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Could the age threshold for TAVI be relaxed to below 65 years? Pros and cons

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Transcatheter aortic valve implantation (TAVI) has emerged as the treatment of choice for symptomatic severe aortic stenosis (AS) across the whole surgical risk spectrum. Current European guidelines recommend surgical aortic valve replacement (SAVR) for patients under 75 years at low surgical risk, whereas American guidelines advocate for shared decision-making between SAVR and TAVI in patients aged 65 to 80 years, taking into account life expectancy and valve durability. Although SAVR with mechanical valves offers excellent durability, it is partially offset by significant challenges, including a higher thrombotic risk and the lifelong need for anticoagulation. In addition, recent TAVI trials have shown potential benefits for younger, lower-risk populations, generating a growing interest in expanding its indications. Based on all these considerations, whether the age threshold for TAVI should be lowered below 65 years remains a topic of debate.

Pros

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Over the past two decades, TAVI has become the standard treatment for symptomatic AS in high-, intermediate-, and low-risk patients. With proven efficacy and increasing safety, TAVI's applications are expanding. The recent EARLY TAVR trial[1] suggests potential benefits for asymptomatic patients with severe AS, while ongoing trials, such as PROGRESS (ClinicalTrials.gov: NCT04889872) and the Evolut EXPAND TAVR II Pivotal Trial (ClinicalTrials.gov: NCT05149755), are evaluating TAVI for patients with moderate AS, potentially supporting earlier intervention in patients' lifetimes.

The 2021 European Society of Cardiology (ESC) guidelines recommend SAVR using either mechanical or bioprosthetic valves in patients under 75 years who are low risk for surgery or unsuitable for transfemoral TAVI (Class I, Level of Evidence [LoE] B). Meanwhile, the 2020 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend SAVR or TAVI after shared decision-making, balancing longevity and valve durability for patients from 65-80 years (Class I, LoE A). For younger patients, mechanical valve replacement or pulmonary autograft is advised. The ACC/AHA task force reports highlight the durability of surgical bioprostheses beyond 10 years, whereas long-term data for TAVI remain limited, primarily based on high- to intermediate-risk cohorts, with durability evidence in low-risk patients with the latest-generation devices still developing. Mechanical valves, while durable, carry thrombogenic risks and necessitate lifelong anticoagulation, often with warfarin, which poses lifestyle restrictions and increases bleeding risk. This, coupled with the option of transcatheter valve-in-valve (ViV) procedures for bioprosthetic valve failure, has driven an increased use of bioprostheses across all ages[2].

In the 65- to 75-year age range, recent findings from the NOTION-2 (ClinicalTrials.gov: NCT02825134) and DEDICATE (ClinicalTrials.gov: NCT03112980) trials demonstrated TAVI's non-inferiority, or even superiority, over SAVR regarding survival, stroke prevention, and reduced valve-related hospitalisations. However, patients under 65 made up less than 10% of the participants in these trials. Lifetime management of AS requires a comprehensive, patient-centred approach, incorporating initial procedural planning (SAVR or TAVI), valve selection, and long-term monitoring to optimise outcomes. For younger patients with life expectancies of three decades or more, multiple interventions (2-4) may be anticipated. Redo-TAVI poses risks, such as coronary obstruction, making future planning essential, even prior to the first procedure. Advanced computed tomography imaging, valve sizing, and commissural alignment, along with leaflet

interventions, can help reduce the risk of coronary obstruction in subsequent interventions. While ViV-TAVI for surgical bioprosthesis dysfunction has shown comparable outcomes to native valve procedures, it is linked with increased stroke risk and haemodynamic compromise, particularly in patients with small annuli. Cerebral protection devices and surgical valve fracture techniques with oversized balloons have been suggested to address these concerns, though their long-term effects remain unclear.

Although ViV and redo-TAVI procedures show promise for managing bioprosthetic valve degeneration, high-risk situations remain. For example, redo-SAVR is complex and has high complication rates, while TAV-in-TAV-in-TAV or TAV-in-TAV-in-surgical aortic valve procedures involve risk of compromised valve function, as additional frames within the aortic root may impair haemodynamics and accelerate degeneration. Limited data are available on patients requiring a third intervention. An aortic root cleaning procedure may be required to restore function, though it carries significant stroke and mortality risks.

The choice between SAVR and TAVI as a first intervention depends on factors such as anatomical features, concomitant coronary/valvular diseases, comorbidities and the need for reintervention. Shared decision-making that integrates patient preferences, lifestyle considerations, and clinical goals is essential. Recent trends show TAVI's popularity increasing across all age groups, including patients below 65 years of age, suggesting both cardiologists' confidence and patient preference for less invasive approaches[3]. Age alone should not limit access to TAVI for younger patients; instead, patient life expectancy and clinical profiles should guide treatment choices for a contemporary tailored approach. With ongoing technological improvements, both SAVR and TAVI continue to evolve, underscoring the need for careful planning to ensure optimal lifetime management in AS patients.

Conflict of interest statement

P. Garot reports being a proctor or consultant for Abbott, Boston Scientific, Biosensors, Cordis, GE HealthCare, and Terumo; he serves as a Medical Co-Director and is a shareholder of Cardiovascular European Research Center (CERC), a CRO dedicated to cardiovascular diseases; he is a shareholder of Basecamp Vascular and Electroducer. M. Akodad reports being a consultant for Abbott, Edwards Lifesciences, and Medtronic.

Cons

Michael A. Borger, MD, PhD; Mateo Marin-Cuartas, MD

Reducing the age threshold below 65 years for TAVI is neither patient-oriented nor evidence-based for the following reasons.

Contemporary results for SAVR are excellent, with an 8-year survival rate of 92% in low-risk patients aged 65-74[4]. In addition, SAVR in patients under 65 allows for highly durable options for patients with AS, including mechanical heart valves and the Ross operation.

When Heart Teams consider a patient for TAVI, age is a very quick and simple estimate of life expectancy, which is complex to calculate and varies widely from region to region. Despite its pragmatism as a simple parameter, age alone does not reflect the complexity of Heart Team decision-making when assessing lifetime management issues in AS patients. In this regard, the Heart Team must be aware that the average remaining lifespan of a 65-year-old in Europe is 17 years for males and 21 years for females, time frames that are beyond the reported durability of most biological aortic prostheses. Is it better for a 60-year-old patient to undergo TAVI now, then a high-risk reintervention (see next paragraph) in 10 to 15 years, or SAVR now and then an established ViV-TAVI procedure in 10 to 15 years? The answer seems obvious.

Given the longer life expectancy of young patients, TAVI in this cohort is associated with an increased need for reintervention. Redo-TAVI and surgical TAVI-explant procedures are already rapidly increasing, with worrisome outcomes following redo-TAVI[5] and particularly alarming results after surgical TAVI explant[6]. Large series have demonstrated a perioperative mortality rate of 15-18% for surgery post-TAVI, nearly twice as high as the Society of Thoracic Surgeons Predicted Risk of Mortality for these patients. A further reduction of the age threshold would lead to an unprecedented wave of reinterventions post-TAVI with an unknown impact on public health, affecting the lives of many thousands of patients.

In addition, evidence on durability and long-term outcomes are limited. Low-risk randomised clinical trials (RCTs) comparing TAVI versus SAVR have thus far reported results up to 5 years (except for NOTION, with an average patient age of 79 [ClinicalTrials.gov: NCT01057173]), which is an insufficient follow-up period to assess bioprosthesis durability in young patients. Current durability comparisons between TAVI and SAVR valves are therefore inconclusive, particularly since many SAVR patients from low-risk RCTs received bioprostheses that have been subsequently removed from the market. If the durability of TAVI devices turns out to be worse during longer-term follow-up of low-risk patients, the rate of post-TAVI interventions will increase even more. In addition, the higher need for pacemaker implantation and an increased rate of paravalvular leaks following TAVI and their negative impact on long-term survival have been described[7].

Bicuspid anatomy is more prevalent in younger AS patients, and TAVI outcomes in bicuspid AS patients are not as good as those in tricuspid AS patients. A recent RCT showed particularly worrisome results for TAVI in young, low-risk bicuspid AS patients[8].

Methodological aspects of existing RCTs may limit our ability to accurately determine the best treatment options for younger patients. The mean age of participants in most low-risk TAVI versus SAVR RCTs was close to 75 years, with very few patients randomised under 65 years of age. Moreover, none of the RCTs were powered for age category subanalyses. Furthermore, all low-risk RCTs have a non-inferiority design. Reducing the age threshold for TAVI would be a methodologically incorrect assumption

of the non-inferiority of TAVI in younger patients, which has not been demonstrated yet.

In summary, reducing the age limit below 65 for TAVI would be inappropriate for a myriad of reasons, including a resultant increase in the number of patients undergoing high-risk post-TAVI interventions and a lack of supportive evidence, amongst others.

Conflict of interest statement

M.A. Borger discloses that his hospital receives speaker honoraria and/or consulting fees on his behalf from Edwards Lifesciences, Medtronic, Abbott, and Artivion. M. Marin-Cuartas has no conflicts of interest to declare.

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