Commentary: Don’t count your chickens before they hatch

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Aortic valve disease requires lifelong management with a growing armamentarium of treatment strategies to avoid reoperation and anticoagulation. In a recent clinical trial, investigators evaluated the 5-year outcomes of using a novel bioprosthetic valve with RESILIA tissue to prevent structural valve deterioration (SVD). They reported an astonishing 100% freedom from SVD and 98.7% freedom from all-cause reintervention.1 Building on these near-perfect results, Beaver and colleagues2 have presented their findings at the 7-year mark for this patient cohort, although with some caveats.

Bioprosthetic valves are often favored by patients because these valves avoid the need for anticoagulation. However, these valves have an increased risk of SVD and earlier reoperation. SVD is a complex process. After traditional preservation, xenograft cell death occurs with the loss of calcium-dependent ATPase channels and the gradual influx of calcium into the cells. Intracellular calcium buildup, in turn, leads to precipitation with inorganic phosphates and hydroxyapatite formation, resulting in dystrophic calcification. Mechanical degradation plays an additional role, independent of calcification. During chemical treatment, xenografts lose glycosaminoglycans and elastin, which affects their pliability and mechanical stress response. This mechanical damage accelerates calcium deposition on damaged collagen and elastin fibers, worsens hemodynamics, increases valve stress, and initiates the vicious cycle of SVD. Moreover, host immune responses trigger the complement cascade, platelet adhesion, valve inflammation, and fibrovascular tissue outgrowth, resulting in pannus formation.3

In the study by Beaver and colleagues,2 patients from the COMMENCE trial were reconsented with evaluation of their valve durability and hemodynamics at a mean follow-up of 7.7 years. The authors report 99.3% freedom from SVD at 7 years, suggesting a sustained immunity to degradation. Notably, SVD was based on reintervention due to structural dysfunction, which may be a conservative assessment and, thus, underestimate the true degree of SVD. However, the rate of aortic regurgitation, which is an early indicator of SVD, was miniscule; 96.8% of patients had no evidence of aortic regurgitation, suggesting that hemodynamic deterioration may also be low. Previous meta-analyses assessing the long-term outcomes of stented aortic bioprostheses have suggested that SVD may not present until after 8 years and progresses more rapidly after 10 years.4,5 Therefore, mid-term outcomes may not be the best for predicting future sustainability, although a 99.3% freedom from SVD at 7 years is reassuring.

The choice between mechanical and bioprosthetic valves is most often a decision based on current guidelines and is made by clinicians and their patients between 50 and 65 years of age.6 Although mechanical valves may avoid SVD and potential reoperation, they require therapeutic anticoagulation with the added risk of bleeding and thrombotic events. Therefore, developing a durable bioprosthetic valve could be highly beneficial in managing this patient group. Although the study by Beaver and colleagues2 showed excellent freedom from SVD, the patient cohort comprised only one-third of patients between 50 and 65 years of age, with almost 60% of patients older...
than 65 years of age. Typically, younger patients require more “use” of their valve, which may play a speculative role in the progression of their respective SVD. Moreover, patients in this age group are likely to require reoperation at a later time, unless their valve remains SVD-free decades after implantation. Only time will tell if the bioprosthetic valve with RESILIA tissue is the right fit for these unique patients.

A major limitation of the trial update by Beaver and colleagues is that follow-up data from only 195 patients were obtained, compared with the original enrollment of 689 patients and the 5-year follow-up of 512 patients. A couple of factors played into this loss of follow-up, including the effect of the coronavirus disease 2019 pandemic on the logistical resources needed to continue following these patients. The reported freedom from SVD at 7 years is impressive for those patients who continued to be followed, but the limited number of patients warrants caution when interpreting these results. Nonetheless, the trial follow-up results at 7 years are encouraging. As technologies expand to address aortic valve disease and its lifetime management, treatment options that can avoid both anticoagulation and reoperation in younger active patients will become the choice therapy.

**Conflict of Interest Statement**

The authors reported no conflicts of interest.

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**References**