Chapter

Paravalvular Leaks: From Diagnosis to Management

Fathia Mghaieth Zghal, Abdeljelil Farhati and Mohamed Sami Mourali

Abstract

Paravalvular leaks (PVLs) are complications of a surgical or percutaneous valve replacement. They are persistent defects between the native annulus and the sewing ring, which result in a regurgitant prosthesis. They are observed in 2–18% of patients after a surgical valve replacement (SVR) and in 7–40% after a transcatheter aortic valve replacement (TAVR). Clinical manifestations are heart failure and hemolysis. They develop in 1–5% of PVL patients, and they have a poor prognosis. Surgery was the only available treatment to improve the patient's outcome. But it is a high-risk surgery in frail patients and PVL relapse is not rare. Percutaneous PVL closure has emerged as a promising technique. Nevertheless, it needs a careful assessment, demands high technical expertise, and still has limitations. This chapter focuses on the diagnosis of PVL after a SVR and transcatheter PVL closure (TPVL).

Keywords: surgical valve replacement, transcatheter aortic valve replacement, paravalvular leak, transesophageal echocardiography, 3D echocardiography

1. Introduction

Paravalvular leaks (PVLs) are complications of a surgical or percutaneous valve replacement. They are persistent defects between the native annulus and the sewing ring, which result in a regurgitant prosthesis. They are more frequent after a surgical replacement (SVR) of the mitral (SMVR) than the aortic valve (SAVR) (7–17% and 2–10%, respectively) [1–3]. They can be detected early or several decades after the index surgery [4]. PVL reemerged as a frequent and deleterious complication with transcatheter aortic valve replacement (TAVR) development. Where it was reported variably in 7–40% of patients, it decreased with prostheses and technical improvements. Only 1–5% of PVLs result in patent clinical effect [5]; hemolytic anemia or congestive heart failure. In patients with one or both clinical manifestations, spontaneous evolution is unfavorable, and an intervention is indicated. Percutaneous closure seems an optimal therapeutic solution, less invasive than surgery, and has promising results. Nevertheless, this technique demands high technical expertise, and it has its proper limitations and complications, hence indications should be carefully weighed.

2. Etiopathogenesis

PVL after SVR are several co-contributing factors, related to the anatomy of the valve, the surgical technique, the status of the patient, and/or to the surgeon's experience [6], they are depicted in **Table 1**. In TAVR, massive and asymmetrical calcifications and elliptical annulus shape as the main anatomical contributors, insufficient sizing and insufficient depth implantation as procedural predictors and functional c.

Lass and low left ventricular ejection fraction (LVEF) as patient condition factors [7, 8], the experience of the operator remains important to consider. Infective endocarditis (IE) is a main cause of valve disinsertion and can also be a consequence of a mechanical disinsertion with a secondary bacterial infection [9, 10].

3. Clinical and subclinical manifestations

The three main clinical manifestations of PVLs consist of congestive heart failure (HF), anemia, and IE [9].

Congestive HF occurs in the case of large or multiple PVLs with a severe valve regurgitation.

While *hemolytic anemia syndrome* occurs in small PVLs. They are more frequent in mitral valves with preserved LVEF [10], which results in a high velocity and turbulent systolic regurgitant jet. Hemolysis and anemia may be permanent or intermittent. Hence, a partial improvement during follow-up should not exclude the diagnosis nor lead to investigation cessation.

Infective endocarditis syndrome may be secondary to a previous mechanical known or unknown disinsertion or the cause of the valve disinsertion. It is important to detect IE for specific treatment. TPVL is contraindicated in this case.

Clinical tolerance is not directly correlated to the size of the PVL [9], it is influenced by several factors, including the compliance of cardiac chambers compliance, ventricular functions, the existence and degree of anemia, and the rapidity of installation. Symptomatic patients are at the tip of the iceberg.

Subclinical PVLs are more frequent, they can remain stable and or lead to progressive heart function deterioration, or they can be unmasked by an intercurrent event like IE.

Subclinical PVLs were reported to affect the patient's prognosis in SAVR and in TAVR [11, 12], they require a close follow-up and IE prevention. While symptomatic PVLs have a severe prognosis and an intervention, when feasible, is needed to improve their outcome [13].

Local anatomy	Intervention technique	Patient's status	Operator's/center's expertise
Infection Friability Calcifications Elliptical annulus	Supra-annular aortic valve implantation Continuous mitral valve sutures Annular reconstruction Difficult annular access	Advanced age Endocarditis Low body mass index Denutrition Previous valvular interventions and paravalvular leak relapses	Lack of experience and low activity volume

Table 1.
Factors contributing to paravalvular leak occurrence after a surgical valve replacement.

We should have a high index of PVL's suspicion when a patient presents with one of these figures even if first-line investigations, namely, transthoracic echocardiography (TTE) is negative. This is an essential step toward the diagnosis.

4. Cardiac imaging for paravalvular leak assessment and procedural guidance

Assessment of PVLs relay first on ultrasounds. Imaging modalities are complementary and multimodality imaging is usual.

4.1 Transthoracic Doppler echocardiography

TTE is performed as a first-line noninvasive test. It is essential for detection or suspicion of PVLs through direct or indirect signs. Indirect signs include chambers' enlargement and pulmonary pressure elevation. Direct signs consist of visualization of the defect between the annulus and the prosthetic sewing ring, which should be distinguished from an artifact by simultaneous application of color Doppler and identification of the regurgitant jet. The whole circumference of the annulus should be examined carefully, the number, size, and extension of defects are noticed.

TTE can be sufficient, particularly, in anterior aortic PVLs to determine PVL characteristics, however, its sensitivity and precision are weak in mitral PVLs that can be totally missed by TTE due to acoustic shadows.

TTE is fundamental for the assessment of prosthetic valve flows, left and right ventricles and atria sizes and functions, pulmonary pressures, and other valves' status [14–16].

TTE is usually the main test for periodic follow-up.

4.2 Transesophageal Doppler echocardiography

Two (2D) and Three (3D) dimensional TEE is the reference test for PVL assessment, it is performed after a comprehensive TTE, whether this latter was contributive or not.

TEE is essential for the investigation of mitral PVL, multiple PVLs, and complex ones [14–16] TEE permits to assess accurately the sites of the leaks by exploring the whole circumference of the sewing ring by 2D, 3D, and color Doppler modes. When using 3D imaging a careful gain setting and joint color Doppler imaging are important to eliminate gain dropouts [15].

A double opposite clock face is used to indicate the mitral and aortic PVLs sites. The mitral clock face is divided into septal, posterior, lateral, and anterior dials (**Figure 1**).

The number, shape, area, length, and height of PVLs are determined by 3D TEE [9, 14] which also indicates the defect distance from the ring and the PVL spatial position in relation to the mechanism of the prosthesis. Precise sizing using 3D multiplanar reconstruction is a key to choose an adequate device when a TPVL is indicated. Identification of calcifications and IE signs are important to discuss the feasibility and difficulty of a TPVL or surgical treatment (**Table 2**) [16, 17].

The quantification of the regurgitation is better evaluated by non-orifice-related parameters. In fact, vena contracta and proximal isovelocity methods, are

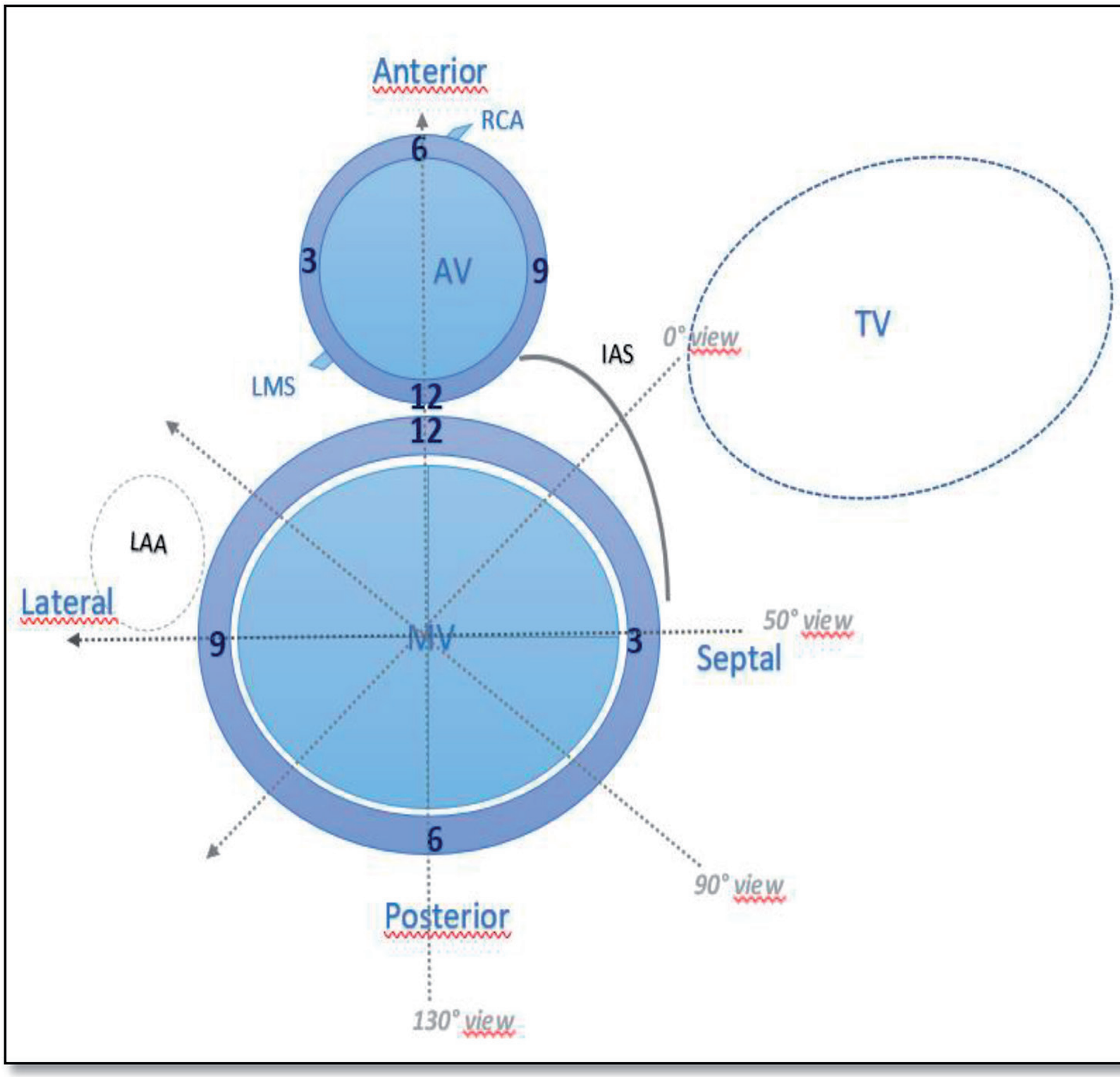

Figure 1.
Schematization of en face view by transesophageal three-dimensional echocardiography. 0, 50, 90, and 130° views: corresponding bidimensional transesophageal echocardiography plans, AV: Aortic valve, IAS: interatrial septum, LAA: left atrial appendage, LMS: left main stem, MV: mitral valve, RCA: right coronary artery, TV: tricuspid valve.

distorted by the irregular shape and location of the defect, they are rarely useful. The severity of the regurgitation is better appreciated by continuity equation, end-diastolic descending aorta velocity or reversal systolic pulmonary venous flow, cavities' dilatation, and pulmonary pressures. The circumferential extension of the defect is also a useful parameter for the severity of the regurgitation as well as the feasibility of TPVL. These parameters are to consider in parallel with the clinical status of the patient.

2D and 3D TEE are essential for TPVL guidance, especially in mitral PVLs, while TTE and fluoroscopy can be sufficient to guide aortic PVLs closure. The utility of per procedure TEE is depicted in **Table 2**. Septal puncture is guided by biplane (45 and 130°) imaging when an anterograde approach is chosen for a mitral PVL reduction, real-time 3D and zoom mode are used to localize the guides and orient the crossing of the PVL then the right positioning of the occluder device. At crucial time of the procedure, the deploying, orientation, and position of the device are to be verified as well as the mobility of the prosthetic valve and its flow (**Figure 2**). Before the release of the occluder

Pre intervention	Per TPVL guiding	Post intervention
Comprehensive cardiac assessment, including chamber sizes and functions, pulmonary pressure, all valves 'morphologies, and flows Research for infective endocarditis Assessment of local anatomy of PVLs: location, shape, number, size/extension, rocking, local, calcifications Gradation of the severity of the regurgitation Gradation of suitability for TPVL, relying on previous anatomical Planification of procedures; choice of the approach, devices and occluders	Septal puncture Spatial catheters and guides orientation Occluder positioning Normal function of prosthetic valve Immediate results Residual leak Complications (tamponade)	Position (migration) Function of prosthetic valve Residual leak/relapse of regurgitation Complications (infective endocarditis…) General cardiac assessment, chambers' size and function, pulmonary pressure.

PVL: paravalvular leak, TPVL: transcatheter paravalvular leak closure.

Table 2.
Role of Doppler transthoracic and transesophageal echocardiography in paravalvular leak management.

device, the residual leak is searched, qualified, and quantified. When significant, it leads to a change of the choice of the device or the indication of a complimentary ad hoc or differed procedure; residual leaks impact the prognosis (**Figure 2**) [16].

Permanent per-procedural monitoring detects at any time of the intervention the occurrence of complications like pericardial effusion or tamponade, embolization of the occluder, impinging, and blocking of the valve.

TEE is important to consider during follow-up if a complication is suspected (i.e., endocarditis, relapse, or extension of PVLs).

4.3 Fluoroscopy

Fluoroscopy is useful to detect rocking prosthetic valves when there is an extensive disinsertion, or an abnormal movement is seen in TTE or TEE. Fluoroscopy is important for TPVL guiding [16].

Fusion imaging combines echocardiography and fluoroscopy, is precious to guide the TPVL, it saves intervention time and increase the success rate [17, 18].

4.4 Intracardiac echocardiography

Intracardiac echocardiography is also an innovative mean to guide TPVL. Unlike TEE it allows to get free from general anesthesia. A series of 21 interventions in 18 patients with intracardiac echocardiography help was reported without any complication related to the imaging technique itself and with an acceptable rate of procedural success [19].

4.5 Magnetic resonance imaging and cardiac tomography imaging

Magnetic resonance imaging and cardiac tomography imaging are useful in a multimodality imaging approach, which is crucial for aortic post-SAVR or post-TAVR PVLs. *Cardiac tomography-fluoroscopy fusion imaging* was used in experienced teams to achieve more reproducible results, higher success, and better short and long terms

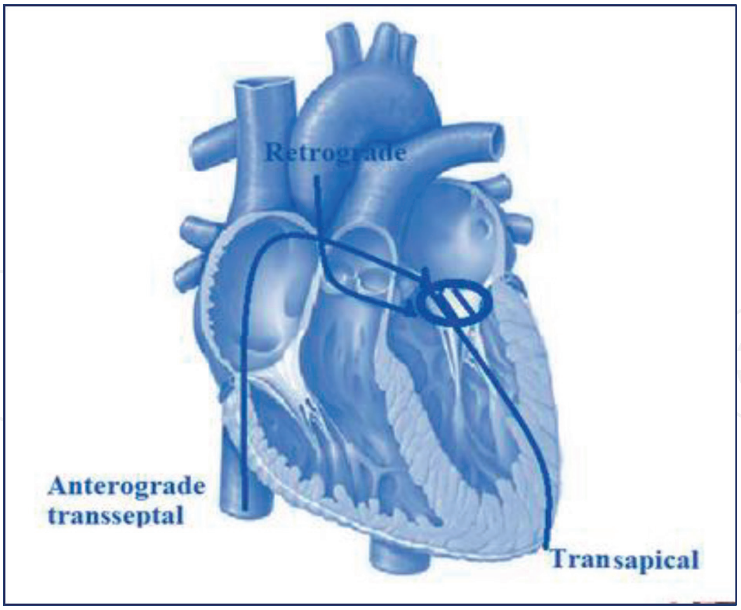

Figure 2.
Approaches for transcutaneous paravalvular leak closure.

outcomes. Also, the extension of indications and treatment with the confidence of complex, multiple PVLs (especially aortic PVLs) were allowed [20, 21].

4.6 Angiography and video-densitometry

Video-densitometric angiography is an emerging method, it was used in prospective trials as a reference tool for post-TAVR PVL assessment. It was reported to have high accuracy and allowed an objective comparison between different TAVR prostheses [22, 23]. For Kitamura M et al. it is helpful in litigious cases and intermediate degrees of regurgitation [24].

Accurate assessment of PVLs remains challenging. American and Japanese imaging and interventional societies collaboration resulted in a key guideline article dedicated to the evaluation of valvular regurgitation after percutaneous valve repair or replacement to help the development and result assessment of these interventions [25].

5. Indications for intervention

Intervention is needed when the patient with PVL is symptomatic or has evolving subclinical consequences, such as left ventricular enlargement and function impairment, significant pulmonary pressure elevation at rest or with exercise, significant hemolysis, and infective endocarditis. In certain situations, the PVL-symptoms causality relationship has to be assessed in case of comorbidities. In other situations, symptoms have to be unmasked by effort tests. TPVL is currently considered in first-line when expertise is available. The first step is to eliminate contraindications to TPVL: evolutive sepsis, extensive disinsertion greater than the third of the circumference, and rocking valves. When these figures are present surgery is chosen. Otherwise, TPVL offers a less invasive solution in generally operated and frail patients.

6. Transcatheter paravalvular leak closure

After a full assessment, defining *the objective* of the procedure is primordial; in the case of heart failure presentation, every PVL reduction is beneficial. When the TPVL is motivated by hemolytic anemia it is important to achieve a total closure of the PVL.

TPVL planification includes the choice of an adequate approach and devices. The procedure is usually performed in a catheter laboratory under general anesthesia and joint TEE and fluoroscopy guidance. Antibiotic prophylaxis is applied by administration of a cephalosporine or vancomycin in case of penicillin anaphylaxis. Nonfractioned heparin is administrated to obtain an active cephalin time between 250 and 300 and prevent catheter thrombosis. These are generally long procedures; the use of fluoroscopy is optimized to 7.5 images/second and the use of a higher image frame rate (15 images/second) is restricted to necessary (device delivery).

Approaches: For the mitral valve, the anterograde transeptal approach is the most used, however, an anterograde transaortic approach is more suitable for septal and posterior PVLs. The combination of both approaches forming an arteriovenous loop and transapical access are alternatives particularly for large or multiple PVLs necessitating the use of multiple devices [21]. The retrograde approach is not feasible in the case of mechanical aortic valve (**Figure 2**).

Device	Amplatzer Vascular plug III	Occlutech paravalvular leak device
En face view		 a1  b1
Profile view		 a2  b2
Material	Multiple layer nitinol mesh	Nitinol braided wires
Advantages	Accommodation to the shape of the channel Relative insusceptibility to deformation	Available in two shapes: square (a1) and rectangular (b1) Available in two types twist (a2) and waist (b2) Stable position in large Paravalvular leaks
Risks	"overhanging" with larger sizes and multiple device implantation	"Dog bone" formation in case of oversizing with a leak across the device

Table 3.
Characteristics of dedicated paravalvular leak devices.

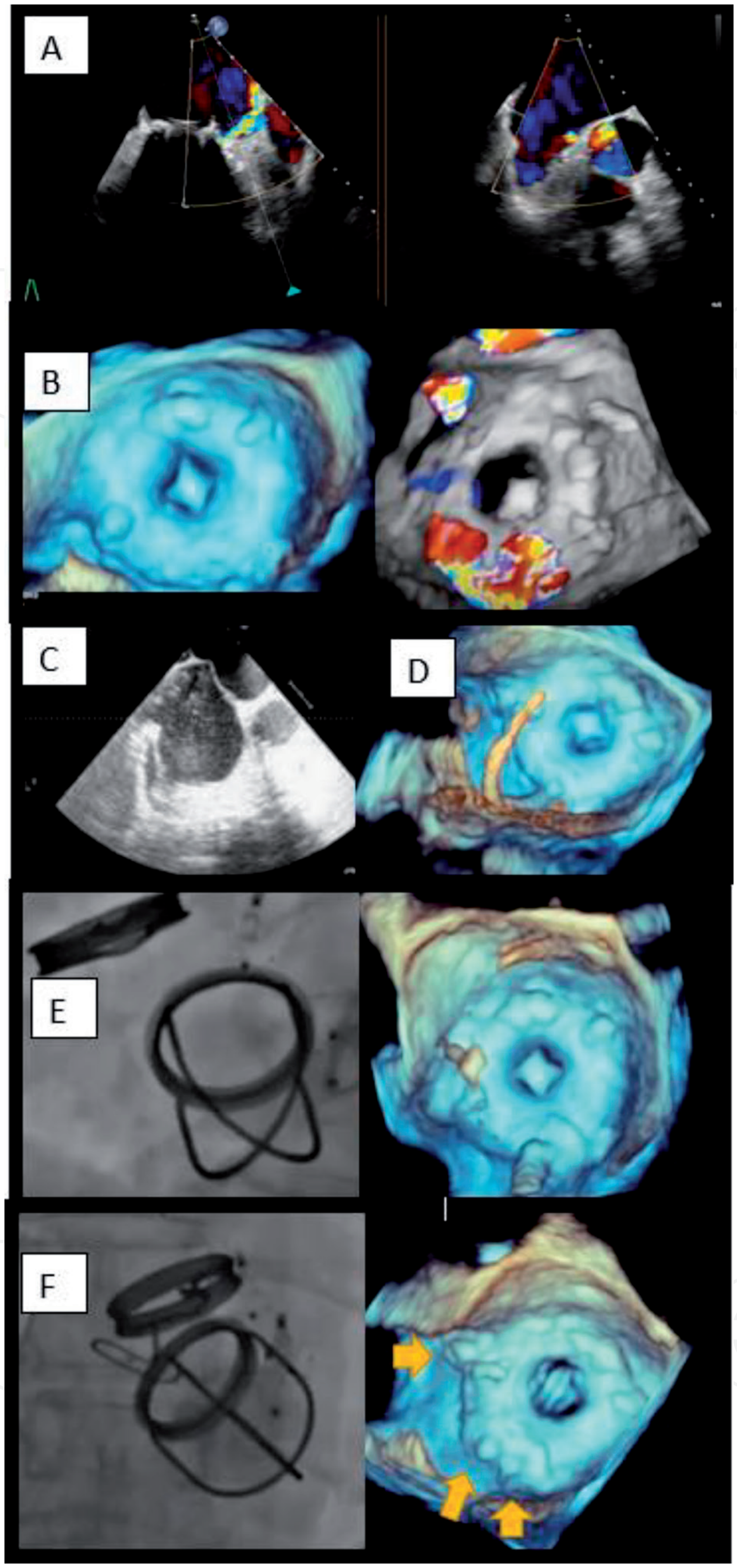

Figure 3.
Illustration of steps of a complex mitral lateral and posterior paravalvular leak transcutaneous closure in a 52-years-old female with an aortic valve prosthesis and a Starr mitral valve prosthesis. A: Paravalvular leak in color Doppler transesophageal echocardiography. B: Assessment of the defect by three-dimensional transesophageal echocardiography. C: The septal tenting. prior to the septal crossing by the wire. D: crossing of the paravalvular leak by the delivery catheter. E: assessment of the occluder device deploying by fluoroscopy and echocardiography and verification of the prosthetic valve flow. F: final result assessment by fluoroscopy and three-dimensional echography after delivery of one lateral and two posterior devices (arrows).

For the aortic valve is concerned, the retrograde approach is the most used, and transapical approach, which is useful for multiple and complex PVLs [26].

Devices: Rare dedicated devices were designed by manufacturers; Amplatzer vascular plug III (Abbott Vascular) and the paravalvular leak device (Occlutech), they are theoretically more suitable than non-dedicated devices. Their characteristics are summarized in **Table 3**.

Other non-dedicated devices were used for TPVL amplatzer vascular plug II and IV (Abbott Vascular), amplatzer duct occluder devices (Saint Jude Medical), atrial septal defect, and ventricular septal defect devices.

All devices are used off-label and do not have FDA approval [27].

The use of multiple devices can be necessary for large or multiple PVLs. This can be achieved one or more times [5].

Delivery sheaths: There is no dedicated delivery sheaths for PVL dedicated devices. Delivery sheaths for atrial septum, ventricular septum, or arterial duct devices adapted for PVL may have an insufficient length for aortic PVLs or nonoptimal diameters. Steerable sheaths facilitate the procedure and are imperative in mitral posteroseptal PVLs.

Figure 3 illustrates the main steps of a TEE-guided mitral TPVL.

6.1 Specific considerations for post-transcatheter aortic valve replacement paravalvular leaks

PVL after TAVR increases late mortality [28]. The assessment relies on a multimodality approach (ultrasounds, MSCT, hemodynamic, and angiography). The closure of TAVR-related PVLs can be considered during the TAVR procedure or subsequent follow-up. During the procedure, many techniques are available to reduce regurgitation. Oversized balloon post dilatation is effective to optimize the valve expansion and ensure a better seal but exposes to an over risk of cerebral embolic events. Snares are used when there is an inadequate depth of implantation. It is to consider with caution when there is heavy calcification as it can result also in their detachment and embolization. Valve-in-valve is used when the previous techniques are not feasible, especially when there is a nonoptimal first valve procedure. This technique can also be used later for surgical or transcatheter degenerated valves [29]. TAVR-related PVL can also be reduced by a TPVL as previously described.

7. Transcutaneous paravalvular leak closure results

Compared to surgery TPVL has lower technical success (about 90% vs. 70–86%) but less short-term adverse events and lower 30 days mortality (about 4 vs. 11%) [27, 30–32]. Mitral TPVL has higher adverse events and mortality rates than aortic TPVL [27]. Three years prognosis and survival are improved when the TPVL is successful without or with the only mild residual leak [33]. Indeed favorable result is obtained in case of the absence of significant residual regurgitation. After a first TPVL, repeated transcutaneous or surgical interventions can be needed during follow-up. The main adverse problems are worsening or new hemolysis in mitral PVLs, significant residual PVL, encroachment of the prosthetic valve, vascular injury, tamponade, hemothorax (transapical approach), device embolization, stroke, relapsing and new PVL, infective endocarditis, and death [3, 27].

8. Wrap-up

Essential steps forward TPVL achievement begin with a clinical suspicion that should include heart failure, anemia, infection, and equivalent syndromes. TTE should be very large. Multimodality imaging assessment is encouraged and facilitates the localization, anatomy evaluation, and measurement of the PVLs, and it prepares and guides the closure intervention. Full patient assessment is also needed, including comorbidities, frailty. Indication should be led by a structural valve specialized heart team. The patient's preferences are taken into account. The planification of intervention is precise and demands a large material set preparation to be able to adapt the technique and address complications, and can miss the diagnosis, particularly in the case of mitral PVL. The procedure is conducted in expertise centers. A long-term close follow-up is then needed as complications can occur at any time of the evolution.

9. Conclusion

Since its first description in 1992, TPVL has undergone an important evolution and become a confirmed technique. It is currently considered as a first-line and vital solution for PVLs reduction by many teams, even if surgery remains the reference technique in guidelines. It is important to note that it demands high expertise and is feasible only in Ref. centers with a multidisciplinary team contribution. It remains limited by dedicated devices availability and lack of financial support.

Author details

Fathia Mghaieth Zghal[1,2]*, Abdeljelil Farhati[2] and Mohamed Sami Mourali[1,2]

1 Faculty of Medicine of Tunis, Tunis El Manar University, Tunis, Tunisia

2 Rabta Hospital, Tunis, Tunisia

*Address all correspondence to: fathia.zghal@fmt.utm.tn; zghal.fathia@gmail.com

References

[1] Ionescu A, Fraser AG, Butchart EG. Prevalence and clinical significance of incidental paraprosthetic valvar regurgitation: A prospective study using transoesophageal echocardiography. Heart. 2003;**89**(11):1316-1321. DOI: 10.1136/heart.89.11.1316

[2] Saia F, Martinez C, Gafoor S, Singh V, Ciuca C, Hofmann I, et al. Long-term outcomes of percutaneous paravalvular regurgitation closure after transcatheter aortic valve replacement: A multicenter experience. JACC. Cardiovascular Interventions. 2015;**8**(5):681-688. DOI: 10.1016/j.jcin.2014.11.022

[3] Cruz-Gonzalez I, Rama-Merchan JC, Rodríguez-Collado J, Martín-Moreiras J, Diego-Nieto A, Barreiro-Pérez M, et al. Transcatheter closure of paravalvular leaks: State of the art. Netherlands Heart Journal. 2017;**25**(2):116-124. DOI: 10.1007/s12471-016-0918-3

[4] García E, Sandoval J, Unzue L, Hernandez-Antolin R, Almería C, Macaya C. Paravalvular leaks: Mechanisms, diagnosis and management. Euro Intervention. 2012;**8 Suppl Q**:Q41-Q52. DOI: 10.4244/EIJV8SQA9

[5] Bhushan S, Huang X, Li Y, He S, Mao L, Hong W, et al. Paravalvular leak after transcatheter aortic valve implantation its incidence, diagnosis, clinical implications, prevention, management, and future perspectives: A review article. Current Problems in Cardiology. 2021:100957. DOI: 10.1016/j.cpcardiol.2021

[6] Jilaihawi H, Kashif M, Fontana G, Furugen A, Shiota T, Friede G, et al. Cross-sectional computed tomographic assessment improves accuracy of aortic annular sizing for transcatheter aortic valve replacement and reduces the incidence of paravalvular aortic regurgitation. Journal of the American College of Cardiology. 2012;**59**(14):1275-1286. DOI: 10.1016/j.jacc.2011.11.045

[7] Milhorini Pio S, Bax J, Delgado V. How valvular calcification can affect the outcomes of transcatheter aortic valve implantation. Expert Review of Medical Devices. 2020;**17**(8):773-784. DOI: 10.1080/17434440.2020.1789456

[8] Nietlispach F, Maisano F, Sorajja P, Leon MB, Rihal C, Feldman T. Percutaneous paravalvular leak closure: Chasing the chameleon. European Heart Journal. 2016;**37**(47):3495-3502. DOI: 10.1093/eurheartj/ehw165

[9] Bernard S, Yucel E. Paravalvular leaks-from diagnosis to management. Current Treatment Options in Cardiovascular Medicine. 2019;**21**(11):67. DOI: 10.1007/s11936-019-0776-6

[10] Choi JY, Suh YJ, Seo J, Choi KU, Hong GR, Lee S, et al. Structural and functional characteristics of mitral paravalvular leakage identified by multimodal imaging and their implication on clinical presentation. Journal of Clinical Medicine. 2021;**10**(2):222. DOI: 10.3390/jcm10020222

[11] Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. The New England Journal of Medicine. 2012;**366**(18):1686-1695. DOI: 10.1056/NEJMoa1200384

[12] Ando T, Briasoulis A, Telila T, Afonso L, Grines CL, Takagi H. Does

mild paravalvular regurgitation post transcatheter aortic valve implantation affect survival? A meta-analysis. Catheter Cardiovascular Intervention. 2018;**91**(1):135-147. DOI: 10.1002/ccd.27336

[13] Genoni M, Franzen D, Vogt P, Seifert B, Jenni R, Künzli A, et al. Paravalvular leakage after mitral valve replacement: Improved long-term survival with aggressive surgery? European Journal of Cardio-Thoracic Surgery. 2000;**17**(1):14-19. DOI: 10.1016/s1010-7940(99)00358-9

[14] Gafoor S, Franke J, Bertog S, Lam S, Vaskelyte L, Hofmann I, et al. A quick guide to paravalvular leak closure. Interventional Cardiology. 2015;**10**(2):112-117. DOI: 10.15420/ICR.2015.10.2.112

[15] Gürsoy MO, Güner A, Kalçık M, Bayam E, Özkan M. A comprehensive review of the diagnosis and management of mitral paravalvular leakage. Anatolian Journal of Cardiology. 2020;**24**(6):350-360. DOI: 10.14744/AnatolJCardiol.2020.10018

[16] Lázaro C, Hinojar R, Zamorano JL. Cardiac imaging in prosthetic paravalvular leaks. Cardiovascular Diagnostic Theraphy. 2014;**4**(4):307-313. DOI: 10.3978/j.issn.2223-3652.2014.07.01

[17] Pascual I, Pozzoli A, Taramasso M, Maisano F, Ho EC. Fusion imaging for transcatheter mitral and tricuspid interventions. Annals of Translational Medicine. 2020;**8**(15):965. DOI: 10.21037/atm.2020.02.169

[18] Kim BH, Koh YS, Lee KY, Chung WB. Three-dimensional Echo navigator system guided transcatheter closure of paravalvular leakage. Journal of Cardiovascular Imaging. 2019;**27**(3):227-229. DOI: 10.4250/jcvi.2019.27.e30

[19] Ruparelia N, Cao J, Newton JD, Wilson N, Daniels MJ, Ormerod OJ. Paravalvular leak closure under intracardiac echocardiographic guidance. Catheterization and Cardiovascular Interventions. 2018;**91**(5):958-965. DOI: 10.1002/ccd.27318

[20] Suh YJ, Hong GR, Han K, Im DJ, Chang S, Hong YJ, et al. Assessment of mitral paravalvular leakage after mitral valve replacement using cardiac computed tomography: Comparison with surgical findings. Circulation. Cardiovascular Imaging. 2016;**9**(6):e004153. DOI: 10.1161/CIRCIMAGING.115.004153

[21] Liu Y, Xu C, Ding P, et al. Transcatheter closure of mitral paravalvular leak via multiple approaches. Journal of Interventional Cardiology. 2021;**2021**:6630774. DOI: 10.1155/2021/6630774

[22] Crouch G, Tully PJ, Bennetts J, Sinhal A, Bradbrook C, Penhall AL, et al. Quantitative assessment of paravalvular regurgitation following transcatheter aortic valve replacement. Journal of Cardiovascular Magnetic Resonance. 2015;**17**(1):32. DOI: 10.1186/s12968-015-0134-0

[23] Asami M, Pilgrim T, Stortecky S, Heg D, Roost E, Windecker S, et al. Impact of valvular resistance on aortic regurgitation after transcatheter aortic valve replacement according to the type of prosthesis. Clinical Research in Cardiology. 2019;**108**(12):1343-1353. DOI: 10.1007/s00392-019-01469-z

[24] Kitamura M, Von Roeder M, Abdel-Wahab M. Quantitative assessment of aortic regurgitation following transcatheter aortic valve replacement. Expert Review of Cardiovascular Therapy. 2021;**19**(7):633-645. DOI: 10.1080/14779072.2021.1924675

[25] Zoghbi WA, Asch FM, Bruce C, Gillam LD, Grayburn PA, Hahn RT, et al. Guidelines for the evaluation of valvular regurgitation after percutaneous valve repair or replacement: A report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Angiography and Interventions, Japanese Society of Echocardiography, and Society for Cardiovascular Magnetic Resonance. Journal of the American Society of Echocardiography. 2019;**32**(4):431-475. DOI: 10.1016/j.echo.2019.01.003

[26] Joseph TA, Lane CE, Fender EA, Zack CJ, Rihal CS. Catheter-based closure of aortic and mitral paravalvular leaks: Existing techniques and new frontiers. Expert Review of Medical Devices. 2018;**15**(9):653-663. DOI: 10.1080/17434440.2018.1514257

[27] Giblett JP, Rana BS, Shapiro LM, Calvert PA. Percutaneous management of paravalvular leaks. Nature Reviews. Cardiology. 2019;**16**(5):275-285. DOI: 10.1038/s41569-018-0147-0

[28] Laakso T, Laine M, Moriyama N, et al. Impact of paravalvular regurgitation on the mid-term outcome after transcatheter and surgical aortic valve replacement. European Journal of Cardio-Thoracic Surgery. 2020;**58**:1145-1152. DOI: 10.1093/ejcts/ezaa254

[29] Stundl A, Rademacher MC, Descoups C, et al. Balloon post-dilation and valve-invalve implantation for the reduction of paravalvular leakage with use of the selfexpanding Core valve prosthesis. Euro Intervention. 2016;**11**:1140-1147. DOI: doi.org/10.4244/EIJY15M11_04

[30] Alkhouli M, Sarraf M, Maor E, Sanon S, Cabalka A, Eleid MF, et al. Techniques and outcomes of percutaneous aortic paravalvular leak closure. JACC. Cardiovascular Interventions. 2016;**9**(23):2416-2426. DOI: 10.1016/j.jcin.2016.08.038

[31] Alkhouli M, Rihal CS, Zack CJ, Eleid MF, Maor E, Sarraf M, et al. Transcatheter and surgical Management of Mitral Paravalvular Leak: Long-term outcomes. JACC. Cardiovascular Interventions. 2017;**10**(19):1946-1956. DOI: 10.1016/j.jcin.2017.07.046

[32] Choi JW, Hwang HY, Kim KH, Kim KB, Ahn H. Long-term results of surgical correction for mitral paravalvular leak: Repair versus re-replacement. The Journal of Heart Valve Disease. 2013;**22**(5):682-687

[33] Alkhouli M, Zack CJ, Sarraf M, Eleid MF, Cabalka AK, Reeder GS, et al. Successful percutaneous mitral paravalvular leak closure is associated with improved midterm survival. Circulation. Cardiovascular Interventions. 2017;**10**(12):e005730. DOI: 10.1161/CIRCINTERVENTIONS.117.005730