Journal of the American Heart Association

EDITORIAL

Aortic Stenosis: The Old Disease With New (and Evolving) Faces

Calvin Woon-Loong Chin, MD, PhD

"A wise man proportions his belief to the evidence"— David Hume

Recent guidelines on the management of valvular heart disease clarified the role of gradient states in stratifying severe aortic stenosis (AS; Figure 1).[1,2] We are perhaps more familiar with the indications of aortic valve replacement (AVR) in high-gradient (HG) severe AS. The guidance on low-gradient (LG) severe AS have added complexity in the diagnosis and management algorithms; but this is necessary to keep pace with evolving knowledge. There are some relevant caveats worth highlighting:

See Article by Snir et al.

1. Although not required to define HG severe AS, aortic valve area of ≤1.0 cm^2 (indexed aortic valve area 0.6 cm^2/m^2) remains an important parameter to establish severity in patients with LG AS.
2. In LG severe AS, AVR is currently recommended in 2 specified groups of patients with *symptoms*:
   a True severe AS in patients with reduced left ventricular ejection fraction (LVEF; also termed classical low-flow low-gradient [LFLG] severe AS). True severe is to be distinguished from pseudosevere AS with further investigations such as dobutamine stress echocardiography or computed tomography calcium score of the aortic valve.
   b Low-flow state (indexed stroke volume ≤35 mL/m^2) in those with preserved LVEF (also termed as paradoxical LFLG severe AS).
3. Currently, there are no specific recommendations proposed in *asymptomatic* patients with LG severe AS; and those with normal-flow low-gradient (NFLG) severe AS.

Prognosis of patients with LG severe AS and preserved LVEF is of topical interest. Patients with paradoxical LFLG severe AS generally have worse outcomes compared with those with moderate disease, HG and NFLG severe AS; and patients with NFLG have better or similar prognosis compared with HG severe AS.[3–6]

With this background, Snir and Celermajer et al in this issue of the *Journal of the American Heart Association (JAHA)* are to be congratulated for providing us with large-scale real-world insights on the prognosis of the different flow-gradient states of severe AS.[7] This study was derived from the National Echo Database of Australia that included more than 8000 patients with severe AS (after excluding those with incomplete data), the largest single study to date.

They had demonstrated that patients with classical LFLG severe AS consistently had the worst prognosis compared with the other subtypes of severe AS. These findings are not surprising but should be interpreted with some caution. Without further information,

Key Words: aortic stenosis ■ risk stratification ■ low-flow low-gradient severe aortic stenosis ■ normal-flow low-gradient severe aortic stenosis ■ classical low-flow low-gradient severe aortic stenosis

Correspondence to: Calvin Woon-Loong Chin, MD, PhD, National Heart Centre Singapore, Duke NUS Medical School, Singapore. E-mail: cchin03m@gmail.com
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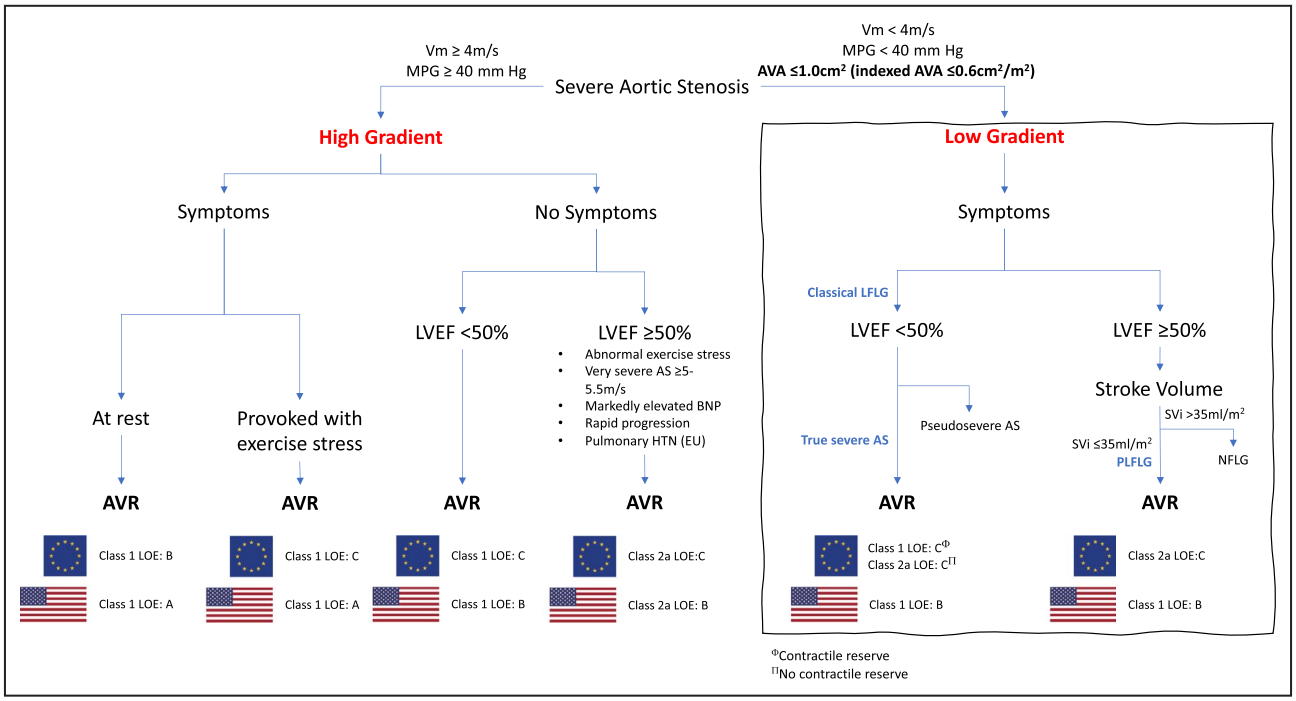

Figure 1. Management of severe aortic stenosis stratified by gradient states.
The recommendations for aortic valve replacement (AVR) in high-gradient severe aortic stenosis (AS) are guided by symptoms and/or reduced left ventricular ejection fraction (LVEF). In the absence of symptoms and preserved LVEF, AVR may be considered in patients with high-gradient severe AS when there is evidence of other abnormal findings. In low-gradient states, aortic valvular area remains an important parameter to establish severity. AVR is currently recommended in 2 groups of symptomatic patients with low-gradient severe AS: true severe in those with reduced LVEF and those with paradoxical low-flow low-gradient severe AS. AVA indicates aortic valvular area; EU, European Union; HTN, hypertension; LOE, level of evidence; MPG, mean pressure gradient; NFLG, normal-flow low-gradient; PLFLG, paradoxical low-flow low-gradient; SVi, indexed stroke volume; and Vm, peak aortic jet velocity.

this group would consist of patients with true severe and pseudosevere AS. Although the predominant cause of death was cardiovascular related, differentiation between true severe and pseudosevere AS is important to identify those with true severe AS who would benefit more from AVR.[8] Patients with paradoxical LFLG and NFLG had lower cardiovascular and similar all-cause mortality compared with those with

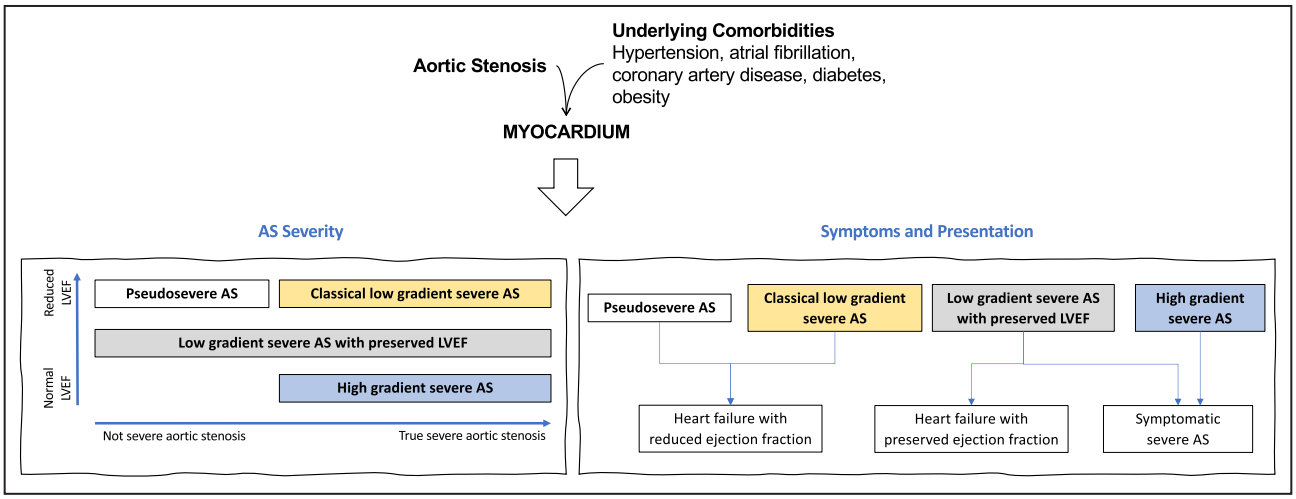

Figure 2. Disease severity, symptoms, and presentation of aortic stenosis.
The complex interaction between the valve and underlying comorbidities on the myocardium ultimately affects the aortic stenosis (AS) severity, symptoms and presentation of the patients. Because of this complexity, conventional echocardiographic assessment of AS severity may not be sufficient to make an accurate diagnosis in some patients; and further investigations are needed to ascertain severity and symptoms of patients. LVEF indicates left ventricular ejection fraction.

HG severe AS. After excluding patients with AVR to elucidate the natural history of severe AS subtypes, both paradoxical LFLG and NFLG were associated with lower cardiovascular and all-cause mortality compared with HG severe AS (supplemental data).

In previous pooled analyses, patients with LG severe AS and preserved LVEF had improved outcomes with AVR compared with conservative management.[4,6] More recent studies suggest AVR may be deferred in those with NFLG severe AS.[9,10] Of note, the survival benefits conferred by AVR were different: HG severe AS was associated with the greatest survival benefit from AVR and paradoxical LFLG with the lowest.[6] Patients with LG severe AS and preserved LVEF have a syndrome akin to heart failure with preserved ejection fraction, sharing similar pathophysiology and clinical comorbidities.[8,11] Altered ventricular-arterial interaction and increased afterload predisposed patients (particularly females) to concentric myocardial remodeling and contractile dysfunction, partly explaining the lower gradients in these patients with severe AS and abnormal ventricular filling in heart failure with preserved ejection fraction.

The impact of AVR on the prognosis of patients with severe AS subtypes cannot be explored adequately in this study. However, it had offered other insights. The authors reported more than 50% of patients with LG severe AS and preserved LVEF (paradoxical LFLG and NFLG) died of a noncardiovascular cause compared with about 35% to 40% of patients with HG severe AS.[7] These observations support the notion that the adverse prognosis associated with LG severe AS and preserved LVEF may not be solely mediated by the degree of AS severity but also contributed by underlying comorbidities; and AVR may not completely reduce the mortality risks in these patients. Managing the comorbidities would be extremely important in these patients as it will not only affect assessment of true severe AS but also influence symptoms and presentation (Figure 2).

The differences in findings can be attributed to study design and patient populations but further underscore disease heterogeneity. Notwithstanding the study limitations, the important conclusion is LG severe AS is not a benign condition. The clinical challenge is to select appropriate patients who would benefit more from AVR. Further investigations will be required to ascertain disease severity and improve risk stratification in these patients.[8]

ARTICLE INFORMATION

Affiliation

National Heart Research Institute, Singapore.

Disclosures

None.

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