Decision Making in Valve Replacement: TAVR vs SAVR

Clinical Practice Today CME

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Learning Objectives

Upon completion, participants should be able to:

- Describe the differences in general criteria for TAVR and SAVR
- Understand the risks and benefits of available devices and how using these devices compares with standard medical therapy

Introduction

Valvular aortic stenosis (AS) is a progressive disease caused by calcification of the aortic valve, with underlying pathophysiologic processes similar to those of atherosclerosis.[1] The prevalence of moderate or severe AS increases with advancing age and currently affects about 3% of individuals aged 75 years or older.[2] Although asymptomatic AS does not increase the risk of death, patient prognosis deteriorates substantially once the disease becomes symptomatic.[2] Without surgical intervention, the 1-year mortality rate for patients with severe symptomatic AS is 50%, and the 2-year mortality rate is 70% to 80%.[2]

Surgical aortic valve replacement (SAVR) improves symptoms and reduces mortality for many patients with severe AS.[1] However, many patients with severe AS are considered poor candidates for surgery due to advanced age, poor left ventricular (LV) function, or medical comorbidities that increase the risk of operative complications or mortality.[1] Indeed, only 50% of patients with severe AS are referred for surgical intervention, and only 40% undergo SAVR.[3] For patients who are considered high-risk surgical candidates, a less invasive approach to treatment may be preferred.[1]

Introduction (cont.)

As an alternative to surgery, transcatheter aortic valve replacement (TAVR) involves the displacement and functional replacement of the native aortic valve with a bioprosthetic valve. In most cases, the valve is delivered on a catheter through the femoral artery (transfemoral). Other access sites for catheter delivery are used for those lacking adequate femoral arterial access. Once in the ideal position across the aortic valve annulus, the valve is deployed via a balloon-expandable or self-expandable system. Since the first TAVR procedure in 2002, transcatheter intervention has become an established alternative to SAVR in patients who are considered inoperable due to prohibitive surgical risk.[4] More recently, the role of TAVR has expanded to include patients with severe AS who are considered operable but have a high surgical risk.[5,6] In addition, TAVR has expanded to include patients who have an intermediate risk of death or complications associated with open-heart surgery.[6a]

Introduction (cont.)

In 2014, the American Heart Association and American College of Cardiology (AHA/ACC) published updated guidelines for the management of valvular heart disease.[7] The guidelines include revised staging criteria for AS, updated recommendations regarding the timing of intervention, and new guidance on the choice between transcatheter and surgical intervention. Overall, the 2014 recommendations reflect a shift toward earlier intervention in the course of AS and increased acceptance of TAVR as an alternative to surgery in appropriate patients.[7] More recently, the ACC published an expert consensus document that discusses the decision pathway for TAVR in patients with severe AS.[7a]

Disease Staging and Risk Assessment

Before choosing between TAVR and SAVR, clinicians must first determine whether any form of intervention is indicated for patients with AS.[2,7a] This decision-making process begins with accurate staging, point-of-care checklists and algorithms, and surgical risk assessment.[2,7a] The 2017 consensus document also notes that as new valves and implantation methods are developed for TAVR, different patient populations may become candidates for the procedure.[7a]

Disease Staging and Risk Assessment (cont.)

Disease Staging System

The 2014 AHA/ACC guidelines introduced a new system of classification for valvular heart disease with 4 progressive stages, similar to the AHA/ACC classification system for heart failure.[7] For each valve lesion, staging is based on valve anatomy, valve hemodynamics, hemodynamic consequences, and symptoms.

The proposed stages are defined as[7]:

- **Stage A:** At risk
- **Stage B:** Progressive
- **Stage C:** Asymptomatic severe
- **Stage D:** Symptomatic severe

Disease Staging and Risk Assessment (cont.)

Disease Staging System (cont.)

Within this updated staging system, additional modifications to the classification of AS help differentiate the potential indications for intervention (Table 1). Specifically, stage C is divided into 2 subcategories: asymptomatic severe AS (stage C1) and asymptomatic severe AS with LV dysfunction (stage C2). Stage D is subdivided into 3 categories: symptomatic severe high-gradient AS (stage D1); symptomatic severe low-flow/low-gradient (LFLG) AS with reduced LV ejection fraction (EF) (stage D2); and symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS (stage D3).[7]

TABLE 1. Recommendations for the Timing of Intervention in Aortic Stenosis

AVR	Class of Recommendation	Level of Evidence
Recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)	I	B
Recommended for asymptomatic patients with severe AS (stage C2) and LVEF < 50%	I	B
Indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery	I	B
Reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥ 5.0 m/s) and low surgical risk	IIa	B
Reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP	IIa	B

AS = aortic stenosis; AVR = aortic valve replacement; BP = blood pressure; LVEF = left ventricular ejection fraction.

TABLE 1. Recommendations for the Timing of Intervention in Aortic Stenosis (cont.)

AVR	Class of Recommendation	Level of Evidence
Reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥ 4.0 m/s (or mean pressure gradient ≥ 40 mm Hg) with a valve area ≤ 1.0 cm^2 at any dobutamine dose	IIa	B
Reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥ 50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms	IIa	C
Reasonable for patients with moderate AS (stage B) (aortic velocity 3.0-3.9 m/s) who are undergoing other cardiac surgery	IIa	C
May be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk	IIb	C

AS = aortic stenosis; AVR = aortic valve replacement; BP = blood pressure; LVEF = left ventricular ejection fraction.

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Disease Staging and Risk Assessment (cont.)

Surgical and Interventional Risk Assessment

Several risk calculators are available to estimate the risk of surgical intervention in patients with severe AS. The Society of Thoracic Surgeons (STS) predicted risk of mortality (PROM) score is widely used to assess operative risk in patients being considered for surgical intervention.[8] It incorporates risk factors such as age, comorbidities, previous cardiovascular interventions, perioperative cardiac status, and hemodynamic status.[9] Many of the major TAVR clinical trials used the STS-PROM score to determine eligibility for enrollment.[8] The STS-PROM score is an effective quantitative tool, but it does not consider some data known to influence the risk of open cardiac surgery, such as ambulatory status, pulmonary resistance, and overall frailty. The STS risk calculator is publically available on the STS Web site for risk estimation in individual patients (www.sts.org).[9]

Disease Staging and Risk Assessment (cont.)

Surgical and Interventional Risk Assessment (cont.)

One of the limitations of the STS score is that it was not designed to estimate risk in patients who are being considered for nonsurgical interventions, such as TAVR.[7] The 2014 AHA/ACC guidelines proposed a new risk-scoring system that builds on the STS score by incorporating three additional indicators of surgical and interventional risk: patient frailty, the number of compromised organ systems, and procedure-specific impediments.[7] The updated approach to risk assessment (Table 2) indicates a shift away from sole reliance on score-based treatment decisions and places increased emphasis on individualized patient assessment.

TABLE 2. Surgical and Interventional Risk Classification for Patients With Severe Aortic Stenosis

	Low Risk (Must Meet All Criteria)	Intermediate Risk (Any 1 Criterion)	High Risk (Any 1 Criterion)	Prohibitive/ Extreme Risk (Any 1 Criterion)
STS-PROM[a]	< 4%, AND	4%-8%, OR	≥ 8%, OR	Predicted risk with surgery of death or major all-cause morbidity > 50% at 1 year, OR
Frailty[b]	None, AND	1 index (mild), OR	≥ 2 indices (moderate to severe), OR	
Major organ system compromise not to be improved postoperatively[c]	None, AND	1 organ system, OR	No more than 2 organ systems, OR	≥ 3 organ systems, OR
Procedure-specific impediment[d]	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

[a]Use of the STS-PROM score to predict risk in a given institution with reasonable reliability is appropriate only if institutional outcomes are within 1 standard deviation of STS average observed/expected ratio for the procedure in question.
[b]Seven frailty indices: Katz Activities of Daily Living (independence in feeding, bathing, dressing, transferring, toileting, and urinary continence) and independence in ambulation (no walking aid or assist required or 5-meter walk in < 6 s). Other scoring systems can be applied to calculate no, mild-, or moderate-to-severe frailty.

TABLE 2. Surgical and Interventional Risk Classification for Patients With Severe Aortic Stenosis (cont.)

[c]Examples of major organ system compromise: cardiac—severe LV systolic or diastolic dysfunction or RV dysfunction, fixed pulmonary hypertension; CKD stage 3 or worse; pulmonary dysfunction with FEV_1 < 50% or $DLCO_2$ < 50% of predicted; CNS dysfunction (dementia, Alzheimer disease, Parkinson disease, CVA with persistent physical limitation); GI dysfunction—Crohn disease, ulcerative colitis, nutritional impairment, or serum albumin < 3.0; cancer—active malignancy; and liver—any history of cirrhosis, variceal bleeding, or elevated INR in the absence of VKA therapy.
[d]Examples: tracheostomy present, heavily calcified ascending aorta, chest malformation, arterial coronary graft adherent to posterior chest wall, or radiation damage.

Disease Staging and Risk Assessment (cont.)

Surgical and Interventional Risk Assessment (cont.)

The 2017 ACC consensus document further discusses patient risk assessment and the decision pathway for TAVR.[7a] First, patients should be adults with calcific valvular AS; they must be assessed for underlying surgical risk based on the 2014 AHA/ACC guidelines, the STS-PROM score, and other measures. Importantly, the multidisciplinary team of various cardiovascular subspecialists must be closely involved in the decision-making and procedural processes.

Disease Staging and Risk Assessment (cont.)

Surgical and Interventional Risk Assessment (cont.)

The decision pathway is divided into 4 main sections[7a]:

- Preprocedure evaluation, which is based on individualized clinical and imaging evaluation, risk category, patient goals and expectations, and futility consideration as assessed by the entire heart valve team; this should be performed as the first step in the decision-making process
- TAVR imaging and assessment, which includes transthoracic echocardiography, multi-detector CT, and other imaging techniques with critical measures; this should be used in initial assessment and evaluation conducted before, during, and after the procedure
- Key issues regarding performance of TAVR, which involves preprocedural planning and procedural details, anticoagulation, and post-deployment valve assessment
- Post-TAVR management, which includes pain management, discharge planning, and long-term follow-up care

Choice of Valve-Replacement Procedure

Surgical and Interventional Risk Assessment (cont.)
The patient's degree of surgical risk is the primary consideration driving the recommendations for transcatheter versus surgical intervention for severe AS (Table 3). The 2014 AHA/ACC guidelines recommend TAVR for patients who are considered too high risk for surgical intervention and who are expected to survive more than 12 months after the procedure (class I).[7] TAVR is also recommended as a reasonable alternative to surgery in patients who are high-risk surgical candidates (class I).[6,7] For patients at low or intermediate surgical risk, however, SAVR remains the recommended intervention (class I).[7]

TABLE 3. Recommendations for Transcatheter Versus Surgical Intervention in Aortic Stenosis

Recommendations	Class of Recommendation	Level of Evidence
SAVR is recommended in patients who meet an indication for AVR with low or intermediate surgical risk	I	A
For patients in whom TAVR or high-risk SAVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care	I	C
TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival > 12 months	I	B
TAVR is a reasonable alternative to SAVR in patients who meet an indication for AVR and who have high surgical risk	IIa	B

AS = aortic stenosis; AVR = aortic valve replacement; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

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TABLE 3. Recommendations for Transcatheter Versus Surgical Intervention in Aortic Stenosis (cont.)

Recommendations	Class of Recommendation	Level of Evidence
Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS	IIb	C
TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS	III: No benefit	B

AS = aortic stenosis; AVR = aortic valve replacement; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

Choice of Valve-Replacement Procedure (cont.)

Heart Valve Teams and Centers of Excellence

Treatment decision making requires collaboration between patients and a multidisciplinary team of clinicians with experience in AS care.[7] Reflecting the importance of multidisciplinary care, the 2014 AHA/ACC guidelines discuss the role of heart valve teams and heart valve centers of excellence in the management of patients with severe heart valve disease.[7]

The guidelines recommend (class I) that a heart valve team collaborate on the care of patients who are being considered for transcatheter or surgical intervention. At minimum, the team should consist of a cardiologist and a cardiovascular surgeon. Depending on the needs of the patient, the heart valve team may also include structural valve interventionalists, cardiovascular imaging specialists, anesthesiologists, and nurses with experience in managing severe heart valve disease.[7]

Choice of Valve-Replacement Procedure (cont.)

Heart Valve Teams and Centers of Excellence (cont.)
The AHA/ACC guidelines also recommend (class IIa) consultation with or referral to a heart valve center of excellence for[7]:

- Asymptomatic patients with severe valve disease
- Patients who may be best treated with valve repair rather than valve replacement
- Patients with multiple comorbidities who are candidates for valve intervention

To qualify as a heart valve center of excellence, facilities must have experienced clinicians from multiple disciplines, offer all available options for AS diagnosis and management, participate in regional or national outcome registries, demonstrate adherence to guidelines, participate in ongoing quality improvement initiatives, and publically report their mortality and success rates.[7]

Current Transcatheter Heart Valve Devices

The first devices approved in the United States (US) for TAVR in patients with severe symptomatic AS were the balloon-expandable Edwards Sapien bovine pericardial device and the self-expanding CoreValve porcine pericardial device.[10,11] More recently, the next-generation Edwards Sapien XT device was approved as the preferred balloon-expandable heart valve system.[12] However, the latest device, Sapien 3, has replaced the XT as the most common balloon-expandable transcatheter valve in the US, and the EvolutR (a repositionable CoreValve system) has replaced the original CoreValve system for the treatment of high- and extreme-high-risk AS patients in the US (JK Harrison, written communication, January 2017).

The clinical trials for first-generation devices incorporated similar study designs, with evaluation in separate cohorts of high-risk surgical patients (compared with SAVR) and nonsurgical patients (compared with medical therapy).[4,6,13,14] Additional data from postapproval registry studies provide insight on safety and efficacy in patients who do not meet the rigorous inclusion criteria of clinical trials.[15]

Current Transcatheter Heart Valve Devices (cont.)

Edwards Sapien Balloon-Expandable Device

The multicenter, prospective, randomized PARTNER trial (Placement of Aortic Transcatheter Valves) evaluated the safety and efficacy of TAVR using the first-generation Sapien heart valve system in patients with severe symptomatic AS.[4] In the two PARTNER cohorts, TAVR with the Sapien device was compared with SAVR in high-risk surgical patients (PARTNER A) or with standard medical therapy in nonsurgical patients (PARTNER B).[4,14] Based on the positive findings from these pivotal trials, the Sapien heart valve device was approved in 2011 for the treatment of nonsurgical patients and also gained approval for high-risk surgical patients in 2012.[10]

Current Transcatheter Heart Valve Devices (cont.)

Edwards Sapien Balloon-Expandable Device (cont.)

Sapien TAVR versus SAVR. The PARTNER A cohort included 699 patients who were considered high-risk surgical candidates (mean STS score, 11.8%). Prior to randomization, patients underwent an assessment of their peripheral arteries to determine eligibility for transfemoral placement (n = 497) or transapical placement (n = 207). Patients were then randomly assigned to undergo TAVR (n = 348) or SAVR (n = 351). The primary endpoint was all-cause mortality at 1 year.[14]

The 30-day all-cause mortality rate was 3.4% in the TAVR group and 6.5% in the SAVR group (*P* = .07). At 1 year, the rates of all-cause mortality were 24.2% and 26.8%, respectively (*P* = .44). The between-group difference of 2.6 percentage points was within the prespecified margin to demonstrate the noninferiority of TAVR compared with SAVR (*P* = .001).[14] Patients in the TAVR group were significantly more likely than those in the

Current Transcatheter Heart Valve Devices (cont.)

Edwards Sapien Balloon-Expandable Device (cont.)

SAVR group to experience major vascular complications by day 30 (11.0% vs 3.2%; *P* < .001). Conversely, compared with transcatheter replacement, surgical replacement was associated with an increased risk of major bleeding (9.3% vs 19.5%; *P* < .001) and new-onset atrial fibrillation (8.6% vs 16.0%; *P* = .006). The rates of major stroke in the TAVR and SAVR groups were 3.8% and 2.1%, respectively, at 30 days (*P* = .20) and 5.1% and 2.4%, respectively, at 1 year (*P* = .07).[14]

In a 2-year follow-up analysis of the PARTNER A trial, no difference was observed in all-cause mortality between the TAVR and SAVR groups (HR, 0.90; *P* = .41).[16] Additionally, the stroke rate did not differ significantly between the treatment groups (HR, 1.22; *P* = .52). Patients in the TAVR group had an increased risk of paravalvular leak (PVL) compared with those in the SAVR group at 1 year (7.0% vs 1.9%; *P* < .001) and at 2 years (6.9% vs 0.9%; *P* < .001). Moreover, the presence of PVL was associated with increased late mortality (HR, 2.11; *P* < .001), even in patients with mild PVL.[16]

Current Transcatheter Heart Valve Devices (cont.)

Edwards Sapien Balloon-Expandable Device (cont.)

More recently, 2,032 intermediate-risk patients with severe AS were randomized to undergo either TAVR or SAVR. The primary endpoint was death from any cause or disabling stroke at 2 years.[16a] The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group (*P* = .001 for noninferiority). At 2 years, the Kaplan-Meier event rates were 19.3% in the TAVR group and 21.1% in the surgery group (HR in the TAVR group, 0.89; 95% CI, 0.73-1.09; *P* = .25). In the transfemoral-access cohort, TAVR resulted in a lower rate of death or disabling stroke than surgery (HR, 0.79; 95% CI, 0.62-1.00; *P* = .05), whereas in the transthoracic-access cohort, outcomes were similar in the two groups. TAVR resulted in larger aortic valve areas than did surgery and also resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation; surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.[16a]

Current Transcatheter Heart Valve Devices (cont.)

Edwards Sapien Balloon-Expandable Device (cont.)

Sapien TAVR versus medical therapy. The PARTNER B trial included 358 nonsurgical patients who were randomly assigned to TAVR or standard medical therapy.[4] The rates of all-cause mortality in the TAVR and medical therapy groups were 5.0% versus 2.8%, respectively, at 30 days ($P = .41$) and 30.7% versus 50.7%, respectively, at 1 year ($P < .001$). This landmark clinical trial also demonstrated an absolute mortality reduction of 20% in patients treated with Sapien TAVR compared with standard medical therapy.[4]

Current Transcatheter Heart Valve Devices (cont.)

Medtronic CoreValve Self-Expandable Device

The US CoreValve Pivotal Trials evaluated the safety and efficacy of the CoreValve device in patients with symptomatic severe AS.[6,13] TAVR with the CoreValve device was compared with SAVR in the US CoreValve High Risk Study and with previously published mortality data for medical therapy alone in the US CoreValve Extreme Risk Study.[6,13] The US CoreValve High Risk Study was the first trial to show improved clinical outcomes in comparison to conventional open SAVR. Based on findings from these studies, the Medtronic CoreValve device was approved in 2014 for the treatment of severe symptomatic AS in patients with high surgical risk and in nonsurgical (extreme-risk) patients.[11]

Current Transcatheter Heart Valve Devices (cont.)

Medtronic CoreValve Self-Expandable Device (cont.)

CoreValve TAVR versus SAVR. The US CoreValve High Risk Study enrolled 795 patients with symptomatic severe AS who had an estimated 15% or greater risk of death or major morbidity within 30 days of open SAVR.[6] These high-risk surgical candidates were randomly assigned to TAVR with the CoreValve device or SAVR. The primary endpoint was all-cause mortality at 1 year. The primary hypothesis was that TAVR would be noninferior to SAVR. If the noninferiority margin was met, a test for superiority was also planned.

At baseline, the mean patient age was 83 years, and the mean STS score was 7.3% in the TAVR group (n = 390) and 7.5% in the SAVR group (n = 357). In the TAVR group, the self-expanding transcatheter valve was delivered via the iliofemoral route in 323 patients and via noniliofemoral access in 67 patients.[6]

Current Transcatheter Heart Valve Devices (cont.)

Medtronic CoreValve Self-Expandable Device (cont.)

The 1-year rates of all-cause mortality were 14.2% and 19.1% in the TAVR and SAVR groups, respectively, meeting the thresholds for noninferiority ($P < .001$) and superiority ($P = .04$) of TAVR compared with SAVR. No difference was observed between the TAVR and SAVR groups in the 1-year rate of all strokes (8.8% vs 12.6%; $P = .10$) or major strokes (5.8% vs 7.0%; $P = .59$). The combined endpoint of all-cause mortality or major stroke at 1 year favored TAVR compared with SAVR (16.3% vs 22.5%; $P = .03$).[6]

Patients in the TAVR group had a higher rate of vascular complications (6.2% vs 2.0%; $P = .004$), pacemaker implantation (22.3% vs 11.3%; $P < .001$), and moderate or severe PVL leak (6.1% vs 0.5%; $P < .001$) at 1 year compared with patients in the SAVR group.[6] Conversely, patients treated with TAVR were less likely than those in the SAVR group to experience major bleeding (16.6% vs 38.4%; $P < .001$), new-onset or worsening atrial

Current Transcatheter Heart Valve Devices (cont.)

Medtronic CoreValve Self-Expandable Device (cont.)
fibrillation (15.9% vs 32.7%; *P* < .001), and acute kidney injury (6.0% vs 15.1%; *P* < .001). The overall rate of major cardiovascular and cerebrovascular events (MACCE) was lower in the TAVR group than in the SAVR group at 1 year (20.4% vs 27.3%; *P* = .03).[6]

CoreValve TAVR versus medical therapy. The US CoreValve Extreme Risk Iliofemoral Study compared TAVR with historical data of standard medical therapy in patients who were considered to be at extreme surgical risk regarding open SAVR (≥ 50% predicted risk of operative death or irreversible morbidity at 30 days).[13] At baseline, the mean age was 83.1 years, and the mean STS-PROM was 10.3%. Most patients (91.9%) had New York Heart Association (NYHA) class III or IV symptoms. Most patients were treated using iliofemoral access (n = 487). Patients who required an alternative access approach (n = 146) were not included in the iliofemoral analysis. The primary endpoint was all-cause mortality or major stroke at 1 year.[13]

Current Transcatheter Heart Valve Devices (cont.)

Medtronic CoreValve Self-Expandable Device (cont.)
The 1-year rate of all-cause mortality or major stroke was 25.5% (95% CI, 21.6%-29.4%), significantly less than the objective performance goal of 43% calculated from historical data (*P* < .0001). The rate of all-cause mortality or major stroke at 30 days was 9.3% (95% CI, 6.7%-12.0%).[13] Patients had a low rate of major stroke at 1 month (2.4%) and 1 year (4.1%). PVL at 30 days was mostly mild (41.6%) or moderate (11.0%) and showed no correlation with late mortality. Overall, 80% of patients who experienced moderate PVL at 1 month and survived to 1 year had a reduction in PVL over time. An assessment of symptom improvement showed that 90% of patients improved at least 1 NYHA class by 1 year, and 60% of patients improved at least 2 classes.[13]

Researchers also presented results from a continued access study of 873 patients who enrolled after the US CoreValve Extreme Risk Study ended.[13] Among 830 patients treated with iliofemoral access, the risk of all-cause mortality or major stroke was 6.0% at 30 days and 16.1% at 1 year.

Current Transcatheter Heart Valve Devices (cont.)

Next-Generation Sapien XT Device

The Sapien XT device is the lower-profile, next-generation version of the Sapien balloon-expandable heart valve system.[17] Compared with the first-generation Sapien device, the Sapien XT valve incorporates changes to the valve support frame, valve leaflet geometry, and valve delivery system that may influence clinical outcomes for patients undergoing TAVR.[17] The Sapien XT device was approved in 2014 for the treatment of patients with inoperable severe AS and high-risk patients with severe AS.[12]

Current Transcatheter Heart Valve Devices (cont.)

Next-Generation Sapien XT Device (cont.)

PARTNER II: Sapien XT versus Sapien. The PARTNER II trial evaluated the transfemoral TAVR using the Sapien XT device compared with the first-generation Sapien device in 560 patients (mean age, 84.3 years) with severe AS who were ineligible for surgical intervention (mean STS score, 10.7%).[17] Patients were randomly assigned to TAVR using the Sapien XT (n = 284) or Sapien (n = 276) TAVR system.

At 1 year, a similar proportion of patients in the Sapien XT and Sapien groups reached the primary composite endpoint of death, disabling stroke, and rehospitalization (33.9% vs 34.7%; *P* = .86; *P* for noninferiority = .0034).[17] An analysis of secondary endpoints showed no difference between the Sapien XT and Sapien groups in 30-day all-cause mortality (3.5% vs 5.1%; *P* = .36) or disabling stroke at 30 days (3.2% vs 3.0%; *P* = .85). However, the Sapien XT device was associated with a reduced risk of major vascular complications compared with the first-generation Sapien device (9.6% vs 15.5%; *P* = .04), including a reduction in perforations, dissections, and hematomas.[17]

Current Transcatheter Heart Valve Devices (cont.)

Next-Generation Sapien XT Device (cont.)
Several procedural and safety endpoints favored the Sapien XT device. Although no difference was observed between the Sapien XT and Sapien groups in the mean procedure time (101.0 min vs 109.6 min; *P* = .18), patients in the Sapien XT group had a reduction in the mean anesthesia time compared with the Sapien group (197.6 min vs 212.0 min; *P* = .02).[17] Patients in the Sapien XT group were also less likely to require the implantation of 2 or more valves (1.1% vs 3.7%; *P* = .05), less likely to experience aborted procedures (0.7% vs 3.0%; *P* = .06), and less likely to require intra-aortic balloon pump (IABP) hemodynamic support (0.4% vs 2.2%; *P* = .06). A nonsignificant increase was observed in the risk of PVL in the Sapien XT group at 30 days (24.2% vs 16.9%; *P* = .12) and at 1 year (29.2% vs 20.9%; *P* = .20).[17]

The PARTNER II investigators concluded that the Sapien XT device was the preferred balloon-expandable valve system based on improved procedural outcomes, similar 30-day outcomes, a reduction in vascular complications, and similar 1-year major clinical events and valve performance.[17]

Current Transcatheter Heart Valve Devices (cont.)

Next-Generation Sapien XT Device (cont.)
SOURCE XT registry. The European SOURCE XT postapproval registry is evaluating outcomes in high-risk patients with AS who are treated with the Sapien XT device in real-world clinical practice. A recent interim analysis included 2,688 patients (mean age, 81.5 years) from 93 centers in 17 countries who underwent TAVR with the Sapien XT heart valve.[15] Most devices were implanted via the transfemoral route (62.7%), followed by the transapical (33.3%), transaortic (3.7%), and subclavian (0.3%) routes.

The 1-year all-cause mortality rate was 19.5%, and the cardiac mortality rate was 10.8%, one of the lowest mortality rates for TAVR reported to date. The stroke rate at 1 year was 6.3%.[15] Most patients (93.8%) had no or mild PVL at 1 year, suggesting that the problem of PVL in patients undergoing TAVR with the Sapien XT device is improving.[15]

Current Transcatheter Heart Valve Devices (cont.)

CHOICE: Sapien XT versus CoreValve

The German multicenter CHOICE trial was the first head-to-head randomized trial of TAVR devices.[18] The trial enrolled 241 high-risk patients with severe AS and iliac artery anatomy suitable for transfemoral access. Patients were randomly assigned to transfemoral TAVR with the Sapien XT valve (n = 121) or the CoreValve device (n = 120). The Sapien XT valve was deployed during rapid ventricular pacing, whereas the CoreValve was deployed without pacing or slow-rapid pacing. The primary endpoint was the composite endpoint of device success.[18]

At 30 days, the device success rate was 95.9% in the Sapien XT group and 77.5% in the CoreValve group (RR, 1.24; $P < .001$).[18] The difference in device success was attributed to a lower immediate procedural frequency of moderate (or higher) aortic regurgitation as assessed by angiography in the Sapien XT group compared with the CoreValve group (4.1% vs 18.3%; RR, 0.23; $P < .001$). Additionally, the need to implant more than 1 valve occurred at a lower frequency in the Sapien XT group (0.8% vs 5.8%, $P = .03$).[18]

Current Transcatheter Heart Valve Devices (cont.)

CHOICE: Sapien XT versus CoreValve (cont.)

No difference was observed between the Sapien XT and CoreValve groups in the 30-day risk of cardiovascular mortality (4.1% vs 4.3%; RR, 0.97; $P = .99$).[18] Furthermore, there were no differences in rates of major bleeding (19% vs 15%; $P = .36$) or vascular complications (14% vs 13%; $P = .78$). Overall, 18.2% of patients in the balloon-expandable valve group and 23.1% of those in the self-expandable valve group met the composite safety endpoint (RR, 0.79; $P = .42$). Additionally, patients in the Sapien XT group were less likely than those in the CoreValve group to need a permanent pacemaker (17% vs 38%; $P = .001$); the risk of stroke was numerically higher in the balloon-expandable valve group, but this difference was not statistically significant (5.8% vs 2.6%; $P = .33$).[18]

Current Transcatheter Heart Valve Devices (cont.)

CHOICE: Sapien XT versus CoreValve (cont.)
The CHOICE trial investigators concluded that the Sapien XT balloon-expandable valve resulted in greater device success than a self-expandable valve in patients with high-risk AS undergoing TAVR, but with no differences between devices in the risk of cardiovascular mortality, safety, or stroke risk at short-term follow-up.[18] It must be noted that this was a small trial compared with the randomized trials published to date on TAVR. A comparison of long-term outcomes may provide greater insight into the optimal selection of treatment options for patients with severe AS.

Safety Considerations

Reducing the risk of major adverse events associated with TAVR is the focus of ongoing technologic innovation. As previously described, the major complications of TAVR with currently available devices include PVL, vascular complications, and the development of new-onset conduction disturbances that require permanent pacemaker implantation.

Understanding the risk factors for complications may allow clinicians to identify high-risk patients and guide treatment decisions.[19] One recent meta-analysis described the risk factors that increased the likelihood of pacemaker implantation after TAVR.[19] In 11,210 patients who underwent TAVR with first-generation devices, 17% required pacemaker implantation. The risk of pacemaker implantation was 2.5-fold higher among patients treated with the CoreValve device compared with those treated with the Sapien device. The median rate of pacemaker implantation was 28% and 6% for the CoreValve and Sapien devices, respectively. Additional significant risk factors for pacemaker

Safety Considerations (cont.)

implantation included male sex (RR, 1.23; $P < .01$), first-degree atrioventricular (AV) block (RR, 1.52; $P < .01$), left anterior hemiblock (RR, 1.62; $P < .01$), and right bundle branch block (RR, 2.89; $P < .01$) at baseline. Intraprocedural AV block also significantly increased the need for pacemaker implantation (RR, 3.49; $P < .01$).[19]

Investigational Devices

As of January 2017, several new studies are being conducted or starting enrollment in the US. Numerous transcatheter devices are in development with design modifications aimed at addressing the limitations of available devices.[20] Three bioprosthetic valves in late-stage development for the treatment of severe AS include the JenaValve® system, the Medtronic Engager™ system, and the Symetis Acurate™ system.[21] With CE (Conformité Européenne) mark approval for use in Europe, these devices are accumulating additional data in clinical trials as well as postmarketing registry studies.[20]

Investigational Devices (cont.)

JenaValve

The JenaValve device features a porcine root valve fitted with an outer porcine pericardial skirt and mounted on a low-profile self-expanding nitinol stent. The valve catheter is delivered via the left ventricular apex. The stent design includes 3 “positioning feelers” that are clipped to the patient’s native aortic valve leaflets; this allows operators to rely on both axial and radial fixation to anchor the device in an anatomically correct position. The valve can be deployed without the need for rapid pacing, thereby reducing the risk of hemodynamic compromise during implantation. Moreover, the low-profile stent design prevents coronary obstruction and reduces the risk of PVL.[21-23]

Investigational Devices (cont.)

JenaValve (cont.)

After the first successful human implantation of the JenaValve in 2010, the device was evaluated in a prospective, multicenter German trial of 73 patients with severe symptomatic AS.[22,23] Among 67 patients scheduled for TAVR (mean age, 83.2 years), the procedural success rate was 89.6%. Four patients were converted to conventional surgery due to valve dislocation (6%), 2 patients required a valve-in-valve procedure (3%), and 1 patient was converted to another TAVR device (1.5%). The overall 30-day mortality rate was 7.6%. Two patients (3%) developed major cerebrovascular events, and 6 patients (9.1%) required a pacemaker for new-onset conduction disorders. Among successfully treated patients, 86.4% had no or minimal PVL, and no patients had severe postprocedural regurgitation.[23]

Investigational Devices (cont.)

JenaValve (cont.)

The JUPITER Registry follows real-world patients undergoing TAVR with the JenaValve system.[24] In a recent interim analysis, the procedural success rate among 126 patients enrolled to date was 93.7%. For those with a minimum follow-up of 30 days (n = 115), the 30-day risks of all-cause and cardiovascular mortality were 12.7% and 5.8%, respectively. Complications included acute kidney injury (13.0%), permanent pacemaker implantation for new-onset conduction disorders (13.0%), major vascular/access-site complications (7.8%), and acute myocardial infarction (0.9%). No patients have had a major stroke. Based on discharge echocardiography, no patients developed moderate or severe PVL.[24] These findings suggest a high procedural success rate with the JenaValve system in real-world patients with severe AS.

Investigational Devices (cont.)

Medtronic Engager System

The Medtronic Engager device consists of a self-expanding valve and support arms that facilitate anatomically correct positioning and axial fixation. The valve leaflets are constructed from bovine pericardial tissue and mounted within a nitinol frame. This device is delivered via the left ventricular apex.[25] A feasibility study evaluated the Medtronic Engager in 10 patients (mean age, 82.5 years) with severe AS. The device was implanted successfully with anatomically correct positioning in all patients. At 30 days, no patients had mild (or higher) PVL or transvalvular regurgitation. Two patients (20%) required the implantation of a permanent pacemaker.[26] No cases of dissection, coronary obstruction, or other device-related complications were reported. The multicenter European pivotal trial enrolled 125 patients with severe AS.[27] At baseline, the mean age was 82 years, the mean STS score was 5.6%, and 82.4% of patients had NYHA class III

Investigational Devices (cont.)

Medtronic Engager System (cont.)

or IV heart failure. A total of 124 patients underwent transapical TAVR with the Engager heart valve prosthesis, with an overall device success rate of 94.8%. The 30-day rate of all-cause mortality was 8.1%. The majority of patients (70.7%) had no PVL at day 30, although 25% had trace PVL and 4.2% had mild PVL. No cases of moderate or severe PVL were reported. A total of 34 patients (28.5%) required pacemaker implantation at 30 days.[27]

Investigational Devices (cont.)

Symetis Acurate Valve

The Symetis Acurate device consists of a porcine valve mounted on a self-expanding nitinol stent partially encased by a polyethylene terephthalate skirt.[28] The stent incorporates 3 stabilization arms that stabilize the valve in the ascending aorta and prevent tilting during deployment. To minimize the risk of coronary obstruction, the distal edge of the stent is not covered. The device is designed to be self-positioning in an anatomically correct position, allowing for a relatively simple implantation with tactile feedback.[21] It is available in 3 sizes (23 mm, 25 mm, and 27 mm) and is designed for transapical and transfemoral implantation.[21,28]

Investigational Devices (cont.)

Symetis Acurate Valve (cont.)

The Symetis Acurate valve was evaluated in a series of 40 patients (mean age, 82.8 years) with severe AS.[29] The mean STS score was 9.0%. All patients underwent successful valve implantation. The 30-day mortality rate was 12.5%, and the stroke rate was 5.0%. One patient (2.5%) required permanent pacemaker transplantation.[29] Findings from a 6-month follow-up analysis demonstrated promising midterm outcomes.[28] Two additional patients died, resulting in a 6-month survival rate of 82.5%. Two additional patients had a stroke, and 3 patients required a pacemaker. The 6-month freedom-from-MACCE rate was 75.0%. Echocardiography at 6 months showed a low risk of residual PVL, with most patients having no or mild PVL (96.7%) and 1 patient having moderate PVL (3.3%). No cases of severe PVL were reported.[28]

Conclusion

In the past decade, TAVR has substantially changed the treatment of patients with severe symptomatic AS. Based on positive findings from randomized clinical trials over the last 5 years, TAVR is now recommended for patients who are considered an extreme risk for conventional surgical intervention as assessed by a multidisciplinary heart valve team. Centers of excellence with highly developed heart valve teams, strong clinical research records offering the latest valve technology, and high procedural volume hold the promise of improved treatment outcomes for patients with AS in the US. Additionally, next-generation prosthetic valves currently in clinical trials show potential for reducing the risk of major adverse events, improving valve performance, and allowing even better long-term patient outcomes for patients undergoing TAVR. Additionally, ongoing technologic and procedural advances in devices and delivery systems may extend the reach of TAVR to patients with lower or perhaps even standard surgical risk.

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