11. TAC Approval Letter
12. Dean's signature form

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,



G. Srinivas
Member Secretary, IEC

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE (IEC)
SCTIMST, THIRUVANANTHAPURAM



PLAGIARISM SCAN REPORT

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The unique ability of 3D echocardiography to provide high resolution en-face view of ASD helps in proper assessment of defect size and rim adequacy, as well as evaluation for any additional ASD. It is these characteristics of 3D imaging which was utilized in the current study, to determine its feasibility for use in transcatheter ASD closure. The current study included 30 adult patients, deemed suitable for transcatheter ASD closure, who were recruited over a period of one year. The study population was middle aged with mean age being 40.5 ± 12.05 years. Majority of the patients in the study cohort were females. This highlights the fact that ostium secundum ASD has a female preponderance of almost 2:1 and majority of cases are diagnosed in adulthood(17). Dyspnea, palpitations and chest pain were the most common presenting complaints in the current study cohort. The symptomatology usually depends on the defect size. Small defects are usually asymptomatic and go undetected. Larger defects usually present with symptoms in the third decade of life with main symptoms of dyspnea, exercise intolerance, fatigue and palpitations(18). Overt right heart failure is uncommon with ASD, as was seen in the current study. Patients who develop significant pulmonary hypertension may get predisposed to developing right heart failure on long term follow up. ECG analysis showed that majority of study patients were in sinus rhythm. Patients with ASD are predisposed to develop atrial arrhythmias like atrial flutter or fibrillation, secondary to atrial dilatation. It can be noted in one-fifth of ASD patients pre-operatively (19). The typical rsR pattern in lead V1 on ECG was seen in 63% of the study population, which is a marker of right heart overload (1).

2D TTE revealed normal ventricular function in all study participants. None of the patient in the study had more than mild pulmonary hypertension. Majority of the patients had only mild tricuspid regurgitation whereas mitral regurgitation was noted in 10%. The ASD diameter measured on 2D TTE was consistently smaller than that measured on 3D TEE. This is expected as TEE provides better resolution images which helps to image the entire length of atrial septum. The best window for ASD evaluation in 2D TTE is the subxiphoid view, which is usually sub-optimal in adult patients. 2D TEE is the main modality used for ASD assessment and intraprocedural guidance. 3D imaging was also used in cases where good 3D datasets were acquired. There was no significant difference between ASD dimensions measured on 2D vs 3D TEE. A high degree of correlation was noted between 2D and 3D imaging for maximum and minimum ASD diameters. Hascoet et al. evaluated 30 ASD patients using 2D and 3D TEE and compared the ASD dimensions with balloon sizing diameters. There was a high correlation noted between 2D and 3D TEE for maximal ASD diameters in both round and oval ASD(20). Another study by Seo et al. enrolled 107 consecutive patients who underwent transcatheter ASD closure. They also showed that there was very good correlation between maximal ASD diameters as measured on 2D and 3D TEE (21).

3D imaging helps in determining the shape and orientation of the defect, which ultimately affects the device size. The device area was significantly larger than the defect area for both oval and circular defects in the current study. Similar findings were also noted in the study by Roushdy et al. This can be attributed to the fact that device sizing is currently based on maximal diameters obtained on 2D TEE. Device oversizing by 2-4mm is recommended on the basis of maximal ASD diameter. A significant proportion of these defects are oval, which can only be deciphered on 3D imaging. Hence, larger devices are commonly used to ensure complete coverage of defects. In spite of significant differences, there was good correlation between 3D defect area and circumference with device area and circumference. Roushdy et al. also showed good correlation between defect and device measurements.

Oval defects had larger defect area and circumference than round defects on 3D imaging. Consequently, the device area and circumference for oval defects were also larger than those for round defects. Presence of malalignment or floppy rims did not significantly device sizing as 3D defect area was similar amongst these patients.

