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EDITORIAL COMMENT

Guidelines for Aortic Regurgitation and Thoracic Aortic Aneurysms in Asian Population

Need a Second Look?*

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Chronic severe aortic valve regurgitation (AR) is a diagnosis notorious for many physical examination findings that carry famous names from the 1800s and 1900s, such as deMusset, Müller, and Alvarenga-Duroziez. However, despite its early identification in the literature, managing severe AR remains challenging due to difficulty in recognition, staging, and, most importantly, deciding on the right time to intervene. There are multiple etiologies for chronic severe AR,[1] often related to a problem with the aortic valve such as bicuspid aortic valve or rheumatic fever. It is also commonly associated with, or caused by, thoracic aortic aneurysms (TAAs).[1,2]

In 2020, the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines on management of chronic severe AR[1] recommended intervention with Class I indication for symptomatic patients, asymptomatic patients with left ventricular (LV) systolic dysfunction ≤55%, and patients undergoing cardiac surgery for other indications. Patients with evidence for dilated LV were given Class IIa indication (left ventricular end systolic dimension [LVESD] >50 mm or indexed LVESD >25 mm/m^2) with emphasis on the importance of index measurements, especially in women and small patients.[1,3] The guidelines acknowledge recent studies showing that indexed LVESD threshold for optimal postoperative survival may be even <25 mm/m^2.[4,5] Regarding TAAs, there are multiple cutoffs provided by the guidelines[2,6] depending on the etiology. When the indication is incidental to other cardiac surgical procedures, they recommend a diameter threshold of >4.5 cm and/or a growth rate of 0.5 cm/y.

In this issue of *JACC: Asia*, Yang et al[7] report the experience of National Taiwan University hospital in managing patients with chronic severe AR between 2008 and 2020. The authors sought to evaluate their outcomes and assess the validity of applying these guidelines on the management of an Asian population. In summary, all consecutive patients treated for chronic moderate to severe AR were identified from the national echocardiogram database, with inclusion and exclusion criteria clearly defined in the study protocol. A total 711 patients were followed for 4.8 years on average (IQR: 2.0-8.4 years) and divided into 2 groups: patients with bicuspid aortic valve regurgitation (BAV-AR = 149 [21%]) vs those with tricuspid aortic valve regurgitation (TAV-AR = 562 [79%]). Twenty-one patients had Marfan syndrome and 28 had connective tissue disease. Fifty-one patients with BAV-AR and 201 with TAV-AR had surgical intervention. In the BAV-AR group, 14 patients had aortic valve surgery (AVS) + aortic surgery (AoS), whereas the remaining 37 had AVS alone. In the TAV-AR group, 101 patients had AVS+AoS and 100 AVS alone. A total of 185 patients (26%) died during the follow-up period: 28 (4%) in the surgical group and 157 (22%) in the nonsurgical group. In the BAV-AR group 15 patients died: 2 in the AVS+AoS group and 13 in the nonsurgical group. In the TAV-AR group 170 patients died: 6 patients in the AVS+AoS group, 20 in the AVS group, and 144 in the nonsurgical group. BAV-AR had significantly better 10-year survival than TAV-AR, but the difference between the 2 groups disappeared after adjusting for age and other factors.

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As expected, patients who had surgery had better overall survival compared with those without surgery (worst survival). Interestingly, patients with AVS+AoS had better survival as compared with those with AVS alone, mostly driven by TAV-AR. After adjustment for age and comorbidities, AVS+AoS showed a trend toward better survival (HR: 0.45; 95% CI: 0.19-1.08; $P = 0.07$). There were a total of 18 aortic dissections during the study period (17 in TAV and 1 in BAV; 17 with type A). The overall incidence was 3.7% ± 1.0% at 10 years (incidence rate: 48.6 [95% CI: 29.7-75.4] per 10,000 person-years), driven by the TAV-AR group.

The authors then went the extra mile and compared their outcomes with the United States. The group did a similar study in the United States and followed patients with chronic severe AR at a tertiary referral center between 2006 and 2017.[8] When the authors compared the 2 populations, they found a stark difference in aortic size in patients with TAV-AR. Patients in Taiwan had larger aorta size, particularly the indexed value, with a higher rate of concomitant aortic surgery (46%) as compared with the United States (30%). They also observed an excess risk of death in TAV-AR as compared with the general population in both countries, yet the TAV-AR survival-gap was larger in Taiwan compared with the United States. The authors attributed those findings to their patients' larger baseline indexed LV size (ie, at a relatively advanced stage in AR disease course), larger aorta, and late surgical timing, partially because of smaller body surface area in Asian patients.

The paper highlights an important gap in the guidelines, which are mostly based on studies from the Western hemisphere dominated by the Caucasian race, without adequate representation of the Asian population. I agree with the authors that findings from this study are both reassuring and concerning at the same time. The good news is that Asian patients with BAV-AR being treated according to the ACC/AHA guidelines are doing well. The study shows low mortality, low risk of AD, and similar life expectancy to the general population. Meanwhile, the concerning news is that patients with TAV-AR are not doing so well when compared with the U.S. population. Although this comparison is observational without proper propensity match, the findings shine a light on significant differences between the United States and Taiwan, mostly related to management of TAV-AR associated with TAA. The indexed measurements show that TAV-AR patients in Taiwan are referred with much larger aorta compared with the U.S. (indexed sinus of Valsalva 25.1 ± 5.2 vs 20.5 ± 3.2 and indexed midascending aorta 26.5 ± 5.6 vs 21.0 ± 4.8), and 50% of patients with TAV-AR had AVS+AoS compared with 25% of the U.S. cohort. The significant differences in post-AVS indexed LV dimensions between the 2 studies also confirm that Asian patients are referred to surgery at a more advanced stage than their U.S. counterparts.

Looking at the bigger picture, surgical patients had better survival than nonsurgical patients, regardless of AoS, and patients who had AVS+AoS showed a trend toward better survival when compared with those with AVS alone. Both maximal aorta size and indexed maximal aorta size were independently linked to poor survival after adjustment for covariates. Collectively, those findings emphasize the importance of aortic size and raise questions regarding the validity of a 45-mm cutoff for concomitant aortic surgery in this population. Perhaps, indexed aortic measurements are warranted in the Asian population, especially in patients with TAV-AR.

In summary, when we look at the ACC/AHA guidelines and their applicability to Asian population based on this article, we find the following: Guidelines for management of BAV-AR and its associated TAAs are appropriate. Guidelines for management of TAV-AR are reasonable, if the LV index measurements are followed. However, guidelines for management of TAV-AR associated with TAAs need a second look, and perhaps revisions, to include indexed measurements of the aorta, rather than the absolute 45 mm cutoffs.

Lastly, this study eloquently highlights the importance of indexed measurements when applying guidelines to patients around the globe, and calls for vigilance and caution when writing and applying those guidelines. The study also demonstrate reassuring results to Taiwanese patients with aortic valve regurgitation; surgical outcomes in Taiwan are superb and equivalent to outcomes in the United States. Therefore, early referrals and prompt intervention should be encouraged.

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REFERENCES

1. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2021;77(4):e25–e197.

2. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2010;56(25):e50–e103.

3. Saisho H, Arinaga K, Kikusaki S, et al. Long term results and predictors of left ventricular function recovery after aortic valve replacement for chronic aortic regurgitation. *Ann Thorac Cardiovasc Surg*. 2015;21:388–395.

4. Yang LT, Michelena HI, Scott CG, et al. Outcomes in chronic hemodynamically significant aortic regurgitation and limitations of current guidelines. *J Am Coll Cardiol*. 2019;73:1741–1752.

5. de Meester C, Gerber BL, Vancraeynest D, et al. Do guideline-based indications result in an outcome penalty for patients with severe aortic regurgitation? *J Am Coll Cardiol Img*. 2019;12:2126–2138.

6. Hiratzka LF, Creager MA, Isselbacher EM, et al. Surgery for aortic dilatation in patients with bicuspid aortic valves: a statement of clarification from the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016;67:724–731.

7. Yang L-T, Lo H-Y, Lee C-C, et al. Comparison between bicuspid and tricuspid aortic regurgitation: presentation, survival and aorta complications. *JACC: Asia*. 2022;2:476–486.

8. Yang LT, Benfari G, Eleid M, et al. Contemporary differences between bicuspid and tricuspid aortic valve in chronic aortic regurgitation. *Heart*. 2021;107:916–924.

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