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Late gadolinium enhancement cardiac magnetic resonance in aortic stenosis: Where do we stand today?

Short title: Late gadolinium enhancement CMR in aortic stenosis

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Related article
by Orłowska-Baranowska et al.

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Aortic stenosis (AS) is the most frequent valvular heart disease and its prevalence is expected to triple over the next years due to ageing of the population [1]. In the early adaptive phase, left ventricular (LV) systolic pressure increases in response to the narrowing of the aortic valve, in an effort to compensate for the increased afterload and maintain an adequate cardiac performance and functional status [2]. However, as AS progresses, the LV enter a decompensation phase and the disease takes on a malignant course with a dramatic increase in mortality, especially when symptoms and/or LV dysfunction develop [3]. This transition from the adaptive to maladaptive/symptomatic phase is mainly driven by severe structural alterations in the myocardium, such as LV hypertrophy and intramyocardial fibrosis [4].

The fact that myocardial scarring is an advanced step of LV remodeling in the setting of AS has been recently confirmed in large-scale studies and meta-analyses, showing that focal fibrosis, as evidenced by late gadolinium enhancement (LGE) cardiac magnetic resonance (CMR), is present in more than half of patients referred for aortic valve replacement (AVR) and its presence is associated with increased mortality [5–7]. Interestingly, Thornton et al. [7] showed that both infract and non-infract LGE patterns on CMR were powerful independent predictors of mortality (all-cause and cardiovascular) in symptomatic patients with severe AS, regardless of the type of valve intervention. Although this is an intriguing finding that underscores the importance of LGE evaluation for better risk stratification of patients with severe AS, it does not answer "the one million dollar" question: Can CMR with LGE guide management of AS patients?

Orłowska-Baranowska et al. [8] tried to shed light on this important topic by conducting an observational study of 91 asymptomatic patients with severe AS, the results of which were published in the *Polish Heart Journal*. All 91 patients underwent CMR with LGE and 68 of them (75%) finally underwent AVR due to clinical progression of the AS. A number of early post-AVR complications (hospitalization time after AVR, length of hospitalization in intensive care unit after AVR, need for extra corporeal membrane oxygenation or continuous renal replacement therapy, new episode of atrial fibrillation or post-pericardiotomy syndrome) and echocardiographic outcomes (change in wall thickness and LVEF at 12 and 24 months after the procedure) were evaluated. The authors found that LGE positive patients developed symptoms earlier than LGE negative patients (median time of symptoms onset: 18 vs. 28 months, $P = 0.01$). However, when the analysis was restricted to the subgroup of patients who underwent AVR, no difference was observed with regard to the post-intervention echocardiographic and clinical outcomes based on the LGE status from the baseline evaluation.

This work by Orłowska-Baranowska et al. [8] further confirms the emerging role of CMR in risk stratification of patients with AS, showing that LGE is a potential harbinger of early symptoms development in asymptomatic patients with severe stenosis. However, the post-AVR findings of the study should be interpreted with caution and in the context of some methodological remarks in the study design. First and foremost, the median time interval between CMR examination and AVR procedure was 2 years. During that period of time, the researchers did not perform a follow-up

CMR for LGE status update in patients who initially had a LGE-negative scan, and thus a kind of cross-over bias may have skewed the post-intervention findings. In addition, only a small number of patients (68 patients) were included in the analysis of the post-intervention outcomes, rendering the findings of limited or even dubious clinical significance.

There is no doubt that CMR can effectively risk-stratify symptomatic patients with severe AS and, as shown by Orłowska-Baranowska et al. [8], CMR's prognostic utility extends to asymptomatic patients as well. However, whether CMR can be used to optimize the timing of intervention in AS remains an open question. Currently, this hypothesis is being tested in the randomized EVOLVED trial (Early Valve Replacement Guided by Biomarkers of Left Ventricular Decompensation in Asymptomatic Patients with Severe Aortic Stenosis; NCT03094143), which compares early AVR with standard of care (i.e., wait for symptoms development) in patients with LGE on CMR and asymptomatic severe AS. This trial together with others investigating the role of early intervention in the clinical context of asymptomatic severe AS are anticipated to provide strong recommendations on the optimal timing of intervention in this patient population (Figure 1). Until the recommendations of these trials become available, an individualized therapeutic approach should be followed, taking into consideration the patient's risk profile and their preference.

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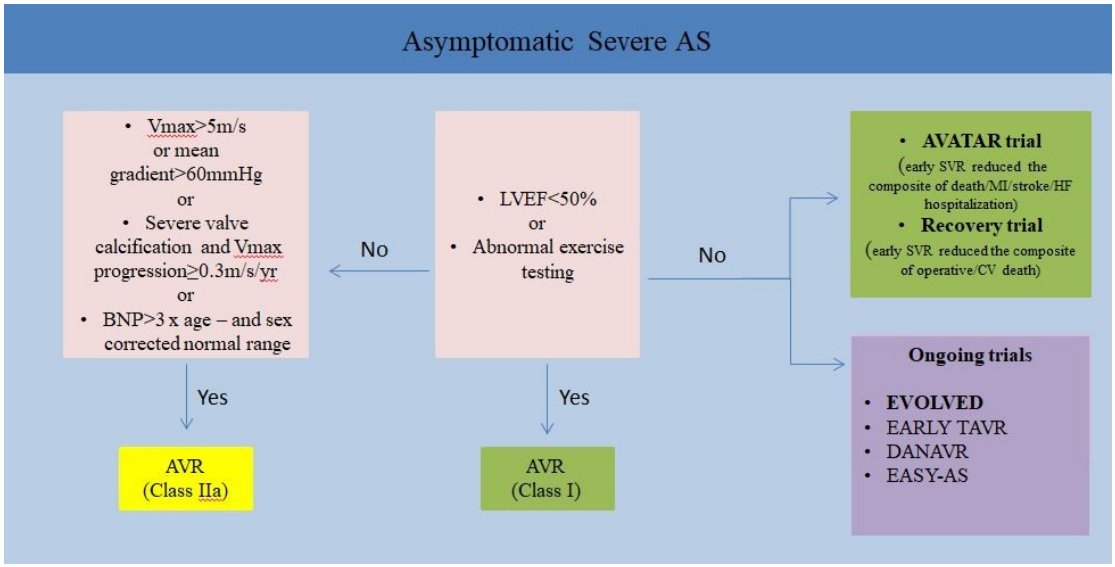

Figure 1. Current management and ongoing trials in asymptomatic aortic stenosis

Abbreviations: AS, aortic stenosis; AVR, aortic valve replacement; BNP, B-type natriuretic peptide; CV, cardiovascular; HF, heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; SVR, surgical valve replacement; Vmax, maximum velocity