# Pre- and Intraprocedural Imaging Considerations in Paravalvular Leak Closure

Adriana Postolache, Simona Sperlongano, Mathieu Lempereur, Raluca Dulgheru, François Damas, Nils Demarneffe, and Patrizio Lancellotti

**Abstract**

Paravalvular regurgitation or leak (PVL) is not an uncommon complication of prosthetic valve disease and can be associated with severe heart failure, hemolytic anemia, or both. The management of these patients often having multiple comorbidities is challenging and the choice between surgical intervention, transcatheter closure and medical treatment should be decided by the Heart Team on a case-by-case basis. Transcatheter PVL closure has emerged as an attractive and efficient treatment option for these patients and the success of the procedure relies on a careful pre-procedural evaluation, for selecting the patients suitable for a transcatheter intervention, and expert imaging guidance during the procedure. Pre-procedural evaluation should determine the location and the number of the jets and the severity of the PVL. Echocardiography holds a central role in the pre-procedural evaluation of patients with PVLs, but other imaging modalities, such as cardiac magnetic resonance imaging (CMR) and cardiac computed tomography (CT) can offer useful adjunctive information for grading the severity of the regurgitation and for selecting the type and the size of the prosthesis. The intervention is performed under fluoroscopic and transesophageal/intra-cardiac echocardiographic guidance. The use of fusion imaging can facilitate the delivery of the device. Echocardiography has an important role on the procedural guidance, being especially useful for selecting the size of the device(s), confirming the correct location of the device(s) and its lack of interference with the prosthetic valve function or adjacent structures (such as the coronary arteries for aortic PVLs) and for evaluating the presence of complications. A good communication between the echocardiographer and the interventional cardiologist, at every step of the procedure, is essential for the success of the intervention.

**Keywords**

Paravalvular leak · Pre-procedural planning · Intra-procedural guidance · Transcatheter mitral paravalvular leak closure · Transcatheter aortic paravalvular leak closure · Transcatheter tricuspid paravalvular leak closure

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**Learning Objectives**

1. Describe the indications and the contraindications for transcatheter paravalvular leak closure;
2. Describe how to evaluate the severity of PVLs by using an integrative multiparametric and multimodality approach;
3. Describe the principles of the procedural guidance during percutaneous paravalvular leak closure;
4. Describe the key points of pre- and intra-procedural evaluation for mitral, aortic and tricuspid PVL closure.

**Case Study on Transcatheter Mitral PVL Closure**

A 67-year-old female comes to our attention during a follow-up outpatient visit reporting worsening of dyspnea over the last few months. She is affected by type 2 diabetes mellitus on insulin therapy, permanent atrial fibrillation, and stage IIIA chronic kidney disease. Her mobility is poor due to a recent femur fracture with endoprosthesis implantation. She had a previous mitral valve surgical replacement (1991) with a Carbomedics 25 mm bileaflet mechanical prosthetic valve. Blood tests show chronic severe hemolytic anaemia (which is partially responsible for the symptoms) and no evidence of infection. Transthoracic echocardiography (TTE) is performed as the initial imaging test. On TTE, left ventricle is not enlarged and its systolic contractility is preserved, left atrium is severely dilated, and moderate aortic regurgitation and severe tricuspid regurgitation are found. TTE also reveals the presence of a mitral prosthesis paravalvular leak (PVL), which appears significant on color Doppler analysis.

The TTE evaluation of our patient suggested the presence of mitral prosthesis regurgitation, limited by acoustic artifacts of the mechanical valve, so a transesophageal echocardiography (TEE) was performed to confirm the diagnosis. A TEE showed normal functioning of the 2 mitral leaflets, with a mild (non-significant) intraprosthetic washout. Multiple PVLs were detected, the larger located anterior-medially. The "en face" view (surgical view) of the mitral prosthesis on 3-dimensional (3D) TEE displays a large antero-medial echo dropout area outside the sewing ring, confirmed by color Doppler, due to a calcified and fibrotic annulus, resulting in disruption of the sutures. The jet density and turbulence, the wide vena contracta, the large proximal isovelocity surface area (PISA) shell, and the systolic retrograde flow into the pulmonary veins support the severity of the mitral paravalvular regurgitation.

## Background and Definitions

Prosthetic paravalvular regurgitation or paravalvular leak (PVL) is an abnormal communication between the ring of a surgical or transcatheter prosthesis, and the native valve annulus. A few cases of PVL have also been described in patients with mitral valve repair.

It is not an uncommon complication of prosthetic valve disease, occurring in 7–17% of patients with mitral and 2–10% of patients with surgical aortic prostheses [1, 2]. The incidence of PVL is higher in transcatheter prosthetic valves, even though the incidence of significant aortic regurgitation in patients undergoing transcatheter aortic valve implantation (TAVI) has significantly decreased in the last 20 years, with 0.6–5.3% of patients undergoing TAVI having at least moderate PVL, in more recent trials [3–6]. Taking into consideration the increase in transcatheter valvular replacements, the incidence of PVL is likely to increase in coming years.

Paravalvular regurgitation may result from an interaction of factors related to the intervention (poor technique, use of sutures without pledgets, use of continuous sutures for the mitral prostheses, supra-annular prostheses, inappropriate size of a transcatheter valve) and factors related to the local tissue (important annular calcifications, tissue friability, the presence of infection).

The clinical presentation is highly variable, ranging from an incidental finding on the follow-up echocardiographic study to severe heart failure, hemolytic anemia, or infective endocarditis. The vast majority of PVLs are mild and are considered benign, in the absence of infective endocarditis, with only a few cases being associated with hemolysis. Approximately 2–5% of PVLs on surgical valves are clinically relevant, being associated with heart failure, hemolytic anemia, or both [7].

The diagnosis, in particular, estimating the severity of PVL, and the management of these patients are challenging. Figure 1 presents a proposed management plan for patients with PVL. The choice between redo-surgery, transcatheter closure and medical palliative treatment should be made by the Heart Team, on a case-by-case basis. According to the latest ESC and ACC/AHA guidelines on valvular heart disease, surgical reintervention remains the first treatment option for patients with PVL associated with heart failure or severe hemolytic anemia needing repeated blood transfusions, whereas transcatheter intervention can be considered in patients at high or prohibitive cardiac risk, with anatomically suitable PVLs for a percutaneous closure [8, 9].

Transcatheter PVL closure has emerged as an attractive treatment option in these patients who often have many comorbidities and are at high

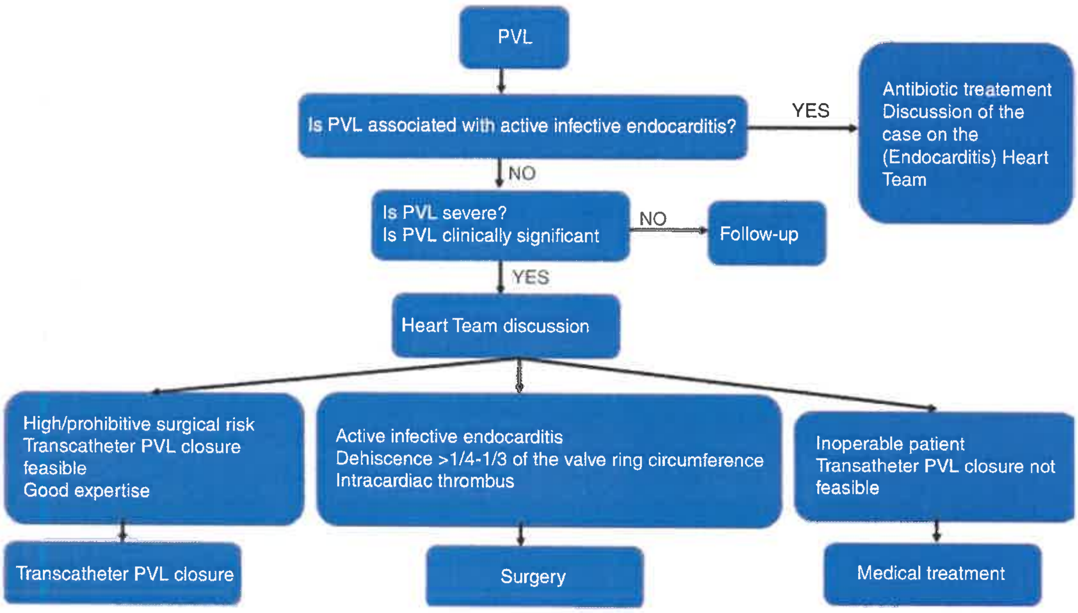



**Fig. 1** Proposed management plan for patients with paravalvular regurgitation. The detection of paravalvular leak (PVL) on an echocardiogram should prompt for the search of infective endocarditis. In the absence of infective endocarditis, non-severe PVLs usually do not need and intervention as only few cases can be associated with severe hemolytic anemia. Patients with severe, clinically significant PVLs should be discussed in the Heart Team meeting, and the choice between surgical (re)intervention, transcatheter closure and medical treatment should be made on a case-by-case basis

surgical risk. In centers with good expertise, transcatheter PVL closure has a high feasibility rate (>90%), a good success rate (reduction in PVL to <mild in >70% of cases), which is associated with an improvement in heart failure symptoms, mid- and long-term survival and, in most cases, a decrease in hemolytic anemia severity [10, 11]. Although the success rate for the surgical reintervention is higher than for transcatheter closure (<mild residual regurgitation in >90% of cases), this comes with the price of a higher peri-procedural mortality and complications risk, and a risk of PVL recurrence, without an advantage on long-term survival [10]. Nowadays, many high-volume centers consider the transcatheter intervention as the first treatment option in feasible patients, with surgical reintervention being reconsidered afterwards in case of failure of the transcatheter procedure [10].

Based on current knowledge, transcatheter closure is contraindicated in patients with active infective endocarditis, in patients with a significant dehiscence of the prosthetic valve ring, involving >1/4–1/3 of the circumference, and in patients with intracardiac thrombus [7]. It can however be considered, after the resolution of the infectious process and the disappearance of the thrombus, in patients that are judged to be inoperable by the Heart Team.

The key steps for having a successful transcatheter PVL closure are:

- Careful pre-procedural evaluation for selecting the patients suitable for transcatheter intervention and for planning the intervention;
- Expert imaging guidance during the procedure, with constant communication between the operator(s) and the imager.

## Principles of Pre-procedural Assessment Before Transcatheter PVL Intervention

The evaluation of para-valvular regurgitation is difficult and should try to determine the following points:

- The location and the number of the jet(s);
- Estimate the severity of PVL.

Pre-procedural evaluation is helpful for planning the procedure, by selecting the best approach for delivering the device(s) in the individual patient, and it offers an estimation of the type and size of the device(s) that would best close the defect.

### Location and Number of the Jet(s)

Echocardiography is the first and main imaging modality for the diagnosis of prosthetic valve dysfunction, and transthoracic (TTE) and transesophageal echocardiography (TEE) are usually used together, as complementary exams. With regards to the location of the regurgitant jets, TTE is limited for the evaluation of mechanical mitral PVLs, when often, the jet can only be visualized in an off-axis view (such as the sub-costal view), and TEE is key for diagnosis. On the other hand, for aortic PVLs, TTE and TEE are more complementary, with TTE being useful for the visualization of anteriorly located jets, whereas posterior jets are better visualized by TEE [12]. 3D echocardiography, in particular 3D TEE, facilitates a more precise location of PVLs [12]. To improve the communication between the different actors involved in the patient's management, it is recommended that the location of the regurgitant jet(s) should be described on a clock face or on anatomical criteria, as shown in Fig. 2 [7, 12, 13].

### Grading the Severity of PVL

This is without a doubt the most difficult part of the evaluation of PVLs and an integrative, multiparametric, and, in many cases, a multimodality imaging approach should be used [7, 12, 13].

*Echocardiography* is the main imaging modality used for estimating the severity of PVL and, in a similar way to native valve regurgitation, an integrated approach, which takes into consideration qualitative, semi-quantitative and quantitative parameters, from all echocardiographic methods (2D, color, PW, CW Doppler, 3D echocardiography) is recommended for determining the severity of PVLs [7, 12, 13]. We outline some of the important points in the evaluation of PVLs:

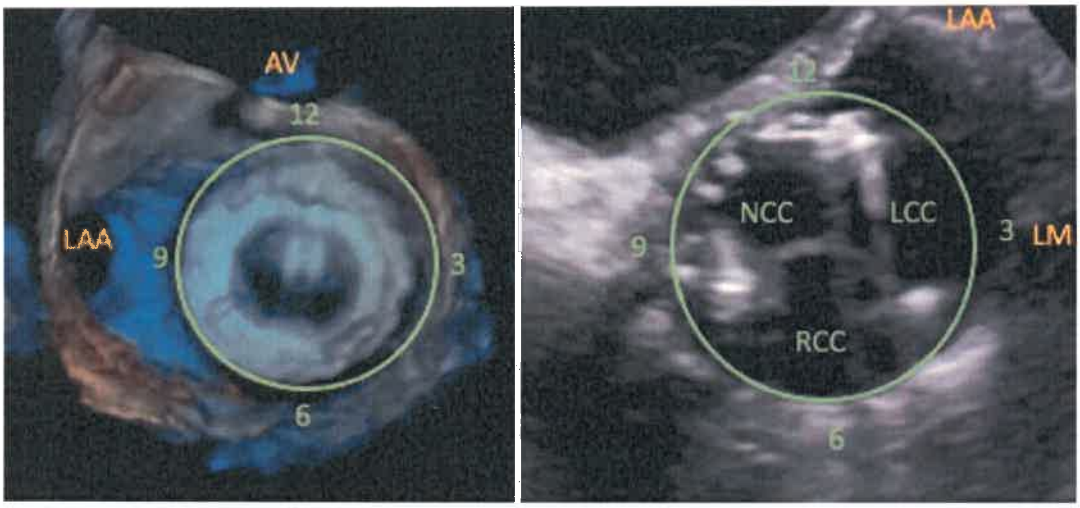



**Fig. 2** Localization of paravalvular regurgitant jets. To improve the communication between the Heart Team members it is recommended that the location of the regurgitant jet(s) should be described on a clock face or on anatomical criteria. For the mitral position, the 3D surgical-en face view of the mitral prosthesis should be viewed as a clock face, with the aortic valve located at 12 o'clock, the interventricular septum at 3 o'clock at the left atrium auriculum at 9 o'clock position. Most mitral PVLs are found between 10 and 2 o'clock and between 6 and 7 o'clock. For the aortic prosthesis, most centers prefer to describe the location of the jets in relation to the corresponding "aortic cusps" or on an "en face" clock way, similar to the mitral location, with the right coronary cusp located at 6 o'clock and the left main origin at 3 o'clock. Most aortic PVLs are located around the non-coronary and the left-coronary cusp. *AV* aortic valve, *LAA* left atrial auriculum, *LM* left main coronary artery

- The presence of excessive rocking motion of a mitral prosthesis (>15° from the annulus), or the presence of discordant motion of an aortic prosthesis in comparison to the aortic annulus, indicate severe mitral and, respectively, aortic PVL [7, 12].
- A semi-quantitative evaluation based on the circumferential extent of the regurgitant jet(s) is useful, in particular in the case of multiple leaks, with a value >30%, being in favor of severe paravalvular regurgitation [7, 12, 13].
- The vena contracta method can be used, in case of a single leak, provided that the proximal area can be visualized.
- As the jets are often multiple and their shape is non-circular, the PISA method is, in most cases, not applicable [7, 12].
- The volumetric method can be performed but is cumbersome and its reproducibility is rather low [7, 12].
- The presence of parameters with a high specificity for severe regurgitation, such as systolic retrograde venous reflow in mitral and tricuspid PVL(s), diastolic flow reversal in the aorta, in aortic PVL, can be very useful for grading the severity of prosthetic regurgitation.
- The development or aggravation of preexistent ventricular dilatation or dysfunction (in the absence of another cause), or an increase in pulmonary artery pressure suggests the presence of a significant regurgitation [7, 12, 13].

The PVL Academic Research Consortium recommends the use of a 5-grade system for defining the severity of PVL: trace, mild, moderate, moderate-to severe and severe [7, 13].

*Cardiac magnetic resonance imaging (CMR)* can measure the regurgitant volume and the regurgitant fraction, even in the case of multiple jets, and should be considered in particular when the echocardiographic grading of PVL severity is discordant to the patient's symptoms or the degree of LV dilatation/dysfunction [7, 12, 13].

*Cardiac computer tomography (CT)* angiography with 3D/4D reconstruction can be used in cases where TTE and TEE are unable to clearly delineate the extent and the location of PVL, as can be the case for mechanical valves with significant shadowing during sonographic imaging [7, 12, 13]. CT can identify not only the leak location and the size of the defect, but can also evaluate the tract trajectory, the presence of calcification within the tract and the surrounding structures. The information obtained from CT can also be used for fusion imaging, facilitating the wiring and the cannulation during the procedure [14]. Also, in more recent years, 3D printing on CT data can help to understand the defect and can help in selecting the devices(s) [15, 16].

*Fluoroscopy* can show the presence of excessive prosthetic motion, indicating severe PVL.

Our patient's clinical case was discussed by the Heart Team and an interventional treatment was chosen because of the patient's symptoms and the severe anaemia, refractory to medical therapy. The patient was deemed at too high surgical risk, considering her clinical condition (NYHA class III), her comorbidities, and the previous surgery (EuroSCORE II >8% for a single elective procedure on the mitral valve and >13% for 2 procedures on both the mitral and the tricuspid valve). Therefore, the patient was scheduled for percutaneous closure of the main mitral PVL.

## Intra-procedural Guiding of Transcatheter PVL Closure

Transcatheter PVL closure is performed under fluoroscopic and echocardiographic guidance.

Fluoroscopy is superior to echocardiography at visualizing the catheters, the wires, the prostheses, but, except for calcified and metallic structures, it does not allow for the visualization of cardiac structures. On the other hand, echocardiography offers the possibility for visualizing the intra-cardiac structures in multiple planes. While 3D TEE is the echocardiographic modality used in most centers, intracardiac echocardiography (ICE) can be used, depending on local availability and expertise, in aortic PVLs [17]. 3D TEE guided procedures are performed under general anesthesia, which can also pose a risk in these high-risk, often old and frail patients, whereas ICE-guided procedures can be performed under conscious sedation. The combination of the TEE and ICE is also possible, with ICE used at the beginning of the procedure, for guiding transseptal puncture, and 3D TEE used for guiding the implantation of the device. Fusion imaging, superimposing the live 2D/3D echocardiographic images, or the pre-procedural 3D CT data, on the fluoroscopic image, can facilitate the passage of the guide wire through the defect and thus improve the success rate, while decreasing procedure time and radiation exposure [14, 18, 19].

### Approach

The approach used for passing the wires and delivering the prostheses is chosen prior to the intervention, based on the location of the paravalvular leak and certain patient characteristics. The approach can be retro-grade or antero-grade, trans-septal, trans-aortic or trans-apical and is described in more detail on the following sections on mitral, aortic and tricuspid PVL closure.

### Type and Sizing of the Prostheses/ Devices

The type of device(s) chosen for closing a PVL depends on the local availability and the size and shape of the defect.

There is no specifically designed device for PVL closure approved by the FDA. As such, in the USA, different self-expander occluder devices are used in an off-label fashion, the most used being the Amplatzer family of plugs:

- the Amplatzer vascular plugs (AVP II and IV)
- the Amplatzer duct occluder (ADO I and II)
- the Amplatzer atrial septal occluder (ASO)
- the Amplatzer muscular ventricular septal defect occluder (AMVSDO) [20].

Of these, the AVP II and IV, which can be recaptured after deployment, are the most often used devices in the US.

In Europe, the AVP III device, which has an oblong shape, and the Occlutech device, specifically designed for PVL closure and which comes on a rectangular- or a square-shape, are also available [20]. Although there are a few comparative data, the AVP III and the Occlutech devices seem to have a somewhat higher technical and clinical success rate (>90%), and a lower risk of complications than the other devices [21–23].

The size of the device(s) is based on the echocardiographic measurement of the 2D and, preferably 3D, dimensions of the jet at the vena contracta. With the exception of the Occlutech device, the chosen device(s) should be larger than the dimensions of the defect, in order to avoid embolization, but not so large as to interfere with valve function, particularly in the case of mechanical prostheses PVL [20]. Pre-procedural CT data can also be used for selecting the right size of the device, in particular in aortic PVLs [15, 16, 20]. Table 1 presents a comparison of the different imaging modalities used for the pre-procedural and intraprocedural evaluation of trans-catheter PVL closure.

After selecting the size of the device, careful 2D and 3D imaging throughout the procedure is necessary for:

- Evaluating the position of the catheter and the device(s);
- Confirming the correct, full deployment of the device(s) in the intended position;
- Confirming the lack of interference of the device with the prosthetic valve function or adjacent anatomical structures (such as the coronary arteries for the aortic position);
- Confirming a stable device deployment;
- Evaluating for the presence of residual regurgitation and the need for further intervention;
- Confirming the safe removal of catheters and imaging of the transseptal shunt in case of transseptal approach;
- Evaluating the presence of complications (see Table 2) [7].

**Table 1** Multimodality imaging comparison of patients with paravalvular leak

| Imaging modalities | Advantages | Limitations |
|---|---|---|
| Transthoracic echocardiography (TTE) | Evaluates prosthetic function, LV size and function, pulmonary pressure<br>Better than TEE for visualizing the anteriorly located aortic PVLs | Acoustic shadowing can limit the evaluation of mitral PVLs and posteriorly located aortic PVLs |
| Transesophageal echocardiography (TEE) | Extremely useful for diagnosis in patients with mitral PVL and in patients with posterior aortic PVL<br>The most used imaging modality for procedural guidance | Acoustic shadowing can limit the evaluation of anteriorly located aortic PVL<br>Need for general anesthesia |
| 3D echocardiography | Improves the localization of PVLs<br>Useful for selecting the size of the device and guiding the passage of the guidewires and device deployment | Image resolution can be limited by the lower frame rates |
| Intracardiac echocardiography (ICE) | Allows procedural guidance under conscious sedation | Limited in mitral PVL closure |
| Fluoroscopy | Very useful for procedural guidance<br>A rocking motion of the prosthesis indicates severe PVL | Does not visualize anatomical structures unless calcified |
| Cardiac magnetic resonance imaging | Useful in patient with discordant clinical and echocardiographic evaluation<br>Can quantify regurgitation severity in patients with multiple jets | Artifacts from metallic structures<br>Dependent on patient compliance |
| Cardiac computer tomography | Can be useful in patients with mechanical prostheses and significant acoustic shadowing on echocardiographic images<br>Can be very useful for planning the procedure and selecting the size of the devices<br>Through the use of fusion imaging, can be useful for guiding the device delivery | Artifacts can limit image resolution<br>Radiation exposure and use of contrast agents |

**Table 2** Complications of transcatheter PVL closure

| |
|---|
| Access site related complications:<br>• Femorale venous/arterial approach: dissection, stenosis, perforation, rupture, arteriovenous fistula, pseudoaneurysm, hematoma, irreversible nerve injury, compartment syndrome, distal emolization causing limb ischemia;<br>• Apical approach: Hemothorax, pericardial effusion, coronary laceration |
| Complications of transseptal crossing: intracardiac shunt |
| Bleeding complications |
| New or worsening of hemolytic anemia (may also resolve after several months, after the endothelization of the device) |
| Stroke (hemorrhagic or ischemic) and transient ischemic attack |
| Acute kidney injury |
| Coronary obstruction:<br>• Aortic PVL closure may cause left main or right coronary artery obstruction<br>• Postero-lateral mitral PVL closure may occasionally cause left circumflex occlusion |
| Device interference with the prosthetic valve function after device release:<br>• On fluoroscopy, evidence of mechanical valve obstruction<br>• On echocardiography, a sudden increase in prosthetic valve regurgitation or in trans-prosthetic gradients |
| Device or valve thrombosis that interferes with valve function |
| Device erosion |
| Device or prosthetic valve endocarditis |
| Device embolization:<br>• From the aortic position, may travel anywhere, most often being lodged at the aortic bifurcation or in the iliac arteries and can be removed percutaneously<br>• From the mitral position, small devices can pass the aortic valve and then be removed percutaneously, but larger devices may need surgical intervention for removal |
| Heart block (antero-medial tricuspid PVL closure) |
| Conversion to open surgery |
| Mortality: immediate (<72 h) and 30 days procedure-related mortality |

A good communication between the echocardiographer and the interventional cardiologist, at every step of the procedure, is essential for the success of the procedure.

## Percutaneous Closure of Mitral PVL

PVL is present in 7–17% of patients with mitral prostheses [1, 2]. As mitral surgical reintervention is associated with an increased risk of death in these patients, often associating multiple comorbidities, transcatheter closure represents a valuable treatment option in suitable patients with mitral PVL and heart failure or severe hemolytic anemia.

## Diagnosis and Pre-procedural Assessment of Mitral PVL

The main aspects of the pre-procedural evaluation of patients with mitral PVLs are:

- TTE can show indirect signs of a significant prosthetic regurgitation (increase in trans-prosthetic gradients, LV dilatation or dysfunction), while the jet can be visualized only from off-axis transthoracic images, such as the subcostal view.
- TEE is the imaging of choice for the evaluation of mitral PVLs, offering important information about the location, the shape, the size and the severity of PVL.
- The addition of 3D echo to the transesophageal images, offers a more precise localization of the regurgitant jet(s) around the ring of the prosthetic valve. When using the recommended clock face description for the location of the regurgitant jets (see Fig. 2), most mitral PVLs are found between 10 and 2 o'clock and between 6 and 7 o'clock [24, 25].
- The evaluation of the severity of mitral PVL follows the same principles described earlier and a multiparametric approach is recommended, with emphasis on those parameters with a high specificity for severe regurgitation. According to the Paravalvular Leak Academic Research Consortium, the parameters in favour of a severe mitral PVL are:
  - An excessive rocking motion of the sewing ring;

- The presence of LV dilatation or the increase in pulmonary artery pressure, in the absence of another cause;
- An increase in pressure gradients (mean gradient >5 mmHg);
- A dense, holosystolic or triangular CW Doppler envelope of the regurgitant jet;
- The ration between the mitral prosthetic flow and the sub-aortic flow on PW Doppler ≥2.5;
- A large, visible proximal convergence;
- a large vena contracta ≥7 mm;
- the presence of systolic flow reversal in the pulmonary veins, which is specific for severe PVL;
- the circumferential extent of the regurgitant jet(s) on color Doppler ≥30%
- a regurgitant volume ≥60 mL, a regurgitant orifice area ≥40 $mm^2$ and a regurgitant fraction ≥50%, according to the volumetric method [7].

• CMR should be considered when the echocardiographic grading of PVL severity is discordant to the patient's symptoms or the degree of LV dilatation/dysfunction [7, 12].
• Cardiac CT is seldom necessary for the characterisation of mitral PVLs.

## Intraprocedural Imaging Modalities and Measurements During Transcatheter Mitral PVL Closure

Transcatheter closure of mitral PVLs is, in general, performed under general anesthesia, with real-time 3D TEE and fluoroscopic guidance. ICE is often limited for guiding mitral PVLs closure. The use of fusion imaging, can facilitate the passage of the guide wire through the defect and improve the success rate.

There are 3 main approaches for delivering the prosthesis: the antegrade transseptal, the most commonly used, the retrograde transaortic and the retrograde transapical. The choice between the 3 approaches is made depending on the location of the jet and on patient characteristics:

• the antegrade transseptal approach is not applicable in patients with prior PFO/ASD transcatheter closure;
• the retrograde transaortic approach is not applicable in patients with associated aortic prosthesis or in patients with prior interatrial septal closure;
• the retrograde transapical approach, has the highest technical success rate but is associated with a higher risk of complications (hemothorax, pericardial effusion, coronary laceration); it is reserved to patients with prior interatrial septal closure or those with medially located defects.

The size of the device(s) is based on the shape of the defect and the 3D dimensions of the jet(s) at the vena contracta, as described earlier.

Once the device is in place, it should not be released before making sure that it doesn't impede on prosthetic function, and careful evaluation for the presence of complications (see Table 2) is recommended.

## Post-procedural Assessment

Post-procedural assessment is usually performed at 30 days and should include a clinical evaluation for heart failure symptoms, a biological evaluation for the presence of hemolytic anemia, and an echocardiographic evaluation. The transthoracic echocardiogram can evaluate the function of the prosthetic valve, the dimensions and the function of the left ventricle and pulmonary artery pressure, but for mitral prosthesis, transesophageal echocardiogram is necessary for confirming that the device is in place and for evaluating the importance of residual regurgitation (Table 1). The timing of the transesophageal echocardiogram is variable in different centers, between 1 and 3 months after the intervention. Based on the results of this evaluation, in patients with persistent symptomatic significant PVL, the choice between another percutaneous PVL closure attempt and surgical intervention should be discussed.

## Percutaneous Closure of Aortic PVL

Aortic PVL in present in 2–10% of patients with surgical aortic prostheses [1, 2]. Although the incidence of at least moderate aortic PVL in patients undergoing TAVI has significantly decreased in the last 20 years, some studies showing rates similar to the ones seen in SAVR patients, the incidence of mild PVL remains higher in TAVI than in SAVR patients [3–6].

The approaches to PVL after SAVR and TAVI are different. In patients with PVL after SAVR, the choice between surgical reintervention and transcatheter PVL closure should be decided by the Heart Team on a case-by-case basis. In TAVI patients, the approach depends on the cause/mechanism of the PVL:

- In case of a PVL due to a low implantation of the prosthesis, a valve-in-valve procedure is the best way to close the leak;
- In case of a mal apposition of the valve to the annulus or valve under-expansion, post-dilatation of the valve can improve the leak;
- In the case of a large calcification pushing against the frame of the prosthesis, post-dilatation carries the risk of annular rupture and percutaneous PVL can be considered, but is more difficult than in SAVR patients owing to significant annular and valvular calcifications, the presence of sealing skirts, and the, generally, smaller sized defects [20, 26–28].

### Diagnosis and Pre-procedural Assessment of Aortic PVLs

The main aspects of the pre-procedural evaluation of patients with aortic PVLs are:

- Echocardiography is the imaging technique of choice to identify and quantify aortic PVLs, TTE and TEE being used together and offering complementary information. Due to the acoustic shadowing of the prosthesis, posterior PVLs are more difficult to visualize on TTE, whereas anterior PVLs may be under-detected or under-estimated on TEE [29]. Sometimes, on both TTE and TEE, off-axis and intermediary views are needed to reveal lateral and medial paravalvular jets.
- 3D imaging, especially when performed during TEE, is ideal for PVL evaluation, allowing a better definition of the jet location, trajectory and shape. Most aortic PVLs are located around the non-coronary and the left-coronary cusp [25, 30]. Also, TTE and, in particular TEE, can be used for determining the origin of the coronary arteries, an important aspect of the pre-procedural evaluation of patients with aortic PVL, as a low implantation of the coronary arteries poses a risk of coronary ostia obstruction after the device(s) deployment.
- The evaluation of the severity of aortic PVL follows the same principles described earlier, and a multiparametric approach is recommended, with emphasis on those parameters with a high specificity for severe regurgitation. According to the Paravalvular Leak Academic Research Consortium and the Valve Academic Research Consortium 3, the parameters in favour of a severe aortic PVL are:
  - the presence of discordant motion of an aortic prosthesis in comparison to the aortic annulus
  - the presence of LV dilatation in the absence of another cause;
  - a short deceleration time (<200 ms);
  - A dense CW Doppler envelope of the regurgitant jet and often multiple jets;
  - An E/A ratio >1.5;
  - A large visible proximal convergence and a large jet width at its origin;
  - a large vena contracta ≥6 mm;
  - the presence of holodiastolic flow reversal in the proximal descending aorta with an end-diastolic velocity ≥30 cm/s;
  - the (sum of the) circumferential extent of the regurgitant jet(s) on color Doppler ≥30%;
  - a regurgitant volume ≥60 mL, a regurgitant orifice area ≥40 $mm^2$ and a regurgitant fraction ≥50% according to the volumetric method [7, 13].

- CMR is particularly useful in patients with multiple jets but can be limited by the presence of metal artefacts.
- Cardiac CT is a very useful adjunctive test to echocardiography for pre-procedural planning in aortic PVLs. It allows a detailed visualization of the size, the location and path of aortic PVLs and is very useful for determining the origin of coronary arteries.

## Intraprocedural Imaging Modalities and Measurements During Transcatheter Aortic PVL Closure

Transcatheter closure of aortic PVLs can be performed under general anesthesia, with real-time 3D TEE and fluoroscopic guidance, or under conscious sedation with ICE and fluoroscopic guidance. ICE imaging from the right ventricular outflow tract may improve the identification of leaks located anteriorly, which are frequently challenging to identify at TEE due to the prosthesis' acoustic shadowing. The use of fusion imaging, by superimposing the real-time 2D/3D echocardiographic image or the 3D reconstruction of the pre-procedural cardiac CT data on the fluoroscopic image, can facilitate the passage of the guide wire through the defect and improve the success rate, with a decrease in procedure time [14, 18, 19].

Aortic PVLs are usually corrected with a retrograde trans-aortic approach and 3 techniques can be used for delivering the device:

- A catheter-only technique, can be used in small defects which can be closed with a single device;
- An "anchor wire" technique, in which a wire is placed in the left ventricle, allows for sequential deployment of multiple devices if needed.
- An arterio-arterial rail can be used, when a more stable support for device(s) delivery is needed. The Glide wire crosses the defect, then is advanced in the left ventricle and then through the aortic prosthesis into the descending aorta and from there it can be snared and exteriorized to the contralateral femoral artery. It is rarely necessary and is not recommended in patients with mechanical aortic PVLs, in which cases, for more stability, the snaring of the catheter through a transseptal or a transapical approach can be used [31].

The size of the device(s) is based on the shape and the size of the defect as determined mainly based on the 2D and 3D dimensions of the jet at the level of the vena contracta, although, in the case of aortic PVLs, the information obtained from the pre-procedural CT can also be very useful [15, 16, 20].

An important step of the procedure is checking for the normal functioning of the aortic prosthesis, the mitral valve apparatus (in particular for leaks located around the "non-coronary" cusp) and ruling out coronary ostia obstruction after the device(s) deployment. In this respect, coronary angiography may be necessary to confirm coronary flow once the device has been positioned.

*In our patient*, the procedure was performed on general anesthesia, under fluoroscopic and transesophageal guidance, and an anterograde transseptal approach was chosen by the interventional cardiologist. At the beginning of the procedure, the presence of intracardiac thrombi was excluded by conventional TEE. 3D TEE identified the position of the main PVL, located anterior-medially, between 1 and 3 o'clock on the "en face" view of the mitral valve. 3D TEE also defined the anatomy and the size of the defect, helping the selection of the most appropriate closure device, in this case the Amplatzer Vascular Plug II of 10 mm. Figure 3a, b both conventional and 3D TEE were used to assist the interventional cardiologist in the transseptal puncture and in guiding the wire and the catheter through the defect. Once the position of the catheter was considered adequate, the device was deployed under ultrasound guidance. Immediately after the device deployment, its proper seating was ensured by TEE and a residual, no more than mild paravalvular regurgitation was detected by

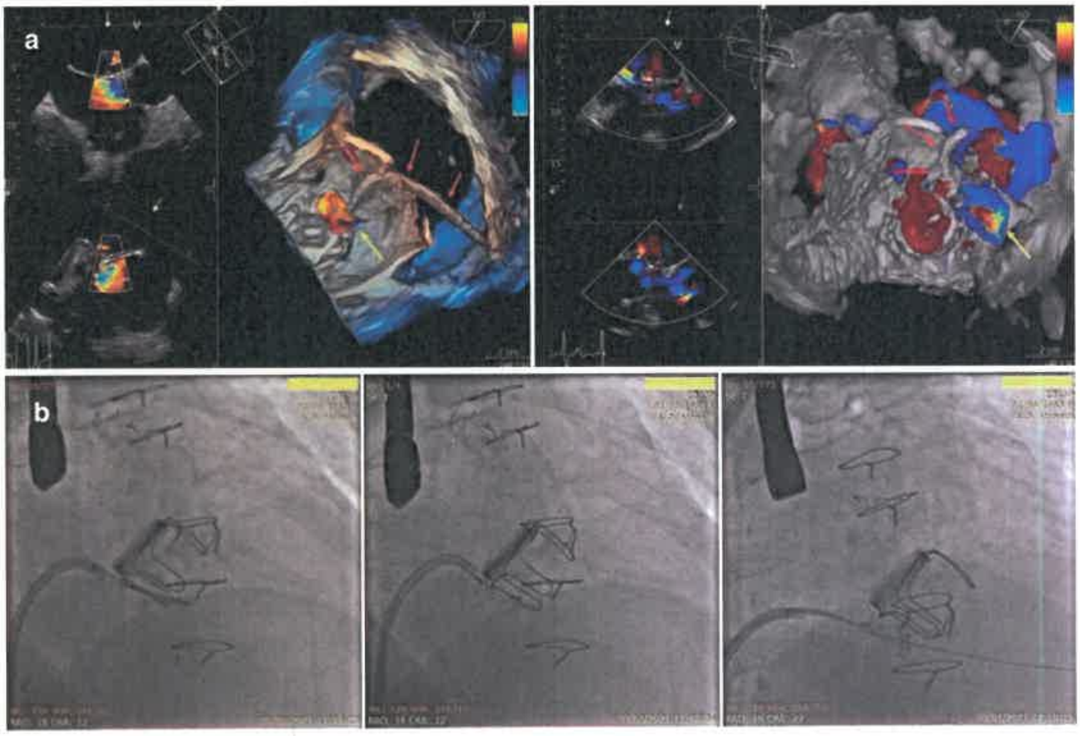


**Fig. 3** (**a**) Intra-procedural 3D TEE imaging to guide mitral PVL closure. In this "en face" view of the mitral valve, PVL appears as a large echo dropout area outside of the sewing ring, located anterior-medially (between 1 and 3 o'clock), confirmed by color Doppler (yellow arrows). 3D TEE images assist the interventional cardiologist in guiding the device release system through the defect (red arrows). (**b**) Intra-procedural fluoroscopic imaging to guide mitral PVL closure. After transseptal puncture, the catheter is guided through the mitral PVL and the Vascular Plug is released, allowing an almost complete obliteration of the defect. [*Images courtesy of professor Paolo Golino, head of Cardiology Unit of University of Campania "Luigi Vanvitelli", Monaldi Hospital, Naples (interventional cardiologist: prof. Paolo Golino, echocardiographer: dr. Gemma Salerno)*]

color Doppler. The 30-day follow-up evaluation showed, mild paravalvular regurgitation and improvement of heart failure symptoms.

## Post procedural Assessment

The goals of the post-procedural assessment of aortic PVL closure are similar to those of mitral PVL closure. The transthoracic echocardiogram can evaluate the function of the prosthetic valve, the dimensions and the function of the left ventricle, estimate filling and pulmonary pressures and can be sufficient for evaluating the presence of residual regurgitation. Transesophageal echocardiogram can however be necessary in patients with suspected significant paravalvular regurgitation, in particular in the case of posteriorly located jets. In our patient, the 30-day follow-up evaluation was good, with mild paravalvular regurgitation and improvement of heart failure symptoms.

### A Second Case Study of Transcatheter Aortic PVL Closure

A 76-year-old female patient with symptomatic severe aortic stenosis and at low surgical risk, underwent, according to the Heart Team decision, a surgical aortic valve replacement. The surgeon opted for a mini-invasive aortic valve replacement via right anterior thoracotomy and implantation of a sutureless Perceval M valve. The valve needed repositioning due to malposition near the non-coronary sinus leaflet, due to heavy calcifications. The pre-procedural transesophageal echocardiogram (TEE) described a mild para-valvular aortic regurgitation and the hemodynamic status was good at the end of the surgical intervention.

She was then transferred to the intensive care unit where, the next day, her condition deteriorated, and she developed cardiogenic shock. Transthoracic echocardiographic images were difficult. Control TEE showed severe paravalvular aortic regurgitation with a jet located around the non-coronary leaflet (the region where the most important calcifications were described on the surgical protocol) (Fig. 4a).

The case of the patient was once more discussed in the Heart Team meeting and, given the high risk associated with a surgical reintervention on a patient on cardiogenic shock, it was decided to proceed with percutaneous PVL closure.

The procedure was performed under general anesthesia with transesophageal and fluoroscopic guidance. The 2D vena contracta was 4.7 mm (Fig. 4b). Using a 6F femoral access, the PVL orifice was crossed with an Aquatrack® (Cordis) wire using a JR4 guiding

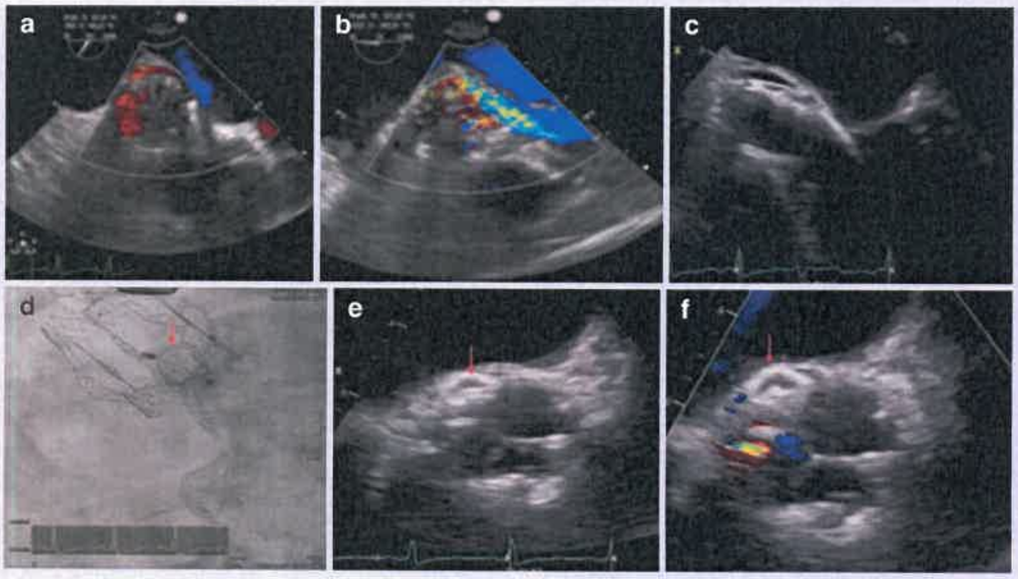



**Fig. 4** (a–f) (**a**) and (**b**) present the pre-procedural TEE examination showing the presence of a regurgitant jet all around the cusp located in the non-coronary sinus (**a**), with a 2D vena contracta measured at 4.7 mm (**b**). The resolution of the 3D images was low in this patient. Based on the crescent shape of the regurgitant orifice and the dimension of the vena contracta, an Amplatzer vascular Plug III 12/5 mm was considered to be the best device for closing the leak. The delivery catheter is seen passing through the defect (**c**) and the device is then delivered after assuring the correct location of the device, without interference with the prosthetic valve function. The device (red arrow) is then released, as seen on the fluoroscopic (**d**) and echocardiographic short-axis images (**e**), with mild residual paravalvular regurgitation on color Doppler (**f**)

catheter (Fig. 4c). After exchange with an Amplatz Super Stiff™ (Boston Scientific) wire, the delivery catheter was advanced and an *Amplatzer™ Vascular Plug III* (12 mm long axis × 5 mm short axis) (Abbott) was implanted (Fig. 4d, e) with a mild residual paravalvular regurgitation and no evidence of interference of the device with the prosthetic valve function (Fig. 4f).

The clinical evolution was good, and the patient was transferred on the flour the next day following the percutaneous paravalvular leak closure. She, however developed a pseudo-aneurysm at the femoral artery puncture site, which was resolved with an ultrasound-guided thrombin injection. The patient left the hospital 6 days after the percutaneous PVL closure.

The 30-day follow-up transthoracic echocardiographic evaluation showed a good functioning aortic prosthesis, with a mild paravalvular regurgitation.

## Percutaneous Closure of Tricuspid PVLs

Percutaneous closure of tricuspid PVLs has not been as well described as mitral or aortic PVL closure, probably because hemodynamically significant tricuspid PVL, leading to severe heart failure, liver dysfunction or severe hemolysis, is rare. A few cases of transcatheter PVL closure have been reported in literature, particularly in patients with underlying congenital heart disease [32–34]. A right internal jugular or femoral vein approach is used and the procedure is usually performed under fluoroscopic and TEE guidance, although TTE can also be used [32–34]. The sizing of the device(s) is based on the size of the defect determined from the echocardiographic images and the procedure is performed in a similar way to mitral PVL closure. A particular possible complication of antero-medial tricuspid PVL, due to its proximity to the nodal tissue, is the occurrence of heart block [34].

## Conclusions

Paravalvular leak is not an uncommon complication of surgical or transcatheter prostheses and can be associated with severe heart failure or severe hemolytic anemia. Percutaneous PVL closure is a useful and safe alternative to conventional surgery for the treatment of these patients. Echocardiography plays a pivotal role in the pre-procedural diagnosis and patient selection as well as peri-procedural interventional guidance. Other imaging technologies can offer important information for pre-procedural evaluation and, with the use of fusion imaging, can also facilitate the implantation of the devices(s).

**Key Points**

- The presence of active infective endocarditis, of intracardiac thrombus or of a significant prosthetic valve dehiscence are contraindications for percutaneous paravalvular leak closure.
- Pre-procedural evaluation is extremely important for evaluating the feasibility of a transcatheter approach and for planning the procedure.
- The device should not be released before confirming its correct location, and its lack of interference with prosthetic valve function or surrounding structures.

## Chapter Review Questions

1. Which of the following affirmations related to transcatheter paravalvular leak (PVL) closure is FALSE? (choose all correct answers)
   A. It is an effective treatment option for reducing hemolytic anemia.

B. The presence of intracardiac thrombus is an absolute contraindication for performing transcatheter PVL closure.
C. It should be considered in suitable patients with moderate PVL;
D. According to the latest guidelines, surgery is the first treatment option for patients with clinically significant PVL.

**Answer: A, B, C**

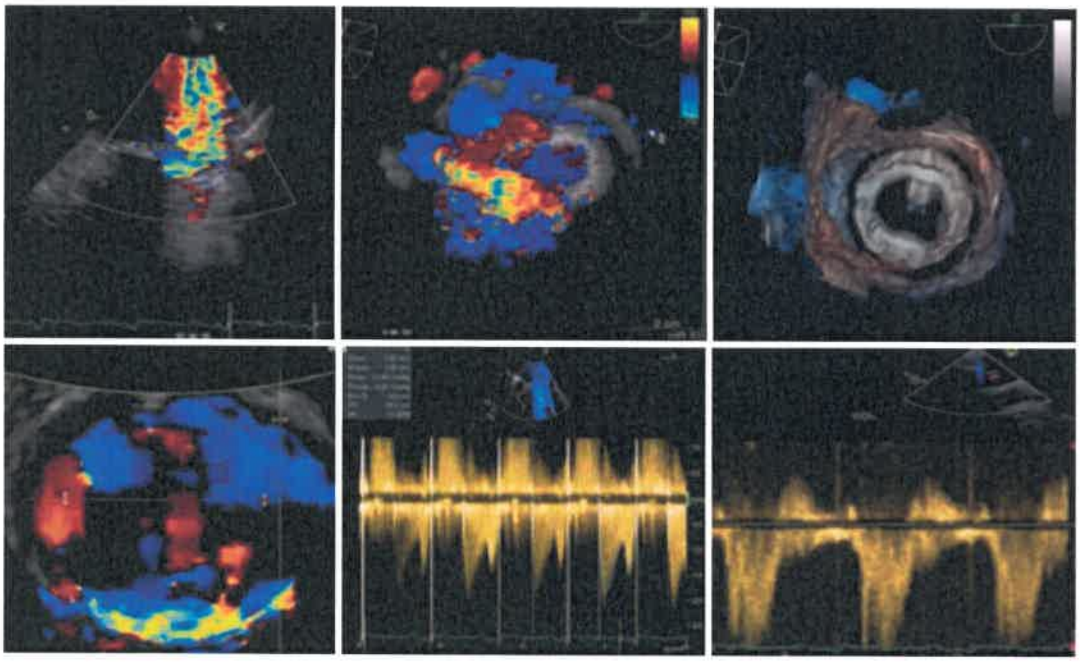
The effectiveness of transcatheter PVL closure for treating hemolytic anemia is less straightforward than for heart failure treatment. Although, in most cases, hemolytic anemia is reduced after transcatheter PVL closure, there are also a few cases of aggravated hemolytic anemia after transcatheter closure.

The presence of intra-cardiac thrombus represents a RELATIVE contraindication for performing transcatheter closure, related to the risk of embolism, but transcatheter PVL closure can be performed afterwards, once the thrombus has disappeared under anticoagulant treatment.

In general, non-severe PVL has a good prognosis and does not require treatment, although some studies suggest its presence is associated with a higher risk of infective endocarditis.

A 75 years-old patient with a history of mechanical mitral valve replacement for infective endocarditis performed 8 years prior to the actual presentation, was hospitalized for heart failure in the context of atrial fibrillation. The transthoracic echocardiogram showed a mildly reduced ejection fraction with diffuse hypokinesia and increased mitral prosthesis gradients (mean gradient of 7 mmHg but for a heart rate of 110 bpm), whereas the disks mobility was normal. The patient was referred for electrical cardioversion and transesophageal echocardiogram was performed for excluding intracardiac thrombus. The exam showed the presence of a posteriorly located paravalvular leak (PVL) whose evaluation can be seen in the following image.

2. Which of the following affirmations is true (choose all correct answers)
   A. The patient has moderate PVL
   B. PVL is severe
   C. The patient should be discussed in the Heart Team meeting, but transcatheter PVL closure using a transseptal approach can be performed
   D. the exclusion of infective endocarditis is necessary.



**Answer: B and D**

The transesophageal images show the presence of a posteriorly located paravalvular regurgitation with several echocardiographic parameters in favor of a severe PVL: the 2D vena contracta is >7 mm, the circumferential extent represents 30% of the annular circumference, there is an increase in trans-prosthetic gradients, but the mobility of the disks is normal and there is a systolic flow reversal in the pulmonary veins. The patient had systolic flow reversal in all pulmonary veins, a sign which is specific for severe mitral regurgitation.

The evaluation for the presence of infective endocarditis is necessary in all patients diagnosed with a previously unknown paravalvular regurgitation. Our patient had already been operated on for infective endocarditis and, as such, he is at higher risk for infective endocarditis recurrence. The lab tests in our patient showed the presence of a hemolytic anemia and an inflammatory syndrome. Blood cultures were negative (the patient had been prescribed an antibiotic 2 weeks prior, for a suspected pulmonary infection). On the transesophageal echocardiogram, there was no image suspected of a vegetation, but the PET-CT was positive with an intense fixation of the tracer all around the mitral prosthesis. The patient was diagnosed with culture negative active infective endocarditis, which is a contraindication for transcatheter PVL closure. His case was discussed on the Endocarditis Heart Team meeting and surgical reintervention was performed.

3. Select the correct affirmations about aortic paravalvular leak (PVL) (choose all correct answers):
   A. Posteriorly located jets are easily visualized on the transthoracic echocardiogram
   B. A vena contracta >6 mm suggests severe PVL
   C. Holodiastolic flow reversal with an end-diastolic velocity in the descending thoracic aorta >20 cm/s, is highly suggestive of severe aortic PVL
   D. Left ventricular dilatation can be a sign of severe aortic PVL.

   **Answer: B, D**

   Posteriorly located aortic PVLs are more difficult to visualize and can be missed on the transthoracic images, but they are better visualized on the transesophageal images.

   The vena contracta >6 mm and the development or an increase of left ventricular dilatation in the absence of another cause, indicate the presence of a severe aortic PVL. The end-diastolic velocity in the descending thoracic aorta >20 cm/s suggests moderate-to severe aortic regurgitation, whereas a velocity >30 cm/s suggests severe aortic prosthetic valve regurgitation.

4. Which of the following aspects about percutaneous mitral PVL closure is INCORRECT:
   A. It can be performed under fluoroscopic and intracardiac echocardiography imaging guidance
   B. Fusion imaging can facilitate the passage of the catheters through the leak and decrease procedure time and radiation exposure
   C. Transesophageal echocardiography is essential for confirming the correct location of the guiding catheter and the device inside the leak
   D. Before releasing the device, careful evaluation is necessary for confirming the lack of interference of the device with the prosthetic valve function

   **Answer: A**

   Percutaneous mitral PVL is performed under transesophageal and fluoroscopic guidance, and the use of fusion imaging can facilitate the passage of the catheters through the leak and decrease procedure time and radiation exposure. Intracardiac echocardiography is limited for guiding the delivery of the device in the mitral position. Confirming a correct location of the device and its lack of interference with the prosthetic valve function are essential steps of the procedural evaluation.

5. The following aspects about percutaneous aortic paravalvular leak (PVL) closure are true (choose all correct answers):
   A. Careful echocardiographic and angiographic evaluation is necessary for ruling out coronary ostia obstruction after device deployment
   B. It is always performed on general anesthesia, under fluoroscopic and transesophageal imaging guidance
   C. In patients with PVL after TAVI related to a low implantation of the prosthesis, transcatheter PVL is the best way for closing the leak
   D. A retrograde transfemoral approach is used.

   **Answer: A, D**

   Transcatheter aortic PVL closure can be performed under general anesthesia, on fluroscopic and transesophageal guidance, or under conscious sedation, on fluoroscopic and intracardiac echocardiography guidance. A retrograde transfemoral approach is used. An important step in the procedural evaluation is ruling out coronary ostia obstruction after device deployment, a possible complication of aortic PVL closure. In patients with paravalvular leak after TAVI related to a low implantation of the prosthesis, a valve-in-valve is usually the best choice for treating paravalvular regurgitation.

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