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EDITORIAL

Beyond Sex-Based Differences: Exploring the Complexities of Aortic Stenosis in Women

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Editorial referring to the article: Degenerative Aortic Stenosis in Women: Challenges and Perspectives

Sex is an important biological variable in the pathophysiology of cardiovascular disease.[1,2] In fact, it could determine great differences in manifestation, treatment, and outcomes of several heart disorders. At the level of the aortic valve, there are sex-specific factors related to the pathogenesis of aortic stenosis (AS) that influence hemodynamics changes resulting from pressure overload response, and they should be considered in the management of patients.[1] Despite the fact that sex-based differences in AS exist, they are often not fully recognized and understood, leading to unequal treatment outcomes between males and females.[3,4]

This issue of the *International Journal of Cardiovascular Sciences* presents a comprehensive review of the growing evidence on sex disparities, from the pathogenesis to the treatment of severe degenerative AS, focusing on women.[5]

In this review, entitled "Degenerative aortic stenosis in women: challenges and perspectives," the authors have pointed out that, in clinical presentation, women are often older and have higher prevalence of hypertension and diastolic dysfunction than men.[5] Regarding the pathogenic process of degenerative AS, the authors emphasize that, compared to men, women have more concentric ventricular hypertrophy and higher transaortic gradients.[5] Concentric ventricular remodeling was recognized as a predictor of worse outcome in women, but not in men.[4] For a given severity degree of AS, women have less valve calcification, measured by computed tomography, with more valvular fibrosis and denser connective tissue than men.[5,6] This contrast may have a significant prognostic value since the level of valvular calcification is an independent predictor of disease progression, especially in asymptomatic individuals and could be used to guide referral for intervention.[6]

Also, it is important to note that women may exhibit milder symptoms, and they could often be masked by self-limitation resulting from elderly behavior, which delays the indication for intervention.[5,6] In fact, historically, there has been a divergence in the referral of women with severe AS for surgical aortic valve replacement, which is less performed in this sex. This discrepancy could be related to women's higher post-operative mortality, higher frailty, and elevated risk of patient prosthesis mismatch, due to smaller annular sizes.[5-7] However, after the advent of transcatheter aortic valve replacement (TAVR), this disparity has decreased, with an equal representation of women in the utilization of this procedure in the main studies.[8,9] Curiously, despite worse pre-procedural female profile and higher rates of bleeding and vascular complications, TAVR has demonstrated improved long-term survival in women, compared to men.[10] Moreover, women have shown improved reverse remodeling of myocardial hypertrophy post-procedure, compared to men.[11]

This study highlighted the discussion of this critical topic, adding relevant information about innate physiological differences in AS between men and women, but gaps still remain in the current knowledge, and future randomized trials are necessary to elucidate them. Furthermore, the equality in representation of women among TAVR studies does not necessarily translate to equal care and, particularly, optimal timing of valve intervention. Future research should focus on exploring the advantages of using sex-specific guidelines for indicating valve procedures, taking into account the inherent physiological sex variations in AS phenotypes and identifying healthcare factors that may contribute to unequal treatment of women with severe AS.

Keywords

Aortic Valve Stenosis; Women; Sex Differences; Transcatheter Aortic Valve Replacement; Hypertension, Ventricular Hypertrophy.

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