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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Natural History, Diagnostic Approaches, and Therapeutic Strategies for Patients With Asymptomatic Severe Aortic Stenosis

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CME Objective for This Article: At the end of this activity the reader should be able to: 1) determine the prevalence and clinical importance of asymptomatic severe aortic stenosis; 2) identify the appropriate complementary investigation to perform for patients presenting with asymptomatic severe aortic stenosis; 3) identify indications and recommendations for aortic valve replacement; and 4) identify the pros and cons of an early invasive aortic valve replacement strategy compared to medical surveillance for patients with asymptomatic severe aortic stenosis.

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Natural History, Diagnostic Approaches, and Therapeutic Strategies for Patients With Asymptomatic Severe Aortic Stenosis

ABSTRACT

Aortic stenosis (AS) is one of the most common valvular diseases encountered in clinical practice. Current guidelines recommend aortic valve replacement (AVR) when the aortic valve is severely stenotic and the patient is symptomatic; however, a substantial proportion of patients with severe AS are asymptomatic at the time of first diagnosis. Although specific morphological valve features, exercise testing, stress imaging, and biomarkers can help to identify patients with asymptomatic severe AS who may benefit from early AVR, the optimal management of these patients remains uncertain and controversial. The current report presents a comprehensive review of the natural history and the diagnostic evaluation of asymptomatic patients with severe AS, and is followed by a meta-analysis from reported studies comparing an early AVR strategy to active surveillance, with an emphasis on the level of evidence substantiating the current guideline recommendations. Finally, perspectives on directions for future investigation are discussed.
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Aortic stenosis (AS) affects ~5% of adults above the age of 65 years (1). It is one of the most common valvular diseases in developed countries, and its prevalence is projected to increase over the next decade with an aging population (2,3). Untreated, symptomatic severe AS is associated with a dismal prognosis (4–6), with as many as one-half of patients dying within 1 or 2 years (7–9). Aortic valve replacement (AVR), either surgical or via a transcatheter approach, is the only treatment shown to improve survival (10–14). Current guidelines recommend surgical AVR (SAVR) as a Class I indication for appropriate patients with severe symptomatic AS. Transcatheter AVR (TAVR) is recommended with a Class I indication for severe symptomatic AS patients who are not candidates for SAVR and with a Class IIa recommendation as an alternative to SAVR in "high-risk" AS patients (15,16).

As many as 50% of patients with severe AS report no symptoms at the time of diagnosis (17–19). The optimal timing of intervention for these patients is uncertain and controversial (17,19–28). Although current guidelines recommend AVR for selected patients with asymptomatic severe AS (**Table 1**) (15,16), in practice, a "watchful waiting" or active surveillance strategy is adopted for the vast majority of asymptomatic patients, with intervention planned once symptoms emerge or left ventricular (LV) systolic dysfunction develops. This strategy has some practical challenges: 1) interpreting symptoms or the lack thereof is notoriously difficult, particularly in elderly sedentary patients; 2) with AS progression being highly variable and unpredictable, rapid deterioration may occur; 3) a standardized algorithm for active surveillance has not been defined or validated; 4) late symptom reporting may result in irreversible myocardial damage with worsened prognosis, despite AVR; 5) operative risk increases with patient age and LV dysfunction; and 6) the risk of sudden death in patients with severe AS without classic symptoms is ~1% to 1.5% per year. Given the current low periprocedural mortality rates for isolated SAVR and TAVR, earlier intervention has been increasingly advocated (11–14,18,19,25–31); however, the current conservative strategy of watchful waiting in patients with asymptomatic severe AS has never been compared with early AVR in a randomized trial.

The present report will review the natural history of asymptomatic severe AS and subsequently summarize the potential roles of exercise testing, biomarker assessment, and imaging to guide the optimal timing of AVR. A meta-analysis from reported studies comparing an AVR strategy with a watchful waiting approach will also be presented. Finally, perspectives on directions for future investigation are discussed.

NATURAL HISTORY AND DIAGNOSTIC EVALUATION OF PATIENTS WITH ASYMPTOMATIC SEVERE AS

DEFINITION OF SEVERE AS AND CURRENT RECOMMENDATIONS FOR AVR. Current American College of Cardiology (ACC)/American Heart Association