

EDITORIAL COMMENT

Symptom vs Objective Evidence for Optimal Timing of Aortic Valve Replacement*



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In this issue of *JACC: Advances*, Playford et al¹ examined the presence of symptoms, comorbidities, and cardiac damage in 2,213 patients with moderate and 3,416 with severe aortic stenosis (AS) from a large database in Australia to understand the importance of symptoms in management of AS. Symptoms were common, present in 41.3% of moderate and 47.7% of severe AS. Dyspnea was the most common symptom and echocardiographic data were similar for those with or without symptoms in both moderate and severe AS. Comorbidities were also common with hypertension present in more than 50% in both groups. Presence of any symptom was not associated with the degree of cardiac damage which was associated with AS severity and mortality in both symptomatic and asymptomatic individuals. The authors concluded that symptoms are more associated with comorbidities than related to its AS severity and proposed that the current guideline for management of AS based on symptoms needs to be revised. This timely and provocative paper draws attention to the limitations in our current taxonomy of AS, diagnostic criteria, and therapeutic paradigms.

Consideration of aortic valve replacement (AVR) in patients with AS is usually guided by patient's symptoms. Ross and Braunwald in their historical description reported that death occurs soon

(6 months-2 years) after the onset of dyspnea, chest pain, or syncope after reviewing the history of 11 patients who were found to have severe AS at autopsy.² They were much younger than contemporary patients and AS was mostly of rheumatic in etiology so that their symptoms were purely related to hemodynamically significant advanced AS. Fifty years later, Braunwald provided a "Then and Now" perspective in AS, pointing out that AS now is mostly degenerative, high risk patients can be identified early by advanced imaging, and AVR can be done by transcatheter means resulting in entering "the promised land" for patients with AS who can be treated at an earlier stage of the disease.³ Authors showed that symptoms are not specific to AS and in some patients not even heart related. It is therefore possible that a patient with noncardiac dyspnea and barely severe AS by current AS severity criteria can receive AVR while an elderly asymptomatic patient with critical AS is not considered for AVR. Since the presence of symptom was detected by Natural Language Processing in this study, it is possible that a careful history taking would have discriminated cardiac from noncardiac symptoms. We hope that any symptom in a cardiac patient needs to be confirmed by careful examination and objective data to support its cardiac cause.

Echocardiographic assessment of left ventricular filling pressure by E/e' has been shown to be associated with dyspnea and increased mortality in patients with not only severe, but also moderate AS.^{4,5} With aging, diastolic function becomes abnormal accentuated by comorbidities such as hypertension, diabetes, coronary artery disease, and obesity. This superimposed myocardial dysfunction is probably responsible for symptoms in patients with less than severe AS as currently defined. The extent of myocardial dysfunction can be assessed by echocardiographic

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global longitudinal strain or myocardial fibrosis by cardiac magnetic resonance imaging. Both can identify high risk patients not only in severe but also in moderate AS.⁶

The current severity criteria for AS can cause a confusion, AS is classified as severe, moderate, and mild based on aortic valve (AV) velocity and AV area of ≥ 4 , 3, and 2.5 m/s, and of <1.0 , 1.5, and 2.0 cm², respectively. These values, however, depend on flow status and even with normal flow state, 4 m/s aortic velocity matches best with AV area of 0.8 rather than 1.0 cm².⁷ The mismatch between AV velocity and AV area is therefore apparent in predicting the hospitalization and survival of the patients with AS in both normal and low flow state.⁸ Ito et al showed that stroke volume becomes reduced and mortality is abruptly increased when AV area reaches 1.2 cm². There is also sex-difference in stroke volume. Women with a smaller stroke volume have a lower AV velocity and mean gradient for a given absolute or indexed stenotic valve area.⁹ Contemporary AS co-exists with underlying myocardial disease such as diastolic dysfunction and cardiac amyloidosis, which also contribute to patients' symptoms and outcome.¹⁰ Therefore, we need more comprehensive assessment of patients with AS incorporating multiple variables in addition to AV velocity and area.

As authors proposed from their thought-provoking data, severity criteria and therapeutic paradigm of AS need a revision. Severe AS should be based on parameters predicting a good and improved outcome after AVR. It appears that patients with AV area <1.3 cm² and evidence of increased filling pressure (by E/e' or pulmonary capillary wedge pressure) or myocardial dysfunction (strain, cardiac magnetic resonance imaging or computed tomography) benefits from AVR.^{11,12} Another means to identify the patients with AS who can benefit from AVR is topographical clustering.¹³ Then, the group of the patients with AS who

can benefit from AVR should be classified as severe AS. In real world, a substantial portion of the patients with significant AS or valvular heart disease are not clinically identified.¹⁴ Such a patient may sustain significant irreversible cardiac damage that cannot be corrected by AVR. Early detection of AS or valvular heart condition can be facilitated by careful auscultation and also application of artificial intelligence to a widely available test such as 12 lead electrocardiogram.¹⁵ In most clinical situations, significant AS is diagnosed by an echocardiographic examination. However, the severity of AS can be underestimated by not performing a comprehensive examination. Almost 2/3 of the patients with AS, the highest aortic velocity is detected by the right parasternal window which is frequently not performed.¹⁶

In summary, Playford et al¹ have made a major contribution to the field of AS by demonstrating a poor clinical outcome in patients with moderate AS, prognostic power of diastolic filling pressure, and nonspecific nature of symptoms in patients with AS.^{1,5,17} We have abundant data, mature technology, and resources to correctly identify high risk patients with significant AS based on objective evidence to determine optimal timing of AVR before irreversible myocardial damage.

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Dr Oh consults for Medtronic Inc in valve projects; has the potential to receive equity distribution from Anumana for ECG-AI algorithm to detect aortic stenosis; and is the recipient of a research grant from REDNVIA as national PI for the EVOID AS trial that tests whether a DPP-4 inhibitor can reduce the calcification of aortic valve. Dr Rihal has reported that he has no relationships relevant to the contents of this paper to disclose.

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