Original Contribution

Review

Transcatheter Closure of Secundum Atrial Septal Defects

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ABSTRACT: Atrial septal defect (ASD) is one of the most common congenital heart defects, accounting for 7%-10% of all congenital heart disease (CHD) in children and 30%-33% of defects diagnosed in adults with CHD. This review highlights the evolution of transcatheter ASD closure, indications, follow-up, outcomes, and complications with a focus on the erosion issue with certain devices.


Key words: atrial septal defect, transcatheter ASD closure

Atrial septal defect (ASD) is one of the most common congenital heart defects, accounting for 7%-10% of all congenital heart disease (CHD) in children and 30%-33% of defects diagnosed in adults with CHD. If left untreated, there is significant risk of atrial arrhythmias and late morbidity; therefore, closure of hemodynamically significant defects (right ventricle volume overload as evidenced by transthoracic echocardiography or Qp:Qs >1:5:1) is advised in childhood.1 Historically, surgery has been the gold standard; however, the initial description of transcatheter closure by King and Mills in 19762 laid the groundwork for the development of refined and clinically acceptable transcatheter alternatives to surgery. This initial work by King and Mills was truly revolutionary, and 25-year follow-up data on the 5 patients who underwent transcatheter closure were reported in 2003 with 4 of these patients alive and well.3 Unfortunately, following this huge step, work on transcatheter closure of ASD lay fallow for a number of years until 1983, when Rashkind reported successful delivery of a single foam-covered six-ribbed device with hooks at the ends of three of these ribs.4 Modifications of this basic design led to the development of the Clamshell device, a double-hinged paired umbrella with four arms that folded on themselves.5 Clinical studies with this device were halted due to concerns regarding device fracture and residual shunting.6-8

In 1993, Das et al reported on a new device called the Angel Wing, which was the first self-centering device and had two Dacron-covered square disks and nitinol frames with midpoint tension spring eyelets.9 One of the authors of this paper (ZMH) implanted the first Angel Wing device in June 7, 1995;10 however, because of the relative stiffness of the frame and the design of the attachment mechanism, it was not easy to retrieve by catheter and due to 2 cases of device erosion, the device was redesigned and named the Guardian Angel. However, that device was never used in humans. The real breakthrough with transcatheter ASD closure came with the development of the Amplatzer septal occluder in the mid 1990s (Figure 1). This device design consists of a nitinol wire mesh that is tightly woven into two disks with a connecting waist between the two disks corresponding to the approximate thickness of the interatrial septum. The first clinical report was published in 1997.11 United States Food and Drug Administration (FDA) approval followed in 2001. Although many other devices have been reported, the other mainstream device in clinical use today in the United States is the Helex septal occluder (Figure 2). This device consists of a single nitinol wire covered by an ultrathin membrane of expanded polytetrafluoroethylene. In its occlusive configuration, the device forms two round flexible discs that straddle the septum.

Anatomy of the Atrial Septum

The atrial septum is formed by the septum primum, which originates from the atrial roof and septum secundum. Formation of the septum occurs through several stages. The septum primum grows as a crescenteric flap, leaving an opening between the left and right atria called the ostium primum. With growth of the septum primum, the ostium primum narrows.
and a second opening (ostium secundum) is formed. As the septum secundum grows anteriorly to meet the septum primum posteriorly, it leaves a small opening called the foramen ovale (FO), providing a continuous pathway for shunting of blood across the pulmonary vascular bed in fetal life. Thus, the foramen ovale is not a true deficiency in the atrial septum. Following birth, and decrease in pulmonary vascular resistance, the hooded morphology of the septum primum collapses over the foramen ovale to provide functional closure. The muscular rims of the foramen ovale are known as the limbus and form the raised margin around the FO. Autopsy studies have showed rims of the foramen ovale to provide functional closure. The muscular

Table 1. American Heart Association guidelines for closure of atrial septal defects.

| Class I | (1) Transcatheter secundum ASD closure is indicated in patients with hemodynamically significant ASD with suitable anatomic features (level of evidence: B). |
| Class IIa | (1) It is reasonable to perform transcatheter secundum ASD closure in patients with transient right-to-left shunting at the atrial level who have experienced sequelae of paradoxical emboli such as stroke or recurrent transient ischemic attack (level of evidence: B). (2) It is reasonable to perform transcatheter secundum ASD closure in patients with transient right-to-left shunting at the atrial level who are symptomatic because of cyanosis and who do not require such a communication to maintain adequate cardiac output (level of evidence: B). |
| Class IIb | (1) Transcatheter closure may be considered in patients with a small secundum ASD who are believed to be at risk of thromboembolic events (eg, patients with a transvenous pacing system or chronically indwelling intravenous catheters, patients with hypercoagulable states) (level of evidence: C). |
| Class III | (1) Transcatheter secundum ASD closure is not indicated in patients with a small secundum ASD of no hemodynamic significance and with no other risk factors (level of evidence: B). (2) Transcatheter ASD closure should not be performed with currently available devices in patients with ASDs other than those of the secundum variety. This would include defects of septum primum, sinus venosus defects, and unroofed coronary sinus defects (level of evidence: C). (3) Transcatheter ASD closure is contraindicated in the management of patients with a secundum ASD and advanced pulmonary vascular obstructive disease (level of evidence: C). |

Indications for Closure

The indications for closure of an ASD in the pediatric population are outlined in Table 1. Under usual circumstances, flow through an ASD occurs from left to right, but to a variable degree depending on the size of the ASD, the ventricular compliance, and the pulmonary vascular resistance (PVR). Excessive flow through the defect will eventually lead to right atrial and ventricular volume overload. If the shunt is large and results in significant right heart volume loading, the patient may experience symptoms of shortness of breath, reduced exercise tolerance, or palpitations in the second or third decade of life. Intervention in older patients has also been shown to be advantageous, with Konstantinides and colleagues demonstrating significant improvement in the survival rate in symptomatic patients older than 40 years undergoing surgical ASD closure compared to those treated medically. Transcatheter ASD closure is deemed feasible if the balloon-stretched diameter of the defect is less than 35 mm and the defect has sufficient rims (>5 mm) of surrounding atrial tissues. However, transcatheter closure has been routinely performed in defects with deficient rims, particularly of the anterosuperior atrial septum. Attempted closure in patients with 2 or more deficient rims is not advised and device embolization is thought to be higher in patients with significantly deficient posterior and inferior rims. Weight restrictions have lessened over time and multiple reports have demonstrated safe and effective closure in patients weighing less than 15 kg. The American Heart Association recommendations for closure in adults reflect those for children as well as documented orthodeoxia-platypnea, and ASD with left-to-right shunt and PVR less than two-thirds of the systemic vascular resistance. Contraindications for ASD device closure include elevated PVR in excess of 7 Wood units (indexed), although closure in patients with secundum ASD and pulmonary arterial hypertension can be successfully performed in selected subjects and is associated with good outcomes. Other contraindications include acute or recent sepsis, or contraindications for antithrombotic therapy.

Procedure

Prior to defect closure, it is crucial to identify the number of defects, defect size, location, morphology, and the surrounding atrial septal tissue to determine whether the defect is amenable to transcatheter closure or not. Baseline assessment of cardiac structures that may be affected by the procedure should also be carried out. Echocardiography remains the noninvasive gold...
standard imaging tool for detecting an interatrial communication. Three-dimensional transthoracic and transesophageal and intracardiac echocardiography have also been used.

Although transcatheter closure of small-to-moderate sized defects with good rims is frequently straightforward, it should be performed only in laboratories and by experienced operators equipped to deal with complications and unexpected challenges of the procedure, and surgical back-up should be available. Conscious sedation may be used if intracardiac echocardiography (ICE) is used to guide closure; however, general anesthesia is preferred when TEE is used or with younger patients as they may not be cooperative. Access is obtained usually in the right femoral vein. If ICE is used, an additional sheath is needed in the left or right femoral vein depending on the patient’s weight. If the weight is >35 kg, we access the femoral vein in the right using two separate punctures a few millimeters from each other; however, if the weight is <35 kg, we access the contralateral vein. The main advantages of ICE over TEE during this procedure include avoidance of anesthesia, better view of the left atrium and the posterior-inferior rim of the septum, and need for fewer personnel, because the interventional cardiologist will be able to perform the interventional procedure independently with the need for an anesthesiologist or echocardiographer. The foremost disadvantage is the additional cost of the imaging catheter. Intravenous heparin should be given to keep an activated clotting time >200 seconds throughout the procedure as the risk of thrombus in the left atrium will predispose the patient to stroke. A thorough hemodynamic evaluation

Figure 3. Stepwise angiographic images of Helex septal occluder deployment. (A) The catheter is advanced in the right upper pulmonary vein. (B) Defect balloon sizing. (C) Left atrial disk deployment. (D) Right atrial disk deployment. (E) The device is released.

Figure 4. Stepwise intracardiac echocardiographic images of Helex septal occluder deployment. (A) Atrial septal defect. (B) Left-to-right shunt through the atrial septal defect. (C) Balloon sizing of the defect. (D) The delivery system crossing the defect to the left atrium. (E) Device deployment. (F) The device is deployed with no residual shunt.
should be carried out before device deployment and special attention should be given to the pulmonary artery pressures, PVR, Qp:Qs, left atrial pressure, and the left ventricular end-diastolic pressure. Right upper pulmonary venous angiography may be performed, since it profiles the atrial septum and the defect size and may serve as a roadmap during device deployment. This view is obtained with 35° left anterior oblique and 35° cranial angulation. Intraprocedural echocardiography is used to assess the size of the defect and the septal rims in multiple planes, with confirmation of pulmonary venous drainage (particularly right-sided) to the left atrium and the degree of atrioventricular valve regurgitation. Balloon sizing of the defect is recommended in all ASD device closure cases; however, some operators may choose not to balloon-size based on the size and location of the defect. Once the defect is crossed and a catheter advanced into the left upper pulmonary vein, a stiff exchange-length guidewire is positioned in that vein. Following this, an appropriate-sized sizing balloon (St Jude Medical or NuMED, Inc) is advanced across the defect. The balloon is inflated under echocardiography guidance until no residual shunt through the defect is seen (stop-flow technique). At this stage, the diameter of the balloon is measured by cine recording and echocardiography. In the case of the Amplatzer devices, a device approximately no more than 2 mm greater than the stop-flow diameter is usually chosen. The Helex device is usually not recommended for defects greater than 18 mm in diameter and a device:balloon size ratio of 2:1 is chosen for best results. The delivery sheath is then advanced over the wire and once the tip of the dilator crosses the defect, the dilator is held and the sheath advanced over the dilator into the left upper pulmonary vein. The wire and the dilator are then slowly withdrawn and the sheath held below the level of the heart to allow back-bleed to eliminate any possibility of air embolism. The device is then loaded and advanced to the tip of the sheath (Figures 3-6).

The delivery sheath is pulled out of the pulmonary vein into the left atrium, and at this point the delivery cable is fixed firmly while retracting the sheath over the cable and deploying the left atrial disc in the left atrium. Then, the entire assembly (sheath/cable) is withdrawn toward the septum. Once the left disc is within a few millimeters of the septum, the connecting waist is deployed partially in the left atrium with continuous traction toward the defect. The purpose is to “stent” the
defect with the waist. Then, with continuous traction toward the right atrium, the right atrial disc is deployed in the right atrium. Once the entire disc is deployed, the delivery cable is then pushed toward the septum to approximate the two discs of the device to each other.

The mechanism for deployment of the Helex device is outlined in Figures 3 and 4. Echocardiography and cine fluoroscopy should be used to document and monitor all stages of device deployment with full assessment prior to device release.

Various strategies have been described to promote stability of the device in the setting of a deficient anterosuperior rim, including use of the Hausdorf sheath, the pulmonary vein deployment technique, use of the dilator to maintain the left atrial disc on the left atrial aspect of the septum during deployment, and use of a balloon across the defect to maintain the device in a stable position.22-24 Recently, the manufacturer of the Amplatzer device (St Jude Medical) introduced a new delivery system (TorqView FX) that has an inner softer cable that does not produce much tension on the device. Once the right atrial disc is deployed, the stiffer cable is retracted and the softer inside cable is pushed; this allows better alignment of two discs with the atrial septum.

**Follow-up**

Within 24 hours of device implantation, an echocardiogram should be done on all patients to evaluate the device position and any residual shunt and to look for any potential complications (device erosion, embolization, etc). Twelve-lead electrocardiogram should also be performed, since rare cases of heart block have been reported with large devices.25 Hill and colleagues reported an increased incidence of atrial arrhythmias and conduction abnormalities early after device closure.26 Post-procedure follow-up visits for all patients should be done at 6 months, 1 year, and then every 1-2 years thereafter. At each visit, physical exam, electrocardiogram, and echocardiography should be performed. If complete closure is documented at the 6-month follow-up visit, aspirin and SBE prophylaxis may be discontinued. It has been well documented that right ventricular size will improve rapidly in the first month; however, long-standing right ventricular dilatation may improve more slowly and may not normalize completely.27

**Clinical Outcomes**

In 2002, a trial comparing surgical closure and transcatheter closure with the Amplatzer septal occluder demonstrated comparable closure rates.28 However, complication rates in the surgical group were significantly higher than the device closure group (24% vs 7%, respectively), and the length of the procedure and the hospital stay were shorter in the patients who underwent transcatheter closure.

Furthermore, in 2007 a multicenter pivotal study compared transcatheter ASD closure with the Helex device to surgical closure.29 There was no significant difference in the efficacy and safety between the two groups; however, the length of sedation and the hospital stay were shorter in the patients who underwent transcatheter closure.

Patel et al studied 113 patients >40 years old and demonstrated that ASD closure using the Amplatzer septal occluder in these patients was safe and effective with minimal complications.30 They reported a remarkable decrease in symptoms, which included fatigue, dyspnea, exercise intolerance, and palpitations, as well as decrease in the right ventricle size.30 In
Complications

The most common complications are outlined in Table 2. Complications that relate to the procedure and the device are rare. The following complications may occur during transcatheter ASD closure: device migration; device malposition; cardiac erosion/perforation leading to tamponade and death; aortic rim with or without deficient superior rim and the use of an over-sized device. The United States FDA held a panel meeting in May 2012 to examine the issue of device erosions. The final recommendations of the FDA Circulatory Device System are still pending at the time of this writing.

Table 2. Reported complications.

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<th>Chan</th>
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<td>Left atrial appendage perforation</td>
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Another study, percutaneous ASD closure was found to result in early and remarkable cardiac geometric improvements that nearly reverted the right-to-left volumetric imbalance completely. Most of this remodeling occurs within a few weeks after ASD closure. Even in patients >60 years old, transcatheter ASD closure is safe and effective, and right ventricle remodeling is still reported.

ASD Closure Devices

Many devices have been developed, with only two devices receiving FDA approval in the United States. These are the Amplatzer septal occluder and the Helex septal occluder.

1. **The Amplatzer septal occluder.** The Amplatzer septal occluder is one of two closure devices being used in the United States manufactured by St Jude Medical. It is a self-centering device that consists of two circular retaining discs made of nitinol wire mesh and linked together by a short connecting waist. While the waist centers the device in the defect and occludes it, the retaining discs provide stability on opposite sides of the defect. The size is determined by the size of the waist and ranges from 4-40 mm; however, the 40 mm device is not approved in the United States. It is delivered by a long sheath available in different sizes.

2. **The Gore Helex septal occluder.** The Gore Helex is the second device approved for use in the United States and is manufactured by WL Gore & Associates. No cases of migration or erosion have been reported for this device. The occluder is manufactured by WL Gore & Associates. No cases of migration or erosion have been reported for this device.
Transcatheter Closure of Secundum ASDs

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composed of an expanded polytetrafluoroethylene material with hydrophilic coating, which is supported by a nitinol frame. The occluder has a double disc shape that bridges the defect. A 2:1 ratio between the device size and the defect size “balloon-stretched diameter” should be used for optimal results, and the device diameter should not exceed 90% of the measured septal length. The septal tissue margins should be sufficient in size and integrity to prevent device embolization, and residual leaks are more common when the defect size is measured to be more than 18 mm.

In one large study, 87% of 342 patients had the Helex device implanted successfully. There were significant adverse events (mostly device removal for different reasons) in 5.8%. Overall composite success was seen in 91.5%. Significant residual shunt and frame fracture were reported; however, no device erosion or cardiac perforation have been reported thus far with the Helex.

A newer modification of this device, the Gore septal occluder (GSO) just received United States FDA approval for initiation of an IDE clinical trial. It is also comprised of a nitinol wire frame covered with expanded polytetrafluoroethylene (ePTFE). The wire frame is formed from five wires shaped into the right and left atrial discs, the eyelets, and the lock loop. The five-wire design provides conformability, allowing each individual wire within a right or left atrial disc to conform to the heart anatomy. The ePTFE includes a hydrophilic surface treatment to facilitate echocardiographic imaging of the occluder and surrounding tissue during implantation. Figure 7 depicts this new device.

3. The Occlutech Figulla Flex II device. The Occlutech Figulla Flex II (Occlutech gmbH) is a self-expanding nitinol wire mesh, very similar to the Amplatzer device in shape, but with a different design that eliminates the left atrial microscrew. This is fully recapturable and repositionable, and allows 50% reduction of meshwork material on the left atrial side with greater flexibility compared with Amplatzer device. Furthermore, the delivery cable mechanism is different and allows pivoting of the device, which facilitates positioning across the septum, an advantageous feature especially in large defects. Figures 8 and 9 depict the device and its delivery cable.

4. Transcatheter Patch device. The Transcatheter Patch utilizes a balloon-mounted, porous, polyurethane patch in combination with a defect bridging system for device apposition and immobilization until patch integration into adjacent tissue occurs. This device is flexible, biodegrades in situ and eventually will be replaced with native tissue. It is manufactured by Custom Medical Devices.

5. Cardioseal/Starflex. The Cardioseal/Starflex family of devices consists of two square patches of polyester fabric hand-sewn to a stainless-steel skeleton. Usually, it is used to close defects <16 mm. The manufacturer of these devices (Nitinol Medical Technologies) ceased to exist due to financial problems and the technology was sold to WL Gore & Associates.

6. Bioabsorbable devices (Biostar, Biotrek). Biostar and Biotrek are unique in using bioabsorbable materials to optimize the biological response of the defect closure and reduce the burden of prosthetic material that remains in the heart once the closure is achieved. The Biostar has an engineered porcine intestinal collagen layer scaffold, while the Biotrek uses the synthetic polymer poly-4-hydroxybutyrate. The manufacturer of these two devices is the same as the CardioSeal and ceased to exist.

7. Cardia devices. There are multiple generations of Cardia occluders (manufactured by Cardia Inc). Overall, the device has a double umbrella, with a frame of four arms. These devices have evolved and improved remarkably over the last 1-2 decades. There is a plan for a clinical trial in the United States.

8. Solysafe septal occluder. The Solysafe septal occluder consists of a self-centering device with two foldable polyester patches attached to eight metal wires made of phynox, which has been used in surgical implants for years. The course of the wires and the device’s patch enable the device to self-center in defects of variable diameters, with a maximum diameter given by the distance between the wires. With five device sizes, defects with stretched diameter up to 30 mm can be effectively closed. Gielen et al reported a very high incidence of device fracture.

Figure 7. Gore septal occluder.

Figure 8. The Occlutech device.

Figure 9. Loading the Occlutech device on the delivery system.
in their most recent study. The incidence of device fracture was 82.3% after 5 years of implantation. The device was also associated with erosions and was therefore discontinued by the manufacturer (Swissimplant AG).

9. PFM device (ASD-R). Manufactured by PFM gmbH, the PFM is a double-disc device made of nitinol wire, which is woven tightly in a single piece without welding or hubs on either side, which may reduce the risk of clot on the disc. A self-centering waist is achieved by reverse configuration of the left atrial disc.

Conclusion
Despite the recent concern about device erosions associated with some devices, albeit very rare, transcatheter ASD closure has continued to be a very safe procedure with comparable results to surgical closure, and long-term follow up studies have shown that the overall outcomes remain excellent. Device closure of the appropriate defect is an alternative attractive option to open surgical techniques. The United States FDA Circulatory Device System recommendations regarding device erosions are still pending and perhaps will shape the future of ASD device closure in the United States.

References