EDITORIAL

# Searching for the Best Strategy for Patients with Severe Aortic Stenosis

*Buscando la mejor estrategia para pacientes con estenosis aórtica severa*

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In Europe and North America, calcific aortic stenosis (AS) is the most common valvular heart disease (VHD) leading to aortic valve replacement. The prevalence of AS continues to grow with the aging of the population, meaning an increase in the number of patients requiring treatment for this disease. The "surgical" approach was the first option to treat these patients, and enabled the opportunity to solve associated conditions such as aortic dilatation or coronary artery disease (CAD). Conventional surgical aortic valve replacement (SAVR) for the treatment of acquired AS is associated with improved survival compared to conservative management, and is related with excellent results. The proof-of-concept first case of transcatheter aortic valve replacement (TAVR) performed by Cribier and colleagues in 2002 opened a door to this new less invasive therapeutic option. (1) During the last years, randomized clinical trials (2-4) demonstrated superiority of TAVR over conservatively managed patients not amenable for cardiovascular surgery, as well as non-inferiority of TAVR compared to SAVR in patients at high operative risk. Subsequently, non-inferiority of TAVR vs. SAVR was reported for intermediate-risk patients (5-7), and more recently, two trials by Mack et al. (8) and Popma et al. (9) provided strong evidence that TAVR is non-inferior and possibly superior to surgery over 1-year and 2-year follow-up. These results have set the ground for an increase in the number of TAVR procedures, surpassing the numbers of SAVR performed in Germany and the United States in the last couple of years. (10) This trend is likely to continue in the next years, taking into account that the vast majority of patients undergoing SAVR in the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database were in the low-risk group (80% were at low risk, 14% at intermediate risk, and 6% at high risk). (11)

The new TAVR studies have led to a paradigm shift in how we select the best strategy to treat patients with severe aortic stenosis. We require accurate information not only about the risk of perioperative mortality and major morbidity, but also, importantly, –before we can generalize the TAVR trial outcomes to all patients and medical institutions– on what the local results are where patients are to be treated.

Consideration of national and local results is relevant because the excellent results observed in the TAVR trials may be difficult to replicate locally. In particular, advanced preoperative cardiac imaging, the expertise of the Heart Team, including patient selection and the ability to supply expeditious surgical bail-out if required, together with intensive postoperative care, are aspects that may vary substantially from country to country and region to region. Consequently, the study from Borracci et al. -the results of which are reported in this issue of the Journal- aimed to analyze this question with a single-arm meta-analysis of studies reporting in-hospital mortality after SAVR in low- and intermediate-risk patients in Argentina, as a benchmark for future comparisons with their local TAVR outcomes. (12) Four observational studies reported in-hospital mortality and postoperative complications with a pooled population of 1192 patients. Fifty-nine percent were men, with a mean age of 74 years (range 33-92), and 67% underwent isolated aortic valve replacement. In-hospital mortality was 3.1% when considering the pooled risk. When patients were separated into low- and intermediate-risk, mortality rates were 2.7% and 6.1%, respectively. Importantly, the observed mortality was higher than expected as derived by the STS predicted risk of mortality (PROM). Mean STS PROM score was 1.5% in the low-risk group (O/E ratio=1.8), and 5.1% in the intermediate-risk group (O/E ratio=1.2). Other major complication rates were reported as follows: postoperative stroke 1.3%, myocardial infarction 0.4%, need for permanent pacemaker 2.7%, mediastinitis 1.4%, and reoperation for bleeding 2.6%.

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Overall, the pooled results from the four Argentinian reference centers reflect the real world in developed countries, when the results of contemporary registries are analyzed. The study from Thourani et al. (11), which evaluated 141,905 patients undergoing SAVR at STS-participating institutions between 2002-2010, showed similar 30-day all-cause mortality of 5.8% with a mean STS score of 5.48% in the intermediate-risk group, but a lower mortality of 1.7% in the low-risk group with a mean STS score of 1.67% (O/E ration 1.0). However, the study from Thourani et al included only first-time isolated SAVR. The reported rate of other major postoperative complications in both risk groups was lower in the study from Borracci et al., only reporting a higher rate of deep sternal infection.

It is important to note that operative mortality reported in the STS database has decreased for intermediate-risk surgical patients in the last two decades (from 6.4% to 5.4%), but not in the low-risk group, where it remains stable at 1.7%. (11). Low-risk patients also continue to constitute the majority of patients undergoing SAVR. In view of the excellent results achieved for TAVR in the recently published low-risk studies, one can argue that further improvements are required in low-risk conventional SAVR patients.

Outcomes in the low-risk TAVR trials (8, 9) were exemplary. The rate of death in SAVR patients at 30 days was 1.1% in the PARTNER 3 trial and 1.3% in the study from Popma et al. These excellent results are certainly multifactorial, partly due to surgical expertise but also due to patient selection with a narrowly defined patient population. Nevertheless, excellent surgical results using sutureless, rapid deployment biological valve prostheses have been reported in a broader risk-spectrum of patients, with a hospital mortality of 1.6% and 0.8% in low- and intermediate-risk patients, respectively. (13) Importantly, a less invasive approach was used in 74% of the abovementioned cases. This reflects the potential benefit of introducing minimal invasive surgical programs along with new technologies that facilitate these approaches.

TAVR results are also rapidly improving. In the large German experience (10), intraprocedural complications during TAVR have declined from 9.4% in 2012 to 3.9% in 2014, and severe TAVR complications such as annular rupture, aortic dissection, or coronary occlusion now occur in <0.3% of patients. A marked reduction of in-hospital mortality rates has also been observed, decreasing from 10.4% in 2008 to 4.2% in 2014. Despite this trend, when low- and intermediate-risk groups were compared, the 30-day mortality was lower with isolated SAVR than with trans-vascular TAVR (1.5% vs. 3.7% and 3.7% vs. 4.1%, respectively). (14) Overall, TAVR has been demonstrated to be associated with an increased risk of permanent pacemaker implantation, major vascular complications, and prosthesis associated aortic regurgitation, but with a lower incidence of new-onset atrial fibrillation, bleeding requiring transfusion, and acute kidney injury requiring hemodialysis. (15)

The expansion of TAVR into the lower-risk population will change the way we select the best strategy for a particular patient. Estimated operative risk will likely no longer play a central role. The decision process will be dictated by life expectancy (in relation with the age of the patient and local demographics), the durability of the prosthesis, the ability to perform future valve-in-valve procedures, and the need to address associated conditions such as aortic dilatation or coronary artery disease. In addition, the patient´s lifestyle and preferences, and the local expertise of the Heart Team will need to be taken into consideration. The search of the best strategy for a particular patient should be guided by a "locally adjusted" informed shared decision. In this regard, the current study by Borracci et al. supplies us with important information regarding SAVR outcomes in Argentinian reference centers. Further adjustments may be required when considering results in other Argentine hospitals.

## Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

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