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Chapter 19 Frequently Asked Questions PFO Closure With the Amplatzer or Gore Cardioform Devices

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CHAPTER

19

Frequently Asked Questions: PFO Closure With the Amplatzer or Gore Cardioform Devices

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PFO Closure for Stroke, Myocardial Infarction, Peripheral Embolism, Migraine, and Hypoxemia
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INTRODUCTION

A 30-year-old woman had a stroke 3 months ago and is now referred to you after being evaluated by a neurologist. There is no obvious source of the stroke, but a patent foramen ovale (PFO) was identified by transesophageal echocardiography (TEE) with right-to-left shunting. Your new patient has a lot of questions and you do not have a lot of time. We have written this chapter based on frequent questions that we have received over the years. You may choose to print this out and give to your patient, or adapt it to your practice.

PERCUTANEOUS CLOSURE OF INTERATRIAL SHUNTS: PFO OR ATRIAL SEPTAL DEFECT

In the past, the only way to close a hole in the heart that produced an abnormal connection between 2 chambers was to perform open-heart surgery. For over 25 years, catheter-based devices have been available as an alternative to open-heart surgery, and some devices have been approved by the Food and Drug Administration (FDA) since 2001. They permit us to close abnormal connections (shunts) between the right and left atrium (an atrial septal defect or ASD) without needing open-heart surgery. This technique is performed in the cardiac catheterization laboratory by an interventional cardiologist. During this procedure, a small tube called a catheter is placed in the heart from the large vein in the groin. A special spring-loaded device is passed through the catheter and straddles the hole between the 2 heart chambers. The procedure takes less than an hour and is performed without the necessity for general anesthesia. The patient can usually go home the same day. Imaging with X-ray fluoroscopy or echocardiography are used to guide the atrial septal defect procedure according to the operator's choice.

What Is a PFO?

The foramen ovale is a small passageway in the heart that all people have at birth. The foramen ovale permits oxygen-rich blood to pass from the placenta in the mother's womb to the left side of the baby's heart. From there, this blood can travel to the vital organs in the baby's body. Once the baby is born, the lungs expand with air, and the pressures inside the heart change. This forces a flap to close over the PFO passageway. After a few months, this flap normally seals over with scar tissue which prevents any further blood from mixing between the left and right sides of the heart.

However, in over 20% of people, the foramen ovale passageway does not seal over and it remains patent (able to open). In the vast majority of people, this does not cause any problem. However, in adulthood small blood clots form in the veins of the lower body in all people. They are usually harmless because of their small size, even if they travel to the lung. A large blood clot is dangerous and can cause a pulmonary embolus, but we are talking about clots that are usually 1–3 mm in size. If there is a PFO, however, the blood clot may cross over and reach important and delicate organs such as the brain, the eye, or the coronary arteries supplying the heart. Even very small blood clots may cause damage there. Some people, for instance, develop a stroke that cannot be explained by the usual causes. This is called a *cryptogenic (unknown cause) stroke*. It has been observed that a high percent of people (60%–70%) with a stroke of unknown cause, have a PFO. Hence, such a crossover of a blood clot (paradoxical embolism) is assumed as the reason for their stroke.

What Is a Cryptogenic Stroke?

"Cryptogenic" means of unknown cause. A stroke or a transient ischemic attack (TIA—a neurologic deficit that resolves completely within a day) is usually caused by one of the following: (1) hardening or fissure of the arteries that lead to the brain, (2) a blood clot from the heart or the aorta that lodges in the brain, or (3) an abnormality of the arteries in the brain. All of these conditions block the blood flow to a region of the brain and impair its function. If the patient does not have any of these problems or any other known cause for the stroke (there are many), then the stroke is said to be "cryptogenic."

There is a high association of people with cryptogenic stroke and a PFO. This is especially true in younger people, 20–60 years old, who usually are not at a high risk of having a stroke due to hardening of the arteries. The recurrence rate in people who have a cryptogenic stroke and a PFO is about 1% per year, but this risk appears to be constant and additive, so the longest study showed a 10% recurrent stroke risk over 10 years.

Estimate of Incidence of Cryptogenic Stroke Due to PFO

There are 700,000 strokes/year in the United States; 100,000 of these are cryptogenic. The prevalence of PFO among cryptogenic stroke patients is estimated to be between 60% and 70%. Therefore 60,000−70,000 strokes/year in the United States are potentially caused by paradoxical embolism through a PFO. From an individual's perspective, if 20% of all people have a PFO, then there are approximately 65 million people in the United States who have a PFO and do not know about it. If we estimate that there are 60,000 cryptogenic strokes per year due to a PFO, then the risk to develop a stroke for a person with a PFO is 1 in 1000 people per year. This risk may be higher if the PFO is opening up very often, is big, or has a large amount of blood crossing it.

How Does a PFO Cause a Stroke?

Our current theory is that a small blood clot may form in the veins of the leg and pass from the veins into the right atrium of the heart. Normally a small blood clot in the right side of the heart will travel to the lungs and be trapped and not cause any notice. A very large blood clot can plug up a large artery in the lungs and cause significant problems. This is termed pulmonary embolism. However, blood clots that pass through a PFO are usually much smaller, about 1−3 mm in diameter. If a person happens to have a PFO and also happens to develop a blood clot in the veins, there is a small chance that the blood clot could travel from the vein to the right side of the heart, through the PFO, into the left side of the heart, and from there it could go to the brain and cause a stroke or to another sensitive organ. Although the chance of this is small, the possibility of this coincidence increases as you get older and perhaps develop other illnesses that promote blood clots, like varicose veins. On average, approximately 1 in 1000 people/year with a PFO may develop a stroke. The risk is dependent on the characteristics of the PFO and does not include damage to other organs, such as the heart and the eye.

Although it is difficult to prove that the PFO is the intermediary passageway for a blood clot to cause a stroke, there are some lines of evidence that suggest this may be the case:

1) Although a PFO is found in 20% of the population, a PFO is found in 60%−70% of people who have a cryptogenic stroke.
2) If the PFO is closed, the chance of developing a subsequent recurrent stroke is reduced dramatically (about 75%).

What Alternative Treatments Are Available?

If someone has a cryptogenic stroke, and a PFO is documented by TEE (a form of imaging the heart where the ultrasound probe is placed in the esophagus through the mouth), there are currently 3 ways of trying to prevent another stroke.

1) The patient can be placed on a potent blood thinner called warfarin (Coumadin, the traditional blood thinner), apixaban, dabigatran, edoxaban, or rivaroxaban. Blood thinners have been used for over 50 years and are given to patients who have atrial fibrillation, a common arrhythmia especially in elderly people causing strokes from blood clots that form in an upper heart chamber, or prosthetic heart valves to prevent blood clots from forming on the foreign substance. Although these blood thinners can be used safely, they harbor a definite risk of internal bleeding. This is especially bothersome for our active patients who participate in athletic activities. Weaker blood thinners, such as acetylsalicylic acid and clopidogrel, have also been used because they cause less bleeding, but their protection is suboptimal.
2) The PFO can be closed surgically. This requires open-heart surgery where the circulation is maintained by passing the blood through a heart−lung bypass machine. In addition to the obvious trauma of the operation and the required recuperation, there is much concern that the bypass machine causes small particles to go to the brain. Some patients report subtle memory or personality changes following open-heart surgery and we suspect this may be due to the bypass machine. Such surgery is rarely performed as an isolated intervention anymore.
3) In October 2016, the FDA approved the use of the Amplatzer PFO Occluder (Abbott, Chicago, Illinois) device for PFO closure, and in March 2018, use of the Gore Cardioform Septal Occluder (W.L. Gore and Associates, Flagstaff, Arizona). Outside of the United States, these and similar devices have been available for over 25 years. Placing these devices is a lot easier on the patient than having open-heart surgery. The procedure is done in the cardiac catheterization laboratory using X-ray imaging and often some form of echocardiography to guide the catheter that is used to place the device. The procedure is relatively simple, takes less than an hour to perform, and does not require hospitalization.

RANDOMIZED CONTROLLED CLINICAL TRIALS OF PFO CLOSURE FOR STROKE: THE RESPECT, REDUCE, CLOSE, AND DEFENSE-PFO TRIALS

The best way to determine if a procedure or a drug should be used is to test the new procedure against the current standard clinical treatment. The RESPECT trial was performed with the Amplatzer PFO Occluder device. The 5-year results of this trial showed that for patients who had a cryptogenic stroke, the recurrence rate on medical therapy was 1.7% per year. For the patients who were assigned to the PFO closure group, the risk of recurrent stroke was reduced by 70%, which was statistically significant.

The REDUCE trial tested the Cardioform Closure Device by the W.L. Gore company. It is made from Gore-Tex and has springs that form 2 discs on the left and right atrial sides of the septum or wall between the 2 upper chambers of the heart. The REDUCE trial showed a significant reduction in preventing recurrent stroke in people who had a "cryptogenic stroke."

The CLOSE trial in Europe demonstrated clinical benefit of PFO closure in people who had a large shunt or an atrial septal aneurysm (a term used when the thin wall between the upper 2 heart chambers appears pliable and redundant). None of the patients who had their PFO closed had another stroke during a follow-up of up to 6 years. In the medically treated groups, the recurrent stroke rate was about 1% per year. No definitive difference could be proven if coumarin blood thinner was used versus an antiplatelet blood thinner such as acetylsalicylic acid or clopidogrel, but overall coumarin appears more effective.

A fourth randomized clinical trial, the DEFENSE-PFO trial in South Korea, also demonstrated a profound clinical benefit of PFO closure in people who had similar anatomical variants as in the CLOSE trial. The study included patients with a large PFO or hypermobile septum or atrial septal aneurysm. Similar to the CLOSE trial, none of the patients who had their PFO closed had another stroke during a follow-up of 2 years.

An Explanation of the Procedure to Close a PFO With the Amplatzer or Gore Cardioform Device

The patient comes to the hospital on the morning of the procedure and is brought to the cardiac catheterization laboratory. Some sedation may be given, such as an intravenous tranquilizer or even a morphine-derivative. Intravenous heparin, a short-acting blood thinner, is given while we are working inside the heart. We numb up the groin to access the femoral vein with a needle. A tube is placed into the femoral vein, similar to starting a large IV. An echocardiography probe may also be passed through a vein in the leg into the right atrium to image the heart. A special long tube called a catheter and a long wire are passed under X-ray guidance into the heart, across the PFO, and into the left atrium. The device is loaded into a special delivery catheter. The device is placed in the left atrium and the distal disc is opened. The disc is then pulled snug against the left side of the PFO. When we are convinced that the device is in the correct position, we unfold the second disc in the right atrium side of the PFO. This encloses or sandwiches the PFO between the 2 discs of the device. The device is then released from its delivery catheter. The final position is observed with injecting some contrast medium or with intracardiac echocardiography before the procedure is finished. Some centers use TEE during the procedure and this requires stronger sedation or even brief general anesthesia with a respiratory tube. The patient is observed in the monitoring area of the hospital. If there are no complications, the patient is discharged that evening.

PFO Closure for Migraine Headaches

The frequency of PFO is increased in people who have migraine with aura; about 50% of these people have a PFO compared to 20% in the general population. Many groups have found that when they close a PFO for indications such as stroke, the patients who also had migraines often described a reduction in the frequency and severity of their migraine episodes, and quite a few tell us that the migraines are completely gone. This observation was tested in 2 randomized controlled trials called the PRIMA and the PREMIUM studies. They included patients with very severe and frequent migraines, between 6 and 14 days of headache per month, in people who were unresponsive to multiple medications. The frequency of migraine days was reduced to a greater extent in people who had their PFO closed (an average reduction of 3.2 vs. 2.0 days). It was especially effective in people who had migraine with frequent episodes of aura (greater than 50% of their attacks were with aura).

What Possible Complications Can Occur?

No procedure is risk-free and you have to compare the potential benefits with the potential risks. Complications with the use of the Amplatzer and Gore Cardioform devices are rare, and the following events have been described:

1) Atrial fibrillation: In the trials, up to 5% of people who had a device implanted developed atrial fibrillation. This was usually transient (a single episode) but could last on and off for several (2–6) weeks. Since blood clots can form during atrial fibrillation and cause a stroke, there may be a need for blood thinners and antiarrhythmic medication for 1–3 months.

2) Chest pain: About 1 in 500 people develop severe chest pain, which we believe is due to excessive scar tissue formation over the device. If this does not go away within the first 1–3 months, either spontaneously or with antiinflammatory medical therapy, then the only way to treat this is to remove the device. Since there is so much scar tissue, the device cannot be removed with a catheter and you would have to undergo open-heart surgery.

3) Blood clot: This could form on the device. Since these devices are made of foreign substances, the body may respond by forming blood clots on it. We used TEE at 1–6 months post implant in thousands of patients to determine if there were any blood clots on the device, but have not observed any blood clots on our patients who have received Amplatzer or Gore devices. This somewhat unpleasant method to check the device is no longer routine. Within 3–6 months, the body covers these devices with fibrous scar tissue. We believe that this prevents future clots from forming. To help prevent these blood clots from forming, we place patients on weak blood thinners for a short period of time. We are currently using acetylsalicylic acid for 1 year and clopidogrel for 1 month after implant, medications that inhibit platelets in the blood from initiating blood clots. Other centers may use shorter periods for these drugs.

4) Infection: Since these devices are foreign substances, they could catch bacteria that pass through the bloodstream. Bacteria may get into a person's bloodstream during surgery, but also during dental cleaning. To prevent infection of the freshly implanted device, patients should avoid dental work for 3 months and take antibiotics prophylactically, that means 1 h before any dental procedures and when other invasive procedures are performed. This is the same recommendation as for patients who have a prosthetic heart valve, but in most centers, this recommendation is limited to the first 3–12 months after PFO closure.

5) Erosion: Worldwide, there have been 1,000,000 Amplatzer devices implanted to close ASDs (large holes in the heart) or PFOs. There are 200 reports (<1 in 5000) where the device has caused an erosion in the wall of the heart. This rare event, however, has generally required open-heart surgery to correct the condition and resulted in death in a few patients. Most of these episodes occurred with the larger ASD devices.

Of the 40,000 Gore Cardioform devices delivered to date, there are 2 reports of perforation of the heart wall due to a fracture of one of the scaffold wires. This can cause blood to form in the sac around the heart (hemopericardium) and may require emergency evacuation as well as surgical removal of the device.

6) Major complication: It is extremely rare to have a severe complication such as a stroke, heart damage, or death from a PFO closure procedure. These serious problems have not occurred in our practice.

What Side Effects Can Occur With the PFO Closure Device?

In addition to the possible complications associated with this device, there are 2 side effects that some people have described.

1) Since this is a foreign substance in the heart, it is possible that the device can irritate the heart chambers in which it is placed. This often causes palpitations or irregular heartbeats and potentially could cause persistent arrhythmias, that is, sustained irregular heartbeats. Depending on how bothersome and chronic these palpitations are, the patient may be given medications to treat the arrhythmia or need a blood thinner.

2) Some patients report an increased incidence of headaches in the 1–2 months following placement of the device. Most of these patients have had a history of migraine in the past, so it is difficult to know whether this effect is caused by the device. On the other hand, a number of reports suggest that chronic migraine headaches may be diminished in the long run following closure of the PFO.

3) More than 10% of people are allergic to nickel, which is contained in almost all septal closure devices. The shedding of nickel from these devices is, however, minimal and temporary. Although device explantation for that reason has been described, the respective risk is so small that prior testing is not warranted.

What Instructions Must I Follow After I Have a PFO Closure Device Placed?

Some operators deem no restrictions necessary. To prevent dislodgment of the device, we recommend that no strenuous physical activity be performed for 1 month following the device implantation. If you have a desk job, you could return to work 2 days after the procedure. Do not lift anything heavier than 10 pounds for 2 weeks.

You will need to take acetylsalicylic acid (at least 81 mg) for 3–12 months and clopidogrel 75 mg for 1 month. You should return within 1–3 months for a follow-up transthoracic (in some centers transesophageal) echocardiogram or transcranial Doppler ultrasound examination.

You will need to take antibiotics, usually amoxicillin, before any dental work, at least in the first months. This will prevent any infection getting started on the device. If you are allergic to penicillin, an alternative antibiotic can be used.

Could My PFO Have Contributed to My Transient Ischemic Attack?

It is definitely possible. The question is, did you have a TIA, which is assumed to be due to a small blood clot (an embolus) that came from the legs, up the veins to the right side of the heart, and then crossed through the PFO over to the left atrium, and went up to your brain, or did you actually have a complex migraine? A complex migraine also causes transient neurologic deficits (numbness, tingling, and weakness), which can last 20 min to a few hours. Neither a TIA nor a complex migraine causes a defect to be seen on a brain MRI. Migraine is more common in people with a PFO (about 50% of people with PFO have migraines) and is thought to be due to a chemical or venous (low oxygenated) blood that goes across the PFO and travels to the brain where the chemical triggers a migraine in susceptible people. Things that we would evaluate in your history include a history of migraines, previous headaches, and visual disturbances like shimmering waves or bright zigzag lines.

If you have had previous transient numbness on the same side and place, it would be unusual for a blood clot to go to the same spot on 2 different occasions. If that is the case, a complex migraine with transient neurologic deficit would be the more likely diagnosis. However, a complex migraine may well be triggered by a PFO and PFO closure might cure it.

Why Was My PFO Not Previously Detected? Is Echocardiography the Only Way to Diagnose This?

The best noninvasive way to detect a PFO is by using some sort of contrast agent during an echocardiography (either transthoracic or transesophageal or by transcranial Doppler). Each method has its pros and cons, but each requires an intravenous injection of contrast solution creating microbubbles that are detected by the ultrasound. A PFO does not make any murmur that can be picked up during a physical exam, like with a stethoscope. That is why it is never diagnosed by a routine physical exam or an electrocardiogram (ECG). The ultimate way to confirm the presence of a PFO is with a heart catheterization where a guidewire is passed across the atrial septum. That proves that there is still a connection between the upper 2 heart chambers, which should have closed after birth.

I Had a Transient Ischemic Attack; Are There Any Other Tests You Would Recommend for Me?

Another cause of emboli to the brain is an arrhythmia called atrial fibrillation. Even if a simple ECG does not show any abnormality, it would be good to be thorough and get an extended ECG monitor for days or even weeks.

How Soon Should I Have This Procedure?

If you had a TIA, there is less emergency than if you had an MRI-documented stroke. In every case, it is advisable to get it closed as soon as your specialist has concluded that your stroke could have been caused by your PFO.

What Is the Recovery Like?

The catheter-based procedure is very simple. We do it on an outpatient basis. The groin may be bruised for a few days and there are rare cases of bleeding in the groin after the procedure. Most people can go back to work in a few days. The devices are well tolerated but may cause mild transient chest discomfort, like something pulling inside, for the first month. Acetaminophen can be given if needed. People eventually can get back to their regular exercise and have participated in marathon or Ironman races after closure.

Is There Any Exclusion Criteria to Device Closure?

We have not come across a PFO that could not be closed. Even the presence of an inferior vena cava filter is not a problem. If the vein from the groin to the heart is blocked, we have placed the PFO closure device from the neck vein.

Will I Be Able to Feel the Device?

Most people tolerate the device once it becomes covered with scar tissue and do not feel it. Sometimes people tell us that they can feel a tugging sensation, which is not painful, especially when they turn on their left side in bed.

Can I Travel With the Implanted Device? Will the Device Trigger Airport Security Systems?

Yes, you may travel with an implanted device. In case you have a patient identification card, just take it along while traveling. The device will not trigger airport security systems. There is much less metal in the device than in frames for glasses or wedding bands. Furthermore, metal parts in both the Amplatzer and Gore Cardioform devices are made of an alloy of nickel and titanium, which are only weakly magnetic and cannot trigger magnetic detection devices.

Can I Have a Magnetic Resonance Imaging Study After Having the Device Implanted?

Yes, the PFO closure devices are made from nonferromagnetic metal and are therefore compatible with magnetic resonance imaging (MRI). The device, however, cannot be checked by MRI.

Can I Have My PFO Closed if I Am Pregnant?

Pregnancy per se is not a contraindication to placing a PFO closure device, especially if the stroke occurred during pregnancy. However, since the PFO closure device is placed using X-ray guidance during a catheter-based procedure, the risk of X-ray exposure must be weighed against the potential benefits of the procedure. Hence, you should discuss this issue with your treating physician. For the rare cases that cannot wait, there is an option to perform PFO closure without using X-rays at all.

In Your Expert Opinion, Is There Anything Else I Should Know or Consider Prior to Having My PFO Closed?

On the TEE, you may have a large PFO or an atrial septum that is flimsy (atrial septal aneurysm). These factors increase your risk of having a stroke through the PFO. So that pushes us toward strongly recommending to have your PFO closed. Additionally, the separation of the septum (wall) dividing the right and left atrium may be incomplete. This is called an ASD and that alone justifies that the defect should be closed (and there is FDA approval for that). For unusual cases, it is advisable to go to a large hospital, where they have done a lot of PFO/ASD closures (like more than 300).

http://pfofoundation.org: PFO Foundation.