Aortic Valve 2024: Which Valve for Which Patient?

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19 Glossary of Abbreviations
20 AVR, Aortic valve replacement
21 CT, Computed tomography
22 DAPT, Dual-antiplatelet therapy
23 INR, International normalized ratio
24 PPM, Patient prosthesis mismatch
25 PROM, Predicted risk of mortality
26 SAVR, Surgical aortic valve replacement
27 STS, Society of Thoracic Surgeons
28 SVD, Structural valve deterioration
29 TAVR, Transcatheter aortic valve replacement
30 VARC, Valve Academic Research Consortium
Central Picture Legend: Framework for Aortic Valve Shared Decision-Making. In patients 50 to 69 years old.

Central Message: Aortic valve disease management is rapidly evolving with advances in transcatheter and surgical interventions. Informed decision-making is quintessential for providers and patients in this era.
Perspective Statement: Recent advances in aortic valve disease management have influenced valve choice, interventional strategy, and lifetime management. This review highlights contemporary data for aortic valve disease.

Keywords: Aortic valve; Bioprosthetic valve; Mechanical valve; SAVR; TAVR; Guidelines; Lifetime management
Abstract

The lifetime management of aortic valve disease is an evolving landscape. Younger patients are increasingly electing for bioprosthetic over mechanical valves, and novel aortic valve technologies have improved bioprosthetic durability. Recent data suggest reduced risks of reoperation and transcatheter valve replacement within prior aortic valves. This review highlights recent advances and discusses the lifetime management of aortic valve disease.
Introduction

Bioprosthetic aortic valve replacement (AVR), mechanical AVR, and the Ross procedure each have unique risks and benefits. Factors that influence valve choice include age, lifestyle, activity level, childbearing, and comorbidities. Furthermore, transcatheter aortic valve replacement (TAVR), improved outcomes after redo surgical aortic valve replacement (SAVR), the introduction of valve-in-valve TAVR, and improved bioprosthetic durability have influenced the lifetime management of aortic valve disease.

Despite published evidence guiding valve choice in AVR, there remains a lack of consensus on the optimal approach for aortic valve choice. In fact, American and European AVR guidelines differ in recommendations, with American guidelines suggesting bioprosthetic valves be considered at age 50 while European guidelines favor an older age of 65. This review summarizes relevant literature regarding valve choice (bioprosthetic, mechanical, Ross procedure), interventional strategies (TAVR versus SAVR), and lifetime management to help providers counsel their patients with aortic stenosis in a shared decision-making model to select the right valve for each patient.

Epidemiology of AVR, TAVR, and SAVR

With the widespread adoption of TAVR, more overall AVRs are performed each year. From 2012 to 2018, total AVRs in the USA nearly doubled from 58,120 to 98,610, primarily driven by an increase in TAVR from 6,470 (11.1% of total AVRs) to 57,155 (58.0%). Meanwhile, SAVR volume declined slightly from 44,117 in 2008 to 41,455 in 2018. And, more recent data show that these trends have continued through 2021 (Figure 1). These trends likely reflect the
approval of TAVR for prohibitive, high-, intermediate-, and low-risk patients.\textsuperscript{6,8,10} With the overall increase in patients treated with AVR, it is paramount to understand which strategy (TAVR versus SAVR) and which valve (bioprosthetic versus mechanical) provides the best outcomes for each patient in the context of lifetime management.

**Rise in Bioprosthetic Valve Utilization**

Surgical strategy within SAVR reflects increased bioprosthetic valve utilization (Figure 2), particularly among younger patients for whom a mechanical valve is a reasonable alternative.\textsuperscript{11-14} Recent studies report similar longitudinal mortality in young patients in the 50 to 70 age range receiving a bioprosthetic versus mechanical prosthesis.\textsuperscript{11-13} One large analysis in California found a bioprosthetic valve was associated with slightly higher 15-year mortality in patients 45 to 54 years old\textsuperscript{14}, however, in that same analysis, patients aged 55 to 64 years had similar 15-year mortality. Importantly, this data reflects earlier generation valves and a high 7\% reoperation mortality rate.

In New England, Iribarne and colleagues\textsuperscript{11} conducted a multicenter, retrospective analysis of 1449 inverse probability weighted isolated AVR patients (age 50 to 65 years) across 7 centers from 1991 to 2015 and found no differences in in-hospital morbidity, mortality, or length of stay between those who received a bioprosthetic versus mechanical valve. Results from the Cleveland Clinic were similar—Attia and colleagues\textsuperscript{12} evaluated 527 propensity-matched pairs of patients who received an isolated bioprosthetic or mechanical valve between 1990 and 2020. After propensity matching, mean age was 54±14 years for bioprosthetic patients and 54±12 years for mechanical valve patients. There were no differences in major in-hospital complications or in-
hospital mortality. A propensity-matched New York database analysis of patients aged 50 to 69 years with either a bioprosthetic (n=1001) or mechanical valve (n=1001) also showed similar 15-year survival.\textsuperscript{13} As with other studies, bioprosthesis had a higher reoperation rate (12.1\% [95\% CI, 8.8\%-15.4\%] versus 6.9\% [95\% CI, 4.2\%-9.6\%]). As expected, the mechanical prosthesis group had a higher 15-year cumulative incidence of major bleeding (13.0\% [95\% CI, 9.9\%-16.1\%] versus 6.6\% [95\% CI, 4.8\%-8.4\%]).

Collectively, these studies highlight an increase in bioprosthetic valve utilization in younger patients and a higher risk of requiring reoperation compared to mechanical valves. In the setting of isolated AVR, these US studies suggest there are no differences in postoperative morbidity or longitudinal mortality following bioprosthetic and mechanical AVR in patients aged 50 to 70 years old, although there are European studies that favor mechanical valves.\textsuperscript{15}

Criteria for Evaluating Structural Valve Deterioration for Bioprosthetic Valves

Two criteria are commonly used to evaluate bioprosthetic valve durability—the classic “Akins criteria”\textsuperscript{16} and the recent Valve Academic Research Consortium “VARC” criteria.\textsuperscript{17} The Akins criteria are a historical society consensus definition primarily based on reoperation for structural valve deterioration (SVD); while the VARC criteria (now in its third iteration) was developed with the advent of major transcatheter aortic valve trials and includes echocardiography hemodynamic parameters of valve failure.\textsuperscript{18}

Bioprosthetic SAVR Tissue Durability
Novel technologies to improve durability and freedom from SVD have been introduced; however, data are often limited, and importantly, biologic valve durability has been shown to decline after the 5-to-7-year time frame.\textsuperscript{19} Most recently, durability at a mean 7.7 years for the novel RESILIA tissue aortic valve (Model 11000A; Edwards Lifesciences) was reported as part of the prospective, non-randomized, multicenter clinical evaluation (COMMENCE) trial.\textsuperscript{3} Among 225 patients (mean age: 65.1±10.9 years) who were reconsented for extended follow-up beyond the original 5-year follow-up, freedom from SVD defined by “Akins criteria” was 99.3% and freedom from reoperation was 97.2%. Notably, none of the 92 patients younger than 65 years experienced SVD at 7 years, and minimal transvalvular regurgitation was reported. And, in a separate propensity-matched analysis that employed the more recent VARC-3 criteria, Bartus et al.\textsuperscript{20} also found RESILIA did very well compared to a non-RESILIA surgical bioprosthetic AVR data from the PARTNER 2A TAVR Trial (SVD was only 1.0% versus 4.8%; one-sided lower-bound of hazard ratio, 1.15; \( P=0.03 \)). These results highlight the improved long-term durability of the RESILIA aortic valve though follow-up through 10 years is ongoing.

The Avalus bioprosthesis (Medtronic, Minneapolis, MN), another novel valve, has data available through five years as part of the Pericardial Surgical Aortic Valve Replacement (PERIGON) Pivotal trial comparing patients ≤65 years (n=271) versus patients >65 years (n=847).\textsuperscript{21} As expected, younger patients had lower Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM) (1.1%±0.9% vs 2.2%±1.4%, \( P<0.001 \)) and fewer comorbidities with lower 5-year mortality (5.3% vs 14.0%, \( P<0.001 \)), although 5-year valve-related mortality did not differ
(1.3% vs 1.5%, \(P=0.66\)). Notably, no patients experienced SVD, although longer-term follow-up will be required. Additionally, the Epic Supra porcine valve (Abbott, Santa Clara, CA) is another novel option that was found to have 94% freedom from reoperation at 10 years in a large study of 11,685 patients (mean age: 76±7 years) that linked a manufacturer device tracking database to a Medicare claims database.\(^{22}\)

In the era of TAVR, a contemporary analysis of isolated SAVR outcomes was performed combining the STS and National Death Index databases.\(^{23}\) There were 42,586 patients (2011-2019), with mean age of 74.3±5.7 years and mean STS PROM of 1.9±0.8%. Notably, survival at 5 years was 92.9%; however, in very low-risk patients with STS PROM <1% and age <75 years, SAVR survival was 95% at 8 years. This article serves as a “Benchmark” to discuss contemporary isolated SAVR outcomes with patients during the shared decision-making process. This article also highlights that in the major TAVR trials, the SAVR arms often included concomitant procedures (e.g., coronary artery bypass grafting in 14% and other concomitant operations in 5%).

**Aortic Root Enlargement**

An adequately sized prosthesis must be placed, including root enlargement if necessary, to minimize patient prosthesis mismatch (PPM) and to facilitate future valve-in-valve TAVR. At comprehensive valve centers, root enlargement can be performed safely without increased morbidity as Shih and colleagues\(^{24}\) reported in their experience with isolated SAVR with and without aortic root enlargement (2015-2020). Root enlargement was performed in 54 (6.2%) patients, primarily with a bovine pericardial patch (81.5% [44/54]). After propensity matching
for several baseline characteristics including body surface area, there were no differences in stroke, dialysis, pacemaker, bleeding, length of stay, 30-day readmission, 30-day mortality, and 5-year survival.

Notably, in the era of TAVR following SAVR, there has been increased interest to make sure the initial valve is an appropriate size to minimize PPM; however, others have concerns about increased morbidity with root enlargement and the clinical relevance of PPM as it relates to outcomes.

Reoperation Safety

As more younger patients choose bioprosthetic over mechanical valves, the safety of reoperation becomes paramount. Additionally, when considering a SAVR-first or TAVR-first strategy, the risks with TAVR explant must also be examined.

Mahboubi and colleagues reported morbidity and mortality following re-operative surgical AVR have declined and are now similar to those achieved following primary isolated surgical AVR. In 581 propensity-matched pairs (1980-2017), the re-operative AVR and primary isolated AVR cohorts had a mean age of 62±14 years and 61±14 years, respectively, with similar morbidity and mortality (although bleeding, transfusions, and heart block were more frequent in the re-operative cohort). Through 10 years, longitudinal survival was similar. For younger patients considering a bioprosthetic valve over a mechanical valve, these results at a major valve center are encouraging given previous reports of higher reoperation risk.
Although data are limited, TAVR explant morbidity and mortality have been sobering. Fukuhara and colleagues reported their 10-year experience (2011-2022) of reoperation in 66 post-TAVR patients (63.6% [n=42] native TAVR and 36.4% [n=24] valve-in-valve TAVR following SAVR). Median duration from TAVR to reoperation was 1.8 years (IQR 0.3–4.1), median age at reoperation was 72.0 (IQR 63.5–77.0) years, and median STS PROM was high at 8.5% (IQR 4.1–15.7). Importantly, concomitant procedures at re-operation were common with only 18.2% of patients undergoing isolated redo SAVR, which likely reflects reoperations from earlier generation higher risk transcatheter aortic valve cohorts and the desire to address all pathology at reoperation. A TAVR-first approach in this series was associated with higher operative mortality at TAVR explant than TAVR explant following SAVR-TAVR; and these limited data suggest a SAVR-first approach may be preferred to limit the risk of mortality following TAVR explant.

**TAVR Durability**

The first TAVR was performed in France in 2002, yet TAVR adoption has increased faster in the United States than in France, particularly for patients <65 years old despite current guidelines recommending SAVR in patients <65 years old (Figure 3). The 2020 American College of Cardiology/American Heart Association guidelines prioritize age as a decision-making factor for TAVR versus SAVR, while European guidelines prioritize age and surgical risk. Nonetheless, several randomized trials have evaluated the safety, efficacy, and durability of balloon-expandable and self-expanding TAVR valves in various patient populations.

The PARTNER (Placement of Aortic Transcatheter Valves) I, II, and III trials were a series of randomized trials that established the safety and efficacy of balloon-expandable TAVR in high-
medium-, and low-risk patients with initial follow-up of 1 to 2 years.\textsuperscript{33-35} Recently, the 5-year follow-up results from low-risk PARTNER 3 patients were published.\textsuperscript{40} Mean aortic valve gradient (12.8±6.5 mm Hg TAVR versus 11.7±5.6 mm Hg SAVR) and aortic valve area (1.9±0.5 cm\textsuperscript{2} TAVR versus 1.8±0.5 cm\textsuperscript{2} SAVR) were similar between balloon-expandable TAVR and bioprosthetic SAVR at 5 years. However, TAVR valves had slightly higher rates of valve thrombosis (2.5% versus 0.2%) and mild or greater aortic regurgitation (24.5% versus 6.3%). Nonetheless, the rates of aortic valve reintervention (2.2% TAVR versus 2.6% SAVR) and valve-related death (0% TAVR versus 0.2% SAVR) were low and similar between TAVR and SAVR valves.

Similar trials with a self-expanding TAVR valve (CoreValve, Evolut, Medtronic, Minneapolis, MN) were performed in high-risk, intermediate-risk, and low-risk patients in the Pivotal, SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation), and NOTION (Nordic Aortic Valve Intervention) trials.\textsuperscript{36-39} These trials established the safety and efficacy of self-expanding TAVR and were limited to 1- to 2-year follow-up, except the NOTION trial has results through 8 years.\textsuperscript{41,42} Among patients who received either the self-expanding CoreValve (n=145) or various stented bioprosthetic SAVR valves (n=135), there were no differences in major outcomes at 8 years, including death, stroke, and myocardial infarction. CoreValve patients had improved mean aortic valve gradients and aortic valve area through 8 years compared to SAVR patients (Figure 4). Clinically, there was no difference in aortic valve reintervention rate through 8 years (3.6% TAVR versus 2.3% SAVR, \textit{p}=0.51).
Balloon-expandable and self-expanding TAVR are acceptable options for first-time AVR although more longitudinal follow-up is required. Current 2020 American College of Cardiology/American Heart Association guidelines recommend SAVR for patients aged <65 years, shared decision-making for patients aged 65 to 80 years, and TAVR for patients aged >80 years or who have a life expectancy of less than 10 years. However, despite the guidelines, recent data show TAVR has been adopted in 52.5% of patients aged <65 years in the United States (Figure 3).

Mechanical Valves

While mechanical valves offer improved durability compared to bioprosthetic valves, limitations include lifelong anticoagulation with increased risk of bleeding and thromboembolic events, and lifestyle limitations. Additionally, warfarin has dietary restrictions and teratogenicity, prohibiting the use of mechanical valves in pregnant women. Clinical trials have aimed to reduce the burden associated with warfarin therapy by evaluating lower international normalized ratio (INR) goals and warfarin alternatives. The Prospective Randomized On-X Anticoagulation Clinical Trial (PROACT) randomized 375 On-X mechanical aortic valve replacement patients to lower dose warfarin (n=185; target INR: 1.5-2.0) or standard warfarin therapy (n=190; target INR: 2.0-3.0) across 33 US centers between 2006 and 2009. This strategy was employed three months after AVR, and all patients received 81 mg of aspirin daily. Mean age was 55.2±12.5 years, and concomitant procedures were common. Mean INR was lower for the low-dose warfarin group (1.89±0.49 vs 2.50±0.63, P<0.0001) with fewer bleeding events (major: [1.48% vs 3.26%/patient-years; P=0.047]; minor: [1.32% vs 3.41%/patient-years; P=0.021]), and no difference in stroke, transient ischemic attack, total neurologic events, and all-cause mortality.
through 8.7-year follow-up. This trial established an INR goal of 1.5-2.0 as acceptable for patients receiving an On-X mechanical aortic valve.

Unfortunately, all alternative anticoagulation strategies, including the use of dual-antiplatelet therapy (DAPT), apixaban, or dabigatran have not been effective in clinical trials.

Furthermore, a recent combined analysis of the STS and Medicare databases with 7-year follow-up showed patients >65 years receiving mechanical valves had higher mortality compared to biologic Bentall operations and a 20% incidence of readmission for bleeding at 7 years. In the current era, mechanical valves continue to be limited by their requirement for warfarin and associated bleeding events. While alternative anticoagulation strategies have been sought, there is currently no acceptable alternative to warfarin.

Ross Procedure

The Ross procedure is a preferred strategy in children given the autograft’s ability to grow with a child; however, its use in adults is more limited as it puts two valves (pulmonary autograft in aortic position and pulmonic homograft in pulmonary position) at risk for degeneration. Despite these limitations, the Ross procedure may be considered at expert Comprehensive Valve Centers for patients <50 years who prefer a bioprosthetic AVR and have appropriate anatomy (class 2b recommendation, level of evidence B). Experienced centers have recently published favorable results with the Ross procedure in adult patients. In a propensity-matched analysis of patients aged 18-50 years from California and New York databases, El-Hamamsy and colleagues evaluated longitudinal outcomes following the Ross procedure (n=434) versus biological AVR (n=434) versus mechanical AVR (n=434). At 15 years, actuarial survival was higher for patients who underwent the Ross procedure (93.1%; 95% CI, 89.1%-95.7%) compared to biologic or
mechanical AVR and was similar to that of an age-, sex-, and race-matched US general population. The Ross procedure was associated with a lower risk of reintervention compared to biological AVR, but a higher reoperation risk compared to mechanical AVR. At 15 years, the cumulative incidence of any aortic and/or pulmonary valve reintervention after the Ross procedure was 17.2% (95% CI, 13.2%-21.6%).

Some centers have adopted a “wrapped technique” (pulmonary autograft inclusion), which includes a vascular graft sleeve around the neoaortic root to limit dilatation, reducing the rate of reintervention to 4.0% at 10 years compared to 26.8% in an unwrapped cohort. However, this technique does not address pulmonary homograft failure, which is still a common indication for reintervention.

**Bicuspid Aortic Valve Patients**

Notably, patients with bicuspid aortic valves were excluded from TAVR trials. While TAVR can be safely performed in these patients with favorable valve performance, bicuspid valve patients are younger, often have substantial calcium burden and a larger annulus, and SAVR first may be a preferred strategy.

Bavaria and colleagues reported excellent 5-year results with the RESILIA tissue bioprosthesis in native bicuspid aortic valves (n=214) compared to tricuspid valves (n=458). Bicuspid patients were younger (59.8±12.4 years versus 70.2±9.5 years, p<0.001), and none experienced SVD, with minimal paravalvular and transvalvular regurgitation reported (0.7% and 2.9%, respectively).
In a national database analysis of SAVR in low-risk patients with bicuspid (n=9131) or tricuspid (n=56,556) aortic valve disease, Hirji and colleagues\(^5^4\) found bicuspid patients were younger (median: 70 years versus 74 years, \(p<0.001\)) with lower STS PROM (mean: 1.6% versus 2.3%, \(p<0.001\)). The majority received a bioprosthetic valve (91.2% in bicuspid cohort and 92.6% in tricuspid cohort), and 30-day mortality and morbidity were similar between groups, though bicuspid patients had lower risk-adjusted 5-year mortality and 5-year readmission rates.

While randomized trial data comparing SAVR to TAVR for bicuspid valve patients do not exist, Chen and colleagues\(^5^5\) recently conducted a nonrandomized, propensity-matched Centers for Medicare and Medicaid Services database analysis of 797 pairs of bicuspid aortic stenosis patients undergoing isolated SAVR versus TAVR. Before matching, TAVR patients were older with more comorbidities and higher frailty. In matched analyses, at three years, SAVR was associated with improved survival and improved freedom from hospital readmissions, with no difference in the risk of aortic valve reintervention or stroke. While these data are certainly important for guiding valve choice in patients with bicuspid aortic stenosis, randomized trial data are needed.

**Lifetime Management Strategy**

The lifetime management of aortic valve patients considers improved bioprostheses durability, transcatheter alternatives and valve-in-valve TAVR as well as improved re-operative aortic valve surgery. Bagur and colleagues\(^5^6\) advocate the ratio of expected valve durability versus the expected remaining years of life as a basis; however, this does not capture the contemporary landscape for younger patients who are likely to require reintervention. Alternatively, Windecker and colleagues\(^5^7\) share a framework based on life expectancy and age while considering the risk
of reintervention (Figure 5). They propose ordered surgical and transcatheter interventions
dependent on these factors and provide several plausible strategies.

Guideline Review

American and European guidelines differ in recommendations for aortic valve choice. The 2020
American College of Cardiology/American Heart Association guidelines recommend mechanical
aortic valves for patients younger than 50 years (Class 2a recommendation, level of evidence B),
shared decision-making for patients 50 to 65 years old (Class 2a recommendation, level of
evidence B), and biologic valves for patients older than 65 years (Class 2a recommendation,
level of evidence B). For patients of any age with a contraindication to anticoagulation or who
do not desire anticoagulation, bioprosthetic AVR is recommended (Class I recommendation,
level of evidence C).

The 2021 European Society of Cardiology/European Association for Cardio-Thoracic Surgery
guidelines account for surgical risk and risk of reoperation in addition to age. Briefly, a
mechanical aortic valve is recommended in patients at an accelerated risk of SVD (Class 1
recommendation, level of evidence C), patients younger than 60 years (Class 2a
recommendation, level of evidence B), or patients with a reasonable life expectancy for whom
reoperation or TAVR would be high risk (Class 2a recommendation, level of evidence C).
Meanwhile, a bioprosthetic aortic valve is recommended in patients whose life expectancy is
lower than the presumed durability of the bioprosthesis (Class 1 recommendation, level of
evidence C), patients for whom reoperation would be unlikely or low risk (Class 2a
recommendation, level of evidence C), or patients older than 65 years (Class 2a
recommendation, level of evidence C).
Together, these guidelines support mechanical AVR in patients younger than 50 and bioprosthetic AVR in patients older than 65. For patients between 50 and 65 years old, the guidelines differ in their recommendations between a mechanical or bioprosthetic valve as European guidelines recommend mechanical AVR in patients younger than 60 years, and American guidelines recommend shared decision-making with mechanical and bioprosthetic both being reasonable options.

Conclusions

As this review highlights, younger patients are increasingly choosing bioprosthetic valves, bioprosthetic tissue durability is improving, TAVR is becoming increasingly common, and the Ross procedure can be performed at expert centers with outstanding results. Nonetheless, there is a lack of consensus regarding optimal lifetime aortic valve disease management. Shared decision-making is quintessential to aortic valve management in 2024 and beyond (Figure 6).
References


Figure Legends

**Figure 1.** Annual US Trends in Transcatheter Aortic Valve Replacement (TAVR) and Surgical Aortic Valve Replacement (SAVR) Procedural Volume. Reproduced from *The Annals of Thoracic Surgery* with permission from Elsevier.

**Figure 2.** Rise in Bioprosthetic Aortic Valve Utilization. Isolated AVR using biological (blue) or mechanical (red) prosthesis by calendar year. Reproduced from *The Journal of Thoracic and Cardiovascular Surgery* with permission from Elsevier.

**Figure 3.** TAVR Adoption Trends in the United States Versus France. Reproduced from the *Journal of the American College of Cardiology* with permission from Elsevier.

**Figure 4.** NOTION Trial 8-Year Results for Effective Orifice Area and Mean Aortic Valve Gradient. Reproduced from the *European Heart Journal* with permission from Oxford University Press.

**Figure 5.** Lifetime Management Strategy of TAVR and SAVR Interventions. Reproduced from the *European Heart Journal* with permission from Oxford University Press.

**Figure 6.** Framework for Aortic Valve Shared Decision-Making. *In patients 50 to 69 years old.

AVR, aortic valve replacement; CI, confidence interval; INR, international normalized ratio; PPM, patient prosthesis mismatch; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.