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Editorial

# TAVI in low-risk patients. Reality or fiction?

## TAVI en el paciente de bajo riesgo. ¿Realidad o ficción?

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## Introduction

The number of transcatheter aortic valve implantations (TAVI) has increased exponentially with more than 100 000 procedures worldwide. Initially reserved for non-operable very high-risk patients, the indication rapidly spread to intermediate risk patients. Recently, the usefulness of TAVI has been investigated in the segment of younger, low-risk patients with smaller studies and larger randomized trials in these patients. Considering the increase in procedures and improvement in device technology over the past decade, it can be anticipated that TAVI will become a valid alternative to surgical aortic valve replacement (SAVR) if not the preferred therapy for most patients including lower risk patients. Here, we summarize the present knowledge and discuss the pros and cons of TAVI in low-risk patients.

## Risk estimation. How is "low-risk" defined?

Risk assessment in clinical trials as well as in daily routine strongly depends on patient categorization. So far, risk prediction in TAVI is performed using scores adopted from conventional surgery such as the Society of Thoracic Surgeons (STS) score and the EuroSCORE I and II as the most widely and frequently used models. Although several TAVI specific risk scores have been proposed,[1,2] so far none of these novel risk models have succeeded in clinical studies or daily routine.

How is "high-risk" and "low-risk" defined? Commonly, patients are divided into 3 risk categories: (a) high-risk (STS score > 8%, log EuroSCORE > 20%); (b) intermediate risk (STS score 4–8% or log EuroSCORE 10–20%); and (c) low-risk (STS score < 4% or log EuroSCORE < 10%). However, these risk models must be interpreted with caution: first, it is important to recognize that the STS and EuroSCORE have been created to predict operative mortality in the setting of cardiac surgery, and commonly overestimate mortality in TAVI.[3] Second, low risk does not necessarily mean young age. With both risk scores, a patient can be 90 years of age and still be considered almost a low-risk patient. Third, surgical risk scores do not consider important comorbidities, such as active malignancy, chest wall radiation, porcelain aorta, liver cirrhosis or the presence of frailty. Therefore, risk scores should always be just one part of the decision-making process of the interdisciplinary Heart Team.

## TAVI in low-risk patients. Evidence from recent and ongoing clinical trials

The first favorable data on TAVI outcome in low-risk patients came from observational real-world registries.[4–6] With the NOTION (Nordic Aortic Valve Intervention) trial, the first randomized study in low-risk patients with a mean STS score of 3 provided promising results.[7] Comparison of TAVI using the first-generation self-expanding CoreValve with SAVR showed no difference in all-cause mortality after 5 years. Nevertheless, permanent pacemaker implantation rate in the TAVI

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arm was high with 34.1% (SAVR = 1.6%). Although, there is a strong trend of decreasing permanent pacemaker implantation rate in TAVI it is still highly variable in next-generation transcatheter heart valves.[8]

Also, moderate or severe paravalvular leakage was significantly higher in the TAVI group with 15.7% compared to 0.9% after SAVR.[9] However, these numbers have significantly dropped in current studies since computed tomography-based annular sizing prior to TAVI has emerged as the gold standard and transcatheter heart valves with sealing skirts will result in a further decline. Regarding valve durability, which is of major concern especially when treating younger patients, the rate of structural valve deterioration according to the current definition[10] was greater in the SAVR arm compared to TAVI after 6 years (SAVR = 24.0% vs TAVI = 4.8%).[11]

Supporting data on safety in low-risk patients also is available from the LRT (Low-Risk TAVI) trial, a prospective, multicenter comparison of TAVI to historical controls undergoing SAVR. Using newer generation transcatheter heart valves including the Edwards SAPIEN 3, the Medtronic Evolut R and Evolut PRO, 30-day mortality and stroke rate in the TAVI group was 0%. Also, the requirement of permanent pacemaker implantation was only 5% and more than mild paravalvular aortic regurgitation was reported in only 0.5%.[12]

Only recently, 2 eagerly awaited trials investigating TAVI in low-risk patients using the balloon-expandable SAPIEN 3 (PARTNER-3)[13] and a self-expanding, supra-annular transcatheter heart valve (Evolut Low-Risk trial)[14] further proved safety and efficacy of TAVI in Low-Risk patients. While in the Evolut Low-Risk trial TAVI was non-inferior to surgery in terms of a composite endpoint including death or disabling stroke, the PARTNER-3 trial even showed statistical superiority analyzing a composite of death, stroke or rehospitalization at 1 year. In PARTNER-3 death from any cause after 1 year occurred in 1% of patients treated with TAVI compared to 2.5% undergoing surgery. In the Evolut Low-Risk trial the estimated incidence of death from any cause was 4.5% in both groups after 24 months. In terms of valve durability, data from the Evolut Low-Risk trial published so far showed lower aortic valve gradients in the TAVI group compared to patients with surgery at 1 year.[14] Although, both studies further support the use of TAVI in low-risk patients only short- and mid-term outcomes are provided. Therefore, long-term results from these clinical trials as well as data from the NOTION-2 (NCT02825134) and the DEDICATE (NCT03112980) trials are expected to shed further light on the heated debate. However, having in mind that these studies are currently ongoing the most interesting results on long-term valve durability cannot be expected before 2025. Learning from surgical bioprosthetic valves, degeneration often occurs after 8 years and rapidly increases after 10 years.[15]

## Future challenges

Several issues when extending TAVI to younger lower-risk patients will be of major importance. These issues are longevity, permanent pacemaker implantation rate, paravalvular leakage, and valve thrombosis. So far, there is no hard evidence that durability of transcatheter heart valves is inferior compared to surgical valves. However, it will be important to investigate these issues with rigorous follow-up of current trials especially for the treatment of younger and low-risk patients. Regarding paravalvular leakage, there has already been a clear improvement over the last years. Regarding the permanent pacemaker implantation rate which was comparatively high at the beginning of TAVI (19.8–28.6% in CoreValve US Pivotal High Risk Trial [NCT01240902] or REPRISE 2 [NCT01627691]), later trials showed significantly lower rates (4.5–8.3% in CENTERA-2 and SAVI TF).[16,17]

Another challenge will be the group of patients with bicuspid valve disease as data from isolated SAVR reported a prevalence of bicuspid valve diseases in more than 60% in patients under 70 years of age.[18] As most randomized clinical TAVI studies excluded bicuspid valves, data on these patients is scarce. However, in a recent propensity-matched analysis, similar results between bicuspid and tricuspid valves were shown with newer generation transcatheter heart valves.[19]

Furthermore, there is no clear strategy for the optimal post-procedural medical treatment after TAVI so far and future studies need to address the optimal strategy especially in younger lower risk patients.

## Conclusions

When looking at the tremendous success story of TAVI and how the outcome has improved over the years, further refinement of this technology can be expected within the next decade. The extension of TAVI to low-risk patients has already become a reality and may even be superior to conventional surgery. However, treatment of low-risk and especially younger patients must continuously weigh up the risks and benefits and be backed by data from adequate designed trials in order to offer the best possible care to our patients.

## Conflicts of interest

The authors have no conflict of interest to declare.

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