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STRUCTURAL HEART DISEASE (RJ SIEGEL AND NC WUNDERLICH, SECTION EDITORS)

Paravalvular Leak Assessment: Challenges in Assessing Severity and Interventional Approaches

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Abstract

Purpose of Review With increasing use of prosthetic valves to treat degenerative valvular heart disease (VHD) in an aging population, the incidence and adverse consequences of paravalvular leaks (PVL) are better recognized. The present work aims to provide a cohesive review of the available literature in order to better guide the evaluation and management of PVL.

Recent Findings Despite gains in operator experience and design innovation, significant PVL remains a significant complication that may present with congestive heart failure and/or hemolytic anemia. To date, clear consensus or guidelines on the evaluation and management of PVL remain lacking.

Summary Although the evolution of transcatheter valve therapies has had a tremendous impact on the management of patients with VHD, the limitations and complications of such techniques, including PVL, present further challenges. Incidence of PVL, graded as moderate or greater, ranges from 4 to 7.4% in surgical and transcatheter valve replacements, respectively. Improved imaging modalities and the advent of novel surgical and percutaneous therapies have undoubtedly yielded a better understanding of PVL including its anatomical location, mechanism, severity, and treatment options. Echocardiography, used in conjunction with cardiac computed tomography and cardiac magnetic resonance, provides essential details for diagnosis and management of PVL. Transcatheter intervention has become a favored approach in lieu of surgical intervention in select patients after previous surgical or percutaneous valve replacement. PVL treatment with vascular plugs, balloon post-dilation, and the valve-in-valve methods have shown technical success with promising clinical outcomes in appropriately selected patients.

Keywords Paravalvular leak (PVL) · Bioprosthetic valve · Transcatheter aortic valve replacement (TAVR) · Vascular plug (VP) · Balloon post-dilation (BPD) · Valve-in-valve (ViV)

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Introduction

Valvular heart disease (VHD) is rising in prevalence, currently affecting roughly 2.5% of the general US population and up to 13.3% in those > 75 years of age. Valve disease–related deaths account for nearly 2% of total mortality in the USA, 99% of which are attributable to aortic and mitral valve (MV) disease [1]. With an aging population and evolving volume of surgical and transcatheter valve replacements, prosthetic-related complications are expected to rise.

Paravalvular prosthetic regurgitation, or paravalvular leak (PVL), has been demonstrated in 5–18% of all implanted surgical valves, with an incidence of 2–10% in the aortic and 7–17% in the mitral position. Likelihood of PVL in surgical patients is increased with previous or active endocarditis or highly calcified native valvular annulus. PVL is significantly more prevalent in patients who have undergone transcatheter aortic valve replacement (TAVR) which has been a significant area of investigation due to its adverse impact on outcomes [2, 3]. The landmark PARTNER I trial demonstrated that even mild PVL is associated with worse clinical outcomes and increased mortality, further emphasizing the importance of PVL diagnosis and management [4, 5]. Clinicians generally treat PVL in patients who have received surgical valve replacements more frequently than in those with previous percutaneous treatment. This may be due to the previously established gold standards in surgical valve replacement for VHD prior to the more novel transcatheter approaches. The PARTNER trials compared surgical aortic valve replacement (SAVR) to TAVR and concluded that TAVR was noninferior to SAVR in all-cause mortality in intermediate and high-risk patients. A separate analysis conducted with low-risk patients found a higher 3-year survival rate in SAVR vs TAVR, 83.4% vs 72%, respectively [3, 4, 6, 7]. Although the majority of post-TAVR PVL was mild (7.8–40.8%), moderate (5–37.9%), and severe (0.5–13.6%) leaks were substantial. The largest meta-analysis of TAVR outcomes estimated the incidence of residual moderate or severe aortic PVL after TAVR to be 7.4–11% [8, 9]. The wide range of PVL incidence may be due to the lack of standardization across centers in procedural technique, differences in operator experience, choice of prosthetic, imaging modalities, and the challenges of grading PVL. Due to improved patient selection, systematic use of multidetector computerized tomography, increasing operator experience, and device iteration, rates of PVL are presently at an all-time low. In fact, an optimal quality TAVR center should be expected to achieve an outcome of moderate to severe PVL in < 5% of high-risk patients [10, 11].

While most PVL remain clinically silent, 1–3% of patients with PVL require subsequent valve intervention as they manifest with symptoms of congestive heart failure, hemolysis, or in most cases, both [12]. Previously, complications from PVL were managed medically or with repeat surgical replacement. Since Hourihan et al. first reported the utility of transcatheter PVL closure in 1992 [13], this approach has continued to grow in favor among interventional cardiologists with advancing technologies offering significant technical and clinical success rates with decreased morbidity and mortality in high-risk surgical patients.

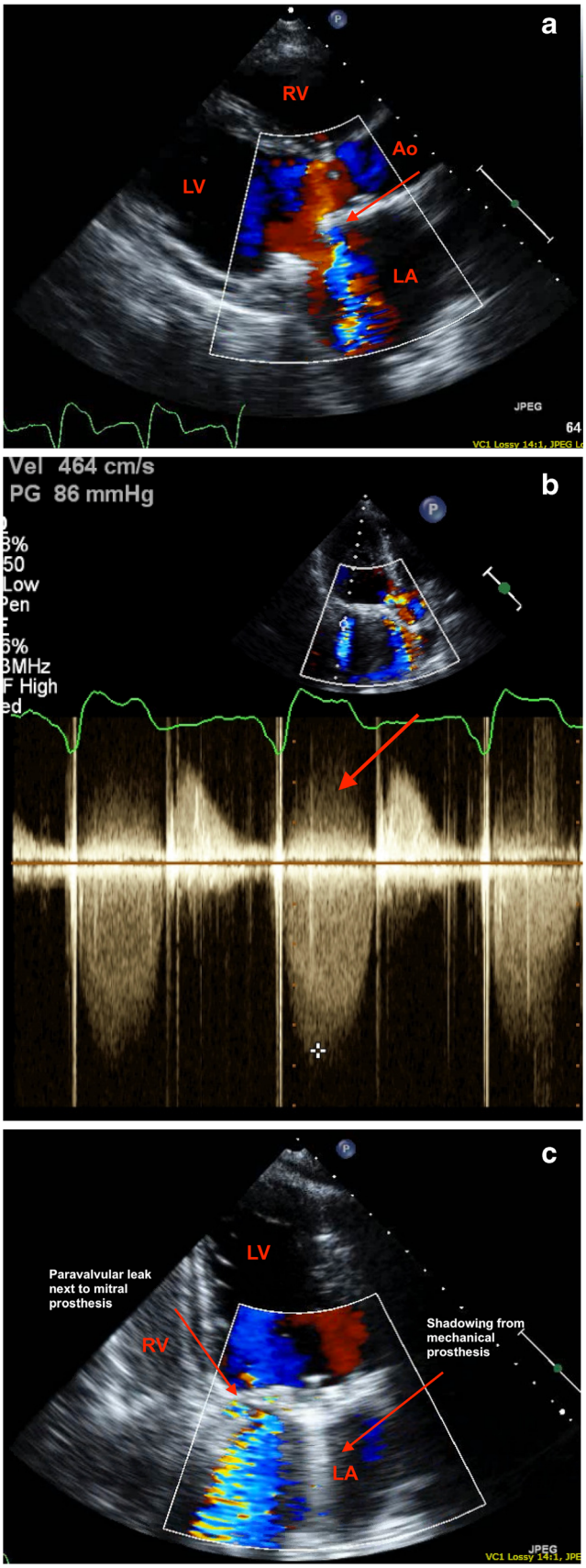
Evaluation of PVL

Echocardiography

Along with careful clinical assessment and physical exam, transthoracic echocardiography (TTE) is the first-line diagnostic imaging modality for all patients with suspected PVL [2, 14]. Echocardiography is widely and readily available, non-invasive, and provides a direct evaluation of prosthetic valve function. TTE provides good visualization of the extent of the jet, but origin and mechanism of the jet may be difficult to ascertain (Fig. 1a). Two-dimensional (2D) and Doppler assessment of the prosthetic valve should be performed to accurately determine atrial and ventricular size and function, pulmonary artery systolic pressure, valvular disease, and mobile masses on either prosthetic or native valves. Doppler evaluation can be especially valuable in evaluating prosthetic valves for leak by identifying elevated Doppler velocities, flow reversal in the descending aorta in aortic PVL, or pulmonary vein flow reversal in mitral PVL or holodiastolic regurgitation jet (Fig. 1b).

TTE is often limited by acoustic shadowing and artifact from mechanical components of prosthetic valves and accrued bioprosthetic leaflet or annular calcification, precluding visualization of the prosthetic valve of interest (Fig. 1c). These imaging limitations may result in an absence of color Doppler signal, which leads to an underestimation of PVL severity and poor etiology differentiation (i.e., valvular vs. paravalvular regurgitation) [15]. Additionally, acoustic shadowing and artifact limit imaging of the left atrium as well as the posterior aortic annulus with TTE.

Transesophageal echocardiography (TEE) is recommended to accurately determine the grade, mechanism, and location of PVL (e.g., eccentric valvular vs. true paravalvular regurgitation) (Fig. 2a). TEE is also the preferred imaging modality for intraprocedural guidance [2]. Like TTE, TEE imaging may be limited by acoustic shadowing or artifact, primarily of the anterior aortic annulus. TEE is consequently the imaging modality of choice in patients with MV prosthesis, while PVL may be best evaluated in patients with aortic valve (AV) prosthesis with TTE or TEE. Three-dimensional (3D) TEE may be a superior imaging modality to visualize prosthetic valve dehiscence (Fig. 2b) and localize PVL origin (Fig. 2c, d). Traditional MV scallop anatomical landmarks can be distorted in the post cardiac surgical patient and traditional TEE 2D



◀ **Fig. 1** A 47-year-old male with a history of MV endocarditis status post (s/p) mechanical MV replacement with Bjork-Shiley valve s/p redo surgery and replacement with Carbomedics (CarboMedics, Inc.; Austin, TX) valve due to recall who presented with progressive dyspnea and found to have severe PVL. RV, right ventricle; LV, left ventricle; LA, left atrium; Ao, aorta. **a** 2-D Transthoracic echocardiography, parasternal long-axis view, demonstrating paravalvular regurgitation (*red arrow*) originating from the anterior portion of the Bjork-Shiley mechanical valve entering the left atrium. Extent of jet can be visualized, but origin and mechanism can be difficult to ascertain. **b** Continuous wave Doppler across the mechanical valve mitral prosthesis demonstrating evidence of regurgitation in systole (*red arrow*). **c** Shadowing often presents a challenge with mechanical prosthesis

views may not accurately pinpoint suspected areas of PVL and/or dehiscence. 3D visualization of a MV prosthesis can allow for more accurate evaluation with postprocessing allowing for the entire valve in the "surgeon's view" to localize a defect. However, 3D TEE has lower spatial and temporal resolution than 2D and requires more technical expertise. In particular, drop-out artifacts with 3D TEE may occur and lead to inappropriate diagnosis of PVL. Multiple views of 2D and 3D echocardiography imaging should be integrated for confirmation and accurate representation of the valvular and cardiac anatomy. As discussed above, the evaluation of PVL is challenging after valvular prosthesis, but the assessment of recurrent or residual leak after percutaneous closure poses even further challenges. TEE long-axis (Fig. 3a) and short-axis (Fig. 3b) views in conjunction offer best view of dehiscence and PVL origin next to previously placed device.

The adult congenital heart disease (ACHD) population poses specific challenges given the complexity and variance of anatomy and prior procedures. Pulmonic valve pathology, including pulmonic PVL, is not well visualized with standard TTE or TEE. Intracardiac echocardiography (ICE) offers utility for evaluation of PVL in all valves where standard imaging is not sufficient and is especially applicable in ACHD patients with pulmonic valve prostheses [16]. CT, CMR, and 3D printing may provide additional information to assist in periprocedural planning.

Cardiac CT

Cardiac computer tomography (CT) is a useful imaging technique when TTE and TEE are inconclusive in determining grade or location of PVL especially due to excessive acoustic shadowing in cases with severe calcification and mechanical prosthesis. Cardiac CT is predominantly used in preoperative planning in patients who are to undergo TAVR as it can provide size and shape of the valvular annulus, as well as the location and degree of annular calcification, decreasing the risk of PVL [17, 18]. Cardiac CT angiography (CCTA) can also accurately visualize leaflet motion and function in

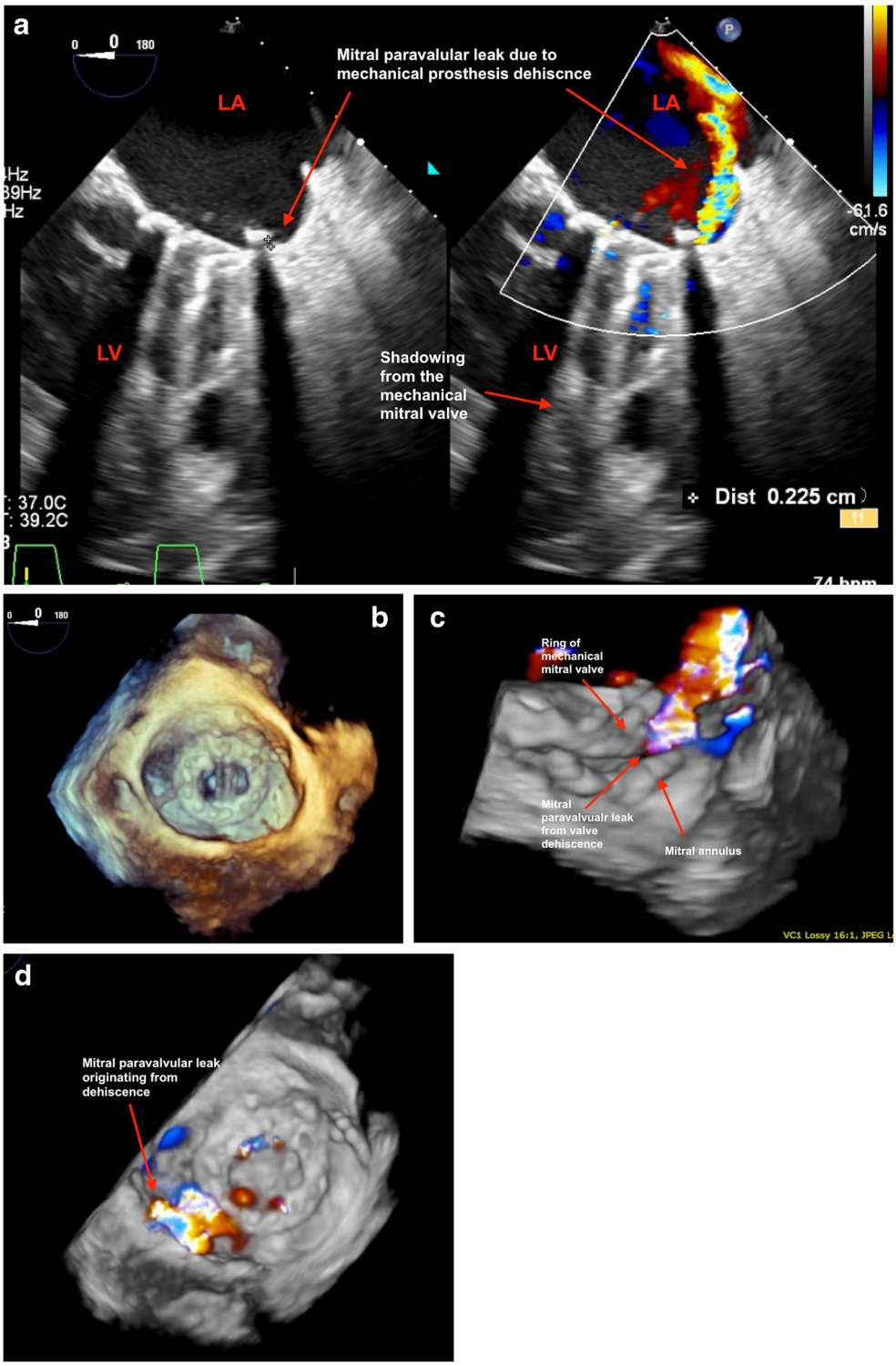
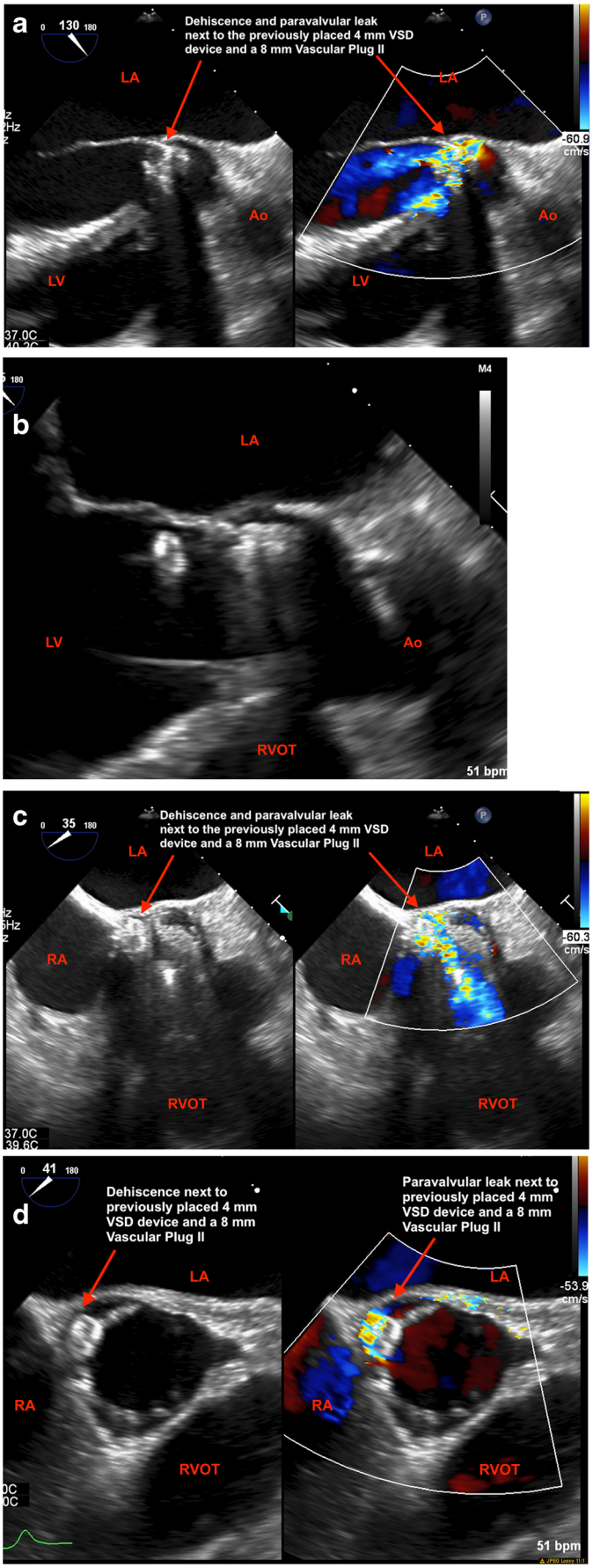


Fig. 2 TEE imaging of the same patient as mentioned above in Fig. 1. LV, left ventricle; LA, left atrium. **a** TEE providing better localization of jet and visualization of dehiscence. **b** Good localization and visualization of mechanical prosthesis in mitral position including valve ring with 3D TEE. Origin of PVL in the dehiscence next to mitral prosthesis with 3D TEE in 3D volume **c** and short-axis view **d**

mechanical valve prosthesis with retrospective ECG gating protocols (i.e., visualizing the valves open/close in systole and diastole). Limitations of cardiac CT include the need for intravenous contrast, exposure to radiation, and poor temporal resolution in patients with rapid heart rates.

Cardiac MRI

Like cardiac CT, cardiac magnetic resonance imaging (CMR) can also be used to assess PVL degree and location in patients where TTE and TEE have been inconclusive. CMR is able to provide accurate flow-imaging and volume-based


a
Dehiscence and paravalvular leak next to the previously placed 4 mm VSD device and a 8 mm Vascular Plug II
LA
Ao
LV
b
LA
LV
Ao
RVOT
51 bpm
c
Dehiscence and paravalvular leak next to the previously placed 4 mm VSD device and a 8 mm Vascular Plug II
LA
RA
RVOT
d
Dehiscence next to previously placed 4 mm VSD device and a 8 mm Vascular Plug II
Paravalvular leak next to previously placed 4 mm VSD device and a 8 mm Vascular Plug II
LA
RA
RVOT
51 bpm

◀ **Fig. 3** A 49-year-old male with history of bicuspid AV, s/p St. Jude (St. Jude Medical Inc.; St. Paul, MN) mechanical AV replacement, subsequent moderate to severe PVL, treated with a 4-mm muscular VSD device and a 8-mm AVP II device now with worsening dyspnea and PVL. RA, right atrium; RVOT, right ventricular outflow tract; LA, left atrium. **a**, **b** TEE long-axis view of AV illustrating a slit-like path where the PVL originates in the dehiscence next to the previously placed devices. **c**, **d** TEE short-axis view of AV illustrates the dehiscence and origin of the PVL next to the previously placed devices

measurements especially relevant in patients with multiple PVLs [19]. An advantage of CMR is the capability to image all prosthetic valves, and can be performed in patients with mechanical valve prostheses with appropriate protocols [20]. Limitations of CMR include the overestimation of PVL (as total regurgitant volumes are measured [2]), and poor image quality in patients with mechanical valves when compared with bioprosthetic valves (due to the ferromagnetic components of the valve) [21]. Therefore, it is important to have prior TTE or TEE imaging to assess degree of valvular vs paravalvular regurgitation to more accurately assess degree of PVL. Like cardiac CT, arrhythmias, particularly tachyarrhythmias, decrease accuracy of PVL assessment.

Fusion Imaging

There is an interest to integrate the above imaging modalities due to their respective limitations and the difficulty of accurate PVL assessment, especially for intraoperative guidance. Clegg et al. discussed the utility of a 3D echo-x-ray navigation system that successfully integrates TEE imaging and fluoroscopic images that is now commercially available for percutaneous interventions for structural heart disease, including PVL. Benefits may include enhanced anatomic understanding, improved delivery system navigation, and improved multidisciplinary team communication [22].

Grading PVL Severity

Severity of PVL is assessed using various anatomical and physiologic parameters, including qualitative, semiquantitative, and quantitative 2D, 3D, and Doppler parameters, obtained by TTE and TEE. Cardiac CT, CMR, and cineangiography may also be used to offer supplemental data to assist in PVL severity evaluation. PVL severity is graded using different schemes including the following: a 3-class, angiographic 4-class, or unifying 5-class grading schema. This review will utilize a modified 3-class grading schema: class 1: mild; class 2: mild-moderate and moderate; class 3: moderate-severe and severe [2, 23].

Structural Parameters

Several critical structural parameters are utilized in grading of PVL and include the size, shape, number, and location of the PVL defect(s) or dehiscence in relation to other anatomical landmarks, as well as left ventricle (LV)/left atrium (LA) size and function [23]. 2D echocardiography in parasternal long-axis and parasternal short-axis views are most useful in assessing position and shape of dehiscence and severity of PVL associated with mitral and aortic prosthetic valves. 3D echocardiography is useful for anatomical localization in relation to surrounding structures intra-op or pre-procedure planning. PVL-graded moderate severity or greater is often associated with inappropriate positioning of the TAVR valve stent position (either too low or too high), irregular stent shape due to eccentric calcium or raphe, and/or free space between stent and native annulus due to valve under-sizing or under-expansion. These abnormalities of stent position and shape, however, lack sensitivity and specificity for grading PVL.

A significant increase in LV diameter or decrease in LV function by echocardiography should raise level of suspicion for PVL. The consideration of LV size and function becomes more useful in the context of chronic PVL (> 3 months after valve replacement), as a large proportion of patients with PVL graded moderate or greater have no significant change of LV diameter or function within the first 3 months of valve replacement. Patients with moderate, moderate-severe, and severe PVL typically have mildly, moderately, and severely dilated LV, respectively [23].

Doppler Parameters

Images obtained by color Doppler and Doppler with both TTE and TEE are critical to accurate classification of PVL severity as they allow for complete visualization of the paravalvular region and all PVL jets. Doppler flow can also assist in determining direction and cardiac phases in which abnormal flow occurs, and can be an invaluable non-invasive hemodynamic tool in distinguishing paravalvular regurgitant flow from other associated defects with prosthetic valve implantation, including ventricular/atrial septal defects, or aorta to cardiac chamber fistulas. PVL jets are commonly multiple, eccentric, and follow irregular serpiginous tracks, making them challenging to quantify as most Doppler measurements are based on evaluation of single, central, and circular orifices. Poorly visualized and eccentric regurgitant orifice reduce reproducibility of vena contracta (VC) and proximal isovelocity surface area (PISA) assessment [24]. Multiple views with TTE and TEE help to alleviate the impact of acoustic shadowing and artifact obstructing visualization of PVL jets. The three most crucial Doppler parameters for semiquantitative assessment of PVL severity are features of the regurgitant jet including circumferential extent and width at its origin.

Jet features, including number of jets visualized, visualization of the jet path along the stent, and proximal flow convergence, by echocardiograph have been shown to be important to assessing PVL severity. The number of jets correlates with the regurgitant fraction measured by CMR [23]. Generally speaking, the more jets visualized the more severe the PVL. However, this is not to say that multiple small jets cannot contribute to trace or mild PVL and one large jet cannot lead to severe PVL. PVL jet paths that are clearly visible along the whole length of the stent are often associated with moderate or greater PVL. Proximal flow convergence is often a marker of moderate-severe to severe PVL [23].

The circumferential extent of the PVL jet(s) is measured using the parasternal short-axis plane by visually estimating the number of minutes the PVL jets occupy if the full annulus was a clock face and dividing by 60 to get a percentage. Mahjoub et al. and the American Society of Echocardiography proposed this method to describe the valvular anatomy, unifying nomenclature between the interventionalist and echocardiographer [25, 26]. The AV and left atrial appendage (LAA) act as landmarks for the 12 o'clock and 9 o'clock positions, respectively to communicate locality of PVL [27]. The 2012 Valve Academic Research Consortium 2 updated the guidelines for use of cutoffs regarding this parameter and its corresponding PVL severity. 10–20%, 20–30%, and > 30% circumferential extent corresponded to mild to mild-moderate, moderate, and moderate-severe to severe PVL, respectively [28]. Scanning the height of the entire stent using the short-axis plane is critical, as PVL circumferential extent may vary significantly depending on the plane of interrogation. This parameter becomes more complex and less reliable when multiple or eccentric jets are present. Jets may be at different levels in a multiple-jet PVL, and eccentric jets may be directed across the short-axis plane, causing an overestimation of the circumferential extent, and consequently PVL severity. PVL severity may also be underestimated when a jet does not occupy a large circumferential extent but has a large radial width. Therefore, this parameter should be integrated with other views and parameters to give the most accurate assessment of PVL severity, as this parameter correlates poorly with PVL severity measured by CMR.

Apart from the aforementioned "clock" method, other forms of unifying nomenclature used between clinicians include the Carpentier and "quadrant" method [29]. The Carpentier method is used to describe the complex structure of the MV by 6 regions (A1–3, P1–3). The posterior leaflet is divided into 3 scallop regions by clefts and assigned P1–3. The anterior leaflet is not divided into leaflets, but assigned A1–3, relative to their respective opposed posterior scallop (P1–3) [30]. The "quadrant" method described by Spoon et al. uses the anatomical relationships of the atrial septum, LAA, and AV to separate the MV into 8 quadrants to localize PVL [31].

The width of the jet at its origin may be the most important parameter to consider for grading severity of PVL. It is measured using the parasternal and apical views and is an estimate of the ratio of the jet width to the LVOT diameter to obtain a percentage. Accurate assessment of the jet width can only be made if the origin of the jet is visualized, which may be difficult. A jet width percentage of 15–30, 30–45, 46–60, and > 60% corresponds to a PVL severity of mild-moderate, moderate, moderate-severe, and severe, respectively [23].

CMR Imaging

Regurgitant fraction by phase-contrast velocity mapping has become one of the most applicable and most frequently used parameters to help assess and grade PVL severity due to CMR's ability to measure regurgitant volumes irrespective of jet characteristics, measurement of regurgitant volume with multiple valve types, and having high reproducibility of measurements. Inherent limitations to CMR imaging assessment of PVL severity include poor cardiac gating in patients with arrhythmias, artifact disrupting image quality, and overestimation of regurgitant due to coronary artery diastolic flow. Regurgitant volume and fraction cutoff values used to grade PVL severity are not well validated and vary substantially between studies. CMR therefore is used in conjunction with echocardiography to confirm PVL severity and should not be used in isolation.

Management of PVL

While only surgical and transcatheter interventions provide definitive treatment of PVL by correcting the anatomical defect or dehiscence, medical therapy remains the mainstay for symptomatic management in patients with heart failure and/or hemolysis due to PVL. Medical management of heart failure from PVL should be approached similarly to the management of heart failure from other causes and should include both preload and afterload reduction. Folic acid and iron supplementation should be offered to patients whose PVL is causing hemolysis. Blood transfusion may be indicated depending on the severity of the hemolysis and symptoms. Indications for PVL closure include heart failure including unexplained reduction in ejection fraction, LV enlargement, and symptomatic or transfusion-dependent hemolytic anemia [32].

Surgical Intervention

The 2017 AHA/ACC Focused Guidelines Update for the management of valvular heart disease has considered surgery a class I indication for patients of acceptable operative risk

with mechanical valves and severe PVL [33]. However, the rapid development of transcatheter PVL closure techniques has resulted in fewer patients requiring open surgical repair for PVL. Moreover, repeat surgery is associated with an increased risk of complications and mortality. Surgical intervention of PVL is therefore reserved in patients with active endocarditis, prosthesis dehiscence involving > 1/3 of the annular circumference, previously failed transcatheter closure, or in patients undergoing CABG or another concomitant valve surgery [14]. Surgical repair of PVL results in closure of smaller defects with re-suturing or complete replacement of the valve with a newer prosthesis. Bouhout et al. investigated the long-term results after surgical treatment of PVL in both the aortic and mitral valves in 190 patients. Operative mortality occurred in 7% of patients. Survival at 1, 5, and 10 years was 85%, 73%, and 56%, respectively. The cumulative incidence of PVL recurrence was high at 3%, 14%, and 32%, at 1, 5, and 10 years, respectively. The number of previous surgeries was a predictor of survival and PVL recurrence. Freedom from New York Heart Association (NYHA) class ≥ III was 96%, 82%, and 58%, at 1, 5, and 10 years, respectively. The freedom from rehospitalization for heart failure was 92%, 83%, and 67%, at 1, 5, and 10 years [34].

Transcatheter Intervention

The 2017 AHA/ACC Focused Guidelines Update for the management of valvular heart disease assigns a class IIa indication of transcatheter repair [33]. Percutaneous repair of PVL or prosthetic regurgitation can be performed with a reasonable success and may be preferred initial therapeutic option, particularly in patients at significant risk for redo open-heart surgery [35•]. A retrospective cohort study found that patients undergoing transcatheter intervention for PVL had experienced less in-hospital morbidity and 30-day readmission when compared with patients who underwent surgical intervention [36]. Transcatheter repair of PVL is contraindicated with acute endocarditis and is difficult to perform with extensive dehiscence (> 1/3 of annular circumference) or in transcatheter valve malposition. Transcatheter intervention is indicated in symptomatic patients or those with class 3 PVL. Procedure can be performed using three different techniques depending on the size, location, and mechanism of PVL. Percutaneous options for treating PVL include the following: vascular plug (VP), balloon post-dilation (BPD), and valve-in-valve (ViV) [37].

It should be mentioned that an extensive review of the available literature regarding these transcatheter approaches did not provide any consensus on a recommended approach or clear guidelines on these topics. Most of the available information comes from smaller studies, case reports, and single-center experiences. Indeed, more systematic and trial data are needed to make more definitive conclusions about management strategies. Rather than a pre-defined recommendation, each individual case merits its own investigation and as such anatomic, patient-related factors as well as operator experience should determine approach.

Vascular Plug

Available literature suggests that transcatheter closure via vascular plug or septal occluders is the most frequently utilized method across the country and globally. Self-expanding occluder devices have been used off-label, as no currently available device carries FDA approval specifically for the treatment of PVL. The Amplatzer vascular plug (AVP; St. Jude Medical Inc.; St. Paul, MN) family of occluder devices constitute the majority of VPs used for PVL closure. Namely, the AVP II and IV are most commonly used in the USA. The AVP III, unique for its oblong shape and only available in Europe, is the most used device [2]. Ventricular septal defect (VSD) devices are also often used during percutaneous closure procedures depending on the size and location of PVL defect.

A meta-analysis of 12 studies evaluating the benefits of the VP method in PVL closure encompassing 362 patients revealed a technical success of 82.3% and 86.9%, and a procedural success of 73.7% and 84.1% in mitral and aortic procedures, respectively. Technical success was defined as successful delivery of a VP, while procedural success was defined as the delivery of a VP resulting in an immediate reduction in PVL by at least one grade (e.g., moderate to mild). A superior functional class improvement or improved hemolytic anemia was observed in successful vs. failed PVL reductions, driven by a reduction in NYHA functional class. Technical success, however, was not associated with a statistically significant lower rate of cardiac mortality [38]. However, in a large consecutive cohort of patients undergoing percutaneous mitral PVL closure, successful percutaneous reduction of the PVL to mild or less was associated with significant mid-term survival benefit [39•].

Although incidence of PVL after TAVR has been reduced with the newer generation valves, improved understanding of valve positioning, and size selection, significant PVL continues to predominantly result from eccentric calcium or raphe associated with bicuspid AV (Figs. 4 and 5). VPs should be considered for patients with single or 2 PVL defects in anatomically suitable locations, based on operator preference. More than one device can be used for single large or multiple defects, and are placed more frequently in the management of mitral PVL vs aortic. We illustrate 3D TEE intraprocedural guidance of 2 AVP II to correct moderate-severe PVL to mild residual PVL (Fig. 6). As improvements in valve design continue to progress, the incidence of PVL may continue to decline. For example, the addition of a polyethylene terephthalate (PET) skirt to the Sapien 3 (Edwards Lifesciences, Irvine,

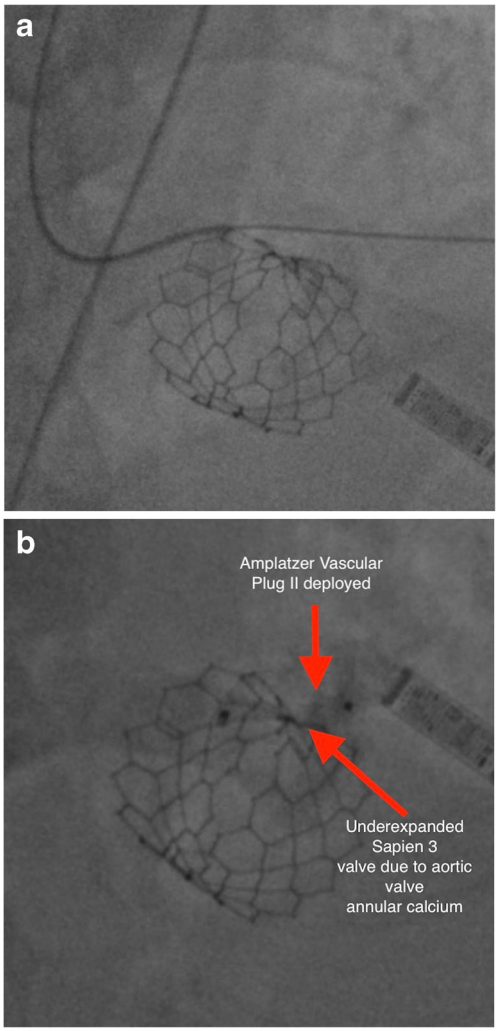


Fig. 4 **a** Cine imaging of crossing of PVL with AL1 diagnostic catheter and glide wire. **b** Cine imaging of valve after AVP II deployment

CA) has been shown to reduce PVL due to eccentric calcification, as the skirt provides an improved seal around the annulus [40].

Balloon Post-dilation

PVL due to incomplete apposition of the AV due to severely calcified cusps or under-sizing can often be treated with further dilation of the prosthesis using either repeat balloon inflations or implementation of an oversized balloon. These techniques reduce the degree of PVL by better expansion and sealing of the paravalvular space. This technique is also occasionally employed in expansion of under-expanded self-expanding prosthetic valves. The valvular annulus dimension as well as the maximum diameter of the implanted prosthetic valve needs to be considered to avoid trauma to the annulus or prosthesis. However, overexpansion of prosthetic valves by BPD can be used to safely treat patients with a larger annulus size, depending on the stiffness and degree of calcification of the native valve and annulus [41].

BPD is typically used when VP cannot safely be deployed, circumferential PVL, or PVL with multiple jets. It can, nevertheless, be used as the first step if there are multiple leaks or if the valve was undersized for the annulus of interest, especially in acute setting right after valve implantation during TAVR [42]. Overexpansion of severely under-size valve can result in leaflet shortening with resultant central valvular regurgitation, stent fracture, and aortic rupture due to penetration by eccentric calcific nodule. Although there have been no large studies illustrating the clinical impact of BPD in PVL closure, multiple case reports emphasize the significant reduction and minimal residual PVL when this method is used. With improvement in pre-procedure CT, dedicated software to accurately assess annulus size and intra-op echocardiogram including 3D TEE use of BPD has decreased.

Valve-in-Valve

ViV is a relatively novel technique employed in patients with degeneration of bioprosthetic, or most commonly following TAVR with the first TAVR ViV procedure described in 2007. Tandar et al. presented significant correction of PVL with ViV with near complete resolution of moderate PVL [43]. Treatment of PVL with a second valve ViV is an alternate therapy that may be required if the PVL is due to an incorrect implant depth, too high or low, relative to the annulus [14, 44]. The occurrence of PVL due to lack of adequate coverage of the valve annulus necessitates ViV implantation. VPs and BPD are often not suitable in this scenario. ViV is only applicable for TAVR or bioprosthetic valves and cannot be used in mechanical prosthesis. More recently, with improvement in imaging modalities, optimal placement of a properly positioned new valve has significantly reduced the incidence of PVL due to valve malposition, thereby resulting in improved hemodynamic results.

Aortic regurgitation (AR) following TAVR is most commonly due to PVL. Although the optimal technique of ViV has not yet been described, Jubran et al. suggest that positioning the second valve should be guided by the location of the initial valve relative to the aortic annulus. Initial valves that were supra-, intra-, and infra-annular were treated with second valves that were implanted lower, higher, and higher than the initial valves, respectively, with subsequent decrease in AR (aortic PVL) in all patients [45].

A retrospective single-center Canadian study investigated the mid-term outcomes of patients who underwent aortic and mitral ViV for surgical biological valve dysfunction (stenosis, regurgitation including PVL, or both). In this study, transcatheter ViV implantation showed encouraging mid-term clinical and hemodynamic outcomes in a high-risk elderly cohort of patients. Overall survival in 73 patients who underwent either

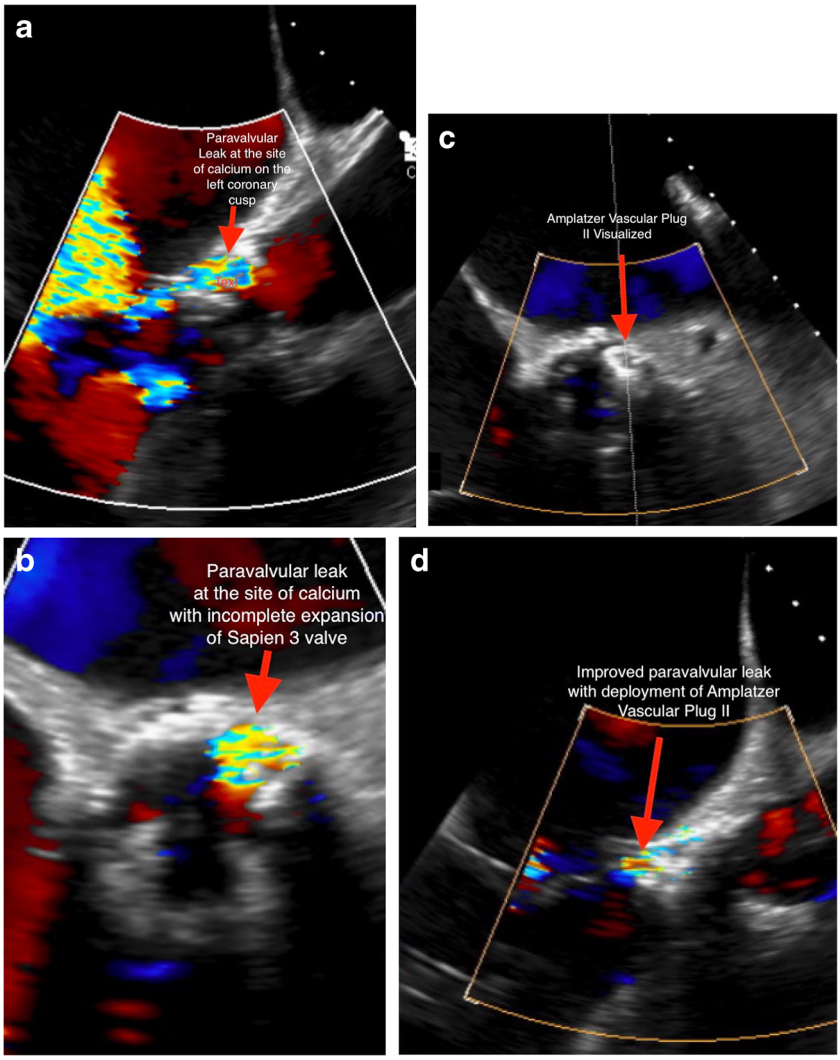


Fig. 5 **a** Baseline TEE of severe PVL at left coronary cusp; **b** cross-sectional image of severe PVL; **c** AVP II visualized on TEE, and **d** mild PVL after AVP II deployment

aortic or mitral ViV implantation was 88.9%, 79.5%, 69.8%, 61.9%, and 40.5% at 1, 2, 3, 4, and 5 years, respectively. The median survival rates were 4.5 and 4.4 years following aortic and mitral ViV implantation, respectively. Poorer estimated survival was observed in patients who had small aortic surgical valves (19 and 21 mm) relative to those with surgical valves of ≥ 23 mm suggesting a potential role of patient-prosthesis mismatch. Significant clinical improvement in heart failure symptoms was observed following ViV implantation in the majority of patients. In all patients who had a 2-year follow-up data, NYHA functional class I and class II were observed in 82.8% and 100% patients with aortic and mitral ViV implantation, respectively. The majority of patients who had longer follow-up after ViV implantation had NYHA functional class I and class II heart failure symptoms [46].

There is limited data when a PVL becomes too large for ViV implantation. Although available case reports prove its valuable and promising utility in management of PVL, none mention failure due to size of PVL. If original valve is severely undersized, overexpansion can potentially result in old stent fracture or aortic rupture due to penetration by eccentric calcific nodule. If new valve in a previously smaller valve fails to expand, it can result in poor leaflet opening and mobility, increasing risk of leaflet thrombosis.

Future Directions

Specific valves and techniques are dependent upon the interventional cardiologist's available resources and preference. As with VP and BPD, ViV is most commonly accomplished by the retrograde approach for aortic, and the transapical or transseptal approach for mitral PVL. Unfortunately, there is no consensus regarding the aforementioned transcatheter methods of PVL closure. Larger retrospective and prospective studies need to further investigate how to more accurately diagnose and treat PVL. Registries, similar to the transcatheter valve therapy registry, are also needed to track real world outcomes of these therapies.

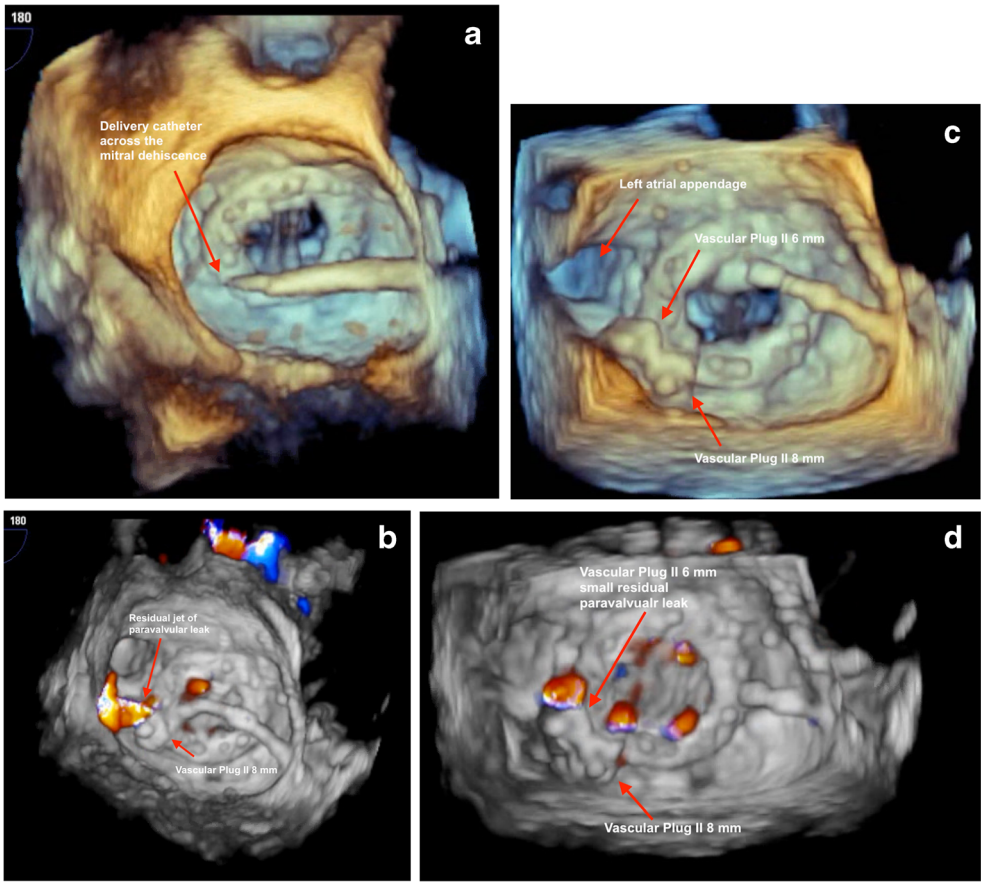


Fig. 6 Patient depicted in Fig. 1 above undergoing TEE and fluoro-guided percutaneous closure of mitral PVL with AVP II 6 mm and 8 mm. **a** Delivery catheter crossing the valve; **b** first VP placed with residual PVL; **c** second VP placed with good detail of surrounding anatomy; **d** Mild residual leak after 2 VPs

Compliance with Ethical Standards

Conflict of Interest Jamil A. Aboulhosn reports receiving research support from, and being a proctor and a consultant for, Edwards Lifesciences; and being a consultant for Medtronic Inc.

All of the other authors have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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