Techniques and Outcomes for the Treatment of Paravalvular Leak

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Paravalvular prosthetic regurgitation is a potentially serious condition resulting from degeneration of annular tissue, affecting 6% to 15% of surgically implanted prosthetic valves and anuloplasty rings. In conditions of tissue friability from any cause, annular calcification, or infection, paravalvular defects can form and lead to varying degrees of regurgitation. Surgical factors associated with the development of paravalvular regurgitation include prostheses in the mitral position, supra-annular aortic prostheses, use of continuous sutures in the mitral position, and use of sutures without pledgets. Paravalvular defects are often crescentic and irregular in shape and may follow a serpiginous track from the downstream to upstream chamber. Chronic paravalvular mitral and aortic regurgitation can lead to left ventricular (LV), left atrial (LA) volume, and pressure overload, resulting in clinical heart failure. Because of noncompliance of the receiving chamber, the volume of regurgitation needed to induce symptoms may be relatively modest, such that standard volumetric measurements of regurgitation severity may not be applicable. In addition, conventional measures of mitral regurgitation severity such as the proximal isovelocity surface area method or pulmonary venous Doppler lack validation in this setting. Secondary elevation in pulmonary arterial pressure may result in right-sided heart failure. Paravalvular regurgitation is the most common cause of hemolytic anemia in patients with prosthetic heart valves. Increased red blood cell shear stress because of turbulent flow through the defect causes mechanical trauma and red blood cell fragmentation. Clinically significant hemolysis is more common in smaller defects with high-velocity jets, in patients with increased red blood cell fragility because of iron and folate deficiency, and in those with preexisting anemia because of the increased turbulence occurring from reduced blood viscosity and increased cardiac output. Moderate to severe paravalvular leak (PVL) after both surgical and transcatheter aortic valve replacement is associated with increased mortality.

Clinical Presentation

Patients with mild paravalvular regurgitation are often asymptomatic; however, when the degree of regurgitation becomes more severe, signs and symptoms of congestive heart failure may develop. Even smaller volumes of mitral or aortic regurgitation into a noncompliant chamber can produce symptoms. In patients with less than severe regurgitation, significant hemolytic anemia may be present, or a mixed presentation may occur. Signs of significant hemolysis may include fatigue, conjunctival and palmar crease pallor, jaundice, choluria, and petechiae. Patients with hemodynamically significant paravalvular regurgitation often have an audible murmur of varying intensity and when congestive heart failure is present may have signs of pulmonary hypertension, right ventricular dysfunction, and elevated jugular venous pressure. Because the murmur may be soft, a high index of suspicion is necessary when evaluating patients for possible paravalvular regurgitation. In patients with mitral prostheses, a pansystolic murmur is never normal and warrants close evaluation with detailed echocardiography. Similarly, a diastolic murmur of aortic regurgitation in a patient with aortic prosthesis warrants evaluation. Cardiac cachexia seems to be a not infrequent accompaniment to the presentation with patients presenting with weakness, sarcopenia, and weight loss. Patients with PVL may remain asymptomatic or well compensated for years then suddenly decompensate. In this circumstance, even a modest therapeutic reduction in regurgitation may be sufficient to restore them to their previous compensated state.

Diagnosis

Two-dimensional (2D) transthoracic echocardiography with comprehensive Doppler evaluation is the imaging test of choice for initial evaluation of patients with suspected paravalvular regurgitation. Typically, a turbulent eccentric jet is seen originating from outside the prosthetic sewing ring, and a gap is visualized between the annulus and sewing ring (Figure 1). An important limitation of transthoracic imaging of prosthetic valves is the problem of shadowing from the sewing ring or annular calcification, which may obscure color flow Doppler images. Elevated Doppler velocities across a prosthesis are often a clue to the presence of significant paravalvular regurgitation and should trigger further evaluation. A detailed transesophageal echocardiogram (TEE) is often
necessary to make a definitive diagnosis, exclude LA thrombus, evaluate prosthesis function, characterize the severity of regurgitation, and to accurately localize the defect. Furthermore, in cases of suspected endocarditis, TEE is essential to identify the presence of vegetation(s) and potential-related complications and sequelae. Patients with confirmed endocarditis require intravenous antibiotic therapy for at least 2 weeks, but preferably the full course of treatment if possible, with confirmatory negative blood cultures before proceeding with PVL closure.

**Anatomic Defect Localization**

TEE is particularly well suited for evaluating mitral paravalvular defects and is ideal for guiding their closure. With 2D TEE, the site of the paravalvular defect is determined by careful systematic scanning of the entire sewing ring in multiple imaging views. The mitral valve prosthesis and its bed can also be imaged from a single echocardiographic view using 3D TEE, thus obviating the often extensive TEE probe manipulation needed to obtain diagnostic 2D images. In addition to easily delineating mitral paravalvular defect location, 3D TEE provides crucial information on the defect(s) shape (often irregular and crescentic), size, and circumferential extent, hence suitability for percutaneous repair that is often not feasible with 2D TEE. A simple triangulation method can be used for localizing mitral paravalvular defects based on standard spatial coordinates and 3 anatomic landmarks: that is, the anteriorly located aortic valve, the anterolaterally located LA appendage, and the medially located atrial septum.

In contrast, aortic paravalvular defects are often best visualized using transthoracic echocardiography or intracardiac echocardiography given the more anterior location of the aortic valve. However, in posterior aortic defects, acoustic shadowing may result in the need for 2D TEE for adequate visualization. Paravalvular aortic regurgitation can be especially difficult to quantify because of strong color flow Doppler signals occupying the relatively small LV outflow tract that may lead to overestimation, or acoustic shadowing that may lead to underestimation. In these instances, aortography may be a useful tool provided that there is no concomitant aortic prosthetic regurgitation. However, because of the normal prosthetic washing jets and inability to accurately guess the orthogonal angle, aortography is often problematic for assessment of paravalvular regurgitation.

ECG-gated cardiac computed tomography (CT) angiography with volume-rendering reconstruction is another highly useful tool for determining the exact location of PVLs as well as the shape, trajectory, and size. Postprocessing imaging software allows for preprocedural determination of the optimal orthogonal fluoroscopy plane to be used during the procedure, thus facilitating efficient crossing of the defect with the wire using predetermined fluoroscopic gantry angles. Cardiac CT is especially helpful for procedural planning of aortic PVL closure, because these defects can be difficult to localize with echocardiography. At our institution, cardiac CT has become a standard preprocedural assessment tool for virtually all aortic PVL closures.

**Indications for PVL Closure**

Indications for percutaneous PVL closure include the presence of (1) symptoms of dyspnea or clinically significant hemolytic anemia and (2) moderately severe or severe paravalvular prosthetic regurgitation. Important contraindications to PVL closure include (1) active endocarditis; (2) regurgitation involving more than one-third of the circumference of the prosthetic annulus or an unstable or rocking prosthesis; and
intracardiac thrombi or vegetation that may be dislodged during the procedure.

Although medical therapy can improve symptoms, progression of heart failure from volume and pressure overload as well as need for repeated blood transfusions often cannot be corrected without closure of the defect. Given the increased morbidity and mortality of repeat cardiac surgery and the added risk associated with paravalvular tissue friability and heavy calcification, percutaneous closure is the preferred treatment choice. In the recent American College of Cardiology/American Heart Association guidelines for the management of valvular heart disease, percutaneous repair of paravalvular prosthetic valve regurgitation is recommended as a class IIa indication for patients with either intractable hemolysis or New York Heart Association class III or IV heart failure who are at high risk for surgery and have anatomic features suitable for catheter-based therapy when performed in centers with expertise in this procedure. Because essentially all such redo surgeries are moderate to high risk, we usually take the strategic approach of percutaneous PVL closure as the first-line treatment, followed by surgical repair when percutaneous approach is not possible or unsuccessful. A decision algorithm for evaluation and closure of PVL is shown in Figure 3.

Procedural Methods

Successful PVL closure requires knowledge and skill in the use of multiple complex catheter techniques including transseptal access, LA navigation, wire snaring, LV apical puncture, creation of wire rails, and vascular plug delivery (Table I in the Data Supplement). Knowledge of abnormal cardiac anatomy and ability to integrate CT, TEE, and fluoroscopic images in 3

Figure 2. Cardiac computed tomography angiography (CTA) and 3-dimensional (3D) transesophageal echocardiogram (TEE) for paravalvular defect localization and sizing. Top left. Cardiac CTA is used to determine the location of paravalvular defect, estimate defect size, and determine optimal crossing angles for the device deployment. Top right. Post mitral paravalvular leak closure, cardiac CTA demonstrating 2 Amplatzer Vascular Plug II (AVP II) plugs in place along the anterior margin of the mitral valve prosthesis. Bottom left. 3D TEE dome-view demonstrates an oblong-shaped mitral paravalvular defect adjacent to the left atrial (LA) appendage (arrow). Bottom right. After measuring the distance from the sewing ring to the LA wall, 2 12-mm AVP II devices were used to close the defect with trivial residual mitral regurgitation (bottom figures used with permission from Mayo Foundation for Medical Education and Research. All rights reserved).
dimensions are also critical. In addition, the interventionalist must have detailed knowledge of the prosthetic valve features including type of prosthesis, radiographic appearance, and the presence of other prosthetic valves to facilitate the procedure. Bioprosthetic valves typically accommodate a larger device size or number of nested devices because of a lower risk of device interaction with leaflet function. In contrast, the spatial relationship of mechanical prosthesis occluder discs relative to the defect(s) is a key determinant of the size and number of devices that can be implanted without interfering with prosthetic valve function.

In patients undergoing closure of para-aortic defects, conscious sedation may be used as long as TEE imaging is not anticipated. For mitral paravalvular defect closure, general anesthesia is preferred for patient comfort and safety because of longer procedural time and TEE requirement for interventional guidance. Efficient, accurate communication between the echocardiographer and interventionalist is essential with the use of simple, anatomically based nomenclature to facilitate localization and crossing of the defect. Low-resolution biplane fluoroscopy at low frame rates (usually 7.5 frames/s) allows for simultaneous orthogonal x-ray plane visualization while minimizing radiation exposure. Procedures can take 120 to 240 minutes, especially early in the learning curve, and careful attention to radiation dose and safety is advisable.

### Mitral PVL Closure

Paramitral defect closure can be accomplished using an antegrade transseptal, retrograde transaortic, or retrograde transapical approach. Of these approaches, the antegrade transseptal is the most often used. Figure 4 demonstrates the general approach we take for procedural planning of mitral PVL closure.

#### Antegrade Transseptal Approach

In the antegrade transseptal approach, the fluoroscopy gantries are oriented with the right anterior oblique projection showing the sewing ring tangentially (on its side and showing tilting discs of a mechanical valve sharply) and the left anterior oblique–caudal view shows the valve en face. These views facilitate 3D navigation and allow immediate detection of valve obstruction (if mechanical prosthesis), as well as immediate recognition of paravalvular versus valvular cannulation when initially crossing the defect. For most mitral PVL closures, a 14F sheath is placed in the right femoral vein. Transseptal LA catheterization is performed under fluoroscopic and TEE guidance using standard techniques and systemic heparinization is initiated with frequent assessment of the activated clotting time to ensure adequate levels of anticoagulation (we prefer keeping the activated clotting time ≥300 seconds). Transseptal puncture is often difficult in this population because of distorted cardiac anatomy, septal patching or scarring, and the need for more precise localization of the puncture. It is important to make the puncture near the level of the defect (superior–inferior axis) and in the case of medial defects, posteriorly/inferiorly on the septum to allow room to steer and flex equipment in the LA.

For thickened or fibrotic atrial septal tissue (eg, patients with previous atrial septal repair, multiple previous transseptal cannulations, and radiation heart disease), a SafeSept transseptal guidewire (Pressure Products Medical Supplies Inc, San Pedro, CA) may aid in obtaining transseptal access owing to the sharp wire tip and J shape that it assumes after crossing the septum, allowing the use of less force and reducing risk of perforation of the opposite wall of the LA. Radiofrequency and electrocautery are other useful adjunctive tools for obtaining difficult transseptal access.
A telescoping coaxial system is introduced into the LA, including a transseptal LA sheath (most commonly an 8.5 French Agilis NxT Steerable Introducer, St. Jude Medical, St. Paul, MN), a 100-cm 6F coronary guide (typically a multipurpose catheter), and a 5F 125-cm multipurpose diagnostic catheter (Table II in the Data Supplement). Depending on the location of the defect, other curved-tip catheters (such as a JR4) may be used instead. The system can be steered in 3 dimensions with multiple degrees of freedom using the deflectable LA sheath allowing the entire mitral valve ring to be probed efficiently. An exchange-length extra support angled hydrophilic 0.035-in wire (Glidewire, Terumo Medical Corp., Somerset, NJ) is passed through the telescoping catheter system with a torque device, allowing the use of finely tuned movements to localize and cross the defect. Three-dimensional TEE allows for localization of the defect sector and visualization of the wire and catheter. After the wire has crossed the defect, it is looped in the LV and passed through the aortic valve and into the descending thoracic aorta to reduce the risk of losing wire position (provided there is no aortic mechanical prosthesis). After obtaining adequate wire purchase, the 5F diagnostic catheter is crossed through the defect, followed by steady advancement of the 6F coronary guide catheter into the LV. These catheters usually cross without the need for excessive force; however, if either catheter does not cross, additional techniques may be required, such as guidewire snaring and creation of an arteriovenous rail to provide more wire support.

After the left ventricle is accessed with the 6F guide, the number and size of device occluders to be used must be determined. Although small and round defects usually require a single occluder, crescentic or oblong defects are best closed using multiple devices (Figure 2). Large paravalvular defects occupying ≤25% of the sewing ring are most effectively closed with staggered nesting of the devices. Our preferred device is the Amplatzer Vascular Plug II (AVP II; St. Jude Medical, St. Paul, MN; Figure 5). Favorable features of the AVP II device include its low profile and its fine nitinol mesh construction allowing for deliverability through a variety of catheters. In addition, it is the lowest cost of the commonly available closure devices. An AVP II of ≤12 mm will fit through a 6F coronary guide catheter without difficulty. Generally, if a 6F multipurpose guide passes easily through the defect without resistance, we start with a 12-mm AVP II device. If considerable force is required to advance the 6F guide or a smaller catheter is required to cross the defect, we use a smaller device (either 10- or 8-mm AVP II). It is important to note that the use of this device and others for PVL closure is off-label as there is currently no Food and Drug Administration–approved device for this indication. Other devices including the Amplatzer Duct Occluder, Amplatzer Septal Occluder, and Amplatzer Muscular VSD Occluder (all manufactured by St. Jude Medical, St. Paul, MN) may also be used. An important caveat is that the nitinol mesh of these devices is stiffer and of larger caliber and is associated with a higher risk of hemolysis.

With single AVP II device placement, the distal third of the occluder is extruded into the LV followed by careful withdrawal of the entire assembly toward the annular plane and mitral valve prosthesis. Careful assessment of mitral prosthetic leaflet motion should be performed and if there is evidence of impairment, the entire assembly should be readvanced into the LV and alternative strategies should be considered including use of a smaller device or device deployment close to the atrioventricular plane. Once the position of the distal disc is snug against the annular plane, this disc is maintained in position, while the rest of the device is slowly extruded as the delivery assembly is carefully withdrawn into the LA; depending on the anatomy of the defect the middle disc may be fully expanded (short length defect) or compressed (within the tunnel of the defect).
Simultaneous Deployment Technique
(Double Wire)
When deployment of multiple devices is planned, one option is a simultaneous technique. A 20F large bore venous sheath is helpful to minimize access site blood loss during the simultaneous deployment procedure. With sheath sizes >14F we typically use either a venous preclose technique (using 2 6F Perclose Proglide devices [Abbott Vascular, Redwood City, CA]) or a figure of 8 stitch for access site management. To facilitate the simultaneous deployment technique, two 0.032-in Amplatz ExtraStiff Guide Wires (Cook Medical, Bloomington, IN) are inserted through the 6F guide catheter and advanced to make gentle loops in the LV. The entire catheter assembly is then withdrawn from the body, leaving only 2 guidewires across the defect in the left ventricle. Two separate delivery systems, each consisting of a 6F multipurpose guide and 5F multipurpose diagnostic, are then loaded and advanced into the LV over each of the guidewires. The guidewires and 5F catheters are then removed and the devices (typically 8- to 12-mm AVP II devices) can be advanced through the 6F guide catheters simultaneously. This technique can also be performed with 3 wires, again using 0.032-in extra stiff and 6F guides as noted above.

Sequential Deployment Technique
(Anchor Wire)
The sequential deployment or anchor wire technique has become our preferred approach for most PVL closure procedures. This technique is especially useful for defect sizes that are too small for the simultaneous deployment technique, yet too large to close with only 1 device. After crossing the defect with the hydrophilic guidewire and multipurpose catheter, one 0.032- or 0.035-in stiff wire is placed in the LV. An 8F Cook Flexor Shuttle Sheath (Cook Medical) is then placed across the defect and with the wire still in place, and AVP II device is delivered without losing access to the LV. After the device is deployed, the delivery catheter is removed from the guidewire and then reloaded onto the guidewire, leaving the device on its delivery cable outside of the sheath to facilitate delivery of additional devices using the same sequence.

Sequential Deployment Technique Using Arteriovenous or Transapical Rail
Alternatively, devices can be deployed sequentially using a more stable rail technique. For this approach the hydrophilic guidewire is snared (typically in the ascending aorta) and exteriorized (Movie I in the Data Supplement). To maintain control and prevent slippage of the hydrophilic guidewire, a Hemostat or Kelly forceps are clamped to each end of the exteriorized wire. A second operator is necessary to hold both ends of the wire rail and can increase or decrease wire tension during crossing of the leak and deployment of the device. All catheters are removed and replaced with an 8F Flexor Shuttle sheath. With the arteriovenous rail in position, the first closure device can be placed through the shuttle sheath alongside the existing exteriorized guidewire rail. After the first device is deployed, the sheath is removed over the delivery cable of the first device leaving the first device attached on its cable. The sheath is then placed over the existing arteriovenous rail again. A second and third device can then be placed using the same sequence (Figure 6). Smaller shuttle sheaths such as 7 or 6F may be required for crossing with >1 device in place. Major advantages of this technique are the complete control one has over wire tension and catheter delivery, devices are not released until the end (ie, everything remains reversible), and it provides great flexibility in terms of delivery catheters and devices. It is important to be cognizant of potential negative effects that can be induced by increasing wire tension with the use of an arteriovenous rail. High arteriovenous rail tension occasionally can result in prosthetic leaflet impingement and native aortic valve regurgitation because of transient distortion of valve anatomy (Figure 6). Constant attention to the aortic pressure waveform throughout the procedure can provide clues to such negative effects, and it is important for operators to release wire tension when it is not in use to minimize the duration of these effects. This technique also can be used with a transapical rail. LV puncture for transapical access with a 4F sheath is required for arteriovenous rail formation in the setting of double mechanical prosthetic aortic
Other Techniques

Retrograde cannulation of paraprosthetic mitral defects can also be accomplished with a retroflexed diagnostic catheter through the aortic valve, such as an Amplatzer curve of left coronary bypass curve. After crossing the defect, the wire is snared in the LA via a transseptal sheath and exteriorized, forming an arteriovenous loop/rail. After this, the delivery system of choice can be used in antegrade transseptal approach with closure devices placed as described above.

Transapical puncture is useful particularly when the defect is in a medial location where catheter manipulation and cannulation from a transseptal approach are limited because of short distance between the atrial septum and the medial mitral annulus, or when the interatrial septum is not favorable for transseptal approach (eg, previous septal closure device placement). Once apical access has been obtained, defects can be crossed in a retrograde manner under fluoroscopic and echocardiographic guidance (Figure 7). Transapical access for paravalvular mitral leak closure is associated with a high (∼20%) risk of postoperative bleeding resulting in hemothorax and need for chest tube drainage, particularly when a 6F sheath size is required to deliver devices. An alternative to percutaneous transapical puncture is performing a small thoracotomy to expose the apex with subsequent surgical repair under direct visualization. In cases of PVL associated with dehiscence of a mitral and mitral valves, because crossing a mechanical prosthesis with a wire can result in acute severe regurgitation and patient decompensation.

Figure 6. Arteriovenous rail and wire-induced aortic regurgitation. With the use of an arteriovenous rail, attention to hemodynamic effects of increased wire tension is critical. In this case, increased wire tension resulted in aortic regurgitation, as evidenced by the drop in aortic diastolic pressure (top left and top right). By advancing wire into the left ventricle and lowering tension, the aortic diastolic pressure rose indicating a reduction in wire-induced aortic regurgitation. Two Amplatzer Vascular Plug II devices were used sequentially (shown) to close the mitral paravalvular defect.
annuloplasty ring, transcatheter valve in valve may be an effective treatment option.14

Assessment of Treatment Success/Failure

Transesophageal echocardiography is used to confirm adequate reduction of perimital regurgitation and fluoroscopy used to confirm normal mechanical prosthetic leaflet motion before device release. In the case of closure for hemolysis, the goal is complete resolution of regurgitation. In addition, measurement of LA pressure may also confirm reduction of the V wave. Importantly, although devices are still attached to the delivery cable, the atrial aspect may be tethered across the prosthetic valve orifice (particularly for lateral defects) toward the atrial septum, producing the appearance of orifice obstruction. However, in these cases, once the device has been released from its cable, the atrial aspect assumes a more neutral position directly over the paravalvular defect within minimal overlay of the valve orifice.

In the case of defects that cannot be crossed with the guidewire, we typically will spend 30 to 60 minutes of wire probing, with different catheters if necessary, before aborting the procedure. If repeated prosthetic leaflet impingement by a plug occurs, we will often attempt 1 to 3 additional device sizes or types before declaring the procedure unsuccessful.

Aortic PVL Closure

Periprosthetic aortic regurgitation accounts for ≈20% of PVL closure procedures. With the increasing use of transcatheter aortic valve replacement (TAVR) therapy in recent years, the incidence of peri–aortic regurgitation has risen. These defects can almost always be approached using a retrograde cannulation technique and are often smaller than perimital defects, usually necessitating only 1 device for successful closure. Transthoracic echocardiography is often adequate for defect localization, with the exception of posterior defects, in which TEE or intracardiac echocardiography may be required. As mentioned previously, cardiac CT angiography is highly useful for preprocedural planning and determination of optimal orthogonal fluoroscopic gantry angles to be used to cross the defect while visualizing the valve tangentially. In general, the left anterior oblique angle derived from CT angiography is more important for crossing than the cranial–caudal angle, and selection of a less steep cranial–caudal angle will help to minimize radiation exposure both to the patient and to the operator (Figure 8). In our experience, perhaps because of less aortic annular motion compared with mitral annular motion during the cardiac cycle, CT angiography seems to provide better visualization of aortic paravalvular defects compared with mitral defects.

Typically, a 6-8F sheath is placed in the femoral artery for aortic PVL closure. Periaortic defects are crossed using a 0.035 stiff angled glide wire within a telescoped 125-cm 5F multipurpose coronary catheter inside a 6F multipurpose guiding catheter. In larger aortic roots or more difficulty with navigating the guidewire, an Amplatzer left coronary 1 catheter may better facilitate direction of the guidewire across anterior defects, whereas a Judkins right 4 may be more useful for posterior defects. In smooth defects, an anchor wire technique may not be necessary, but in most defects with serpiginous courses, the defect should be crossed with a catheter and

Figure 7. Transapical access for paravalvular leak closure. In this patient with paraprosthetic mitral regurgitation, a transapical route was used because of the presence of an Amplatzer closure device in the interatrial septum. Top left, Angiography confirms appropriate access in the left ventricular apex. Top right, The defect is crossed in a retrograde manner. Bottom left, A 10-mm Amplatzer Vascular Plug II (AVP II) device is deployed. Bottom right, A 6-mm AVP II device is deployed in the transapical access site for closure.
the glide wire is exchanged for a 0.032 Amplatzer extrastiff exchange-length guidewire. Knowledge of the compatibility of combinations of catheters, wires and closure devices are crucial to ensure the success of the procedure (Table III in the Data Supplement).

PVL Closure After TAVR

PVL is more common with TAVR compared with surgical aortic valve replacement, with the incidence of moderate or severe residual paravalvular regurgitation estimated at 7.4%. Given the lack of direct visualization of the aortic valve annulus, lack of surgical excision of the old calcified valve, motion of the beating heart, and lack of repositioning capability of currently available transcatheter valves, paravalvular regurgitation during TAVR can result from a variety of mechanisms including annulus–prosthesis mismatch (undersized prosthesis), prosthesis malpositioning, or heavy valve calcification resulting in valve underexpansion and underapposition. Extent and location of aortic valve calcification and the angle of the LV outflow tract to the ascending aorta are both associated with paravalvular regurgitation after TAVR. Moderate-to-severe paravalvular regurgitation may be more common with the Corevalve (Medtronic, Minneapolis, MN) prosthesis compared with the Sapien (Edwards Lifesciences, Irvine, CA) prosthesis. However, with increasing operator experience and standardization of techniques such as multidetector CT-guided optimal oversizing, the incidence of PVL after TAVR has been declining. Furthermore, newer devices such as the Sapien 3 valve with its improved outer skirt design and the Lotus valve (Boston Scientific, Marlborough, MA) with its adaptive seal and repositionability hold promise in further reducing the incidence of PVL after TAVR. Data from The Placement of Aortic Transcatheter Valve (PARTNER) trial has shown that even mild PVL after TAVR is associated with increased mortality.

TAVR-associated PVLs can be divided into those that occur with an adequately positioned and expanded transcatheter valve relative to the native aortic annulus and adequately positioned, but undersized or underexpanded valve relative to the native annulus, and those that occur because of prosthesis malpositioning. PVLs occurring because of transcatheter device positioning too high or too low relative to the aortic annulus (so called infraskirtal or supraskirtal) leaks may necessitate a valve-in-valve implantation either lower or higher to achieve paraprosthetic sealing rather than a vascular plug. PVLs occurring because of either an undersized device relative to the native annulus or an underexpanded device can be treated by balloon postdilatation and valve in valve. In the case of heavy annular or LV outflow tract calcification, postdilatation or valve in valve may not be adequate for reducing PVL, and a vascular plug closure may be more effective. The remainder of PVLs are bordered by an adequately expanded and properly sized transcatheter prosthesis on 1 side and native annulus on the other, thus providing adequate tissue for anchoring of vascular plugs.

For PVL closure in patients after TAVR with the Sapien prosthesis, A VP IV devices have the advantage of being deliverable using standard diagnostic catheters and are often more suitable because of the smaller size and heavy calcification associated with such defects (Figure 9). A VP IV devices range in size from 4 to 8 mm, are delivered through any catheter that can accommodate a 0.038 wire, and have a smaller profile compared with the A VP II plug. Retrograde wire cannulation may be problematic because native leaflets are left in situ, and bulky calcification is frequently present.

For PVL closure in patients after TAVR with the Sapien prosthesis, AVP IV devices have the advantage of being deliverable using standard diagnostic catheters and are often more suitable because of the smaller size and heavy calcification associated with such defects (Figure 9). AVP IV devices range in size from 4 to 8 mm, are delivered through any catheter than can accommodate a 0.038 wire, and have a smaller profile compared with the AVP II plug. Retrograde wire cannulation may be problematic because native leaflets are left in situ, and bulky calcification is frequently present.

For the Corevalve prosthesis, paravalvular regurgitation typically results from either calcification of the annulus resulting in inadequate stent apposition or from deep/low ventricular implantation depth resulting in the covered skirt being seated below the native aortic annulus, allowing blood to regurgitate.
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Through the holes of the uncovered portion of the stent frame, PVLs that occur because of the Corevalve position being too high or too low are generally not treatable with a vascular plug, because the absence of valve apposition at the annular level creates a large defect. The aortic frame struts of the Corevalve prosthesis presents a unique challenge for crossing the defect while avoiding the lattice. A high crossing position across the frame struts is recommended to allow easier device deliverability. The AVP IV device again is the device of choice given its ability to be delivered through a 0.038 diagnostic catheter (Figure 10). Given the proximity of the frame to the coronary arteries, it is useful to perform postprocedure aortic angiography to demonstrate coronary patency, as well as residual PVL.

Outcomes

Most PVL closures are performed for symptoms of heart failure (90%), with ≈30% of patients also having signs and symptoms of hemolysis. Successful PVL closure is generally defined as ≤1+ residual regurgitation and is achieved in 80% to 90% of cases.9,11,12,20

Figure 9. Paravalvular leak closure after transcatheter aortic valve replacement (TAVR). A, Right anterior oblique aortogram demonstrating anterior paravalvular defect in a patient with a 26-mm Sapien prosthesis. B, Amplatzer vascular plug 4 can be delivered through standard diagnostic catheters and may be more suitable for closing post-TAVR defects. C, Right anterior oblique cinefluoroscopy demonstrating Amplatzer Vascular Plug-4 plug deployment through the aortic paravalvular defect.

Figure 10. Paravalvular leak closure after Corevalve transcatheter aortic valve replacement. A, Right anterior oblique cinefluoroscopic view demonstrating crossing of anterior paravalvular defect with a wire. B and C, A 8-mm Amplatzer Vascular Plug-4 device (arrows) deployed within paravalvular leak. D and E, Transthoracic echocardiogram parasternal short axis view demonstrating anterior periaortic regurgitation preprocedure (D) and no residual leak post procedure (E).
Managing and Avoiding Complications

Procedural complications include prosthetic leaflet impingement (4%), device embolization (<1%), need for emergency surgery (0.9%), and bleeding (5.2%). Prosthetic leaflet impingement can almost always be recognized immediately by either cinefluoroscopy or echocardiography. When this occurs despite repeat attempts at extruding the device through the delivery catheter, smaller devices should be attempted. Device embolization is rare and can be prevented by ensuring stable device positioning by pushing the device with the catheter and pulling on the delivery cable while observing for device movement on fluoroscopy. If the device pulls or pushes through the defect, the device should be either redeployed or a larger sized device should be used. If device embolization occurs after it has been released from the cable, the device can usually be snared and removed through a femoral arterial sheath (Movies II–IV in the Data Supplement). Transeosophageal guidance helps to minimize the risk of complications related to transseptal access. High-dose heparinization to keep the activated clotting time ≥ 300 seconds minimizes the risk of thrombotic complications. Vascular access site bleeding risk can be minimized by the use of ultrasound-guided access, reversal of anticoagulation with protamine at the end of the procedure, and vascular closure devices where appropriate.

The 30-day complication rate from the largest published series was 8.7% (including sudden and unexplained death, 1.7%; stroke, 2.6%; emergency surgery, 0.9%; and bleeding, 5.2%). Of note, the learning curve for PVL closure is significant, with a considerable reduction in major adverse cardiovascular events, procedure duration, contrast volume administered, and length of hospital stay after the first 50 case experience, with an overall success rate of 90% in experienced centers (Figure 11).11

Long-term outcomes are favorable in patients who undergo a successful PVL closure and do not have severe comorbidities. Among survivors, 72% of patients who initially presented with heart failure were free of severe symptoms and need for cardiac surgery 3 years after PVL closure.21 Severity of residual regurgitation seems to be an important predictor of outcome. Three-year estimate of survival free of death or need for surgery for those with no, mild, or moderate or severe residual regurgitation was 63.3%, 58.3%, and 30.3% (P=0.01), respectively21 (Figure 11). A recent meta-analysis of 362 patients has demonstrated that successful PVL closure is associated with improvement in functional class or hemolytic anemia (odds ratio, 9.95; 95% confidence interval, 2.1–66.7), reduction in need for surgery (odds ratio, 0.08; 95% confidence interval, 0.01–0.40) and even associated with lower cardiac mortality (odds ratio, 0.08; 95% confidence interval, 0.01–0.90;
Although limited by sample size and retrospective design of included studies, this analysis provides independent data supporting improved clinical outcomes after PVL closure.

**Future Directions**

Important areas of ongoing research in the field of percutaneous PVL closure include continued assessment of long-term outcomes of patients undergoing the procedure. Furthermore, the assessment of invasive hemodynamic effects of PVL closure may help identify patients who are more or less likely to derive clinical benefit from the procedure. It is currently unknown whether hemodynamic parameters including stroke volume and intracardiac pressures may predict outcomes in PVL closure patients. Outcomes of PVL closure after TAVR are currently unknown and future data in this population are required. Finally, ongoing work to create purpose-built devices specially designed for PVL closure holds promise for improving procedural efficacy and success.

**Conclusions**

Percutaneous PVL closure is an effective therapy for patients with heart failure or intractable hemolysis who are at high risk for surgery when performed in centers with expertise in this procedure. Procedural execution requires detailed preprocedural heart-team–based planning, intraprocedural imaging guidance, and skill in complex structural interventional catheter-based techniques.

**Disclosures**

None.

**References**


Techniques for Treatment of Paravalvular Leak


Key Words: aortic valve regurgitation | echocardiography | heart failure | heart valve prosthesis | mitral regurgitation | transcatheter aortic valve replacement
Techniques and Outcomes for the Treatment of Paravalvular Leak
Mackram F. Eleid, Allison K. Cabalka, Joseph F. Malouf, Saurabh Sanon, Donald J. Hagler and Charanjit S. Rihal

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### Table 1. Required Skills for Performing PVL Closure

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<tr>
<th>Interventionalist Requirements</th>
<th>Echocardiographer Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac anatomic nomenclature</td>
<td>Cardiac anatomic nomenclature</td>
</tr>
<tr>
<td>Transeptal access</td>
<td>Transesophageal echocardiography</td>
</tr>
<tr>
<td>Biplane fluoroscopy use</td>
<td>Transthoracic echocardiography</td>
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<td>Echocardiographic image interpretation</td>
<td>3 Dimensional echocardiography</td>
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<tr>
<td>Left atrial navigation</td>
<td>Fluoroscopic image interpretation</td>
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<tr>
<td>Wire rail creation</td>
<td>Procedural equipment &amp; steps</td>
</tr>
<tr>
<td>Wire snaring</td>
<td></td>
</tr>
<tr>
<td>Left ventricular apical puncture</td>
<td></td>
</tr>
<tr>
<td>Catheter, wire and device compatibility</td>
<td></td>
</tr>
<tr>
<td>Occluder/vascular plug device use</td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Paravalvular Leak Closure Equipment

<table>
<thead>
<tr>
<th>Common Equipment</th>
<th>Mitral Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-8F arterial sheath</td>
<td>14F venous sheath</td>
</tr>
<tr>
<td>.032 &amp; .035 exchange length Amplatz extrastiff wire</td>
<td>6F arterial sheath</td>
</tr>
<tr>
<td>.035 exchange length stiff angled Glidewire</td>
<td>Brockenbrough needle</td>
</tr>
<tr>
<td>5F 125cm multipurpose catheter</td>
<td>7-8F Mullins dilator</td>
</tr>
<tr>
<td>6F 100cm multipurpose guide</td>
<td>Inoue wire &amp; dilator</td>
</tr>
<tr>
<td>6-8F Cook Flexor shuttle sheaths</td>
<td>8.5F small &amp; medium curl Agilis sheaths</td>
</tr>
<tr>
<td>AVP-II plugs (4-16 mm)</td>
<td>6F EnSnare retrieval catheter</td>
</tr>
<tr>
<td>AVP-IV plugs (4-8 mm)</td>
<td>LV puncture needle</td>
</tr>
<tr>
<td></td>
<td>2 Hemostats</td>
</tr>
</tbody>
</table>
### Table 3. Compatibility Table for Catheter, Wire and Device Combinations

<table>
<thead>
<tr>
<th>Catheter only Technique</th>
<th>Anchor Technique with 0.032 or 0.035 wire</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AVP II 6 or 8 mm</td>
</tr>
<tr>
<td><strong>6F coronary guide</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>7F coronary guide</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>8F coronary guide</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>4F Shuttle sheath</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>5F Shuttle sheath</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>6F Shuttle sheath</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>7F Shuttle sheath</strong></td>
<td>Yes</td>
</tr>
<tr>
<td><strong>8F Shuttle sheath</strong></td>
<td>Yes</td>
</tr>
</tbody>
</table>

AVP II = Amplatzer vascular plug II

Yes/No = AVP II does/does not fit into delivery catheter (coronary guide or Shuttle catheter)

Supplemental Videos Legend:

Supplemental Video 1. Arteriovenous rail creation. For antegrade transeptal mitral paravalvular leak closure, an exchange length hydrophilic wire is navigated across the paravalvular defect via transeptal approach and then snared either in the left ventricle or aorta and exteriorized through a femoral arterial sheath to provide enhanced support for device delivery.

Supplemental Videos 2-4. Embolized AVP-II plug retrieval. In this case, a 12 mm AVP-II device embolized into the left ventricle after deployment and release around a mitral periprosthetic defect (Video 2). This device further embolized to the aortoiliac bifurcation (Video 3), where it was then snared and retrieved using a 6F Ensnare retrieval catheter through the femoral artery (Video 4). The patient subsequently underwent successful mitral paravalvular leak closure with two 14 mm AVP-II devices.