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EDITORIAL COMMENT

Aortic Valve Replacement in an Era of Rapid Innovation

Better the Devil You Know*

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Iterative and transformative innovations in prosthetic valve design have resulted in improved long-term outcomes for patients with heart valve diseases. Nonetheless, astute clinicians will often warn their patients that there is no real "cure" for aortic valve disease; there is only a substitution toward a more benign disease that is a prosthetic heart valve. The clinical indication for aortic valve replacement for any individual patient is often very clear. The "how" is more complex as the selection of type of prosthesis and optimal method of delivery for an individual patient has become much more complicated in recent years. Physicians have an exponentially growing toolbox to treat heart valve disease. The landscape is rich with a growing list of readily available valve prostheses, particularly when selecting an aortic bioprosthesis. Use of a "heart team" approach for such complex decisions is sometimes beneficial (1).

Each aortic bioprosthesis has subtle differences in biomaterial sources (bovine pericardium or porcine valve), configuration (stented, stentless, or sutureless), and varied proprietary processing strategies with anticalcification treatments to help delay or prevent structural valve degeneration (SVD). Surgeons often show a preference for a particular bioprosthesis based on ease of implantation as specific to their own technical approaches, experiences, training, and eccentricities. It is sometimes difficult to navigate through the considerable marketing hype in this area and identify pragmatic innovations in design that can actually enhance outcomes. Not all valve innovations are beneficial; let us not forget the unfortunate saga of silver-coated sewing rings (2). Surgical aortic valve replacement (SAVR) with a

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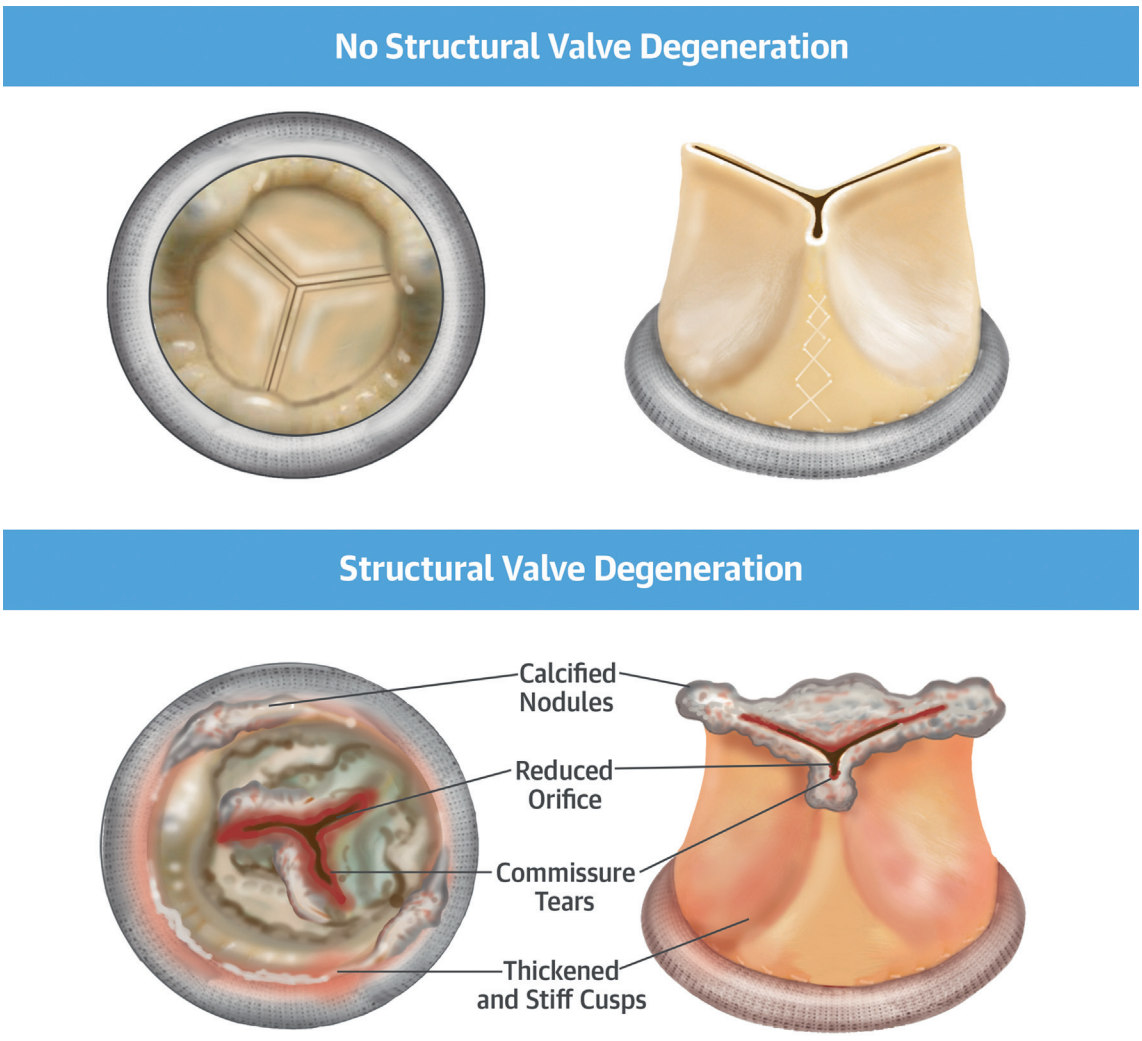
FIGURE 1 SVD of a Bioprosthetic Aortic Valve



(Upper panels) Mitroflow bioprosthesis without any structural valve degeneration (SVD). **(Lower panels) Left:** Mitroflow bioprosthesis with severe SVD showing a reduced orifice area. Extensive calcified nodules are noted, particularly at the cusp commissures. **Right:** Infiltration and diffuse thickening of the 3 aortic bovine pericardial cusps results in severe stiffening and valve dysfunction with stenosis. Cusp tears at the sewn commissures are also a common mode of failure for the Mitroflow bioprosthesis.

biological valve can now be performed with an exceedingly low procedural risk in experienced hands. As such, the challenge for the treatment of aortic valve disease is not the SAVR procedure itself but rather the unpredictable long-term fate of the slowly degenerating aortic bioprosthesis. SVD is the sine qua non of the disease inherent to a bioprosthesis and the Achilles heel for its use in patients with aortic valve disease (Figure 1), especially when they are on the younger end of the age spectrum.

Which valve bioprosthesis is the most benign with the lowest risk of SVD? In the era of precision medicine, can we inform patients and direct them toward prostheses that are perhaps more benign in them compared with others? Can we use evidence-based decisions to direct appropriate patients toward a mechanical prosthesis when the risk of SVD is high? We are faced with rapid disruptive innovations in which novel devices can be used in clinical practice long before the real-world risk of SVD is

apparent. We must be prudent in our selection of a bioprosthesis—it is still a devilish disease. Therefore, it is imperative that we continually and objectively evaluate the long-term results of implanted aortic bioprosthetics.

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To that end, in this issue of the *Journal*, Rodriguez-Gabella et al. (3) from Laval University provide timely, important, and practical data reflecting 10-year clinical outcomes for a large group of consecutive patients (>600) undergoing bioprosthetic SAVR. The study was performed at a single center with high volumes and established surgical excellence in clinical outcomes. To better know this devil, the study endpoints were the prevalence and timing of SVD in addition to patient survival. How benign is an aortic bioprosthesis? Clinically important SVD was manifest in only 6.6% of patients. More than 30% showed evidence of subclinical SVD according to echocardiography. These data suggest that a contemporary bioprosthesis is indeed a benign disease with excellent long-term durability. Interestingly, the mean age at the time of SAVR was 72 years, and a majority of the patients died by 10 years of follow-up. Most deaths were not cardiac related, suggesting that the aortic valve disease was well treated with SAVR. For the vast majority of patients, there is an excellent durable result, and it is unlikely that clinically important SVD will occur within their lifetime. The possible impact of the data for this rapidly emerging field of AVR is compelling. As such, this study will serve as a critical benchmark for SAVR using a contemporary bioprosthesis.

Previous studies with similar intentions have generated comparable datasets. However, the majority of earlier assessments of a bioprosthesis have focused on a single bioprosthesis with no direct contemporary comparison. Many of these previous studies seem to avoid direct head-to-head comparisons between competing devices. In addition, many are confounded by constrained definitions of SVD. SVD as defined according to rates of reoperation alone may be misleading and poorly sensitive as many patients may experience SVD and not receive a reoperation. SVD may not always be clinically significant, requiring repeat intervention. Subclinical disease may serve as a "canary in a coal mine" and should be reported. The work of Rodriguez-Gabella et al. (3) bridged this gap by assessing SVD in multiple ways, including echocardiographic changes over time, resulting in a more robust analysis.

Multivariable analysis was successful in defining important variables that may influence outcomes (3). Interestingly, the Mitroflow bioprosthesis (older generation without anticalcification treatments) was a predictor of important SVD. To improve hemodynamics, the Mitroflow valve was created with the bovine pericardium on the outside of the valve frame compared with a more traditional design placed within the valve housing. This finding of accelerated SVD is consistent with numerous other reports and highlights the importance of post-marketing surveillance and prudence when selecting a modified bioprosthesis (4). We cannot always assume a new valve design is a better design, even if the modifications are subtle and stepwise. The devil is in the details.

For younger patients, the clinical decision strategy becomes more complicated, with novel surgical approaches such as minimal access incisions with rapid deployment valves and surgically implanted sutureless valves that may best prepare for a future valve-in-valve (VIV) transcatheter aortic valve replacement (TAVR) procedure if required. In this analysis (3), younger patients (<65 years of age) showed a higher prevalence of clinically relevant SVD. The clinical momentum for primary TAVR in younger patients should be tempered by these data. Furthermore, recent data show that younger patients may have an important long-term survival benefit from a mechanical valve prosthesis (5). Understanding contemporary rates of SVD is critical for patients and physicians to make informed decisions when selecting a type of prosthesis. Both patients and resource-challenged health care systems can benefit from the "one and done" approach offered by a mechanical solution.

Innovation has also reached aortic mechanical valves, and they should not be dismissed as archaic and outdated (6). For example, the On-X bileaflet mechanical aortic prosthesis (CryoLife Inc., Kennesaw, Georgia) has superior hemodynamics and can tolerate reduced anticoagulation (international normalized ratio: 1.5 to 2.0), resulting in a 65% reduction in bleeding risk with no increase in thromboembolism (7). Dual antiplatelet therapy is also being explored for this mechanical aortic prosthesis (NCT00291525). The prospect of a future valve-in-valve TAVR to address SVD has helped encourage more aggressive use of bioprosthetic SAVR in younger patients. This approach must be questioned with both the knowledge of recent innovations in mechanical valve design and the clear limitations of valve-in-valve TAVR with respect to smaller valve size, anatomic hazards, and unclear long-term hemodynamics and durability. As such, TAVR for SVD should not be used as a touchstone for selection of a bioprosthesis over a mechanical prosthesis for SAVR in younger patients.

We must be vigilant and more rigorous in our clinical studies of each and every aortic bioprostheses, recognizing that it is still a disease. In this era of rapid innovation, expertise-based randomized clinical trials may help facilitate improved evidence-based decisions for aortic valve interventions (8). The devil you know is better than the devil you do not.

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