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Editorial

Understanding the Natural History of Bicuspid Aortic Valve: Are We Close to Understanding It?

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▸ See the article "Mid-term Clinical Outcomes in a Cohort of Asymptomatic or Mildly Symptomatic Korean Patients with Bicuspid Aortic Valve in a Tertiary Referral Hospital" in volume 27 on page 105.

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Although it is well known that bicuspid aortic valve (BAV) is a risk factor for early onset aortic stenosis (AS) and/or regurgitation, the natural history of BAV is not well understood than expected. This is, in part, because there are only a handful of well-established prospective BAV registries[1-3] and even in these registries, most of them are not community-based except for one.[1] Understanding the natural history of BAV is clinically important because it will not only lead to understanding of the disease but also, to predict what kind of outcome is associated with what type, thus enabling a step further to precision approach to this well-described condition.

The article by Sun et al.[4] in this issue of the Journal of Cardiovascular Imaging is thus welcome. The authors tried to describe the natural history of BAV in a tertiary hospital setting. More than 90% of the patients included in this analysis were minimally symptomatic, i.e. New York Heart Association functional class 0 or I, thus indicating that these patients were most likely to be found incidentally. Although there have also been large registries describing the natural history of BAV in Western countries,[1][2] a registry of true Asians as this report provides new insight. A recent publication encompassing more than 600 BAV patient of both Europeans and Asians each demonstrated that the proportion of specific BAV group is different between the Americans and Asians[3] and therefore, the analysis by Sun et al.[4] provides a window into understanding the racial difference into this relatively common congenital heart disease as well as in comparing the different outcomes between different ethnicity.

Although it is not surprising that BAV with either significant valvular dysfunction or ascending aortic dilatation at the initial detection is associated with future surgical events,[2] it is interesting to note that the dichotomous classification of BAV is associated with future surgical events. Two potential plausible mechanisms are possible. First, certain morphologic features of the BAV may lead to adverse rheologic features that accelerates surgery. Indeed, different subtypes of BAV morphology is associated with different aorta flow patterns and wall shear stress assessed by 4D-flow cardiovascular magnetic resonance.[5] However, the finding is slightly contradictory to previous findings reported earlier that the degree of AS tends to progress much faster in anteroposteriorly located BAV than a right-left located BAV.[6] Second, as *NOTCH1*,[7] *GATA5*[8] and *ROBO4*[9] etc. has been reported to be associated with nonsyndromic BAV, the inherent genetic defects per se may lead to premature aging of the

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valvular tissue, again suggested by multiple lines of in vivo animal studies and in vitro studies as well. However, given the incomplete penetrance with only < 15% of the BAV patients explained by *NOTCH1* genetic variation at most,[10] it remains to be explained which gene is in fact the actual genetic driver. It should also be noted that different criteria for classifying BAV may endow different results[11] and only a larger, more comprehensive clinical research will give a complete insight into whether and why specific types of BAV are associated with specific outcomes.

What is equally interesting is that compared to the progressive nature of AS associated with BAV, the aortic regurgitation (AR) in BAV did not show any progression within a median follow-up of 4 years. Whether this is also a racial difference, the insufficient power to support the difference in AR or the incomplete classification used for the analysis should be evaluated in future larger studies. The prevalence of significant AR has varied study-by-study, however surgical events for severe, symptomatic AR has been reported to be only 3%-6%. This might also be a racial difference as there has been reports demonstrating that the degree of significant AR is more common in Europeans than in Asians.[3] What is missing in previous reports[12] and the report by Sun et al.[4] is that the BAV classification was oversimplified by the location of raphe and did not take into account of the eccentricity of the leaflets. Although it is well known that the BAV drives the eccentricity of the aortic flow,[13] it is not known whether the leaflet eccentricity is associated with the degree of valvular dysfunction per se.

In conclusion, Sun and colleagues are to be congratulated for the work that describes the natural history of BAV in Korean patients. However, more work remains to be done and there are more open questions than closed answers for understanding the complexity between the BAV itself and its association with valvulopathy. Building on the findings from a single center registry like this, a multicenter registry is warranted in the future.

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