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Role of Transesophageal Echocardiography in Transcatheter Occlusion of Atrial Septal Defects

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1. Introduction

The incidence of atrial septal defect (ASD) is 1 in 1000 live births and account up to one third of the acyanotic shunts in the adult population. (Brickner et al. 2000; Yared et al. 2009) Patent foramen ovale (PFO) is found more than 25% of the adults. (Yared, Baggish et al. 2009) Historically, surgical closure of ASDs has been the most common therapy until new catheterbased techniques began to develop pioneered by King and Mills in 1975. (King et al. 1976; Yared et al. 2009) Currently, transcatheter closure of ASDs and PFOs is preferred to surgery in otherwise uncomplicated and favorable anatomy cases because it is technically simple and is associated with negligible morbidity and mortality. These procedures are performed for hemodynamically significant left to right shunting, to prevent stroke from recurrent paradoxical embolism and for the platypnea orthodeoxia syndrome. In addition to the above, closure of the surgically created fenestrations after Fontan operations and also baffle leaks after Mustard and Senning surgeries are all performed in the catheterization laboratory. (Hanrath 2001; Sengupta & Khandheria 2005) Several echocardiographic techniques including transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), intracardiac echocardiography (ICE) and real time three-dimensional transesophageal echocardiography (3D TEE) are being used by many centers. (Silvestry et al. 2009) In this chapter, we will review the role of TEE in transcatheter occlusion of atrial septal defects.

2. Development of interatrial septum

A good knowledge of the cardiac anatomy is needed for the echocardiographers to identify the structures and share them in a common language with the rest of the team involved in the care of the patient before, during and after the procedure.

The major septa of the heart are formed between the 27th and 37th days of development. One method by which a septum may be formed involves actively growing masses of tissue that approach each other until they fuse dividing the lumen into two separate canals (symmetrical growth). Septum may also be formed by active growth of a single tissue mass that continues to expand until it reaches the opposite side of the lumen (asymmetrical growth). (Fig. 1)

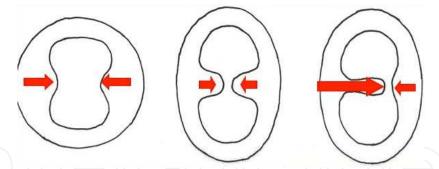


Fig. 1. Formation of septa. Symmetrical (middle) and asymmetrical (right) growth (Courtesy of Dr. Stephen W. Carmichael)

Atrium starts as a common chamber. At the end of the 4th week, a sickle cell shaped crest grows from the roof of the common atrium into the lumen. This is the first portion of the septum primum.

The opening between the lower rim of the septum primum and the endocardial cushions is the ostium primum. (Fig. 2)

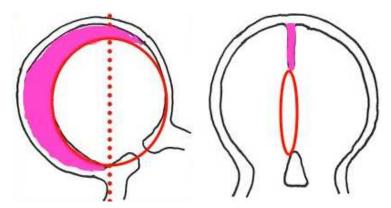


Fig. 2. Septum primum (in pink) and ostium primum (in red) (Courtesy of Dr. Stephen W. Carmichael)

With further development, extensions of the endocardial cushions grow along the edge of the septum primum closing the ostium primum. Before closure is complete, cell death produces perforations in the upper portions of the septum. (Fig. 3)

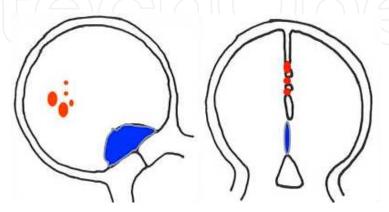


Fig. 3. Closure of ostium primum (in blue) and perforations in the septum (in red) (Courtesy of Dr. Stephen W. Carmichael)

Holes in septum primum coalesce to form ostium secundum. When the lumen of the right atrium expands as a result of the incorporation of the sinus horn, a new crescent shaped fold appears. Septum secundum begins to grow over ostium secundum. Septum secundum is to the right of septum primum and is more rigid. (Fig. 4)

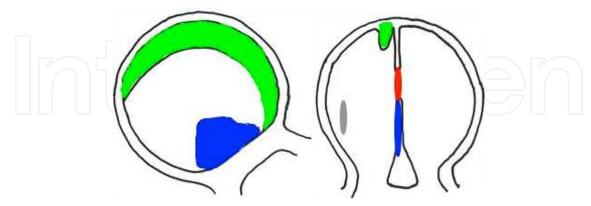


Fig. 4. Septum secundum (in green), septum primum (in blue) and ostium secundum (in red) (Courtesy of Dr. Stephen W. Carmichael)

Free concave edge of the septum secundum begins to overlap the ostium secundum. The tunnel like opening left by the septum secundum is the foramen ovale. Eventually within the first few years of life, the septum secundum fuses with the septum primum in most of the population thus separating the two atria. (Fig. 5)

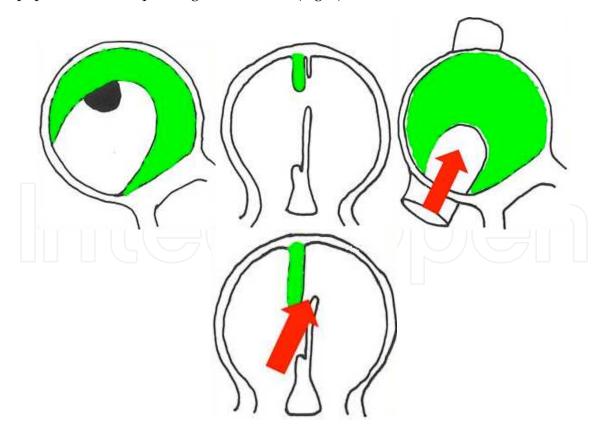


Fig. 5. Septum secundum (in green) and foramen ovale (in red arrow) (Courtesy of Dr. Stephen W. Carmichael)

Ostium secundum ASDs are caused either by excessive cell death and resorption of the septum primum or by inadequate development of the septum secundum.

PFO which is the result of lack of fusion between the septum primum and the septum secundum is not considered a true ASD and stays functionally closed as long as the left atrial pressure is higher than the right atrial pressure. There is a potential for right to left shunting resulting in paradoxical embolism and stroke if the right atrial pressure rises (mostly observed with valsalva) enough to open the PFO. (Johri et al. 2011)

3. Echocardiographic techniques

Echocardiography has been the widely used imaging technique that complements the fluoroscopy during closure of ASDs and PFOs. Compared to computed tomography and magnetic resonance imaging, echocardiography has the major advantage of being portable and real time. In this way, echocardiography can be performed before, during and after transcatheter interventions. (Silvestry et al. 2009) Even though fluoroscopy is the main imaging modality during interventional procedures, it does not provide direct assessment of cardiac anatomy as good as echocardiography. In addition to defining the intracardiac structures important in the ASD closure process, echocardiography is helpful in showing the relationship between catheters or devices and the adjacent structures. (Brochet & Vahanian 2010) The use of echocardiography as an adjunct to fluoroscopy has decreased the amount of total fluoro time to close an ASD.

Once the diagnosis of ASD or PFO and a decision to close it has been made, atrial septum should be assessed immediately before the procedure in the cardiac catheterization laboratory to confirm the diagnosis, during the procedure to help with device occlusion and after the procedure to reconfirm the success of the procedure without complications.

There are multiple techniques for the imaging of the atrial septum.

3.1 TTE

TTE is the simplest technique to use. It can show the device in multiple planes but does not have adequate imaging of the lower rim of the atrial septal tissue, which is above the inferior vena cava (IVC) especially after device placement. In addition to this, since the distance from the septum to the transducer is farther in TTE than TEE or ICE, the color imaging at the atrial septal level may be suboptimal. Access to the patient's body through the sterile field also poses a problem. Even though TTE may be the initial diagnostic tool, it is infrequently used in the catheterization laboratory to aid in ASD closures. (Silvestry et al. 2009)

3.2 TEE

In contrast to TTE, TEE offers better image resolution and definition of anatomy during the transcatheter closure of ASDs. It has become the standard imaging modality in many centers to monitor and guide interventional procedures because of its easy application, lower cost, portability and real time imaging. It is mostly agreed that TEE is superior to fluoroscopy in defining the defect margins and to position the device and/or its arms. (Hanrath 2001) The main limitation of TEE is the need for general anesthesia. (Brochet & Vahanian 2010) It also

requires a dedicated echocardiographer to perform the study. TEE in ASD closure will be discussed further in the rest of the chapter.

3.3 ICE

ICE has been introduced to cardiac imaging techniques more than 10 years ago. It has evolved from cross sectional imaging using a rotating transducer to sector based imaging using a phased-array transducer. There are three ICE catheters available with respective ultrasound systems. Most frequently used ones are 8F or 10 F ultrasound catheters. Some centers prefer ICE to other imaging modalities because of its superiority in imaging especially the inferior rim of the atrial septum, which is important in decision making to close the defect. (Kim et al. 2009) It is advantageous to TEE mostly because it avoids the need for general anesthesia. The cost of the catheter is one of the main drawbacks of using ICE. Even though closure of PFO under the guidance of ICE is safe and effective, ICE may not be sensitive enough to detect all patients with right to left shunting. (Van et al. 2010; Pedra, Fleishman et al. 2011) In addition to this, limited field view for far field device complications, the need for a second venous sheath, the requirement for additional training, potential trigger of atrial arrhythmias are among the disadvantages of ICE. In the setting of a single operator, it may be a more challenge to manipulate the ICE catheter at the same time the closure device. It is up to the center and the interventionalist to prefer ICE to other imaging techniques and there are many catheterization laboratories and interventionalists who prefer this technique during transcatheter closure of ASDs. (Kim et al. 2009; Yared et al. 2009)

3.4 3D TEE

After the introduction of 3D TTE during interventions, a more practical technique, 3D TEE was developed. Real time 3D TEE images have high spatial and temporal resolution that allows detailed views of the cardiac structures. (Lee et al. 2010; Tsang et al. 2011) The use of 3D TEE acquired en face views of the defect and surrounding structures allows accurate measurement of the ASD and any other additional defects like fenestrations. Since the same probe can be used for 2D TEE and 3D TEE imaging and the operator can switch in between the two modalities, this method has become one of the newer and promising techniques in evaluation of the atrial septum during ASD device occlusion.

4. ASD/PFO closure devices

Currently there are a number of devices approved in the USA for closure of ASDs and some of these are also used off label for closure of PFOs. It is very important for the echocardiographer to be familiar with these devices, their design and release mechanisms since the method of implantation is different and unique for each device. (Silvestry et al. 2009)

Atrial septal defect occlusion devices are categorized into two as non-self centered or single pin device and the waist or self-centered device. The cribriform device- AGA Amplatzer multi fenestrated septal occluder (AGA, Plymouth. Minnesota USA) (Fig. 6) and the Gore Helex septal occluder (GL Gore & Associates, Flagstaff, Arizona, USA) (Fig. 7) are among the family of single pin devices. Both the Cribriform and the Gore Helex devices are

approved for closure of small ASDs but are widely used for PFO closure as off label indication. The self-centered devices have two atrial disks that connect with a waist. AGA Amplatzer septal occluder (AGA) (Fig. 6) and the NMT CardioSeal StarFlex septal occluder (NMT Medical, Boston, Massachusetts, USA) (Fig. 7) are the two self centered devices available for closure of ASDs in the USA.

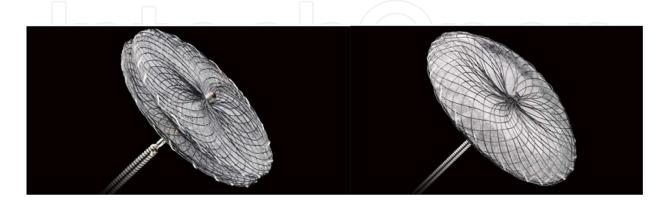


Fig. 6. AGA Amplatzer. Multi Fenestrated Septal Occluder (left) and Septal Occluder (right)

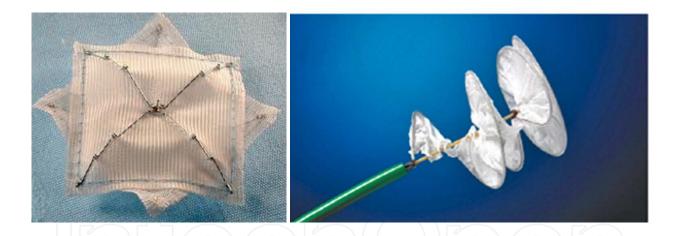


Fig. 7. CardioSeal StarFlex Septal Occluder (left) and Gore Helex Septal Occluder (right)

5. TEE in ASD device closure

5.1 TEE protocol

Even though ASD/PFO closure evaluation asks for certain measurements, for all cases, it is very important to follow a protocol using multiplane views and available windows from gastric to mid and upper esophagus to complete a segmental approach used in evaluation of congenital heart disease. (Fig. 8) In this way, the previous findings seen by other echocardiography modalities will be confirmed and any additional defects will not be missed. (Masani 2001) Many centers already are using TEE protocols that they have developed and these can be incorporated into TEE in interventional studies.

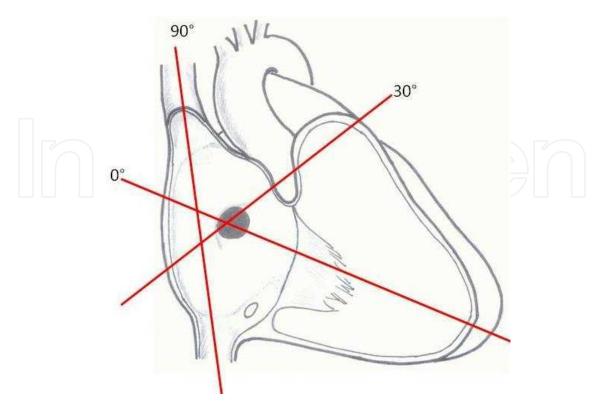


Fig. 8. Multiplane views of the atrial septum. (Courtesy of Dr. Duraisamy Balaguru)

5.2 Imaging of atrial septum pre-, during and post-, device closure

The goals of TEE are: detailed imaging of the defect and its relation to the surrounding structures, identification of patients with suitable anatomy for device closure of their ASD/PFO and guidance for the device positioning and deployment. (Brochet & Vahanian 2010) It should also be kept in mind that the rotation of the transducer to specific angles is a good initial guide but not a strict rule. The defects and other normal structures of the heart may be imaged at closer but different angles.

5.2.1 Pre-procedure

- 1. Evaluation of the entire atrial septum and its surrounding structures; exclusion of additional defects that may render the defect unsuitable for closure
- 2. Defining the defect: ASD vs. PFO
- 3. Color Doppler imaging of the defect and definition of the shunt (left to right, right to left) at rest, with Valsalva
- 4. In cases of PFO requiring further information of the shunt, injection of agitated saline micro bubbles at rest and with Valsalva to visualize any right to left shunting
- 5. Measurement of the defect number and size
- 6. Maximal dimensions of the length of the atrial septum and distance of the ASD from the surrounding structures (rims) (Fig. 12)
- 7. Measurement of the diameter of the stretched balloon across the defect when a sizing balloon is used and identification of any residual left to right shunting (Fig. 15)

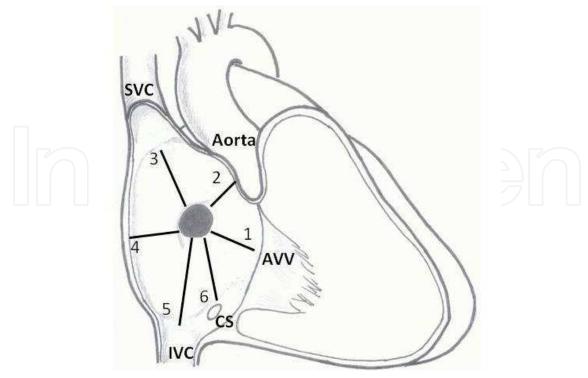


Fig. 9. Secundum atrial septal defect with surrounding rims. (1. Atrioventricular valve rim; 2. Aortic rim; 3. SVC rim; 4. Posterior rim; 5. IVC rim; 6. Coronary sinus rim) (Courtesy of Dr. Duraisamy Balaguru)

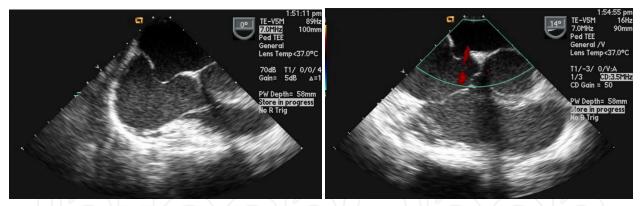


Fig. 10. Atrial septal aneurysm with small left to right shunting

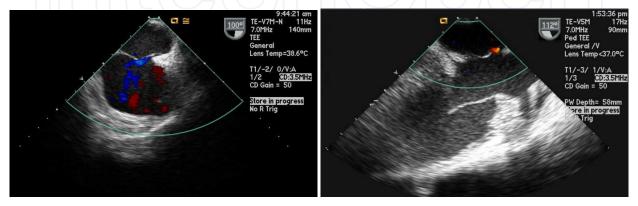


Fig. 11. PFO with bidirectional shunting.



Fig. 12. Four chamber view. Septal defect size, rims (left) and total atrial septal length (right) measurements

A PFO is defined as any anatomical communication through the foramen ovale and a stretched PFO is defined as any left to right flow on color Doppler imaging seen at rest or intermittently. Furthermore, an atrial septal aneurysm is defined as 11-15 mm of total movement of a 15 mm base of atrial tissue. (Silvestry et al. 2009) Sinus venosus, ostium primum or coronary sinus defects cannot be closed by transcatheter intervention and require surgical closure. In addition to this, associated abnormalities of the superior and inferior vena cava, coronary sinus, pulmonary veins and atrioventricular valves that may hinder the device closure should be carefully evaluated. Once the defect is diagnosed as a secundum ASD or a PFO, then the number (more than one defect at the atrial septum or fenestrations) and size of the defect needs to be identified. Currently, defects up to 40 mm in diameter and also multiple defects can be successfully closed with percutaneous transcatheter occlusion. (Silvestry et al. 2009) In addition to the size of the defect, the distance of the defect from the surrounding structures called "rims" play an important role in deciding whether a defect can be closed or not. A surrounding rim of 4-5 mm is considered to be adequate for closure except for the aortic rim which could be less. Posterior, superior (SVC) and especially the inferior (IVC) rim are to be investigated and measured from multiple TEE views for accuracy. (Fig. 14) In the cardiac catheterization laboratory, the operators should be very much familiar with the terminology when rims are mentioned. Alternatively, an easier and according to their relation to less complicated definition of the rims may be specific structures. In smaller patients, especially the pediatric population, the total septal length is also crucial since this may limit the size of the device that can be placed successfully without early or late morbidity. (Momenah et al. 2000)

While interrogating the atrial septum, certain views are recommended for measurements. The diameter of the defect and the color Doppler across it should be obtained from midesophageal four chamber, from short axis at the base of the heart, from gastro esophageal junction and from bicaval view and the largest diameter should be considered while deciding on the size of the device. (Fig 12 and 13) Inferior rim of the defect to mitral valve and tricuspid valve and the total septal length can easily be visualized from mid esophageal four chamber view. (Fig. 12) The short axis view at the base of the heart gives the antero-superior rim (to aortic root), posterior rim (to pulmonary vein) and the total septal length. (Fig 13) With the gastro esophageal junction (0°) or oblique (130°) imaging inferior rim of the defect to the coronary sinus can be seen. Bicaval view is the choice for

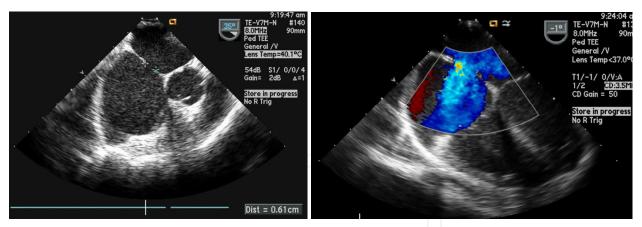


Fig. 13. ASD and aortic rim visualized from short axis view (35°) (left); left to right color flow at ASD (right)



Fig. 14. Bicaval view showing IVC and SVC rims, ASD (left) and fenestrated ASD (right) with left to right shunting

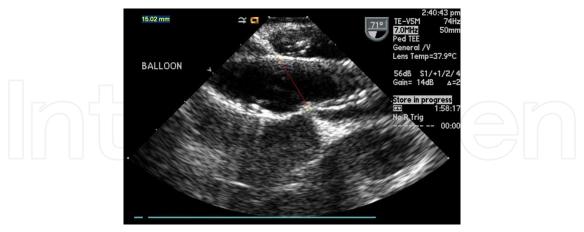


Fig. 15. Balloon sizing of ASD. Note the measurement (in red) at the waist of the stretched balloon

visualization and measurement of the superior rim to superior vena cava and inferior rim to inferior vena cava in addition to the total septal length. (Fig. 14) The color flow entering the RA from vena cava and coronary sinus should not be misdiagnosed. (Masani 2001) Another very important structure is the crista terminalis that extends as a linear structure from the

RA wall close to the IVC to the septum adjacent to the SVC. This structure and the valve of the IVC, Eustachian valve or Chiari network, can both be mistaken as the atrial septum thus ending in a wrong diagnosis. (Masani 2001)

5.2.2 During device closure/deployment

The echocardiographer and the interventionalist work as a team to decide on the device size to be used for ASD/PFO closure. The measurements from both the TEE and cardiac catheterization should be used in choosing the right size device. Once the device is being introduced into the heart and through the defect, the echocardiographer guides the catheterization team with the correct positioning taking into fact the adjacent structures especially AV valves and the entrapment of rims in between the discs (for AGA and Gore Helex septal occluders) and the double umbrella (for NMT CardioSeal). (Fig. 16) Once appropriate placement is confirmed with 2D and no significant left to right shunting seen by color Doppler, the device can then be deployed. (Fig. 17) Small central shunting is frequently seen through the device especially the AGA septal occluders, and this should not hinder the deployment. (Fig. 16) The slight pull of the device by the delivery system is relieved once it is deployed and the device is seen saddling in a much better fashion over the defect.



Fig. 16. AGA septal occluder. Note the device malpositioning- vertical to the atrial septum and the ASD rather than parallel (left) and normal central shunting (right)

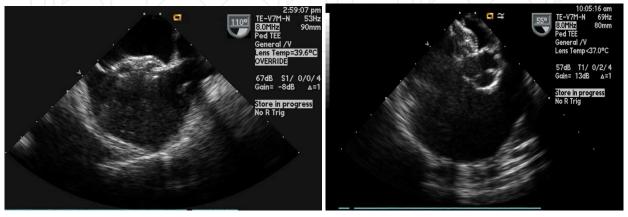


Fig. 17. AGA septal occluder. Correct positioning at bicaval (SVC-IVC) view (left). Straddling the aortic rim (right)

5.2.3 Post device closure

Following deployment, a detailed post procedure TEE should be performed to visualize any impingement on valves, veins and the outflow tract in addition to any residual peripheral shunting. (Fig. 18) In case of acute complications, most of the ASD/PFO occlusion devices can be retrieved in the catheterization laboratory so early post procedure identification of these findings is very important. (Johri et al. 2011)

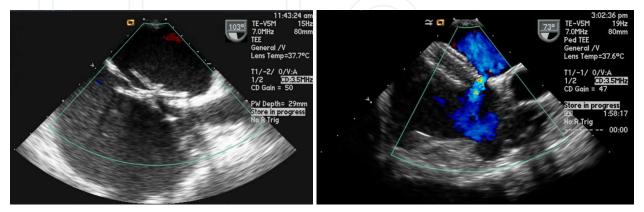


Fig. 18. Gore Helex septal occluder after successful ASD closure (left) and AGA septal occluder with residual peripheral shunting (right)

6. Complications after ASD/PFO device closure

Potential complications after percutaneous device closure of ASDs and PFOs can be categorized into acute/early and chronic/late. In both the acute and late complications TEE plays a very important role. Initially, TEE is helpful in identifying the early complications some of which will be evident in the catheterization laboratory right after deployment.

One of the major but rare complications is device embolization which can embolize to any cardiac chamber or vessel and/or cause valvular dysfunction. Device embolization is commonly secondary to underestimation of the septal defect or the deficiency of the inferior or the superior rims. TEE may be limited in visualization if the device embolizes outside the heart especially beyond the abdominal aorta at the hepatic level or into the peripheral vasculature. (Yared et al. 2009) Once the diagnosis is made by TEE and fluoroscopy, retrieval is attempted in the catheterization laboratory. If unsuccessful, surgical retrieval is done.

Pericardial tamponade though rare is an important complication that may be seen during or acutely after device deployment. Tamponade most frequently is a result of left atrial appendage perforation during the anchoring of the trans septal guide wire though other less commonly encountered reasons may also be from right atrium, right ventricle, or right or left pulmonary vein perforation and though usually a late complication, device erosion through adjacent cardiac tissue. (Yared et al. 2009)

Transient heart block should raise the suspicion of the ASD closure device's impingement on the atrioventricular node. This finding needs to be closely followed afterwards.

Residual shunting seen immediately after device closure may decrease or disappear as the devices endothelizes within several months after deployment. As long as, the residual

shunting is not hemodynamically significant, by many, this finding is not considered to be a complication. (Yared et al. 2009)

7. Pitfalls

Even though TEE is one of the most widely used echocardiographic modalities, it also has pitfalls. It requires expert imaging personal to avoid any wrong diagnosis from misinterpretation of normal and abnormal anatomy of the heart, atrial septum and the defect. Even though it is superior to TTE in imaging because the probe in the esophagus is close to the heart, there may still be disturbance in image quality secondary to air within the esophagus and stomach or the air filled trachea or bronchi. In addition, during prolonged monitoring the transducer may reach its heat limit and may need to be turned off until it reaches a cooler temperature. (Sengupta & Khandheria 2005)

8. Conclusion and future directions

During percutaneous closure of ASDs and PFOs, in addition to fluoroscopy, echocardiographic input is of utmost value to the interventionalist. Among the other imaging modalities which include TTE, ICE and 3D TEE, TEE has long been the standard imaging modality in many centers to monitor and guide interventional procedures because of its easy application, lower cost, portability and real time imaging. With the introduction of smaller transducers, it is also used in the smaller patients, especially the pediatric population. It is the preference, comfort and the expertise of the interventionalist and the echocardiographer to choose the best imaging technique for percutaneous ASD/PFO closure. Since TEE has been used for a long time with good results, it still is the choice of imaging in many of the catheterization laboratories; ICE and 3D TEE are the upcoming competitors.

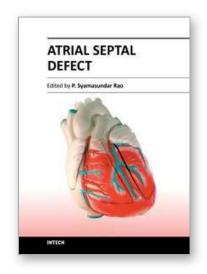
9. References

- Brickner, M. E., L. D. Hillis, R. A. Lange (2000). "Congenital heart disease in adults. First of two parts." *N Engl J Med* 342(4): 256-63.
- Brochet, E. and A. Vahanian (2010). "Echocardiography in the catheterisation laboratory." *Heart* 96(17): 1409-17.
- Hanrath, P. (2001). "Imaging techniques: Transoesophageal Echo-Doppler in cardiology." Heart 86(5): 586-92.
- Johri, A. M., C. A. Rojas, A. El-Sherif et al. (2011). "Imaging of atrial septal defects: echocardiography and CT correlation." *Heart* 97(17): 1441-53.
- Kim, S. S., Z. M. Hijazi, R. M. Lang et al. (2009). "The use of intracardiac echocardiography and other intracardiac imaging tools to guide noncoronary cardiac interventions." *J Am Coll Cardiol* 53(23): 2117-28.
- King, T. D., S. L. Thompson, C. Steiner et al. (1976). "Secundum atrial septal defect. Nonoperative closure during cardiac catheterization." *Jama* 235(23): 2506-9.
- Lee, A. P., Y. Lam, G. W. K. Yip et al. (2010). "Role of real time three-dimensional transesophageal echocardiography in guidance of interventional procedures in cardiology." *Heart* 96(18): 1485-93.

Masani, N. D. (2001). "Transoesophageal echocardiography in adult congenital heart disease." *Heart* 86 Suppl 2: II30-II40.

- Momenah, T. S., D. B. McElhinney, M. M. Brook et al. (2000). "Transesophageal echocardiographic predictors for successful transcatheter closure of defects within the oval fossa using the CardioSEAL septal occlusion device." *Cardiol Young* 10(5): 510-8.
- Pedra, C. A., C. Fleishman, S. F. Pedra et al. (2011). "New imaging modalities in the catheterization laboratory." *Curr Opin Cardiol* 26(2): 86-93.
- Sengupta, P. P. and B. K. Khandheria (2005). "Transoesophageal echocardiography." *Heart* 91(4): 541-7.
- Silvestry, F. E., R. E. Kerber, M. M. Brook et al. (2009). "Echocardiography-guided interventions." *J Am Soc Echocardiogr* 22(3): 213-31; quiz 316-7.
- Tsang, W., R. M. Lang, I. Kronzon (2011). "Role of real-time three dimensional echocardiography in cardiovascular interventions." *Heart* 97(10): 850-7.
- Van, H., P. Poommipanit, M. Shalaby et al. (2010). "Sensitivity of transcranial Doppler versus intracardiac echocardiography in the detection of right-to-left shunt." *JACC Cardiovasc Imaging* 3(4): 343-8.
- Yared, K., A. L. Baggish, J. Solis et al. (2009). "Echocardiographic assessment of percutaneous patent foramen ovale and atrial septal defect closure complications." *Circ Cardiovasc Imaging* 2(2): 141-9.





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Atrial Septal Defects (ASDs) are relatively common both in children and adults. Recent reports of increase in the prevalence of ASD may be related use of color Doppler echocardiography. The etiology of the ASD is largely unknown. While the majority of the book addresses closure of ASDs, one chapter in particular focuses on creating atrial defects in the fetus with hypoplastic left heart syndrome. This book, I hope, will give the needed knowledge to the physician caring for infants, children, adults and elderly with ASD which may help them provide best possible care for their patients.

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