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EDITORIAL COMMENT

A Big Step Forward in the Validation of the Transcatheter Valve-in-Valve Procedure for the Treatment of Failed Surgical Bioprostheses*

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The transcatheter valve-in-valve (VinV) procedure has become a valuable alternative to redo surgery for the treatment of failed surgical bioprostheses. In the recent focused update of the American College of Cardiology/American Heart Association guidelines for the management of valvular heart disease, the VinV procedure was considered a reasonable option (Class IIa, Level of Evidence: B) for severely symptomatic patients with severe bioprosthetic aortic valve dysfunction judged by the heart team to be at high or prohibitive risks (1). The surgical bioprostheses often have a small internal orifice diameter and a nonelastic stent, which may limit the size and expansion of the transcatheter heart valve (THV) that is implanted inside the failed bioprosthesis. This may, in turn, result in suboptimal hemodynamics and high transaortic gradients following aortic VinV. Indeed, elevated gradients are common after VinV and are associated with increased mortality in the VIVID (Valve-in-Valve International Data) registry (2).

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In this issue of *JACC: Cardiovascular Interventions*, Deeb et al. (3) report compelling data from the CoreValve U.S. Expanded Use Study, which was a prospective, nonrandomized study that enrolled 233 patients with symptomatic surgical valve failure who were deemed unsuitable for reoperation (3). In this series, transcatheter VinV procedure with the self-expanding CoreValve THV (Medtronic Inc., Minneapolis, Minnesota) was associated with low rates of mortality (2.2% at 30 days and 14.6% at 1 year) and major stroke (0.4% at 30 days and 1.8% at 1 year). These results are even more impressive given the fact that about one-third of the patients had a small surgical valve (3), a factor that has been previously associated with poor outcomes (2). At 30 days after VinV, still a relatively high proportion (32.3%) of patients in this series had high transaortic gradients (mean gradient ≥20 mm Hg), 3.5% had moderate aortic regurgitation, and 8.1% had a new permanent pacemaker implant. The patients also harbored a spectacular improvement in quality of life following the VinV procedure with an average increase of 30 points in the Kansas City Cardiomyopathy Questionnaire (KCCQ) compared to baseline. High residual gradient after the VinV procedure was associated with less improvement in KCCQ but had no significant impact mortality.

Besides the excellent clinical and functional outcomes achieved by the VinV procedure in this series (3), one of the most striking findings of this study is the impact of pre-existent prosthesis-patient mismatch (PPM) (i.e., PPM of the surgical valve) on the post-procedural outcomes. PPM refers to a prosthetic valve that has a normal function but is too small in relation to patient's body size and thus in relation to patient's cardiac output requirements. PPM is generally defined with the use of the prosthetic valve effective orifice area (EOA) divided

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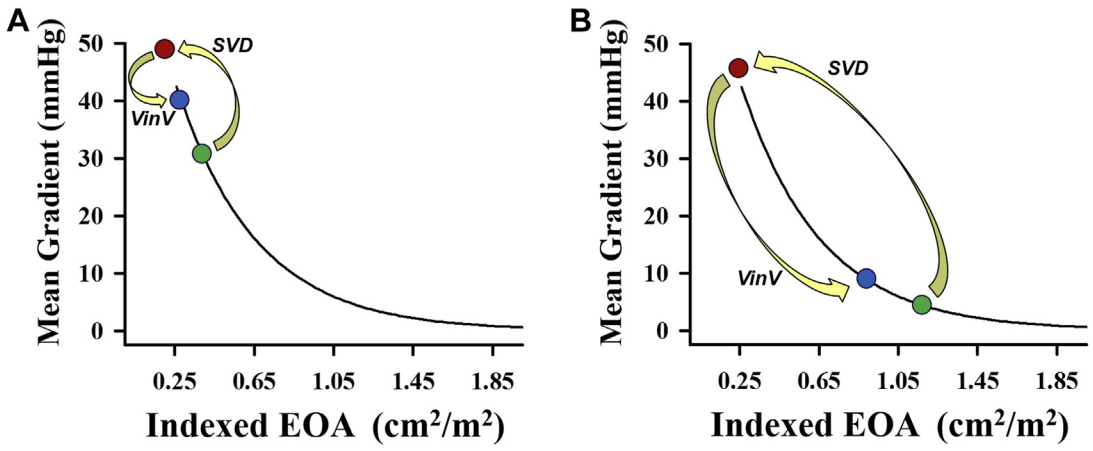
FIGURE 1 Effect of Pre-Existent PPM on Hemodynamic Outcome Following VinV Procedure



(A) A patient with pre-existent severe prosthesis-patient mismatch (PPM) of the surgical valve. This patient already has a small indexed effective orifice area (EOA) and moderately high gradient at 30 days post-initial surgical aortic valve replacement (AVR) **(green circle)**. With structural valve degeneration (SVD) and stenosis of the surgical valve, there is further decrease in EOA and increase in gradient (**red circle**; echo before the valve-in-valve [VinV] procedure). The VinV procedure in this patient results in only modest decrease in gradient (**blue circle**; echo 30 days post-VinV) because most of the elevation in gradient is related to the pre-existent PPM, which is not corrected by the VinV. Compared to the echocardiogram 30 days post-surgical AVR, the indexed EOA is somewhat smaller and the gradient is higher after the VinV procedure because there is inherent loss of EOA associated with the implantation of the transcatheter valve inside the already small orifice of the surgical valve. **(B)** A patient with no pre-existent PPM. In this patient, the severely elevated gradient observed before VinV procedure is mainly related to an acquired prosthetic valve stenosis and the VinV procedure in this patient is associated with a major reduction in gradient and thus hemodynamic and clinical benefits.

by the patient's body surface area and an indexed EOA ≤0.85 cm^2/m^2 is consistent with moderate PPM, whereas a value ≤0.65 cm^2/m^2 indicates severe PPM. In the present study, the authors did not have access to the data of the EOAs of the surgical valves measured early (discharge or 30 days) after the index surgical aortic valve replacement (AVR) (3). So to define PPM, they used the predicted EOA (i.e., the normal reference value of EOA for the model and size of implanted bioprosthesis) indexed to the patient's body surface area. This predicted PPM approach has been well validated and has been shown to associate with outcomes following AVR (4). In the present study, 13% of patients had a pre-existent severe PPM according to the indexed predicted EOA and 42% of patients had moderate PPM (3). The vast majority (77%) of the patients with pre-existent severe PPM had high residual gradient after the VinV procedure. Furthermore, PPM, and especially severe PPM, was associated with 2-fold lower increase in the KCCQ score at 6 months. Further studies including a larger number of patients are needed to determine whether pre-existent PPM has a significant impact on survival following the VinV procedure.

PPM may actually constitute a "triple trouble" for the patients undergoing surgical AVR with a bioprosthetic valve:

- First trouble: Severe PPM is associated with a 1.8-fold increase in mortality and 1.6-fold increase in heart failure rehospitalization after AVR (4).
- Second trouble: PPM may accelerate the structural degeneration of bioprostheses, most likely because PPM increases the flow turbulence through the valve orifice as well as the mechanical stress on the valve leaflets (5). Leaflet mechanical stress is an important factor contributing to the structural degeneration of bioprostheses.
- Third trouble: As very well demonstrated in the present study (3), pre-existent PPM may compromise the hemodynamic and clinical outcomes after the VinV procedure. This procedure can successfully correct an acquired prosthetic valve regurgitation or stenosis caused by structural degeneration but it cannot correct a pre-existent PPM, which is a sequela of the initial surgical AVR (**Figure 1**). In fact, the VinV procedure will often worsen the pre-existent PPM. Indeed, a patient with pre-existent severe PPM has a small indexed

EOA even if the surgical valve is functioning normally. In this patient with little "EOA reserve," a VinV procedure will further and ineluctably reduce the indexed EOA and result in somewhat worse hemodynamics and higher gradients compared to what was observed at the outset of the initial surgical AVR (**Figure 1**).

In the VIVID registry, the effect of pre-existent PPM was not assessed but potential surrogate markers of PPM were found to be associated with mortality including: small (≤21 mm) label size and stenosis as the failure mode of the surgical valve (2). In this registry, patients with high transprosthetic gradients were generally considered having a severe acquired prosthetic valve stenosis due to calcific degeneration of valve leaflets. However, it is likely that in a high proportion of these patients, the elevated gradient was related, at least in large part, to pre-existent PPM. In such patients, a VinV procedure will result in minimal or no reduction or even an increase in gradient (**Figure 1**).

The unprecedented outstanding results obtained by Deeb et al. in this series (3) further buttress the value and indication of the VinV procedure as an alternative to surgery for patients with failed surgical bioprostheses being at high or extreme surgical risks. This study also reveals suboptimal hemodynamic and functional outcomes in patients with pre-existent severe PPM of the surgical valve.

Pre-existent PPM may accelerate the degeneration of the surgical bioprosthetic valves and therefore increase the need for the VinV procedure. Moreover, it may compromise the hemodynamic and clinical results of the VinV procedure. These findings thus emphasize the importance to systematically integrate the information about pre-existent PPM in the risk stratification and procedure planning for the VinV procedure. In patients with pre-existent severe PPM, the balance between risks versus potential benefits should be carefully discussed by the Heart Team. If a decision is ultimately to proceed with VinV in such patients, a THV with supra-annular design, such as the CoreValve, and high valve positioning might be preferred. A randomized trial would be needed to compare the hemodynamic and clinical outcomes of the VinV procedure using a balloon-expandable THV versus a self-expanding THV.

The proportion of biological AVR is rapidly growing, including in the younger population. One of the main reasons for this current trend is the emergence of the transcatheter VinV procedure as a valuable alternative to redo surgery in the case of surgical valve failure. However, the implantation of a bioprosthetic valve with a too small EOA in relation to patient's body size at the time of the surgical AVR would considerably limit or even offset the hemodynamic and clinical benefits of a future VinV procedure. The findings of this study thus provide strong argument in support of the prevention of PPM, and especially severe PPM, at the time of the surgical AVR. Hence, the surgeons should make a particular effort to implant a bioprosthetic valve with the largest possible EOA in relation to patient's body size.

For those patients with severe pre-existent PPM and failed bioprosthetic valves, some investigators have proposed to crack the ring of the bioprosthesis by means of an ultra-high-pressure oversized balloon before the VinV procedure. This approach permits to enlarge the inner diameter of the surgical valve orifice and therefore optimizes the hemodynamic results of the VinV procedure. It should, however, be used with caution to avoid aortic annulus injury. Prosthetic valve manufacturers are also currently developing new generations of surgical bioprosthetic valves with expansible stents to optimize the outcomes of a potential future VinV procedure.

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