During the past decade, occluding devices have significantly evolved, which has made transcatheter device closure of ventricular septal defects (VSDs) an attractive and feasible alternative to surgical closure. Congenital VSDs constitute the most common form of congenital heart disease (CHD) in infants and children. Isolated VSDs account for approximately 20% to 30% of all types of cardiac malformations. In addition, VSDs can be associated with various complex CHD lesions. These defects are classified anatomically based on their location in the ventricular septum: 70% to 80% are located in the membranous portion of the ventricular septum (perimembranous VSDs), 10% to 15% are located in the muscular portion (muscular VSDs), 5% are located below the pulmonary valve (subpulmonary or supracristal VSDs), and 5% are located near the junction of the tricuspid and mitral valves (inlet- or atrioventricular-type VSDs).

Indications for closure of VSDs include a hemodynamically significant shunt and prevention of long-term complications, including pulmonary hypertension, ventricular dilatation, aortic insufficiency, double-chambered right ventricle, and endocarditis. Surgical closure used to be the mainstay of treatment for the majority of VSDs, however, with the introduction of the newer percutaneous VSD closure devices, the results of transcatheter closure have significantly improved, as has been shown in several studies on both muscular and perimembranous VSDs.

We present two illustrative cases of muscular and perimembranous VSD device closure. In addition, we review the technical details for achieving a successful procedure, as well as our recommendations on treating VSDs using the transcatheter approach in the current era.
Case 1

A 24-day-old female infant (3.8 kg) was diagnosed shortly after birth to have a large perimembranous VSD (PmVSD) with inlet extension and a large midapical muscular VSD. She was in heart failure despite maximal medical therapy and was, therefore, referred for device closure of the muscular VSD. Transthoracic echocardiography (TTE) revealed a large PmVSD measuring 9 mm X 10 mm, with inlet extension and a large muscular VSD in the midapical portion of the ventricular septum measuring 6 mm X 6.4 mm. Because the location of the muscular VSD was close to the apex of the ventricular septum, we decided to proceed with percutaneous muscular VSD closure in the catheterization laboratory prior to surgical closure of the PmVSD. The patient was fully heparinized to achieve an activated clotting time $\geq 250$ seconds at the time of device placement. Routine right and left heart catheterization was performed. The right ventricle (RV) pressure was systemic, and the calculated Qp/Qs ratio was 5.5:1; the pulmonary vascular resistance was normal. Figure 1 illustrates the detailed steps of the closure technique as shown by transesophageal echocardiography (TEE). Angiography in the hepatoclavicular view (35° left anterior oblique/35° cranial) was performed to define the location and size of the muscular VSD. A complete assessment of the septum was then performed by TEE. The VSD was measured in multiple views, including the frontal four-chamber and basal short-axis views. Tissue rims and distances from aortic and tricuspid valves were also measured in these views to determine adequacy for device closure.

A 6-mm Amplatzer Membranous VSD Occluder (AGA Medical Corporation, Plymouth, MN) was chosen after measuring the VSD size at end-diastole by TEE and angiographic evaluation. A 4-F Judkins right endhole catheter was then advanced from the venous side across the patent foramen ovale into the left ventricle (LV) and, with use of a guidewire, across the muscular VSD, and was placed in the main pulmonary artery. A .035-inch soft guidewire was then positioned in the main pulmonary artery and snared from the right internal jugular vein with use of a 4-F Amplatz Gooseneck snare (ev3, Plymouth, MN). A 6-F delivery sheath was then advanced from the right internal jugular vein over the snared wire and positioned in the mid-LV cavity. After the sheath was properly positioned, the 6-mm VSD device was screwed onto the delivery cable and was pulled into the loader under a water seal. The loader was then flushed with saline through the side arm. The loader was next screwed into the proximal end of the long sheath, and the device was advanced to the distal tip of the sheath. The LV disk was deployed in the mid-LV cavity. After the sheath was properly positioned, the 6-mm VSD device was screwed onto the delivery cable and was pulled into the loader under a water seal. The loader was then flushed with saline through the side arm. The loader was next screwed into the proximal end of the long sheath, and the device was advanced to the distal tip of the sheath. The LV disk was deployed in the mid-LV cavity. After the sheath was properly positioned, the 6-mm VSD device was screwed onto the delivery cable and was pulled into the loader under a water seal. The loader was then flushed with saline through the side arm. The loader was next screwed into the proximal end of the long sheath, and the device was advanced to the distal tip of the sheath. The LV disk was deployed in the mid-LV cavity. Further retraction of the sheath off the cable deployed the connecting waist inside the septum. Again, before deployment of the right ventricle disk, TEE and/or angiography
confirmed the device position. The RV disk was then deployed by further retracting the sheath off of the cable. Repeat TEE and angiography were again performed before the device was released to confirm adequate positioning. In the event that the device was not well positioned across the VSD or if there was increased valvular regurgitation, the device could have been easily recaptured into the delivery sheath and then redeployed. Ten minutes after the device was released, angiography performed in the left ventricle showed no residual shunt across the muscular VSD. Repeat TEE revealed no residual shunting, as well as no obstruction or regurgitation induced by the device. The patient had transient episodes of arrhythmias during manipulation of the catheters that had no sequelae. Repeat transthoracic echocardiography at 24 hours revealed no residual muscular VSD. The patient then underwent surgical closure of the perimembranous VSD 3 days after the transcatheter procedure.

Case 2
A 55-year-old woman with history of perimembranous VSD presented for evaluation for closure of the defect. The patient was initially diagnosed at the age of 13 years with VSD that was, at the time, hemodynamically insignificant. She complained of fatigue with moderate and vigorous exercise and upon climbing two flights of stairs. She had multiple medical problems, including a diagnosis of possible multiple sclerosis with optic neuritis, neurogenic bladder, fibromyalgia, and hyperlipidemia. The patient was evaluated with cardiac catheterization 2 years before referral to us for device closure. At that time, her Qp:Qs was 2.4:1, her RV pressure was approximately 30% of the LV pressure, her pulmonary vascular resistance was 2.5 Woods units, and she had evidence of a double-chambered RV with a 10-mm to 12-mm gradient across the RV inlet portion. Due to the hemodynamic significance of her shunt and the potential worsening of the double-chambered RV, and her other comorbid conditions, she was referred for percutaneous VSD closure. She underwent cardiac catheterization under conscious sedation and under intracardiac echocardiography (ICE). Hemodynamic assessment revealed her RV pressure was approximately 50% of the LV pressure, with only a 10-mm to 12-mm Hg gradient across the RV muscular bundles. Her calculated Qp:Qs was 2.1:1, and she had normal pulmonary vascular resistance. The size of the PmVSD, as assessed by ICE, was 11 mm to 12.5 mm. The detailed steps of the percutaneous procedure are presented in Figure 2. Briefly, after complete hemodynamic assessment and LV angiography to define the location of the VSD, the defect was crossed using a Judkins right catheter that was advanced over a wire to the pulmonary artery. An arteriovenous wire loop was then established by snaring a wire in the pulmonary artery using an Amplatz Gooseneck snare. This wire was exteriorized from the right femoral vein. The appropriately sized sheath was then advanced from the femoral vein to the RV and into the ascending aorta. The wire was removed, and the sheath was brought back until we were able to advance the tip into the mid-LV cavity. The appropriately sized device (14 mm; 2 mm larger than VSD diameter) was then loaded and the entire assembly system (loader, pusher catheter, cable, and device) was advanced through the sheath to its tip in the LV cavity. The sheath was then slowly pulled back closer to the outflow region of the LV. The LV disk was then deployed between the anterior mitral valve leaflet and the left ventricular outflow tract. After echocardiographic assessment to ensure that the mitral valve apparatus was not affected by the device position, the waist and then the RV disk were deployed next in their respective locations. The LV disk was properly aligned so that the aortic end of the disk (flat) was toward the aortic valve, as evidenced by the appearance of the platinum marker of the LV disk pointing inferiorly (toward the patient’s feet). Echocardiography and repeat angiography were then performed prior to releasing the device to ensure adequate position. Repeat hemodynamics after closure revealed a normal RV pressure, with a minimal gradient (5 mm Hg) across the muscle bundles. ICE revealed tiny residual shunt through the device and no aortic regurgitation. TTE at 24 hours after closure showed good device position across the ventricular septum, with trivial shunt around the device and normal LV size and function. The patient was discharged home the next day on aspirin therapy (81 mg daily) for 6 months.

CONGENITAL MUSCULAR VSD
Muscular VSDs present a particular challenge to surgical closure. Various surgical techniques have been attempted, including right atrial, right ventricular, and left ventricular approaches. The first two provide poor visualization of the defects due to the heavy trabeculations of the RV. The latter, although providing better exposure, has been associated with significant ventricular dysfunction. In addition, the various surgical options remain associated with high morbidity and a significant incidence of residual shunts. Hence, device closure has been contemplated as a better alternative.

Precatheterization Evaluation
An essential element to a successful procedure is to carefully assess and select patients before planning muscular VSD closure. Thus, patients with clinically significant muscular VSDs require detailed echocardiographic assessment prior to planning a catheterization procedure. Such assessment is of paramount importance to determine the exact
location, number, and size of the muscular VSDs, as well as to determine any associated lesions. Evaluation is routinely done using TTE in the four-chamber, parasternal long- and short-axis views.

**Device**

In 1988, Lock et al attempted the first device closure of muscular VSD using the double umbrella device. However, it would be a decade of refining techniques and devices to achieve favorable results before device closure of muscular VSDs became clinically feasible. Currently, the only device approved by the FDA is the CardioSEAL device (NMT Medical, Boston, MA), which received approval for patients at high risk for surgery. However, the design of this device is not ideal for closure of muscular VSDs. The second device that has been evaluated in a US clinical trial is the Amplatzer Muscular VSD Occluder (AGA Medical) and, at the time of submission of this article, is still awaiting FDA approval. The Amplatzer Muscular VSD Occluder is made of .004-inch to .005-inch nitinol wire.

**Techniques and Results of Percutaneous Muscular VSD Closure**

In general, the technique for percutaneous device implantation is similar for the different devices. The procedure is routinely performed under general anesthesia and with continuous TEE guidance, which helps to determine the location and number of VSDs, as well as to monitor the atrioventricular valves for any significant regurgitation that might result during or after device implantation. The use of TEE, which can be optional for experienced operators in the case of a single VSD, is of paramount importance when there are "Swiss cheese" VSDs. The detailed steps of the closure technique are demonstrated in Figure 1. In general, the internal jugular venous approach is preferred when the muscular VSD is located in the midposterior or apical portion of the septum, whereas the femoral venous approach is used for more anterior muscular VSDs. The device chosen is usually sized 1 mm to 2 mm larger than the VSD, as determined by TEE or angiography at end-diastole. After device implantation but prior to release, it is essential to evaluate the device position and function of the atrioventricular valves using TEE and angiography because the device can be easily recaptured and redeployed in case of unsatisfactory position. In addition to fully heparinizing patients (activated clotting time between 200 to 250 seconds) during the procedure, we recommend giving an appropriate antibiotic (commonly cefazolin at 20 mg/kg) in three doses at 8-hour intervals. Subacute bacterial endocarditis prophylaxis and aspirin therapy are recommended for 6 months after the procedure. Patients then undergo chest x-ray, electrocardiography, and TTE follow-up at 6 months after closure, and yearly thereafter.

**Results**

The results of transcatheter muscular VSD closure have significantly improved with the use of the Amplatzer Muscular VSD Occluder. A multicenter US trial involving 83 procedures in 75 patients who underwent muscular VSD device closure showed successful implantation in 86.7% of the attempts, with closure rates of 69.6% and 92.3% at 6-month and 1-year follow-up, respectively. Although the procedure is more challenging in infants, some studies have reported success rates of 84% and 100% immediately after and at 1-year follow-up. One limitation to using the percutaneous technique is infant size. We currently recommend performing this approach for patients ≥5 kg in weight. Those who are smaller in size and those who have complex cardiac lesions requiring surgical repair can undergo percutaneous closure of their muscular VSD off-pump through a minimal median sternotomy. The patient in case 1 could have been treated using surgical exposure of the heart (median sternotomy). While the heart was still beating, we could have closed the muscular VSD using the perrventricular approach and then bypass and repair the perimembranous VSD surgically. The surgeon could then proceed to cardiopulmonary bypass to repair the membranous VSD. However, we elected to proceed with a percutaneous approach for the muscular VSD because of our large experience and good results in this patient population.

**PERCUTANEOUS PERIMEMBRANOUS VSD CLOSURE**

As mentioned previously, PmVSDs are the most common type of VSD. Patients with hemodynamically significant defects (left ventricular volume overload, Qp:Qs ≥1.5:1, history of infective endocarditis) are referred for closure. Surgical intervention, although currently associated with minimal mortality, is still associated with some morbidity, including risks of cardiopulmonary bypass, heart block, post-pericardiotomy syndrome, and the cosmetic issues related to scar. The introduction of the Amplatzer Membranous VSD Occluder, which is specifically designed for the membranous septum unlike the previous devices, rendered the percutaneous option to be safe.

**Device**

The Amplatzer Membranous VSD Occluder device is a self-expandable, double-disk device made of .003-inch to .005-inch nitinol wire mesh. The two disks are connected by a 1.5-mm-long waist, the diameter of which corre-
sponds to the size of the device. Unlike the muscular VSD Occluder, however, the LV disk of the membranous VSD Occluder is asymmetric, with the aortic end .5 mm longer, and the other end (LV end) is 5.5 mm longer than the waist. This asymmetry minimizes the risk of interference of the LV disk with the aortic valve. The RV disk, on the other hand, is 2 mm larger than the waist on either side. Currently, the device is available in sizes of 4 mm to 18 mm, in 1-mm increments. The sheaths required for delivery are 7 F to 9 F.

“Greater experience with possibly randomized trials and long-term follow-up are warranted to compare the results of device closure to those of standard surgical repair.”

Technique of Perimembranous VSD Closure

As with muscular VSD closure, patients with PmVSD should undergo careful evaluation to select those who are candidates for device closure. Weight >8 kg has been, and continues to be, an important safety issue. The presence of sufficient rims (more than 2 mm) between the aortic valve and the defect is a prerequisite for considering device closure with the Amplatzer Membranous VSD Occluder. In addition, the patient should have evidence of volume overload due to the VSD. Volume overload is best assessed by TTE. The procedure is usually performed under general anesthesia with TEE guidance, although it can also be performed under conscious sedation with ICE guidance in select cases. The femoral artery and vein are used for access, and full hemodynamic assessment is first performed to determine the degree of shunting. The detailed steps of the procedure are illustrated in Figure 2. The device is sized 1 mm to 2 mm larger than the VSD size, as assessed by echocardiography. One major important step in using the Amplatzer Membranous VSD Occluder is to ensure alignment of the LV disk so that the aortic end of the disk is toward the aortic valve. Alignment is confirmed on fluoroscopy by the presence of a platinum marker on the LV disk pointing inferiorly when correctly positioned. As with other device closure techniques, repeat angiography and echocardiography are performed prior to releasing the device to confirm satisfactory position. Recommendations for anticoagulation and subacute bacterial endocarditis prophylaxis are similar to those for muscular VSD closure. Patients undergo chest x-ray, electrocardiography, and TTE follow-up at 6 months, and yearly thereafter.

Results

The first clinical experience using the Amplatzer Membranous VSD Occluder was reported by Hajiz et al on six patients with PmVSDs with good results. The immediate and midterm results of the international registry on 100 patients undergoing PmVSD device closure were very encouraging as well, with successful deployment in 93% of cases and complete closure rates of 83.6% at 6-month follow-up. The size of the left ventricular end-diastolic dimension was also shown to significantly improve at 6-month follow-up. In 2006, Fu et al reported the results of the US phase-1 trial on a total of 35 patients with perimembranous VSD undergoing device closure and showed a complete closure rate of 96% at 6-month follow-up.

Complications

The incidence of adverse events encountered during and after transcatheter closure of muscular and perimembranous VSDs compares favorably to those associated with surgical closure. Major complications, including device embolization, cardiac perforation, and air embolism, are very rare in the hands of experienced operators. However, it is essential to have the appropriate tools in the catheterization laboratory and a surgical team available in the event of emergent complications.

Arrhythmias are the more commonly encountered complications; most are transient with no significant morbidity, whereas right bundle branch block is seen in approximately 6% of cases after PmVSD closure. The incidence of complete heart block is serious, and the experience with the Amplatzer Membranous VSD Occluder indicates that the incidence is between 0% and 7%. The onset of the heart block has been of significant discussion because, in many patients, the heart block appears days to months after the device has been deployed, which is in contrast to surgical heart block that appears immediately after cessation of cardiopulmonary bypass. Due to this issue, the US clinical trial is still on hold until the manufacturer redesigns the device. The other important issue is the proximity of the device to the aortic and tricuspid valve leaflets. However, experience indicates that the onset of new aortic or tricuspid regurgitation is rare. Other less commonly encountered but potential complications include hemolysis and pericardial effusion.

The availability of devices specifically designed for the muscular and membranous portions of the ventricular septum has made device closure of congenital VSDs a safe and effective approach. Greater experience with possibly randomized trials and long-term follow-up are warranted to compare the results of device closure to those of standard surgical repair.

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COVER STORY

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