The Spectrum of PFO Closure Devices

A closer look at current technology as the indications for PFO closure become clearer.

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A patent foramen ovale (PFO) is a tunnel-like passage in the interatrial septum formed by failure of postnatal fusion of the septum primum and secundum. Persistent PFO is estimated to occur in approximately 20% to 25% of the adult population. Despite its high prevalence, the clinical significance of a persistent PFO remains an area of intense debate. Over the years, PFO has been implicated in multiple clinical conditions for which closure has been proposed, including cryptogenic stroke, migraine, decompression sickness, platypnea-orthodeoxia syndrome, and paradoxical cardio-systemic embolization.

Nonetheless, the recently published multicenter RESPECT trial, which randomly assigned patients with a proven PFO and ischemic stroke, transient ischemic attack, or systemic thromboembolism to PFO closure or medical therapy, is the only study that has conclusively demonstrated a medium-term clinical benefit from PFO closure.

In 2016, in response to this study, the US Food and Drug Administration (FDA) approved the use of the Amplatzer PFO occluder device (Abbott Vascular) in patients with cryptogenic stroke.

The recent results of the REDUCE and CLOSE clinical trials, presented at the European Stroke Organization Conference, showed positive outcomes using PFO occlude devices in the treatment of PFO. In the REDUCE trial, 664 patients with previous embolic cryptogenic stroke were randomized to PFO closure using Gore & Associates’ septal occluder devices or antiplatelet therapy. Results showed that PFO closures were significantly superior to medical therapy at 3.4 years, had a 76.6% relative risk reduction in recurrent clinical stroke, and a 49.6% relative reduction in silent ischemia via brain imaging. Higher rates of atrial fibrillation were reported in the device closure arm, most of which were periprocedural.

The CLOSE trial enrolled 663 patients who suffered a recent cryptogenic stroke and had a PFO with either an atrial septal aneurysm or a large shunt. Patients were then randomized into three groups: PFO closure using one of the CE Mark–approved PFO devices in addition to antiplatelet therapy, chronic oral anticoagulation, or chronic antiplatelet therapy. PFO closures with antiplatelet therapy better reduced the risk of recurrent stroke, with an absolute risk reduction of 4.9%, compared with antiplatelet therapy alone. Like REDUCE, the CLOSE trial also reported a significantly higher incidence of atrial fibrillation. For more detailed coverage of the REDUCE and CLOSE data, please see page 26.

There are currently multiple commercially available PFO occluders with different design features.

**SELF-EXPANDING DOUBLE-DISC PFO OCCLUDERS**

Self-expanding double-disc PFO occluders make up the bulk of the clinically used PFO occluders and utilize a simple common principle to close a PFO. They consist of two self-expanding left and right atrial discs or anchoring devices that are attached through a central waist. Once in position, a combination of mechanical influences and fibrous encapsulation leads to closure of the PFO.

Closure involves three simple stages. First, the PFO is crossed using a guidewire advanced from the right atrium. A compliant balloon is then often used to measure tunnel dimensions to guide the size of the occluder. However, on occasion, balloon sizing can enlarge the PFO, and therefore, some cardiologists omit this stage. This is followed by deployment of the device by sequential unfolding of the left (distal) and right (proximal) atrial discs. Closure should ideally be guided by transesophageal echocardiography or intracardiac ultrasound and can be performed under conscious sedation or general anesthesia. Nonetheless, some experts continue to use fluoroscopy alone.

**Amplatzer PFO Occluder**

The Amplatzer occluder is the only device that has FDA approval for PFO closure in the context of cryptogenic stroke. It is made of two nitinol woven discs with integral
Dacron patches and a fixed short waist (Figure 1). The Dacron patches are designed to stimulate endothelialization. The device comes in multiple sizes with the right atrial disc being larger than the left atrial disc. The exceptions are the smallest 18-mm device, which has equally sized biatrial discs, and the other “cribriform” devices.

**Figulla Flex II PFO Occluder**

The design of the Figulla II PFO occluder (Occlutech AB) is technically very similar to the Amplatzer device, with minor design differences. Notable differences are a lower-profile left atrial disc, absent hub on the left atrial side, and hinged attachment to the delivery cable (Figure 2). The changes are designed to achieve optimal alignment of the atrial septum during deployment and reduce long-term complications, such as device erosion.

There is a polyethylene patch inside each disc to support immediate closure. Like the Amplatzer occluder, this device is also nitinol based.

**Cardioform Septal Occluder**

The Cardioform Septal Occluder (Gore & Associates) is a flexible, retrievable, double-disc device with a petal design made of a nitinol frame covered by expanded polytetrafluoroethylene to facilitate rapid endothelialization (Figure 3). The Cardioform septal occluder showed clinical success rates of 89% to 100% in initial and further experience of a small cohort.\(^9\)\(^-\)\(^1\)\(^1\) The efficacy of Cardioform occluder was similar to the Amplatzer occluder, with a low risk of a major adverse event, such as fracture or embolization, and no difference in procedural time. As of now, no erosion has been described, even in deficient aortic rims\(^1\(^2\); however, large registries may lack the tools to detect this rare event. The Cardioform septal occluder is suitable for secundum atrial septal defect < 18 mm. In the United States, the Cardioform occluder is indicated for the treatment of atrial septal defects; in the United Kingdom, it is approved for use in atrial septal defects and PFO.

**Other Double-Disc Occluders**

Over the years, multiple other double-disc occluders have been designed, but few have had significant clinical success and most have been withdrawn from clinical use. One such device was the Intrasept (Cardia Inc.) consisting of an articulating central post that joins distal and proximal end caps made of sails and umbrellas. The device is designed to allow close alignment in patients with different septal configurations (Figure 4).

The CeraFlex (Lifetech Scientific) is another double disc occluder. It is designed to minimize thromboembolic complications as it has no distal left disc hub. The titanium nitride coating accelerates endothelialization and significantly reduces release of nickel in comparison to other traditional uncoated devices. Furthermore, it has a
flexible delivery cable capable of rotating through 360° to ensure the device is not under tension during deployment.

OCCLUDERS PLACED WITHIN THE PFO TUNNEL

This group of devices is inserted directly into the PFO tunnel and stabilized though two adjustable left and right atrial anchors bringing the septum primum and secundum in close apposition.19 The rationale underpinning this design is to minimize the amount of material exposed to the circulation and thus reduce device-related complications, such as thrombus formation, atrial arrhythmias, and erosion. In addition, the absence of large metallic discs allows for future septal punctures in case of potentially invasive left heart procedures. The FlatStent occluder (Coherex Medical, Inc.) is a commercially available device that utilizes this principle, and recent evaluation has indicated that it is particularly suited for closure of PFOs with long tunnels (Figure 5).14

BIOABSORBABLE PFO OCCLUDERS

The development of completely or partially bioabsorbable PFO occluders is an ongoing area of intense research.15 These devices have a basic self-expanding double-disc design and are deployed in a similar manner to standard metallic double-disc occluders. However, because the polymer constituting the discs (and struts in selected designs) is resorbed and replaced by native tissue, there should theoretically be a reduced chance of thrombosis, arrhythmia, and device erosion. A number of bioabsorbable devices have been evaluated clinically, but early results suggest these devices have a higher degree of residual shunt when compared with more widely used devices such as the Amplatzer occluder.16 There are currently no bioabsorbable devices in routine clinical use.

ANOTHER NOVEL DEVICE

The HeartStitch occluder (Sutura, Inc.) utilizes complex SuperStitch technology, as used in femoral vascular closure devices, to suture the septum primum and secundum. Similar to other devices where there is no or minimal implantable material, the chances of thrombosis, arrhythmia, and erosion should be reduced.

CONCLUSION

Over the past 2 decades, a large array of devices has undergone evaluation for PFO closure. However, it is only in the past 12 months that the Amplatzer PFO occluder has been given FDA approval for routine clinical use. As the indications for PFO closure are becoming more clear, there is a trend away from permanent deployable devices toward bioabsorbable materials or novel technologies that minimize the use of foreign material. Inherent advantages of such technologies are reduced thrombogenicity, avoidance of device-related complications, and maintenance of normal or near-normal native interatrial septum anatomy, as well as the ability to access the left atrium for potential future intervention.

7. Mas E. Closure of patent foramen ovale, oral anticoagulants or antiplatelet therapy to prevent stroke recurrence results. Presented at: The European Stroke Organisation Conference; May 16-18, 2017; Prague, Czech Republic.

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