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APPENDIX

For supplementary videos and their legends, please see the online version of this article.

Surgical Threshold for Bicuspid Aortic Valve–Associated Aortopathy

Does the Phenotype Matter?

We read with great interest the paper by Hardikar and Marwick (1) published in a recent issue of *iJACC*. The authors should be congratulated for their efforts to address the controversial issue of bicuspid aortic valve (BAV)–associated aortopathy in their current meta-analysis. This report is based on a systematic review of the published literature on BAV aortopathy, with a special focus on aortic-related events during long-term follow-up. The most important finding of this meta-analysis is the very low risk of adverse aortic events in patients with BAV disease, which is in contrast to the widespread perception that exists in the cardiovascular—and in particular the cardiac surgery—community. Indeed, some have even incorrectly equated this risk with that observed in patients with connective tissue disorders (e.g., Marfan syndrome). Hardikar and Marwick (1) were able to identify BAV patients that were at higher risk of aortic events, however, according to patients' age and clinical setting.

The major limitation of the aforementioned meta-analysis is the heterogeneity of the published literature on BAV-associated aortic disease. Such heterogeneity was partially addressed by means of stratification by stage of BAV disease (i.e., nonoperated vs. post-operative BAV patients). However, major heterogeneity also exists within the post-operative patients, as demonstrated by the highly significant I^2 statistic (1). In our experience, this phenomenon may be explained by the fact that different forms of BAV disease (so-called BAV phenotypes) are frequently mixed together in published reports (2). The 2 distinct clinical entities of BAV disease, namely, BAV in patients presenting with predominant aortic valve stenosis and dilation of the supra-coronary aorta (i.e., BAV stenosis phenotype), and BAV in patients presenting with predominant aortic insufficiency and dilation of the proximal aortic root (i.e., BAV root phenotype), are characterized by major differences in the patterns and the prognosis of associated aortopathy (3,4). However, very few published studies to date have separately analyzed these 2 distinct patient subgroups.

Hardikar and Marwick (1) used the age of BAV patients as an additional clinical variable to stratify the outcomes of BAV-associated aortopathy. However, age may also be interpreted as an indirect marker of the different BAV phenotypes. Evidence of this can be found in the fact that BAV patients who required aortic root surgery for aortic regurgitation were in the 5th decade of life, whereas patients undergoing isolated aortic valve replacement for BAV stenosis were in their 6th decade. Such findings are also in line with previous reports showing that aortic root dilation with resultant aortic valve insufficiency (i.e., root phenotype) is predominantly found in young, male BAV patients and is associated with a genetic form of BAV-associated aortopathy (3,4).

The finding from Hardikar and Marwick (1) that aortic dimensions progress more rapidly with increasing age of BAV patients may be somewhat misleading and should be interpreted with a caution. The proposed correlation between the rate of aortic enlargement and increasing age may be explained by the fact that the 2 referenced reports by La Canna et al. (5) and Davies et al. (6) included patients with dilated BAV aortas only. It is generally accepted that diameters of already dilated aortas progress more rapidly; this, rather than just patient age, may account for the accelerated growth of the proximal aorta observed in these studies. The annual growth rate of aortic dimensions in distinct clinical phenotypes (i.e., BAV stenosis vs. root phenotype) would be of great clinical value and should be a focus of future studies.

With the literature that is currently available, it is very difficult to accurately define surgical thresholds for BAV-associated aortopathy, because most of the published studies consist of mixed BAV phenotype cohorts and different stages of BAV disease. We strongly recommend a more homogeneous phenotype-specific reporting of outcomes in BAV disease in future studies.

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REPLY: Surgical Threshold for Bicuspid Aortic Valve–Associated Aortopathy: Does the Phenotype Matter?

We would like to thank Drs. Girdauskas and Borger for their interest and comments regarding our paper (1). We also concur regarding the main message of the meta-analysis, which is that aortopathy associated with bicuspid aortic valve has very low adverse event rates—contrary to the perception that this disease is analogous to connective tissue disorders. This main finding is not compromised by the heterogeneity of the literature.

The significant heterogeneity in the literature is not restricted to aortic stenosis and regurgitation, but also involves bicuspid aortic valve morphologies, as well as the nature of the underlying tissue. Indeed, we found that aortic regurgitation was reported in an older age group—had we focused on aortic valve repair publications, we would have an entirely regurgitant population subset. Similarly, had we taken a subgroup of publications from younger age groups, we would have had a stenosis-predominant subset. Only a few authors have looked at stenosis only (2), and hence, it was difficult to compare these subsets without the heterogeneity. An individual patient meta-analysis would overcome the dependence of standard meta-analysis on the case-mix of the original data, but the performance of this would require more effective data archiving than is the current practice.

We agree that the relationship of age with aortic diameter could be confounded by other factors (3,4). However, as those factors also change with age, we thought that age might be a reasonable marker to increase the clinician's alertness. We hope that once we have sufficient longitudinal data from registry studies, these relationships could be analyzed with more accuracy.

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Intracardiac Echo and Reduced Radiocontrast Requirements During TAVR

Acute kidney injury (AKI) is an independent predictor of mortality after transcatheter aortic valve replacement (TAVR) (1,2) and can be curbed by significantly reducing the amount of contrast agent (3). Intracardiac echocardiography (ICE) appears to match the TAVR workflow (4), provides the highest image resolution, and requires only local anesthesia. It is hypothesized that: 1) ICE is capable of effectively guiding TAVR, reducing the radiocontrast agent requirements; 2) low-contrast TAVR can minimize the risk of AKI; and 3) this strategy is safe and can improve the outcome of TAVR.

Sixty consecutive patients underwent transfemoral or transapical TAVR. In all patients, Edwards Sapien Transcatheter Heart Valves (Edwards Lifesciences, Irvine, California) were implanted. Subjects were randomized in a ratio of 1:1. In group 1, angiography served as the primary and ICE as the complementary guiding tool. In group 2, TAVR was primarily guided by ICE and complemented by angiography at the beginning of the procedure. If needed, angiography was repeated after valve deployment. Longitudinal views (4) served as primary ICE views and after deployment, short-axis views of the prosthetic valve were obtained (Online Video 1). In group 2, a pigtail catheter advanced into the noncoronary cusp identified the level of the valvular annulus. Repeat angiography was performed as needed only in group 1. AKI was graded as proposed by the Valve Academic Research Consortium (5).

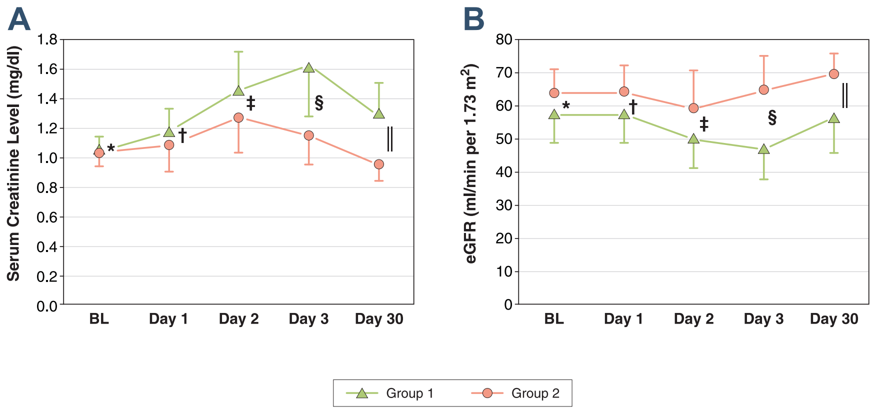

Figure 1. Thirty-Day Follow-Up of Renal Function After TAVR

(A) Serum creatinine levels and group differences on day 30: *p = 0.93, †p = 0.44, ‡p = 0.27, §p = 0.02, ‖p = 0.01, and mean Δ = −0.34 mg/dl (95% confidence interval: −5.7 to −1.6). **(B)** Estimated glomerular filtration rate (eGFR) values and group differences on day 30: *p = 0.21, †p = 0.23, ‡p = 0.18, §p = 0.01, ‖p = 0.03, and mean Δ = 13.2 ml/min per 1.73 m^2 (95% confidence interval: −5.7 to −1.6). No adjustments for multiple comparisons were made. Please see Online Videos 1 and 2. BL = baseline.