# Transcatheter prosthetic paravalvular leak closure

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### Summary

Paravalvular leak affects up to 27% of all prosthetic heart valves implanted by conventional surgery. Patients with paravalvular regurgitation can be asymptomatic or may present with symptoms of congestive heart failure and/or haemolytic anaemia. Assessment and quantification of these paravalvular leaks are difficult since transthoracic colour flow Doppler images may be obscured by annular calcifications and prosthetic material. Surgical re-intervention is the conventional treatment of choice for severe cases but is associated with significant morbidity and mortality, and is not always successful because of underlying tissue fragility. Over the last decade, transcatheter treatment of paravalvular leaks has emerged as an attractive alternative to surgery for high-risk patients and is now favoured as the initial approach in some experienced centres. Transcatheter repair is technically feasible in 60 to 90% of cases according to different published series. Technical success is associated with clinical improvement in 50 to 90% of the cases.

Key words: paravalvular leak; transcatheter closure; valvular heart disease; valvular prosthesis

# Introduction

Advances in cardiac surgery have improved the outcome of patients suffering from valvular heart disease. Valve replacement is often performed at an earlier stage of disease with low operative risk in good surgical candidates without major co-morbidities. Patients with valve replacement nevertheless remain at risk for various early and late complications such as anti-coagulation-related events, thromboembolism, bacterial endocarditis and paravalvular leak (PVL). We review herein the literature on PVL and its treatment including recently developed transcatheter approaches, which are now considered an attractive alternative to surgical re-intervention.

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## Incidence and symptoms

PVL represents a regurgitant jet located between the outer margin of the prosthetic ring and the tissue in the periphery of the native valve.

#### Table 1 Risk factors for PVL

Extensive annular calcification					
Active endocarditis					
Previous valvular surgery (i.e., multiple valvular surgical redo)					
Elderly patients					
Low Body Mass Index					
Large atria					
Surgical technique (i.e., reconstruction of the mitral annulus or the aorto-ventricular junction)					
Surgical experience with heart valve replacement					

PVL is the most common cause of non-structural prosthetic heart valve dysfunction [1]. PVL is found during immediate post-operative assessment in 6 to 17.6% of patients with aortic valve replacement [2, 3] and in 22.6 to 32% with mitral valve replacement [2, 3]. Fortunately, approximately 90% are mild and clinically insignificant [4, 5]. The wide ranges in reported PVL incidence appear to be related to several factors, including inclusion criteria, location of implanted valves and duration of follow-up. PVL are commonly more frequent in the mitral than the aortic position. Risk factors for PVL are summarised in table 1. PVL developing during follow-up may be secondary to suture dehiscence (rupture  $\geq$ 1 suture) or as a consequence of valvular endocarditis [5].

Clinically, PVL are often asymptomatic but may lead to congestive heart failure and/or haemolytic anaemia. Larger leaks usually result in volume overload with congestive heart failure, and multiple leaks in extended haemolysis [5].

### Diagnosis of paravalvular leak

PVL is often suspected at physical examination in the presence of a new murmur. However, confirmation of the diagnosis using transthoracic echocardiography

Correspondence: Stéphane Noble, MD Interventional Cardiology Unit, Division of Cardiology University Hospital CH-1211 Geneva 14 Switzerland stephane.noble[at]hcuge.ch (TTE) can be difficult since colour flow Doppler may be obscured by annular calcifications and mechanical prosthetic materials. The detection and assessment of PVL has been greatly improved with trans-oesophageal echocardiography (TEE) which is now an essential imaging modality to diagnose PVL, describe their anatomical details (shape, number of leaks, location, extension) and to guide surgical or transcatheter therapy.

### Surgical approach to paravalvular leak

Surgical re-intervention has been considered the treatment of choice for years for symptomatic patients with PVL, but surgery is not always successful because of underlying tissue fragility, inflammation or extensive calcifications. The original prosthesis can either be replaced (50%) or it can be re-sutured (50%) [1, 5]. Valve replacement is generally the preferred approach

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#### Figure 1

Image of five different Amplatzer occluder devices. Muscular VSD occluder (A); ASD occluder (B); PDA occluder (C); AVP II occluder (D); AVP III occluder (E). (© St. Jude Medical, Zurich, Switzerland, with kind permission.) ASD = atrial septal defect; AVP = Amplatzer vascular plug; PDA = patent ductus arteriosus;



in cases of intermediate and large PVL. Residual or recurrent PVL are seen in approximately 20% of patients who survive surgical re-intervention [5].

Surgical re-intervention is also associated with an increased risk of morbidity and mortality. As reported by Akins [1], only 46% of patients were free of perioperative complications such as prolonged intubation (>48 h), renal failure, arrhythmia, pneumonia, re-exploration, neurologic or gastro-intestinal events. Redo operative mortality was 6.6% [1].

Over the last decade, transcatheter treatment of PVL has emerged as an attractive alternative to surgery for high-risk patients. Some experienced centres now favour transcatheter closure as the initial approach to PVL [6] with surgical re-intervention reserved for patients in whom percutaneous repair fails or cannot be performed.

#### Transcatheter approach to PVL

PVL transcatheter closure was first reported in 1992 with successful aortic PVL closure in 3 out of 4 patients using the double umbrella Rashkind device [7]. Subsequently, coil embolisation was also used to successfully close PVL [8, 9]. More recently, the technique has been described with the off-label use of various existing Amplatzer devices (fig. 1) for septal occlusion (ASD or muscular VSD) or patent ductus arteriosus closure [10-17]. The oval rather than circular shaped AVP (Amplatzer Vascular Plug) III device (approved in Europe and Canada but not yet in United States for vascular occlusion) has been available since 2008 and has the advantage of being better adapted to close oval or crescent-shaped leaks (the most commonly found shape of PVL).

Precise knowledge of the different Amplatzer device characteristics is crucial in order to select the most appropriate occluder to close a specific PVL. In our experience, the ASD occluder device does not represent a good option since it has the greatest difference between waist and disk diameter (12 to 14 mm more for the disks) which carries a high risk of interference with the prosthetic disk motion. The PDA occluder has a lower diameter difference between disk and waist (5 to 8 mm more for the disks), but the first generation with a single retention disk is at higher risk for device embolisation. The muscular VSD occluder has a similar diameter difference between disk and waist as the PDA occluder (5 to 8 mm more for the disks) and has two retention disks, which makes it our first choice when the AVP III does not provide a satisfactory result or is expected to be sub-optimal (e.g., for large circular rather than ovale defects). The AVP II device (St. Jude Medical, MN, USA) is sometimes used in centres where the AVP III is not available [14, 15].

Transcatheter PVL closure has evolved thanks to advances in imaging techniques such as real-time 3D TEE guidance [18] and material improvements such as steerable trans-septal sheaths (i.e., Agilis catheter, St. Jude Medical) for mitral PVL or new occlusion devices (i.e., Amplatzer AVP III device).

It is important to note that an unstable rocking valve, active endocarditis, bacterial vegetations and thrombus are contraindications for transcatheter interventions. Antibiotic prophylaxis is routinely administered before a PVL transcatheter procedure and activated clotting time should be maintained at least above 250 seconds during the procedure.

## TEE guidance for transcatheter PVL procedures

PVL may be isolated or multiple in numbers. With respect to their shapes, PVL defects are uncommonly cylindric, they are rather crescent or oblong in shape and may be serpiginous. Leak morphology description and sizing by TEE are essential in order to choose the proper type and number of occluder devices to implant (i.e., large defects may require more than one device).

TEE and real-time 3D images not only allow precise assessment of the defect causing PVL but also contribute to procedural success by confirming adequate positioning of the device, assessing and quantifying residual leak and ruling out procedural complications (i.e., interference with valve leaflet/disk motion, device instability or embolisation and pericardial effusion). Of note, the hydrophilic coated Terumo Glidewire<sup>®</sup> (Terumo, Somerset, NJ, USA) used for defect wiring is often difficult to view with ultrasound, nevertheless the echocardiographer is of great help by providing the accurate localisation of PVL [18]. The use of standardised nomenclature between the echocardiographer and the interventional cardiologist is essential, particularly for mitral PVL. We use the "surgeon's view" timeclock method [16] which we adapted to the left anterior oblique-caudal fluoroscopy projection. Indeed, the standard clock-face view provided by TEE and used in the operating room does not correspond to the mitral valve image seen in fluoroscopy. On the "en face" view of the mitral valve in fluoroscopy (left anterior obliquecaudal projection), left and right are reversed compared with the traditional anatomical surgical view (fig. 2). Some centres such as the Mayo Clinic prefer to use a simple triangulation method based on the anatomic relationships of the atrial septum, left atrial appendage, and aortic valve with anatomical terminology (anterior versus posterior, lateral versus medial) [6]. As TEE is used for image guidance, general anaesthesia is recommended for both patient comfort and airway protection. Real-time CT is an emerging technique to guide PVL repair [17].

#### Technical aspect

After wiring the defect, the operator should decide whether to use single or multiple device occluders. A single device is typically used for small and round defects causing haemolysis. Conversely, a crescentshaped defect extending over 25% of the prosthesis circumference is unlikely to be successfully closed with a single device. The use of two devices may be required for complete closure using either a sequential or simultaneous deployment technique. The use of two devices may be preferred when the defect is very close to the prosthetic leaflet/disk. In this setting, using two devices can allow deploying smaller plugs with smaller disk diameters, thus reducing the risk of valve obstruction.

#### Figure 2

- A Surgical view of the heart valves from above, the atria removed and with the surgical time clock drawn around the mechanical mitral valve.
- **B** Trans-oesophageal echocardiography degrees with the corresponding surgical time clock drawn around the mechanical mitral valve.
- C Fluoroscopic left anterior oblique-caudal projection showing mechanical mitral and aortic prostheses and a tricuspid ring. The right coronary artery is filled with contrast and there is a permanent pacemaker lead positioned in the right ventricle apex. The area between 1:00 and 3:00 corresponds to the septal side. 7:00 and 9:00 to the lateral side.

LAA = left atrial appendage; Ao = aortic; TR = tricuspid.

(Modified from: Mahjoub H, Noble S, Ibrahim R, Potvin J, OMeara E, Dore A. JACC Cardiovasc Interv. 2011;4(1):107–14 [16].)





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#### Figure 3

Projections commonly used during mitral PVL closure procedure. In this example, at around 11:00 on the surgical time clock, there is a mVSD occlude device deployed but not yet released.

- A Left anterior-oblique caudal projection (spider view).
- **B** RAO projection.



An important consideration in order to avoid the need to re-cannulate the leak after a first potential failed delivery attempt is to leave a soft hydrophilic safety guidewire (or a 0.014 inch wire) through the PVL alongside the device being delivered.

## Considerations for mitral paravalvular leak

For transcatheter closure of mitral PVL, bi-plane fluoroscopy is extremely helpful to reduce procedural time and limit the movements of the C-arm since the operator must often alternate between two orthogonal views (LAO-caudal and RAO, fig. 3) when probing the leak. Multiple approaches for mitral PVL are possible such as antegrade cannulation of the defect through a transseptal puncture, retrograde cannulation from the left ventricle through the aortic valve, and retrograde cannulation from a trans-apical access (fig. 4). In order to increase wire support, an arterio-venous guidewire loop is often created by snaring the free end of the guidewire that has passed through the leak, the aortic valve up to the ascending and descending aorta in order to exteriorise it from the femoral artery. Subsequently the delivery sheath can be advanced over the rail (fig. 5). Conversely, when retrograde crossing of the mitral PVL is used, the wire found in the left atrium (LA) is snared after trans-septal puncture in order to be pulled out from the femoral vein. The delivery sheath and the device will subsequently be deployed from the LA.

For medial defects, since they are located immediately adjacent to the inter-atrial septum, trans-septal puncture should be posterior, 4 to 6 cm from the medial paravalvular defect in order to be able to manipulate the catheters. The use of a deflectable left atrial sheath

#### Figure 4

Different approaches for mitral PVL closure.

- A Anterograde approach using a trans-septal access.
- **B** Retrograde approach from the femoral artery and through the aortic valve.
- C Trans-apical approach using either a surgical incision or percutaneous approach through the apex.



#### Figure 5

Example of mitral PVL closure through an anterograde approach using a trans-septal access.

- A Wire coming from the femoral vein, through the atrial septum, subsequently crossing the mitral PVL and finally exteriorised through
- the femoral artery.
- **B** Delivery sheath with dilator through the mitral PVL.
- **c** mVSD occluder device with one retention disk deployed.
- **D** Occluder device fully deployed but not yet released.
- E, F Final images once the device released with no interference between the device and the mechanical prosthesis.
- LV = left ventricle; A-V loop = arterio-venous loop.



(e.g., Agilis NxT Steerable Introducer, St. Jude Medical, Maple Grove, Minnesota) has facilitated the success rate of septal leak reduction.

#### Considerations for aortic paravalvular leak

Transthoracic echocardiography has good sensitivity for detecting prosthetic aortic regurgitation but TEE is superior in locating the site of leakage with greater precision (i.e., central vs paravalvular) and assessing extension. The severity of aortic PVL is more difficult to assess and often requires a comprehensive TTE combined with TEE. Aortography or MRI may also help to assess regurgitation severity.

The retrograde approach can be used for transcatheter repair of most aortic PVL. The antegrade approach using trans-apical access might be used as a rare backup option in patients with a failed retrograde approach. In the past, the standard TorqVue<sup>®</sup> sheath (St. Jude Medical, MN, USA) at 80-cm length was sometimes too short to reach the aortic valve using the trans-femoral approach. Therefore, one option was to use longer sheaths available in 6 or 7 French size from different companies such as the 90- to 110-cm Flexor<sup>®</sup> sheath (Cook Medical, Bloomington, IN, USA) or the 90-cm Destination sheath (Terumo, Somerset, NJ, USA). There is now a 120-cm TorqVue<sup>®</sup> sheath (5–7 French). Another interesting option is to use a telescoping co-axial technique, with a 5-F 125-cm multipurpose diagnostic catheter loaded in a 6- to 8-F guiding catheter.

Aortic PVL are usually smaller than mitral PVL, often permitting the use of only one device. There is a potential risk of coronary artery obstruction with aortic PVL closure, since the device may protrude up to the coronary artery ostia. Therefore, post device deployment aortography should be performed before final release of the device to visualise the relationship between coronary ostia and the device. Assessment of the ECG and of the coronary artery flow at TEE may also contribute to exclude coronary flow interference.

#### Alternative approach

With increasing experience with trans-apical transcatheter aortic valve replacement (TAVI), many centres have started to perform hybrid procedures typically with surgical exposure of the apex and trans-catheter techniques to address PVL [15, 17, 19-21]. PVL closure has also been performed using percutaneous puncture of the apex without surgical incision [15, 17, 21]. When a small-caliber catheter or sheath (i.e., 4- or 5-F) is introduced through the apex, no specific apical closure is required. Conversely, for larger sheaths (i.e., 6- or 7-F), in order to minimise the risk of bleeding and haemothorax from the apical puncture site, Ruiz et al. [17] showed the feasibility to use Amplatzer PDA devices to close the trans-apical access. The trans-apical approach might be useful for mitral medially located PVL which are more challenging by retrograde and anterograde approaches, or for wire exteriorisation in the presence of 2 mechanical valves in order to provide more support when necessary.

## Literature review

Until very recently, published clinical experience was limited to case reports and small series without longterm follow-up. The largest series reported in 2009 was from Spain by Garcia [13, 18]. This series showed that the device implantation rate was 63.5% in 52 cases of mitral PVL closure, and a successful device implantation was associated with a significant leak reduction in about half of the cases. In 2011, Ruiz in New York reported his retrospective series using a trans-apical approach (57 patients) [17] and the Mayo Clinic group described their short and long-term experience of the largest series worldwide involving 126 patients (no use of AVP III) [14, 15]. Table 2 summarises the major series published. The Montreal Heart Institute experience of 56 patients, recently presented at EuroPCR [22], is included in table 2.

Transcatheter repair is technically feasible in 60 to 90% of cases with highest success rates in more recent large series. Technical success is associated with clinical improvement in 50 to 90% of the cases. Therefore, successful closure unfortunately does not always result in clinically meaningful symptom improvement and sometimes clinical deterioration may even be possible, typically in relation with new or worsing haemolysis.

#### Table 2

Studies summary.

Studies	Years	Number	Mitral	Aortic	Implantation	Procedural	30-day
		of patients	leak	leak	success	success	mortality
Hourihan	1992	4	0	4	3/4 (75%)	2/3 (66.7%)	NA
Pate	2001-2004	10	9	1	4/10 (40%)	7/10 (70%)	0
					7/10 (70%)		
Cortés	2003–2006	27	27	0	17/27 (62%)	8/17 (47%)	0
Shapira	2003–2006	11	10	3	10/11 (91%)	6/10 (60%)	0
Hein	2002–2006	21	13	8	20/21 (95%)	14/20 (70%)	2/21 (9.5%)
Sorajja	2004–2007	16 (19 P)	14	2	NA	17/19 (81%)	1/16 (6.2%)
Garcia	2003–2009	52	52	0	33/52 (63.5%)	17/33 (51.5%)	NA
Nietlispach	2009	5	4	1	5/5 (100%)	5/5 (100%)	0
Sorajja	2004–2010	115 (141 P)	78%	22%	125/141 (88.6%)	77%	2/115 (1.7%)
			90 pts	25 pts		M 75%	
						A 80%	
						Mec 71%	
						Bio 84%	
Sorajja**	2004–2011	126 (154 P)	78.6%	21.4%	91.3%	76%	3/126 (2.4%)
			99 pts	27 pts			64.3%*
Ruiz	2006–2010	43 (57 P)	76.8%	23.2%	86%	89%	2/43 (4.6%)
			33 pts	10 pts			
Montreal	2001-2010	56 (61 P)	79%	21%	75.4%	70.5%	2/56 (3.6%)
			44 pts	12 pts		(43/61)	

A = aortic; Bio = bioprosthetic valve; M = mitral; Mec = mechanical valve; NA = not available; P = procedures.

\* 3-year survival free from death (all cause).

\*\* Long-term follow-up (115 patients were already included in the study described above).

Regarding long-term clinical efficacy, there is a strong association between 3-year survival and residual regurgitation; and symptoms only improved in patients who had no or mild residual regurgitation [14]. Non-cardiac morbidity was responsible for up to onehalf of deaths at follow-up in the Mayo Clinic experience [14]. In our series, multivariable analysis showed that successful PVL reduction was the only predictor associated with a survival free of death, re-hospitalisation for congestive heart failure or surgical revision (HR 0.34, 95% CI [0.15–0.62]) [22].

## Complications

The main complications following PVL closure are summarised in table 3. Device interference with disk or leaflet movement and device embolisation are the most feared potential complications. In our initial experience, when using a first generation PDA occluder, a major complication was experienced secondary to device migration from the mitral PVL to the patient's aortic mechanical valve causing valve obstruction leading to death. Device embolisation is most commonly described after PDA occluder implantation [6, 14, 23]. In one case the PDA occluder was free in the left atrial cavity and could be taken out by surgery via a right atrium-atrial septum approach [23]. Interestingly, Ussia et al. reported a late Amplatzer 12-mm muscular VSD occluder dislodgment at 2 months associated with sudden recurrent haemolysis and ankle oedema [24]. For mechanical prostheses, TEE and fluoroscopic disk mobility assessment are essential while the closure device is in the defect and still attached to the delivery cable (i.e., before release in order to reposition or retrieve and change device type and avoid prosthetic obstruction). Once released, although infrequent, a device could shift position and subsequently interfere with mechanical disk mobility. In this setting, snaring the device in order to retrieve it might be an alternative to open surgery.

Roger et al. [25] reported a case of bio-prosthetic leaflet erosion with perforation due to an oversized 8-mm ASD Amplatzer device which was interfering with the valve leaflet during each cardiac cycle and presented significant fractures on one of the device's retention disks. Oversized devices might also have an opposite effect and increase the regurgitant defect [26] especially in patients with friable tissue. It is reasonable and probably safer to wait at least 3 to 6 months before attempting transcatheter PVL closure in cases where there is an early leak post-surgery in order to permit better tissue healing around the prosthetic ring and sealing of the prosthesis adjacent to the defect.

Transient haemolysis, although rarely clinically significant, can occur in the early phase following transcatheter PVL closure. A case of early defect progression leading to heart failure and haemolytic anaemia that required surgical reparation before discharge [26] has been reported. In our experience, one patient had to be operated at day five postprocedure because of massive haemolysis. Haemolysis can also occur when there is a significant residual shunt. To avoid unnecessary surgery, temporary erythropoietin administration can be considered.

Stroke or transient ischaemic events represent other uncommon but serious potential peri-procedural complications.

Although transcatheter PVL closure is associated with certain risks, these must be balanced against those of repeat surgery and the symptoms caused by significant PVL. Failure of a transcatheter attempt does not preclude subsequent surgery as an alternative treatment, therefore permitting a stepwise approach to a difficult clinical situation.

#### **PVL post-TAVI**

Aortic PVL represents the Achilles tendon of TAVI with either the Medtronic CoreValve or Edwards SA-PIEN valves, and seems to be associated with increased morbidity and mortality [27, 28]. Transcatheter closure of PVL has recently been successfully performed live at the 2011 CSI meeting by Sievert in Frankfurt, 6 months following an Edwards SAPIEN valve implantation.

#### Table 3

Complications associated with PVL closure.					
Trans-septal puncture-related complication (for mitral PVL)					
Trans-apical approach-related complication (pericardial bleeding, false-aneurysm)					
Complications related to any interventional procedural					
Complications specifically related to transcatheter PVL	Device embolisation				
closure procedures	Device/prosthetic valve interference (mechanical valve)				
	Haemolysis (new or transient worsening)				
	Atrio-ventricular block (new or worsening degree)				

## Conclusions

Since early experience in 1992, transcatheter PVL closure has evolved thanks to advances in imaging techniques, in catheterisation techniques and material, and devices. These improvements have increased procedural success rates and decreased procedural time. PVL device closure remains technically demanding but allows many patients with a high anticipated surgical risk to avoid revision cardiac surgery. Long-term clinical efficacy is strongly related to residual regurgitation. Interventional cardiologists should therefore aim at achieving the best possible result rather than just reducing the leak by using multiple devices when required. Procedural improvements may one day permit the transcatheter technique to become the treatment of choice for PVL closure, even in relatively low-risk surgical patients. However, further refinement of the technique and proper patient selection criteria are still required keeping this field quite exciting for the future.

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