Percutaneous Paravalvular Leak Closure
– Imaging, Techniques and Outcomes –

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Paravalvular leak (PVL) is a known complication of surgical and transcatheter valve replacement procedures. Patients most commonly present with congestive heart failure and/or hemolysis, and repeat surgical procedures to correct the PVL carries increased risk with reduced likelihood of success. As a result, percutaneous approaches to PVL closure have been developed, with a considerable emphasis on multimodality imaging for both diagnosis and procedural guidance in the cardiac catheterization laboratory. Several large series of percutaneous PVL closure have been recently published, with encouraging results with respect to both procedural success and clinical outcomes. Here, we give a comprehensive review of imaging and procedural techniques for percutaneous PVL closure and present the data supporting this novel treatment strategy. (Circ J 2013; 77: 19–27)

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Paravalvular leak (PVL) complicating mechanical or bioprosthesis valve replacement may be seen in 2–12% of patients after mitral valve replacement (MVR) and in 1–5% after aortic valve replacement (AVR).1–3 In the current era of transcatheter AVR (TAVR) moderate/severe aortic regurgitation (AR) is seen in up to 17% of patients, the majority of whom have paravalvular AR.4 Risk factors for PVL in the surgical population include mechanical valve implantation, annular calcification, infectious endocarditis, and previous valve surgery, all of which can result in inadequate suturing of the valve to the native cardiac tissue. In patients undergoing TAVR, risk factors include annular calcification and incorrect preprocedural valve sizing.5

Most patients with PVL present within the first year after valve replacement with symptoms of congestive heart failure (CHF) (85%), though hemolysis is also common (13–47% of patients).6,7 Some patients fare well with medical therapy of CHF and/or erythropoietic agents and periodic transfusion therapy. However, others remain significantly symptomatic and require definitive correction of the PVL. Re-do surgery carries a high recurrence rate, as well as greater risks of morbidity and mortality than the initial procedure.8

Percutaneous approaches to PVL closure have therefore been developed as a less-invasive strategy, and may be accomplished via transseptal (TS) access, apical left ventricular (LV) access, or retrograde arterial access.9 Since the first reports of the procedure in 1992, a number of series have been published, with encouraging rates of procedural success and good clinical outcomes.10–13 In this review, we will summarize the various techniques of percutaneous closure, and provide an overview of the data supporting its use in the treatment of patients with PVL.

Advanced Imaging

Multimodality imaging using transthoracic (TTE) and transesophageal echocardiography (TEE) usually provides the initial diagnosis of PVL, and procedural guidance often requires the aide of 2D and 3D TEE, intracardiac echocardiography (ICE), fluoroscopy angiography, and more recently the combination of computed tomography (CT) and fluoroscopy. We will focus here on preprocedural localization of the PVL and imaging modalities for intraprocedural guidance.

Identifying Mitral PVL

For the sake of consistency in nomenclature, the MV is viewed as a clock-face and leak origin defined by the position on the clock. Figure 1A from the left atrial (LA), or “surgeon’s”, view14. In a large surgical series, the most common location for mitral PVL was anteromedial (between 10 and 11 o’clock) and posterolateral (between 5 and 6 o’clock).7 Similar analysis of a percutaneous series revealed the most common mitral PVLs to be between 10 and 2 (45%) and between 6 and 10 o’clock (37%).12

When using TEE, localizing the PVL requires reconstruction of the clock-face in the mind of the operator. Figure 1B demonstrates the clock-face orientation of the MV as viewed from the left ventricle, which is also the position of the MV in the typical left anterior oblique C-arm angulation. TEE angles are shown in the Figure to demonstrate which portion of the MV is interrogated at each representative angle. Movement of the TEE probe cranial or caudal, and anteflexion or retroflexion of the imaging crystal, cuts the valve at planes parallel to those listed.

Figure 2 shows an example of mitral PVL localization. The
90° TEE view demonstrates the leak origin (Figure 2A), which is confirmed by the 134° view (Figure 2B), both views showing the PVL origin at approximately 11 o’clock. Figure 2C shows the MV with ultrasound beams at each of the angles in panels A and B intersecting at the PVL origin. In this particular patient, the leak was not seen in the 60° TEE view encompassing the medial border of the LA appendage (LAA); if the leak had been seen on that view, it would have implied a wider origin.

TTE can sometimes be used to define the origin of a PVL, but because of shadowing from the MV prosthesis this imaging modality is often inadequate. The mitral clock-face represented on the TTE short-axis image is shown in Figure 3.

**Identifying Aortic PVL**

Position along the perimeter of the aortic valve can also be referenced to a clock-face, as shown in Figure 1A. Aortic PVLs are most commonly encountered at the 7–11 o’clock position (46%), followed by the 11–3 o’clock position (36%). An alternative designation is to identify the origin of the PVL with respect to the native cusp location (ie, right, left, and noncoronary cusps). This can also be helpful in assessing the risk of coronary impingement with percutaneous device placement. The short-axis view of the aortic valve, either by TTE or TEE, is usually the most helpful in defining the leak with respect to the cusps (Figure 4).

**Echocardiography in the Catheterization Laboratory**

As with PVL diagnosis and localization, echocardiography is also instrumental to the closure procedure. We routinely use ICE for puncture of the interatrial septum (IAS), as well as initial wire/catheter guidance if the PVL is well seen (Figure 5). Generally, we place the TEE probe after crossing the leak with a wire (if possible) to minimize the duration of TEE intubation.
Integrating CT and Fluoroscopy

In order to bring intracardiac imaging data to the catheterization laboratory, our group has been involved in the overlay of 3D CT data on to that from real-time procedural fluoroscopy. After identifying the location of the PVL on TEE, markings are made on a preprocedural noncontrast CT (Figure 7A). We then acquire a CT-like image using the catheterization laboratory’s C-arm (syngo DynaCT Cardiac, Siemens Healthcare, Forcheim, Germany) to establish the position of the patient on the table. This allows us to register the preprocedural CT to the DynaCT, and then overlay the markings made on the preprocedural CT on to the real-time fluoroscopic image (Figure 7B). Provision of these stenciled “targets” allows optimal guidance for wires and interventional devices, and in our experience results in reduced procedural time and TEE duration (Figure 7C).

in patients who are usually under conscious-sedation alone (without endotracheal intubation or general anesthesia). In some situations, especially with lateral PVL, the ICE catheter situated in the right atrium is inadequate to provide appropriate procedural guidance, and we use TEE for directing wires and equipment to the PVL origin.

TEE is integral to the PVL procedure for wire/catheter guidance, evaluation of procedural success and the need for additional device(s), and assessment of complications (such as valve impingement by the device). In many situations, we find that the use of real-time 3D TEE imaging allows better visualization of the PVL and the catheters and devices in the LA (Figure 6), overcoming some of the spatial limitations of the 2D imagery provided by ICE and routine TEE.
Techniques for PVL Closure

As previously mentioned, there are a number of possible approaches to both mitral and aortic percutaneous PVL closure. Catheters and devices may be delivered via TS puncture, direct access to the LV apex, or retrogradely via the femoral artery. The choice of access site should be decided on the basis of PVL location, support required for delivery of the bulky closure devices, and presence of other mechanical prostheses that may interfere with wire-snaring/externalization.

TS Approach

In selecting the location for the TS puncture for mitral PVL closure, consideration must first be given to the location of the PVL. Leaks that are lateral are amenable to the routine high stick on the IAS. However, the stick should be lower and more posterior in patients with medial PVL to allow more direct access to the leak origin.

Once the IAS is punctured and dilated, we typically advance an Agilis NxT steerable guide catheter (St Jude Medical) to the LA. This catheter is an 8.5-Fr system, and is available in 3 different distal curves (small, medium, large) based on PVL location and LA size. Some interventionalists prefer to use a curved guide catheter (eg, JR4, Hockey Stick, etc) in lieu of the Agilis. Telescoping a 120-cm 4-Fr angled Glide catheter (Terumo Medical) into the LA via the Agilis provides an even wider range of directions to direct a wire across the PVL.

We typically wire the PVL using an a 0.035-inch stiff-angled Glide wire (SAG; Terumo Medical), but at times we will change to using a hydrophilic 0.014-inch coronary wire if necessary.

Once across the leak, the wire is advanced to the descending aorta. The decision can then be made whether further support is needed, and if so the wire can be snared and externalized via a femoral artery sheath. If the patient has a mechanical AVR, the initial wire can be exchanged in the LV for a stiffer one, such as an Amplatz Super-Stiff or Lunderquist (Cook Medical) via an 0.035-inch compatible microcatheter. The Agilis is then removed and the IAS is dilated. We then
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*Figure 7.* Integration of computed tomography (CT) and real-time fluoroscopy. (A) Areas of interest are marked on the preprocedural CT (LAO projection). (B) CT markings are overlaid onto the real-time fluoroscopic image in the catheter laboratory (LAO). (C) Markings facilitate crossing of the leak (RAO projection). RA, right atrium; IVC, inferior vena cava; Ao, aorta; LAO, left anterior oblique; LPA, left pulmonary artery; PVL, paravalvular leak; MVA, mitral valve annulus; RAO, right anterior oblique; SAG, stiff-angled Glide wire. (Reproduced from Krishnaswamy A et al with permission.)

*Figure 8.* Transseptal approach to medial mitral PVL closure. (A) Agilis steerable catheter in the LA (via right femoral vein), through which an angled Glide catheter and stiff-angled Glidewire (SAG) were used to cross the leak. (B) The wire was advanced to the descending aorta for support. (C) A 9-Fr TorqVue delivery sheath was advanced across the leak to the LV (markings made using DynaCT are also shown). (D) The LV side of the Amplatzer PDA occluder was deployed. Final position of the occluder device in RAO (E) and LAO (F) projections. Asc Ao, ascending aorta; Desc Ao, descending aorta; LA, left atrium; LAO, left anterior oblique; LV, left ventricle; MV, mitral valve; PVL, paravalvular leak; RA, right atrium; RAO, right anterior oblique; TPM, temporary pacemaker. (Reproduced from Krishnaswamy A et al with permission.)

**Figure 9.** Partially advance the Agilis to the LV and pass a second 0.035-inch wire to the ventricle, which allows placement of 2 delivery sheaths and 2 simultaneous devices (but also requires a large, 20-Fr femoral venous sheath) (Figure 9). Alternatively, an 0.014-inch wire may be advanced to the LV via the delivery sheath (once in the LV) alongside the 1st device, thereby keeping access to the leak if necessary after the 1st device is...
PVL wire (crossed via the femoral or TS approach, respectively) via the apex may be the only route that provides better wire support for catheter and/or device delivery. Access is gained at the LV apex under fluoroscopic guidance and using a micropuncture system. Care should be taken to avoid the left anterior descending artery, for which left coronary angiography prior to access may be useful. The approach to PVL crossing and closure is similar to the other approaches. Once the leak is crossed, the wire may be advanced to the descending aorta or snared from the femoral artery (for AV leaks) or advanced to the LA or snared via TS puncture and externalized at the femoral vein (for MV leaks). The degree of support required dictates which of these wire management strategies is the most optimal.

It is best to minimize sheath size at the LV apex in order to perform the procedure percutaneously and without the need for surgical closure of the apex. Therefore, depending on the device required, it may be necessary to externalize the apical wire and deliver the devices via the femoral or TS approach. We have found when using 5- or 6-Fr sheaths at the apex, it is often possible to simply withdraw the sheath; the scarred pericardium usually provides hemostasis. If this approach is chosen, it is of course important to carefully observe, using echocardiography, for apical leak. Alternatively, Jelnin et al have described the successful use of arterial closure systems (Proglide) and PDA occluder devices to seal the apical access point.

Choice of Approach
Access site is decided on the basis of which approach will provide access to the PVL and also allow adequate support for the delivery of bulky catheters and devices. In the case of mitral PVL, the TS approach is most commonly used. Most anterior and lateral leaks can be accessed via the TS approach. Leaks that are posterior and medial may be more difficult to engage, because of the acute angles that are presented after TS puncture; the apical or retrograde aortic approach may be considered either as a default strategy or after failure of the TS approach.

Aortic PVL closure via the TS approach follows the same procedures, though use of a sharply curved catheter (ie, IMA) may be of most use in directing wires from the LV across the aortic PVL. Special considerations include taking care not to traumatize the MV apparatus (delivery of devices retrograde after externalization of the wire is a useful strategy). Patients with a prosthetic MVR are not candidates for this approach.

Femoral Approach
For closing mitral PVL, this approach is not often used, because access to the leak can be difficult, requiring an acutely angled or reverse-curve catheter from the LV after crossing the AV. Additionally, this approach is not feasible in patients with a mechanical AVR. If this approach is used, delivery of devices from the aorta to the MV leak is cumbersome and usually requires the added support of snaring the wire via TS puncture and externalization at the femoral vein.

On the other hand, the femoral approach is the most common for closure of aortic PVL. The step-by-step process is illustrated in Figure 10. The PVL is crossed using a hydrophilic 0.035-inch wire (ie, SAG) via a guide catheter that allows precise control and directability in the aortic root (ie, AL-1 or MP). Once the PVL is crossed, we routinely exchange the SAG for a stiffer wire to provide support (Lunderquist or Amplatz Super-stiff) via an angled Glide catheter. The delivery sheath is then advanced over the stiff wire and the device of choice is deployed in the PVL. If greater support is required for device delivery, consideration can be given to snaring the wire via TS puncture or direct LV apical access. Care must also be taken to avoid impingement of the closure device upon the coronary ostia.

Transapical Approach
Direct LV apical access may be necessary for patients in whom the TS or femoral approach is either inadvisable or has been previously unsuccessful. Additionally, for patients with mechanical AVR or MVR undergoing PVL closure, snaring the PVL wire (crossed via the femoral or TS approach, respectively) via the apex may be the only route that provides better wire support for catheter and/or device delivery.

Figure 9. Simultaneous deployment of 2 closure devices in a mitral paravalvular leak (PVL). (A) After crossing the PVL using a stiff-angled Glidewire (SAG), the Agilis was advanced to the left ventricle and a 2nd SAG advanced to the descending aorta. (B) The Agilis was removed, delivery sheaths were advanced over each wire, and 2 Amplatzer VSD occluder devices were deployed in sequence. VSD, ventricular septal defect. (Reproduced from Krishnaswamy A et al with permission.)
AVP II has discs on either side of the central cylinder, which forms a better seal. The lack of an inner fabric (to promote tissue ingrowth) is a negative point for both the AVP I and II. The Amplatzer ASD occluder has an inner fabric, but is a very large device and may therefore interfere with the valve (especially with a tilting-disc mechanical valve). The Amplatzer VSD occluder also has an inner fabric, but is a very stiff device and is thought to cause more hemolysis than some of the other devices. The PDA occluder is a very easily delivered device that has an inner fabric; its major drawback is the limited number of sizes available.

**Outcomes of Percutaneous PVL Closure**

After the first report of percutaneous PVL closure in 1992, a number of case reports and small series of clinical experience were published. Although the results were variable, overall they lent credence to the idea of percutaneous PVL closure as an alternative to re-do open heart surgery. Recently, 2 groups have provided more comprehensive data on the procedure. Ruiz et al performed 57 PVL procedures (43 patients, majority MV leaks) with a procedural success of 86% and a 30-day all-cause mortality rate of 5.4%; similar surgical series have demonstrated a mortality of 6%. Importantly, 10 patients required a re-do percutaneous procedure, and 2 patients required 3 procedures total. Therefore, it is important to understand that an unsuccessful, or limitedly successful, procedure does not imply complete failure of the percutaneous approach. Furthermore, additional devices may need to be placed after even a successful closure, because of further valve/tissue dehiscence. Another important finding was that although 35% of patients developed worsened hemolysis, the
In the PARTNER IA trial, patients undergoing TAVR with the Edwards SAPIEN (n=348) had a significantly increased rate of PAR than those patients who underwent surgical AVR (n=351) at 2 years (6.9% vs. 0.9%, P<0.001), despite a non-inferior overall clinical outcome.

In a group of 667 patients undergoing TAVR with either the Edwards SAPIEN or CoreValve prosthesis, Tamburino et al reported an incidence of PAR of 21%. Although this variability in PAR reporting underscores the rationale behind the development of the Valve Academic Research Consortium (VARC) outcome classification, it is reasonable to conclude that the incidence of PAR after TAVR is significant.

In the PARTNER I group, the incidence of moderate or severe PAR was an independent predictor of mortality (hazard ratio [HR] 2.11). Even mild PAR was associated with worse mortality at 2-year follow-up. Tamburino et al also identified moderate/severe PAR as a significant independent predictor of mortality (HR 3.8). Substantial attention has therefore turned to minimizing PAR.

Valve undersizing, malpositioning of the aortic prosthesis (too aortic or too ventricular), or bulky calcification of the leaflets are all implicated as causes of PAR. Of these, valve sizing has recently received the most attention. Although surgical sizing of the AV pros thesis allows the luxury of sizing surgical dilators prior to suturing the valve in place, annulus sizing for TAVR must occur noninvasively. Furthermore, accurate sizing is necessary to minimize both undersizing (leading to valve embolization or PAR) and oversizing (annular rupture, heart block, etc). Over time, operators have come to understand that echocardiography is limited by its 2D imaging structure, and quite often underestimates the true annulus size by 1–1.5 mm.

On the other hand, multidetector CT (MDCT) provides a 3D dataset that can be reconstructed in a number of projections and thereby enables more accurate sizing of the annulus. Willson et al recently demonstrated that sizing of the aortic...
annulus by MDCT accurately predicts PAR, and that undersizing by only 0.7 mm could result in moderate/severe PAR. Furthermore, Jilaihawi et al compared a prospective CT- vs. TEE-guided sizing strategy for TAVR and the CT-guided group demonstrated significantly less PAR (7.5% vs. 21.9%, P=0.045). Initial trials of TAVR were conducted using echocardiographic sizing criteria, and operators similarly treated patients using echo-based annulus measurement. With newer data on the methods and benefits of CT-guided annulus sizing and valve selection, as well as improvements in equipment and techniques, we are hopeful of seeing a lower incidence of PAR in the future.

In cases of PAR after TAVR, there are a number of procedural approaches that may be undertaken to reduce the regurgitation. Proper valve positioning is important, especially with the Edwards SAPIEN because it cannot be moved once in place; the CoreValve can be snared and repositioned if it is initially too ventricular. If the valve is well-positioned but PAR exists, consideration may be given to post-dilation of the prosthesis to provide better apposition between the stented valve and the aortic annulus. This is necessary in approximately 10% of patients, and care should be taken to not over-aggressively dilate the valve (thereby risking annular trauma). If PAR is still clinically significant even with post-dilation, or post-dilation is not possible because of concerns about exacerbating central/valvular AR, then a 2nd valve may be positioned within the 1st prosthesis (valve-in-valve). If these methods to seal the PVL are unsuccessful, it is also possible to perform percutaneous PVL closure as described in this review.

Conclusions
PVLs are neither frequent nor uncommon after surgical valve replacement. Although some patients may not suffer clinical consequences of the PVL, others require treatment for CHF or hemolysis. Re-operation in these cases confers substantial risk, and results are not always durable. As such, percutaneous PVL closure has gained greater favor in recent years. Multimodal imaging is the cornerstone of diagnosis and procedural guidance. Currently, operators must use catheters and devices originally constructed for other applications, though equipment specifically designed for PVL closure is under development. TAVR heralds a new era of valve therapy, though even in this arena paravalvular regurgitation is a significant concern and may require percutaneous closure using methods similar to those used for surgical valve PVL closure.

References