

Paravalvular Leak Closure After TAVR

Incidence, impact, and treatment of paravalvular leak after transcatheter aortic valve replacement.

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Transcatheter aortic valve replacement (TAVR) is a rapidly evolving procedure that has assumed a central role in the treatment of severe symptomatic aortic stenosis in high-risk and inoperable patients. Outcomes are comparable to surgical aortic valve replacement (SAVR).¹ Encouraging clinical trial data have led to the widespread adoption of TAVR worldwide. Despite the inherent advantages of TAVR as a therapy less invasive than SAVR, unique challenges remain associated with the procedure in contemporary practice. Perhaps chief among these is the incidence of aortic regurgitation (AR), primarily caused by paravalvular leak (PVL). PVL is far more frequently encountered after TAVR than after SAVR^{2,3} and has been associated with decreased clinical efficacy and a lessened mortality benefit.

INCIDENCE, DETERMINANTS, AND PROGNOSIS OF PVL

PVL is recognized as a significant problem associated with TAVR.^{3,4} Multiple studies have reported the frequency and severity of PVL after TAVR, with relative heterogeneity in data secondary to nonstandardized imaging modalities, timing of assessment, and nonuniform grading scales. In general terms, moderate or severe aortic insufficiency after TAVR occurs in approximately 10% to 25% of cases, and trace to mild aortic insufficiency occurs in 47% to 80%.⁵⁻⁸ There have been no direct comparisons in the rate of PVL between the transcatheter heart valve (THV) systems available in the United States (ie, Sapien [Edwards Lifesciences, Irvine, CA] and CoreValve [Medtronic, Inc., Minneapolis, MN]), so no meaningful statements can be made regarding whether the rate of moderate to severe PVL is different between the two devices.⁹⁻¹³

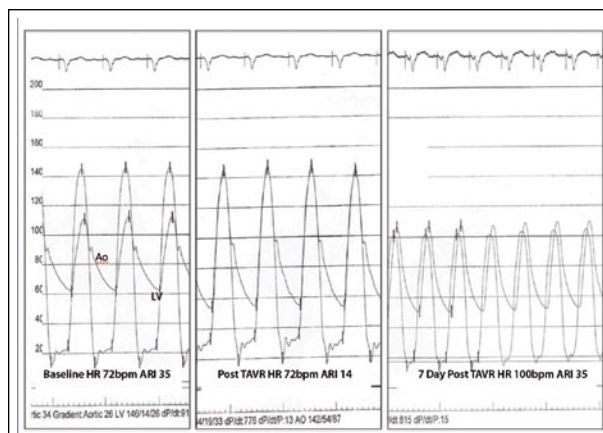


Figure 1. The baseline hemodynamics with a ventricular paced heart rate of 72 bpm, mean aortic gradient of 26 mm, and an AR index of 35. Post-TAVR, at the same heart rate, there is moderate aortic insufficiency with an AR index of 14. Seven days after TAVR, the pacing rate increased to 100 bpm due to persistent pulmonary edema, with an increase in the AR index to 35. (High pacing rates for management of aortic insufficiency after balloon aortic valvuloplasty or transcatheter aortic valve replacement. Ali O et al. *Catheter Cardiovasc Interv.* 83[1]. Copyright © 2014. With permission from John Wiley and Sons, Inc.)²⁰

The etiology of PVL is generally attributable to several anatomic and procedural considerations. Less commonly, PVL is the result of valve malpositioning when deployment was either too high or low in the native annulus. In this case, the fabric skirt of the valve is out of position, and AR is due to blood flow through the uncovered stent struts. More often, PVL is caused by incomplete prosthesis frame apposition to the native annulus secondary to native valve calcification, annular eccentricity, or undersizing of the prosthesis.

Inappropriate valve sizing is one of the most frequent—and also most remediable—causes of PVL. Reliance on two-dimensional transthoracic or transesophageal echocardiography (TEE) tends to result in undersizing of the prosthesis and resultant PVL. Therefore, multidetector CT, often with the aid of proprietary analytic software developed specifically for TAVR, has increasingly become the gold standard for annular sizing. Studies have validated the efficacy of multidetector CT in appropriate sizing and reducing rates of PVL.¹⁴⁻¹⁶ The use of three-dimensional TEE for annular sizing also shows promise, but is highly operator dependent. Assessment of paravalvular AR is challenging at best, and thorough, careful TEE assessment at implantation is critical. Often, a transgastric view of the aortic valve will visualize AR jets that are not well seen in esophageal long and short axis views. The systemic pressure is an important variable in assessing AR, as well.

The importance of AR after TAVR lies in both the diminution of clinical symptomatic benefit and increased mortality. Several studies have demonstrated that moderate to severe AR is an independent predictor of both short- and long-term mortality.^{2,17} Additionally, moderate to severe AR was associated with a 10-fold increase in patients with New York Heart Associate class II or greater symptoms after TAVR. Early reports suggested that mild AR was benign and well tolerated. Unfortunately, 2-year outcome data from the PARTNER trial showed that the presence of even mild PVL or central AR was associated with a late mortality hazard. The effect of PVL and AR was proportional to the severity of regurgitation, but even mild regurgitation was associated with increased late mortality.¹⁸

ASSESSMENT OF PVL

Accurate quantification of PVL is challenging. From a clinical perspective, the degree of PVL, which leads to symptoms or to decompensated heart failure, is highly variable. A PVL that appears qualitatively mild using color Doppler may lead to debilitating symptoms in one patient, whereas a clearly larger leak may be well tolerated in another. Classic hemodynamic findings suggestive of AR at the time of valve implantation (acute reduction in the aortic diastolic pressure) may be suggestive of moderate to severe AR, but this finding is nonspecific and must be interpreted with caution given the concomitant use of general anesthesia, rapid pacing for valve deployment, and alterations in systemic pressures and LV filling pressures. The recently described AR index is the ratio of the gradient between diastolic blood pressure (DBP) and left ventricular end-diastolic pressure (LVEDP) to systolic blood pressure (SBP): $[(DBP - LVEDP)/SBP] \times 100$. As the

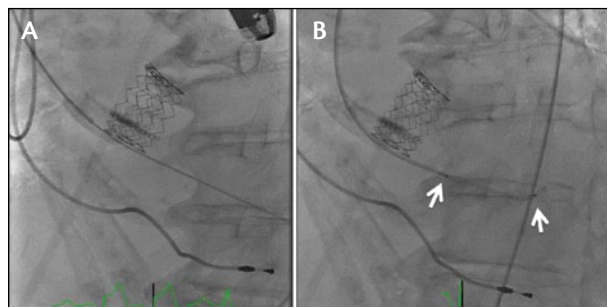


Figure 2. The hydrophilic guidewire is shown across the paravalvular leak, clearly outside of the stent frame (A). A 5-F JR4 diagnostic catheter is shown across the leak (B). The proximal and distal marker dots of the Amplatzer vascular plug 4 are still seen within the catheter (white arrows). Note that Figures 2, 3, and 4 are from the same patient. (Low profile vascular plugs for paravalvular leaks after TAVR. Feldman T et al. *Catheter Cardiovasc Interv.* 83[2]. Copyright © 2014. With permission from John Wiley and Sons, Inc.)²³

AR index approaches 0, the severity of aortic insufficiency increases (Figure 1). An AR index < 25 is associated with greater 1-year mortality.¹⁹

Echocardiography is the gold standard for assessing PVL. Accurate quantification is often difficult due to acoustic shadowing from the intact calcified native cusps and stent frame or the annulus and the common finding of multiple eccentric jets, which are irregular and nonparallel. The eccentricity of the jets often lead to their hugging of the left ventricular wall, making accurate quantification of PVL difficult and subjective. Various techniques and grading systems have been proposed, yet none have been validated or universally agreed upon. Two-year data from the PARTNER trial with the balloon-expandable Sapien THV system also demonstrate that the severity of PVL is not necessarily static over time. Among patients with baseline PVL undergoing 2-year echocardiographic evaluation, PVL was unchanged in 46.2%, improved in 31.5%, and worse in 22.4%.¹⁸

TREATMENT OF PVL

The decision to treat post-TAVR PVL is based on several factors, including presumed etiology (ie, malpositioning vs incomplete annular apposition), severity, and development of otherwise unexplained congestive heart failure in the presence of PVL. In our practice, symptoms associated with heart failure after TAVR have been the trigger for considering intervention.

Several strategies and techniques exist to mitigate post-TAVR PVL. Generally, trivial to mild PVL is well tolerated from a symptomatic standpoint and is treated conservatively with serial echocardiographic follow-up and medi-

cal therapy. Moderate to severe PVL is less well tolerated. When AR is severe immediately after valve implantation, temporary or permanent pacing at heart rates from 90 to 100 bpm may be used as a short-term measure to diminish diastolic filling time and decrease the regurgitant volume prior to more definitive measures (Figure 1).²⁰ PVL that results from grossly malpositioned valves often requires a second valve, or a so-called valve-in-valve procedure, for successful treatment. Another strategy that has been used with the CoreValve system after a too-low implantation deployment is the “snare-and-lift” technique, which uses snare traction to reposition the valve proximally.²¹

More commonly, PVL is the result of incomplete apposition of the prosthesis to the native aortic valve annulus, especially adjacent to large calcific nodules. For both balloon-expandable and self-expanding THV systems, balloon postdilation (BPD) has been used to achieve better stent expansion, with resultant reductions in the severity of PVL. This strategy has been employed both at the time of index implantation and during a later, staged procedure. BPD with a balloon-expandable THV system was associated with at least one degree of improvement in AR in 71% of patients and in residual AR < 2 in 54% of patients using a 1+ to 4+ TEE grading scale.²¹ For both self-expanding and balloon-expandable THV systems, the degree of calcification of the native valve predicts not only the need for BPD, but also its success, with the most calcified valves benefiting the least. However, the gains in reducing PVL with BPD are not without cost. BPD is associated with a trend toward higher rates of new left bundle branch block and a significantly higher rate of cerebrovascular events compared to TAVR without BPD (11.9% vs 2%).²²

For patients in whom BPD is not desirable, feasible, or effective (secondary to restrictive calcification recalcitrant to dilation), the use of percutaneous vascular plugs offers a means by which to reduce PVL. Percutaneous PVL closure is well established in the treatment of surgical prosthetic PVL. Recently, a growing body of reports and case series has described the use of vascular plugs to treat PVL in both balloon-expandable and self-expanding THV systems.²³⁻²⁶ There are unique procedural challenges presented by THV systems as compared to surgical valve prostheses. Vascular plugs utilized for PVL closure in surgical valves generally require large delivery sheaths (6–8 F). Passage of these large sheaths between the native leaflets and the outside of the THV stent frame through highly irregular and calcified channels can be difficult, if not impossible. Additionally, passage of large sheaths could result in dislodgment of the stent valve frame or embolic material.

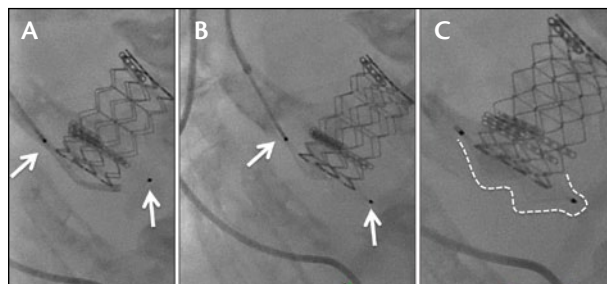


Figure 3. A 5-F JR4 catheter is being used to deliver an Amplatzer vascular plug. In panel A, the arrows denote the proximal and distal marker dots on the Amplatzer vascular plug. The distal marker has been extruded below the stent frame on the left ventricular side of the PVL. Panel B shows the Amplatzer vascular plug after deployment and that it is still attached to delivery cable. Panel C shows an enlarged view of the fully deployed and released AVP, outlined by the dotted line. (Low profile vascular plugs for paravalvular leaks after TAVR. Feldman T et al. *Catheter Cardiovasc Interv.* 83[2]. Copyright © 2014. With permission from John Wiley and Sons, Inc.)²³

The recent development of a low-profile vascular plug (Amplatzer vascular plug 4, St. Jude Medical, Inc., St. Paul, MN) has greatly facilitated the ease and success of post-TAVR PVL closure. The device can be delivered through any catheter through which a 0.038-inch wire will pass. The plug is available in unconstrained diameters of 4 to 8 mm, with constrained lengths of 12 to 21 mm. The procedure is generally performed under general anesthesia and TEE imaging. Preprocedural assessment of echocardiographic images is used to determine the location of the leak relative to fluoroscopic landmarks such as the coronary artery origins, mitral valve, and atrial septum.²³ Positioning of the vascular plugs is primarily guided by fluoroscopy, with TEE assessment of the degree of improvement and to identify additional leaks not previously recognized.

The aortic valve is accessed via a retrograde fashion, and a 5-F Judkins right or multipurpose diagnostic catheter is used in conjunction with a 0.035-inch hydrophilic guidewire to probe the stent frame and ultimately traverse the PVL channel (Figure 2). After passing the hydrophilic guidewire to the left ventricle, careful fluoroscopic and TEE assessment is performed to ensure that the wire is outside of the stent frame. A 4- to 5-F catheter is then advanced across the defect into the left ventricle and used for device delivery (Figure 3). In some cases, the diagnostic catheter will not cross the defect, and the diagnostic catheter can be exchanged for a 4-F hydrophilic Glide catheter (Terumo Interventional Systems, Somerset, NJ), which facilitates passage across the leak. Multiple reports have validated the efficacy of the Amplatzer vascular plug 4 to

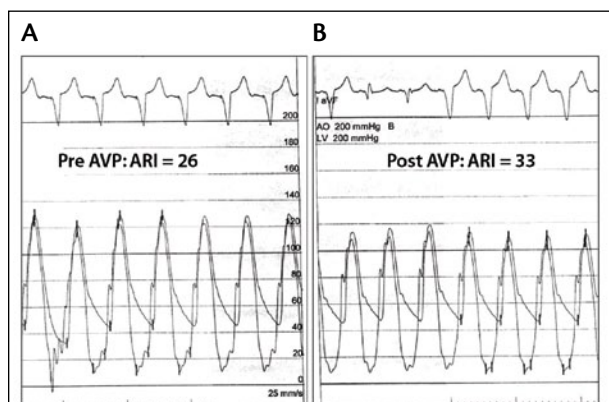


Figure 4. The AR index before and after placement of the Amplatzer vascular plug 4 for PVL. The baseline ARI was 26 (A). After reduction of PVL from severe to trace, the ARI has increased to 33 (B). (Low profile vascular plugs for paravalvular leaks after TAVR. Feldman T et al. *Catheter Cardiovasc Interv.* 83[2]. Copyright © 2014. With permission from John Wiley and Sons, Inc.)²³

treat THV PVL (Figure 4).²³⁻²⁶ More experience is needed to ascertain whether the use of vascular plugs is associated with any excess of cerebrovascular events. Our experience suggests that there is no increased incidence of stroke.

CONCLUSION

Aortic insufficiency due to PVL has emerged as an all-too-common and vexing limitation associated with first-generation THV systems. Ongoing refinement and development of second- and third-generation systems promises to drastically reduce the incidence of PVL. Unfortunately, these THV systems will not be immediately available everywhere—and certainly not soon in the United States. In the interim, treatment strategies for THV PVL are needed. BPD is the least technically demanding and will likely remain the primary initial strategy, particularly for moderate to severe PVL discovered immediately after valve deployment. The limitations of BPD include variable efficacy and an increased risk of embolic stroke. Valve-in-valve and “snare-and-lift” techniques also remain viable strategies, particularly for malpositioned valves. Percutaneous closure with a low-profile vascular plug, such as the Amplatzer vascular plug 4, is a relatively new and promising technique for resolving or mitigating THV PVL. ■

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