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EDITORIAL COMMENT

Many Valves Make Heavy Work*

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In this issue of *JACC: Case Reports,* Nagaraja et al[1] describe performing a transcatheter aortic valve in transcatheter aortic valve replacement, a paravalvular leak closure, a transcatheter mitral valve replacement in mitral annular calcification (TMVR ViMAC), and iatrogenic atrial septal defect closure. By any account, it is a good day's work. Each piece in this puzzle deserves its own attention, but in many ways the decisions that go into mixing and matching these procedures and the timing thereof are what may separate the wheat from the chaff. The prevalence of degenerative mitral annular calcification (MAC) has been found to be high patients who undergo transcatheter aortic valve replacement (TAVR).[2] This can be attributed to age, hypertension, chronic kidney disease, and radiation.[3,4] Simplistically, however, if calcific valvular heart disease is a systemic process, it should come as no surprise that it would be hemodynamically relevant sooner in a 23-mm diameter aortic valve than in a 30- or 35-mm diameter mitral valve. Of course, that does not account for fluid dynamics and pressure differentials across the various valves but may help us understand the blossoming epiphenomenon of calcific mitral stenosis that appears to be evolving among patients with previous aortic valve replacements, as is the case here.

As the structural heart space continues to evolve, we seem to be shedding care patterns borne from decades of surgical valve replacement. In many centers, pre-TAVR coronary angiography has been abandoned in low-risk individuals or patients with worrisome kidney function. Similarly, ideas around staging treatment of polyvalvular heart disease can be conceived of very differently when a catheter-based approach is selected. Had this patient originally gone to surgical aortic valve replacement in 2011, would they have also treated the mitral valve? Perhaps not. It is unclear how stenotic the mitral valve was at the time, but they may have if stenosis was already evident. In the structural heart space, when it is clear that 1 valve is worse than another, working incrementally makes sense to minimize risk and avoid premature biologic valve degeneration.

However, there may be an exception to this rule when it comes to mitral valve replacement. As experience grows using off-label balloon-expandable valves in the mitral position, it has become clear that the primary risk of this procedure is left ventricular outflow tract obstruction (LVOTO).[5] The incidence of LVOTO has been reported at roughly 11%, although may be as high 39.7% in early experience, and it is strongly associated with mortality in these initial studies.[5] In our early experience, 14% of patients had LVOTO, although many of these cases predated contemporary risk assessment.[6] Nevertheless, because LVOTO is such a devastating complication, it is worth mitigating this risk as much as possible. To that end, a pre-existing aortic valve gradient would serve only to compound any iatrogenic outflow tract gradient caused by TMVR, and as such, we have taken to treating aortic valve disease (whether moderate native aortic valve stenosis or degenerating bioprosthetic valve stenosis) aggressively before engaging in TMVR, just as Nagaraja et al[1] report doing in the associated case report.

A multimodality imaging approach is pivotal in the preprocedural planning of such cases, especially to overcome the limitations of the different imaging techniques, properly identify and understand the mechanism of valvular dysfunction, and understand the risk of potential complications such as LVOTO or

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valve embolization or migration.[7,8] In the present case, preprocedural computed tomography analysis revealed a wonderfully large neo-left ventricular outflow tract (LVOT) area and mitral annular sizing reasonable for a 29-mm Sapien valve (Edwards Lifesciences). A neo-LVOT <220 mm^2 or a long anterior mitral leaflet length (>22 mm) should be considered high risk for LVOTO.[5,6] If there is a potential risk of LVOTO, advanced techniques such as alcohol septal ablation can be performed in advance of TMVR, or LAMPOON (Intentional Laceration of the Anterior Mitral leaflet to Prevent left ventricular Outflow tract ObstructioN) can be performed at the time of TMVR (or both can be used) to reduce the risk of LVOTO.[9,10]

The TMVR Registry and the TMVR in MAC Global Registry describe the highly comorbid nature of the patients undergoing ViMAC TMVR, including high rates of chronic kidney disease (53.2%), chronic obstructive pulmonary disease (44.8%, 43.2%), and diabetes (32.8%, 46%). The average Society of Thoracic Surgeons score ranged from 10.1% to 15.3% among cohorts, with over 90% of patients reporting New York Heart Association functional class III or IV symptoms.[11,12] Procedural success, defined by the MVARC (Mitral Valve Academic Research Consortium) guidelines, ranged from 62% to 76%, a rate considerably lower than that of valve in valve TMVR procedures (94% in the TMVR registry). One reason for this discrepancy include the anatomic complexity which is, by its nature noncircular, irregularly calcified, and varied from patient to patient. Thus, the initial experience has been fraught with valve embolization (6.9%), conversion to open surgery (8.6%), and residual significant mitral regurgitation (13%). Reported 30-day mortality exceeded 25% in both registries, although in our own experience, patients who leave the hospital tended to do very well at both 30 days and 1 year.[5]

As with all structural procedures, we have collectively learned from our initial experience. This includes progress in preprocedural imaging and selection criteria, adjunctive procedures, and procedural technique. The initial publication from the TMVR in MAC Global Registry saw a 12% absolute reduction in all-cause mortality comparing the first half to the second half of the cohort (2011-2017). More recently, the MITRAL (Mitral Implantation of Transcatheter Valves) trial prospectively followed 31 patients with TMVR ViMAC treated by transatrial or transseptal access for 1 year.[13] The study reported a 6.7% 30-day and 26.7% 1-year mortality rate for transseptal ViMAC (compared with 21.4%, 38.5% for transatrial access), with 80% technical success and significantly reduced rates of second valve implantation (6.7%) with no valve embolization, conversion to surgery, or paravalvular leak closure.

In conjunction with newer techniques, newer devices offer promise for these patients with MAC. Of course, these new devices will then force further technical innovation. For example, LAMPOON will not help if all devices have a “closed-cell” structure, and our attention will need to shift further to the intraventricular septum. Hopefully, new devices and new techniques will also drive further study of this complex disease state. The future of valvular imaging and structural heart disease is extremely exciting but will likely become only more difficult as we learn how to improve on what we have been doing and how to find new options for diseases not routinely addressed to date.

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