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TAVI in asymptomatic patients with severe aortic stenosis: pros and cons

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Pros: early TAVI, a pre-emptive strategy

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Aortic stenosis is a progressive disease with an unpredictable evolution. While some phases of the disease are latent, the left ventricle and other cardiac structures are constantly exposed to an increasing overload of pressure, with silent cardiac damage (structural and functional) accumulating over time. Often, the expression of symptoms among patients with progressive aortic stenosis appears at a point when a second or third cardiac "disease" occurs, such as a decrease in left ventricle function, diastolic dysfunction, or atrial fibrillation, which all could be irreversible once the aortic stenosis is fixed. Similarly, it is extremely difficult to predict how a patient will "land" in the symptomatic zone, whether it will be a "crash and burn" scenario, more safe with some degree of turbulence, or more smooth and uneventful. Current guidelines recommend surgical aortic valve replacement (SAVR) for patients with severe aortic stenosis if 1) symptoms occur spontaneously or are triggered during a low-level stress test, or among asymptomatic patients if 2) left ventricle function is depressed (<50%), or 3) another open heart surgery is required[1]. Potential benefits of early intervention include reduced mortality, reduced rehospitalisation for cardiovascular reasons, improvement in quality of life, and prevention of progression and occurrence of cardiac damage. Recently, 2 small randomised trials of approximatively 150 patients each demonstrated the benefits of SAVR among patients with asymptomatic critical aortic stenosis (~65 years old, peak velocity ~5 m/s, and no stress test performed)[2] and asymptomatic very severe aortic stenosis (~65 years old, peak velocity ~4.5 m/s)[3].

The current guidelines are silent about the role of transcatheter aortic valve implantation (TAVI) in asymptomatic patients with severe aortic stenosis. Whether TAVI should be performed instead of SAVR is another question. Given the recent data showing the equivalence and even the superiority of TAVI at short- and mid-term follow-up, a less invasive approach may be preferred in asymptomatic patients if cardiac function is to be preserved. We recently demonstrated that SAVR was associated with the occurrence or progression of cardiac damage after aortic valve replacement compared with TAVI, mainly due to the onset of new atrial fibrillation, the lack of regression of left ventricular hypertrophy (remodelling), and the occurrence of new right ventricular dysfunction due to the on-pump phenomenon[4].

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The relative enhanced safety and reduced invasiveness of TAVI compared with SAVR has some appeal if a pre-emptive strategy is contemplated among asymptomatic patients with normal left ventricular function.

Some opponents of TAVI may argue that the durability of TAVI prostheses is still unknown and may preclude the use of TAVI among asymptomatic patients; however, it was shown that most asymptomatic patients with severe aortic stenosis will become symptomatic and require aortic valve replacement ~2 years after their diagnosis, with approximatively 1-2% mortality per year while waiting for symptoms to occur. TAVI valves have demonstrated at least similar valve durability up to 5 years among intermediate- and high-risk patients and should be preferred among this segment of the population to prevent cardiac depletion and the occurrence of adverse events. The role of TAVI among younger patients (65-75 years) is still a matter of active debate, and longer-term follow-up in ongoing trials will help answer this question. If anatomical suitability for initial and subsequent TAVI implantation is confirmed, it is expected that TAVI will become the preferred intervention among both symptomatic and asymptomatic patients. In this regard, the Evaluation of TAVR Compared to Surveillance for Patients With Asymptomatic Severe Aortic Stenosis (EARLY TAVR) trial (ClinicalTrials.gov: NCT03042104) has recently completed its enrolment (~1,000 patients) and is expected to answer this exact question in the near future[5].

Conflict of interest statement

P. Généreux has been a consultant for Abbott Vascular, Abiomed, BioTrace Medical, Boston Scientific, CARANX, Cardiovascular Systems Inc (for the PI Eclipse Trial), Edwards Lifesciences, GE Healthcare, iRhythm Technologies, Medtronic, Opsens, Pi-Cardia, Puzzle Medical, Saranas, Shockwave, Siemens, Soundbite Medical Inc, Teleflex, and 4C Medical for the PI Feasibility study; an advisor to Abbott Vascular, Abiomed, BioTrace Medical, Edwards Lifesciences, and Medtronic; has received speaker fees from Abbott Vascular, Abiomed, BioTrace Medical, Edwards Lifesciences, Medtronic, and Shockwave; has been a proctor for Edwards Lifesciences; and has equity in Pi-Cardia, Puzzle Medical, Saranas, and Soundbite Medical Inc.

Cons: insufficient evidence for TAVI in asymptomatic AS

Bernard Iung, MD

While symptomatic severe aortic stenosis (AS) has been an undisputed indication for intervention for decades, asymptomatic patients with severe AS generally undergo follow-up until symptom onset. Historically, the low rate of cardiac events in asymptomatic AS supported conservative management. Over the last decades, European and American guidelines have defined indications for intervention in selected asymptomatic patients with high rates of cardiac events reported in observational studies[1,6]. Conversely, an argument that supports earlier intervention – as soon as AS becomes severe without waiting for symptoms – is that the risk of delay in the identification of symptom onset thereby exposes the patient to the inherent risk of symptomatic AS.

Recently, intervention in asymptomatic AS has gained new attention due to the RECOVERY and AVATAR randomised trials, which included 145 and 157 patients, respectively, and led to consistent findings supporting early surgery in asymptomatic AS[2,3]. The occurrence of the primary endpoint of operative mortality or postoperative cardiovascular mortality in the RECOVERY trial and all-cause death or major adverse cardiac events in AVATAR was significantly reduced in the early surgery group versus the conservative management group.

The two randomised trials represent a major step forward in evidence-based treatment of asymptomatic AS. However, they do not close the debate. In the RECOVERY trial, AS was more severe than the usual criteria delineate, and the absence of symptoms was based on patient history without systematic exercise testing, while the AVATAR trial included patients with common definitions of severe AS and mandatory negative exercise testing. Primary endpoints were composite in both trials, and the decrease in all-cause mortality was significant only in the RECOVERY trial. The robustness of both trials is limited by the cumulative number of 302 patients and 51 primary events.

The results of the RECOVERY and AVATAR trials support early surgical aortic valve replacement in relatively young (mean age 64 and 67 years, respectively) and very low-risk patients (mean EuroSCORE II 0.9% in RECOVERY and mean Society of Thoracic Surgeons [STS] score 1.7% in AVATAR), who do not represent the majority of AS patients, even the asymptomatic ones. These findings cannot be translated to elderly patients due to the higher risk of procedural complications and the competing risks between AS prognosis and the impact of comorbidities and frailty.

In asymptomatic patients, TAVI is particularly attractive since a minimally invasive intervention seems more acceptable than surgery in patients who do not complain of any symptoms. The recent extension of indications for TAVI to low-risk patients provides the opportunity to consider TAVI in asymptomatic patients, who are frequently at low risk for surgery. However, performing TAVI at an earlier stage of AS leads to interventions in patients with longer life expectancies, and this raises concerns regarding the long-term consequences of TAVI. While paravalvular leak is now less frequent and less severe, the incidence of conduction disorders has not decreased with recent devices. Uncertainties remain on the long-term impact of coronary access and structural valve deterioration[7]. Present data on clinical and echocardiographic follow-up after TAVI are mostly limited to 5-8 years, mostly in

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octogenarians at increased risk for surgery, and cannot be extrapolated to asymptomatic patients with severe AS who do not present with the same features.

Despite recent trials supporting early intervention, it is not time to recommend TAVI in asymptomatic AS. The evidence supporting intervention in asymptomatic AS is currently limited to surgical aortic valve replacement in selected low-risk patients and cannot support unrestricted indications of TAVI in asymptomatic AS. The 20-year story of TAVI has been paved with a succession of randomised trials leading to a progressive extension of indications. We should not abandon this virtuous example and instead should wait for the results from ongoing trials before considering TAVI in asymptomatic AS.

Conflict of interest statement

B. Iung has no conflicts of interest to declare.

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