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EDITORIAL

Paravalvular Regurgitation Following Transcatheter Aortic Valve Replacement: Is it Still an Issue in 2018?

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Paravalvular regurgitation is considered the main Achilles' heel of transcatheter aortic valve replacement (TAVR). With the first generation of transcatheter heart valves (THVs), moderate/severe paravalvular regurgitation (PVR) occurred in 12–23% of patients and was associated with a 2–3-fold increase in mortality.[1–4] The new generation of THVs harbors new features aimed at improving the sealing between the stent and the native aortic annulus. This modification in the valve design, along with optimization of valve sizing and positioning, has contributed to a dramatic reduction in the incidence of moderate/severe PVR (1–6%) compared to the previous generation of THVs. In this issue of the *Structural Heart*, Sannino et al[5] report the results of an elegant study that analyzed the data of 911 patients undergoing TAVR in two sites and in whom PVR was graded using a 3-grade scheme: mild, moderate, and severe using the following Doppler-echocardiographic parameters: (1) number of jet(s), (2) jet path visible along the stent, (3) circumferential extent of PVR, (4) aortic regurgitation index (measured by echocardiography, (5) jet density at continuous-wave Doppler, and (6) pressure half-time (PHT) (Figure 1). The main findings of this study[5] are: (1) moderate/severe PVR occurred in 3.9% of patients and was more frequent with self-expanding versus balloon-expandable and larger versus smaller THVs, (2) neither PVR grade nor the six parameters mentioned above were associated with an increased risk of 1-year mortality, and (3) re-intervention for PVR closure occurred in 1.8% of patients and was associated with a 7.6-fold increase in mortality.

Doppler-echocardiographic parameters to grade PVR

In the present study, Sannino et al.[5] utilized six Doppler-echo parameters that have been previously proposed to assess the severity of PVR (Figure 1).[3,6–8] Each of these parameters, however, has important limitations and should not be used, in isolation, to grade PVR severity. This is the reason why the American Society of Echocardiography and Valve Academic Research Consortium recommend the use of a multi-parameter integrative approach to grade the severity of PVR[7,8] and this is what the authors applied in the present study.[5] One of the most frequently used and reported parameters of PVR severity is the circumferential extent of the PVR jet(s). However, this parameter may overestimate the severity of PVR in the case of eccentric jets and it does not account for the width of the jet(s). Hence, a wide jet with limited circumferential extent may actually correspond to worse PVR severity than a thin jet with larger extent. Some investigators suggested that the AR index is more robust than the PVR circumferential extent because it is primarily based on hemodynamics and less dependent on imaging.[6] The AR index is usually measured invasively by left heart catheterization. However, in the present study,[5] Sannino et al estimated the AR index by Doppler-echocardiography: the LV end-diastolic pressure was estimated by applying the Bernoulli formula to the end-diastolic velocity of the AR flow velocity signal obtained by continuous-wave Doppler. However, the AR index and the PHT are highly influenced by the LV compliance and diastolic dysfunction as well as the aortic compliance. A non-specific elevation of the LV end-diastolic pressure related to advanced LV diastolic dysfunction (as often encountered in patients with severe AS) or a reduced aortic compliance (as often observed in elderly patients) may result in false positive AR index or PHT. In their portfolio of Doppler-echo metrics of PVR, Sannino et al. did not include the width of the PVR jet(s) at their origin.[5] In our experience, the width of the PVR jet at its origin examined in multiple imaging views and planes is probably the most valuable parameter to assess the severity of PVR.[3]

In summary, none of the available Doppler-echo parameters are optimal and one should thus not rely on a single parameter to grade the severity of PVR. A multi-parameter strategy integrating all parameters is a reasonable but nevertheless imperfect approach. If the echo grading is inconclusive, uncertain, or discordant with the symptomatic status, one should consider other imaging modalities such as transesophageal echocardiography (TEE) that allows better visualization of PVR jets and cardiac magnetic resonance (CMR) imaging that allows quantitation of AR volume and fraction (Figure 1).

Association between PVR severity and outcomes

The vast majority of previous studies, trials, and meta-analyses reported a strong association between moderate/severe PVR and increased risk in mortality with hazard ratios ranging between 2.0 and 3.0.[1–3] Some studies even reported an association between mild PVR and mortality (hazard ratio 1.2–1.8).[1–4] The lack of association between moderate/severe PVR and mortality reported in the present study is thus very intriguing.[5] One potential explanation, rightfully proposed by the authors, is the very low

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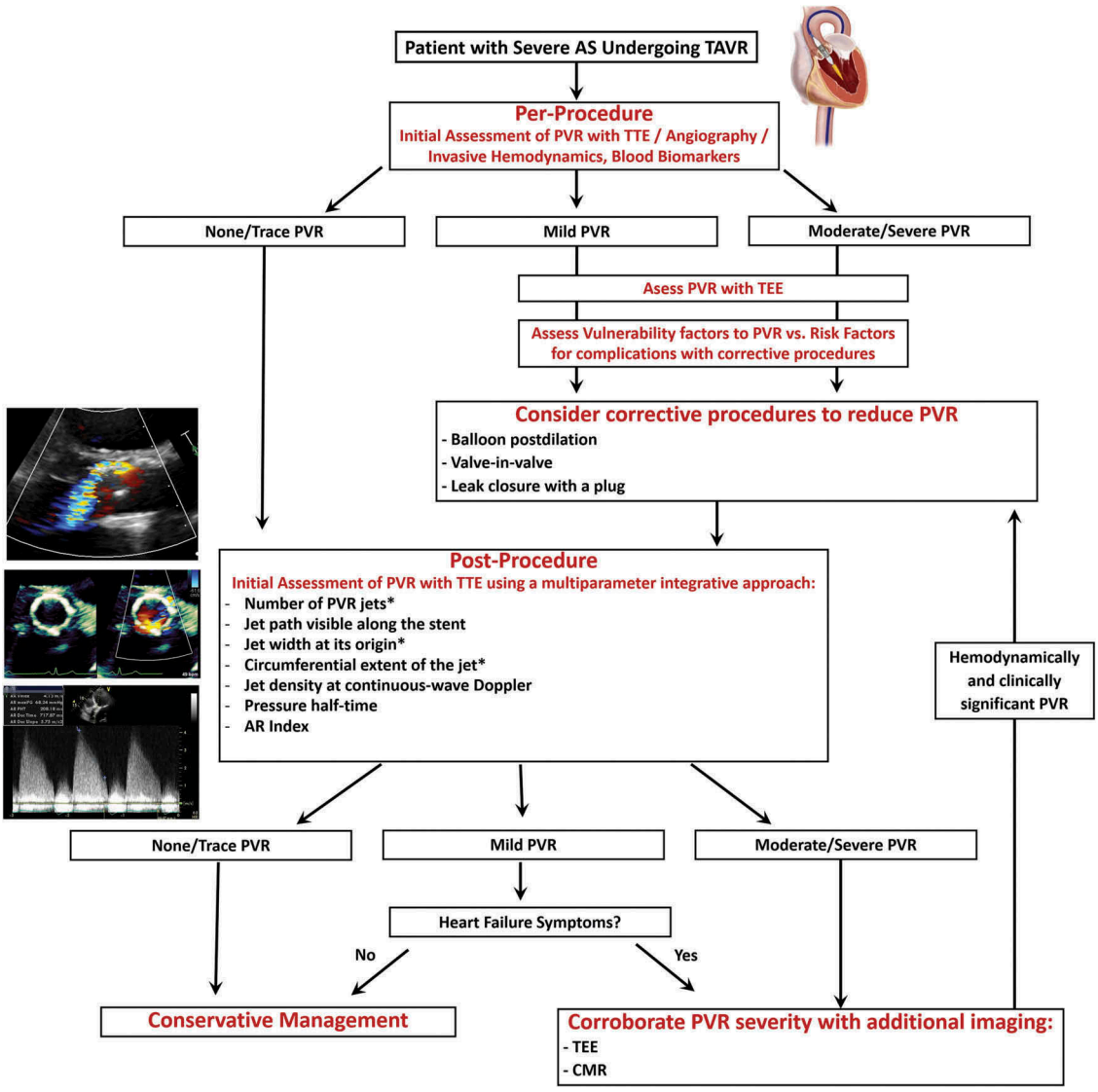

Figure 1. Proposed algorithm for the assessment and management of PVR following TAVR.

Note. *More attention and weight should be put on these parameters to grade the severity of PVR. AR, aortic regurgitation; CMR, cardiac magnetic resonance imaging; PVR, paravalvular regurgitation; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; TAVR, transcatheter aortic valve replacement.

incidence (3.9%) of moderate/severe PVR in this study. When a given complication does not exist or is rare, its impact on outcomes is absent or minimal. However, in the PARTNER 2–SAPIEN 3 registry[3], moderate/severe PVR was associated with a 2.4-fold increase in 1-year mortality, although its incidence (3.5%) was similar to that of the present study.[5] These discrepancies in the results between the SAPIEN 3 registry[3] versus the present study.[5] may be related to the following differences in the study design and methods: (1) Prospective vs. retrospective study, (2) adjudication of PVR in corelab versus site reported, and (3) inclusion of PVR jet width versus AR index among the echo metrics of PVR severity. Hence the differences between the present study[5] versus the previous ones are merely related to differences in the methods to grade the severity of PVR rather than to differences in the impact of PVR on outcomes. Furthermore, even if moderate/severe PVR, per se, was not associated with increased mortality in the present study,[5] reintervention for moderate/severe PVR was associated with a marked increase in the risk of mortality.[5] Finally, Sannino et al. only assessed the impact of PVR on mortality; they did not examine the association between PVR and other major outcomes such as heart failure rehospitalization. The results of the present study[5] should thus not lead to the conclusion that moderate/severe PVR has become benign in the contemporary era. A true moderate/severe PVR has a significant and important impact on outcomes and every effort should be made to avoid this and to eventually correct complications (Figure 1).

Clinical implications

Nowadays, the vast majority of patients have their TAVR performed under conscious sedation and TEE is no longer used to monitor the procedure and assess hemodynamic results immediately after valve deployment. Hence, if at least mild PVR is suspected by the initial imaging or hemodynamic assessment (angiography, transthoracic echocardiography [TTE], invasive AR index), additional and more comprehensive imaging

assessment with TEE should be performed to corroborate PVR severity (Figure 1). Blood biomarkers such the closure time with adenosine diphosphate (CTADP), a surrogate marker for the Von Willebrand factor, may also be used to alert the proceduralist about the presence of significant PVR after THV deployment.[9] Corrective procedures such as balloon post-dilation, or implanting a second valve, should be considered in cases with moderate/severe PVR. When the PVR is considered mild or mild-to-moderate, the decision to perform corrective procedures is based on the assessment of the ratio of vulnerability factors to PVR (no pre-existent native aortic regurgitation, small LV cavity with reduced compliance) versus risk factors for complications (i.e. annulus injury, coronary obstruction, stroke) with these procedures (Figure 1). After the procedure, PVR should be first assessed by TTE using a multi-parameter approach.[7,8] Additional imaging including TEE or CMR should be considered in the following situations: (1) patients with moderate/severe PVR, and (2) patients with mild PVR and persistent or recurring heart failure symptoms. If these additional imaging modalities confirm the presence of clinically and hemodynamically significant PVR, the corrective procedures mentioned above may be considered.

Conclusion

With the improvement in THV design, sizing, and implantation techniques, PVR is less and less an issue in 2018. However, moderate/severe PVR still occurs in up to 5% of patients in the current TAVR era, and when it occurs it is associated with increased risk of mortality and rehospitalization. The compelling data reported by Sannino et al are encouraging because they demonstrate that nowadays in the real life practice, it is possible to achieve very low rates of moderate/severe PVR and valve reintervention. However, the absence of association between moderate/severe PVR and mortality observed in this study should not be used as an argument to lower the guard against PVR. We should pursue our effort to prevent moderate/severe and even mild PVR.

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References

1. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. *J Am Coll Cardiol*. 2013;61:1585–1595. doi:10.1016/j.jacc.2013.01.047.
2. 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 Cardiovasc Interv*. 2018;91:135–147. doi: 10.1002/ccd.27336.
3. Pibarot P, Hahn RT, Weissman NJ, et al. Association of paravalvular regurgitation with 1-year outcomes after transcatheter aortic valve replacement with the SAPIEN 3 valve. *JAMA Cardiol*. 2017;2:1208–1216. doi:10.1001/jamacardio.2017.3425.
4. Kodali S, Pibarot P, Douglas PS, et al. Paravalvular regurgitation after transcatheter aortic valve replacement with the Edwards Sapien valve in the PARTNER trial: characterizing patients and impact on outcomes. *Eur Heart J*. 2015;36:449–456. doi:10.1093/eurheartj/ehu384.
5. Sannino A, Stoler R, Vallabhan R, et al. Assessment of the severity of paravalvular regurgitation and its role on survival after transcather aortic valve replacement. *Struct Heart*. 2019;3: this issue.
6. Sinning JM, Hammerstingl C, Vasa-Nicotera M, et al. Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation. *J Am Coll Cardiol*. 2012;59:1134–1141. doi:10.1016/j.jacc.2011.11.048.
7. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. *Eur J Cardiothorac Surg*. 2012;42:S45–S60. doi:10.1093/ejcts/ezs533.
8. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for non invasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr*. 2017;30:303–371. doi:10.1016/j.echo.2017.01.007.
9. Van Belle E, Rauch A, Vincent F, et al. Von Willebrand factor multimers during transcatheter aortic-valve replacement. *N Engl J Med*. 2016;375:335–344. doi:10.1056/NEJMoa1505643.