JAMA | Review

Transcatheter Treatment of Valvular Heart Disease
A Review

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IMPORTANCE More than 40 million people are living with either mitral or aortic valve disease worldwide, and more than 180 000 heart valve replacement surgeries are performed each year in the US. Transcatheter valve repair has emerged as an important therapeutic option for patients who are candidates for heart valve replacement.

OBSERVATIONS All transcatheter valve therapies involve a multidisciplinary team of interventional cardiologists, cardiothoracic surgeons, radiologists, echocardiographers, nurses, and social workers, termed the *heart team*, to determine the optimal approach for managing each patient. Transcatheter aortic valve implantation (TAVI) is an aortic valve replacement procedure that is performed percutaneously and is currently approved for patients with severe, symptomatic aortic stenosis in all surgical risk categories. The TAVI procedure can be performed using a balloon-expandable or self-expanding valve. In a low-risk cohort of patients (PARTNER [Placement of Aortic Transcatheter Valves] 3 trial), the rates of death from any cause, stroke, or rehospitalization were 8.5% for patients receiving TAVI and 15.1% for patients undergoing surgical aortic valve replacement. Decision-making regarding therapy choice should be based on individual anatomy (including the number of leaflets, annular size, and peripheral arterial anatomy), comorbidities (including concomitant coronary artery disease and aortopathies), and patient preference guide. A mitral transcatheter edge-to-edge repair device is approved by the US Food and Drug Administration for high-risk patients with degenerative and functional mitral regurgitation that has excellent safety and efficacy in these populations. In the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation) trial, the annualized rate of all hospitalizations for heart failure was 35.8% among patients who underwent transcatheter edge-to-edge repair and received medical therapy compared with 67.9% among patients in the medical therapy alone group. Transcatheter tricuspid valve repair and replacement trials are ongoing and show promise for the treatment of patients with tricuspid regurgitation, which previously had limited therapeutic options. Multimodality imaging, which includes transthoracic echocardiography, transesophageal echocardiography, computed tomography, and intracardiac echocardiography, is important for preprocedural planning, device selection, and optimal outcomes.

CONCLUSIONS AND RELEVANCE Approximately 78 000 TAVI procedures and 10 000 transcatheter mitral valve repairs take place yearly in the US to treat patients with severe, symptomatic aortic stenosis and mitral regurgitation, respectively. Transcatheter valve therapies have expanded therapeutic options for patients, including for those who previously had no viable surgical options.

Multimedia

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More than 40 million people are living with either mitral or aortic valve disease worldwide, and more than 180 000 heart valve replacement surgeries are performed each year in the US. As of 2019, transcatheter aortic valve implantation (TAVI) procedures exceeded surgical aortic valve replacement (SAVR) procedures (77 991 vs 57 626, respectively). Due to the aging population and prevalence of disease, TAVI is expected to increase by more than 130 000 procedures by 2026. The TAVI procedure is an aortic valve replacement performed percutaneously that treats patients with severe, symptomatic aortic stenosis. A transcatheter mitral valve repair is a percutaneous procedure used to treat patients with severe, symptomatic mitral regurgitation. With expanded indications for mitral valve repair, and the advent of transcatheter mitral valve replacement, similar exponential growth is also projected for this procedure.

Transcatheter valve repair and replacement has become a cornerstone in the management of patients with aortic and mitral valvular heart disease. Conditions such as aortic stenosis, mitral regurgitation, and tricuspid regurgitation traditionally have been treated surgically. However, transcatheter valve repair and replacement have become available within the past 15 years for the treatment of these conditions. At present, more than 70 000 TAVI procedures are performed each year in the US.[1] The choice of transcatheter valve therapy or surgery should be determined using a shared-decision making process that includes patient preferences, surgical risk, anatomical factors, and a discussion among a heart team composed of interventional cardiologists, cardiothoracic surgeons, radiologists, echocardiographers, nurses, and social workers. This review provides an overview of the various types of transcatheter valve therapies that are currently available in the US (**Table 1**) and in the European Union.

Methods

We searched PubMed for English-language articles of transcatheter valve studies published between January 1, 2002, and April 1, 2021. We included several high-quality clinical trials, including randomized trials, early feasibility studies, and compassionate use studies with sample sizes of 25 patients or greater that evaluated the clinical outcomes of TAVI, valve-in-valve replacement, transcatheter mitral valve repair, and transcatheter tricuspid valve repair and replacement. Based on these criteria, 51 articles were selected. The basis of this review includes data from 17 clinical trials and 1 clinical guideline.

TAVI

Background

According to the current guidelines from the American College of Cardiology/American Heart Association (ACC/AHA),[2] classic severe aortic stenosis is defined as an aortic valve peak velocity greater than or equal to 4.0 m/s, a mean gradient greater than or equal to 40 mm Hg, or an aortic valve area of less than or equal to 1.0 cm^2. Patients should be referred for aortic valve replacement if they have severe aortic stenosis and have symptoms such as dyspnea, heart failure, angina, or syncope. Following the onset of symptoms, mortality rates approach 50% after 2 years if patients do not undergo valve replacement. Medical therapy alone does not alter the prognosis.[3-5] Therefore, expedient referral for aortic valve replacement is important. Patients who met these parameters traditionally were referred for SAVR or were deemed inoperable. However, since 2002 when the first TAVI procedure was performed, TAVI has increasingly been used as an alternative treatment strategy to SAVR even in patients with low surgical risk.[6]

Procedure

The vast majority of TAVI procedures are performed via the transfemoral route. Alternative access using a transcarotid, subclavian, transapical (minimally invasive surgical incision through the apex of the heart), or transinferior vena caval approach can be used if the femoral or iliac arteries have severe atherosclerosis with arterial dimensions approximately less than 5 mm. Planning before the procedure includes a computed tomographic scan to determine proper sizing of the valve (the aortic valve annulus, left ventricular outflow tract, and aortic root dimensions) and to determine the distance of the coronary arteries from the aortic valve annulus and peripheral arterial anatomy (**Figure 1**). The heart team is composed of interventional cardiologists, cardiothoracic surgeons, radiologists, echocardiographers, nurses, and social workers who confer regarding each patient to determine whether TAVI or SAVR is the most appropriate therapy and ascertain the optimal procedural approach (**Box**).

The TAVI procedure is performed by inserting a large bore sheath (14F-18F) into the femoral artery. The aortic valve is crossed with the delivery system in a retrograde fashion. With rapid cardiac pacing to lower the systemic blood pressure, the TAVI device is deployed in the aortic annulus with the native aortic valve leaflet calcium serving as an anchor (Figure 1 and **Video 1**). There are self-expanding and balloon-expandable valves available. The majority of TAVI procedures are performed under monitored anesthesia care with an average hospital stay of 1 to 3 days.

Patients With High Surgical Risk or Deemed Inoperable

The Placement of Aortic Transcatheter Valves (PARTNER 1A and 1B) trials and the CoreValve Extreme Risk Pivotal study[4,7,8] were designed to define the role of TAVI in patients with high surgical risk or deemed inoperable (**Table 2**). These studies were the first to demonstrate survival benefits compared with medical therapy in patients with high or extreme risk for SAVR and led to the initial approval and adoption of the TAVI procedure. The PARTNER 1B trial[4] randomized 358 patients and the PARTNER 1A trial[8] randomized 699 patients with severe, symptomatic aortic stenosis who had been deemed by the heart team as either inoperable (PARTNER 1B) or at high risk (PARTNER 1A) for cardiac surgery. The patients were randomized to TAVI with a first-generation SAPIEN balloon-expandable valve (Edwards Lifesciences) or standard therapy that could include a balloon aortic valvuloplasty. Although the technology had limitations and operator experience was minimal, the outcome of mortality improved from 50% to 30% at 1 year and this result substantially changed the treatment of aortic stenosis.

The PARTNER 1B trial found that in the cohort of inoperable patients, there was a significant reduction in death from any cause in the TAVI group. In the long-term follow-up study,[14] there was a significant reduction in mortality in the TAVI group 5 years after the procedure vs the standard medical therapy group (71.8% vs 93.6%,

Table 1. Transcatheter Valve Therapies Commercially Approved by the US Food and Drug Administration (FDA)

Therapy[a]	First FDA approval date	Indications	Risk type	Major complications	Approximate No. performed in US/y[b]
Transcatheter aortic valve implantation	• 2011 (extreme risk)[c] • 2012 (high risk)[d] • 2016 (intermediate risk)[e] • 2019 (low risk)[f]	Severe, symptomatic aortic stenosis	Any risk	Death, stroke, bleeding, need for permanent pacemaker, and emergent surgery	75 000
Mitral transcatheter edge-to-edge repair (degenerative mitral regurgitation)	2013	Severe, symptomatic, degenerative mitral regurgitation refractory to medical therapy	High surgical risk	Death, stroke, bleeding, single leaflet detachment, and emergent surgery	10 000
Mitral transcatheter edge-to-edge repair (functional mitral regurgitation)	2019	Severe, symptomatic functional mitral regurgitation on optimal medical therapy	Any risk	Death, stroke, bleeding, single leaflet detachment, and emergent surgery	5000

[a] Transcatheter tricuspid valve repair and replacement trials are ongoing but have not been commercially approved in the US.

[b] Estimates are based on data from 2019.

[c] Defined as inoperable.

[d] Predicted by 30-day mortality greater than 7%.

[e] Predicted by 30-day mortality of 3% to 7%.

[f] Predicted by 30-day mortality less than 3%.

respectively; hazard ratio [HR], 0.50 [95% CI, 0.39-0.65], $P < .001$). The CoreValve Extreme Risk Pivotal study[7] enrolled a similar cohort of patients and also demonstrated the safety and efficacy of the self-expanding CoreValve (Medtronic Inc) in patients with severe aortic stenosis who had been deemed inoperable. The study showed that the rate of all-cause mortality or major stroke at 12 months was significantly less compared with the prespecified objective performance goal.

In the PARTNER 1A trial,[8] 699 patients were randomized 1:1 to undergo TAVI with a balloon-expandable, first-generation valve or SAVR. At 1 year, the rates of death were 24.2% in the TAVI group vs 26.8% in the SAVR group ($P = .44$). In the long-term follow-up study,[15] risk of death was similar 5 years after the procedure in the TAVI group and in the SAVR group (67.8% vs 62.4%, respectively; $P = .76$). Using similar inclusion and exclusion criteria, the CoreValve High Risk Pivotal trial[9] enrolled 795 patients with aortic stenosis who had been deemed high risk for surgery and randomized them to TAVI with a self-expanding first-generation valve or SAVR. One year after the procedure, the rate of death was 14.2% among patients in the TAVI group compared with 19.1% among patients in the SAVR group (Table 2). In the long-term follow-up study,[16] all-cause mortality was similar 5 years after the procedure for patients in the TAVI group and in the SAVR group (55.3% and 55.4%, respectively, HR, 0.93 [95% CI, 0.77-1.14]; $P = .50$) and the rates of structural valve deterioration were low.

Patients With Intermediate Surgical Risk

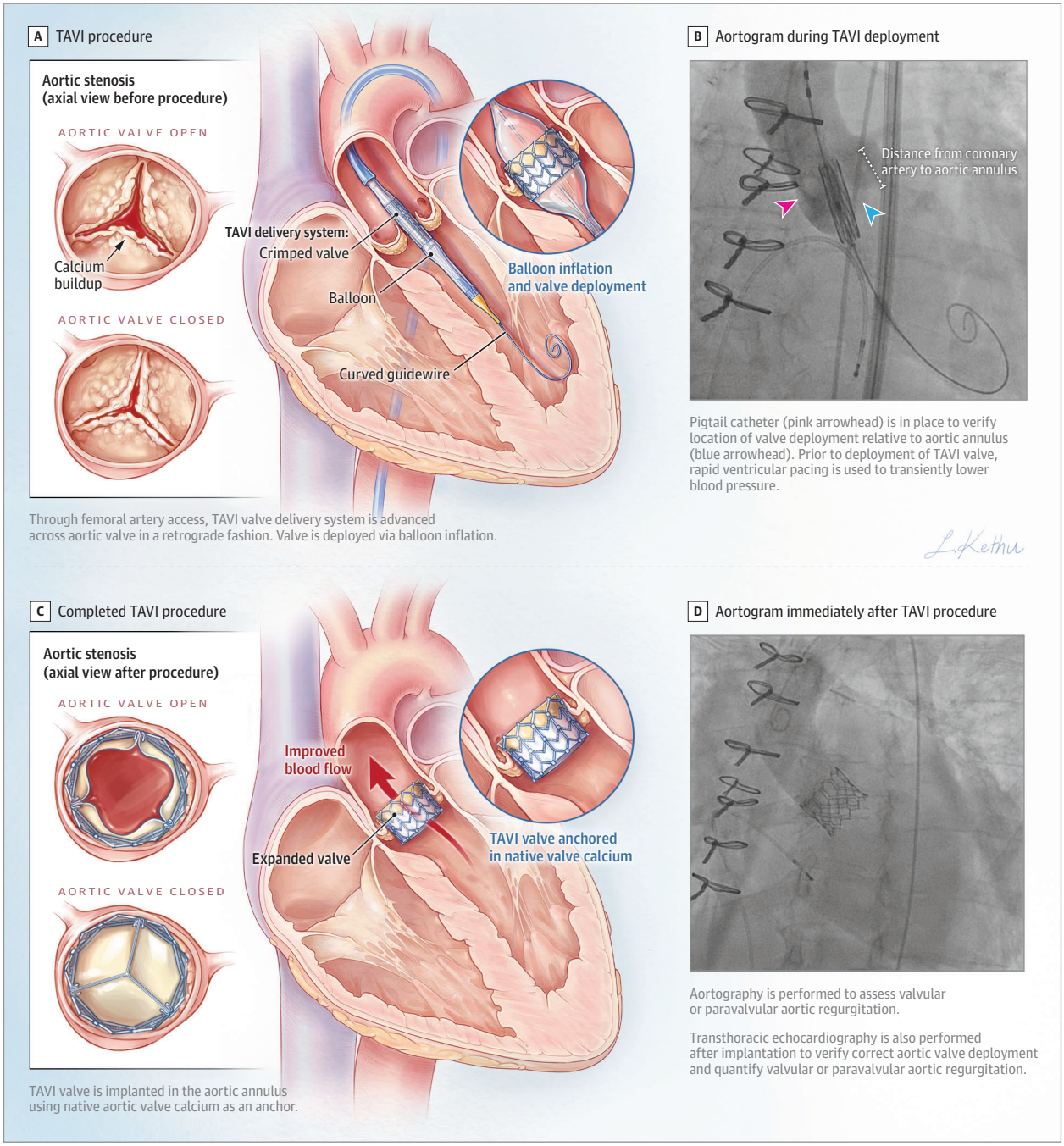
The PARTNER 2 trial[10] enrolled 2032 patients with severe aortic stenosis who had been deemed as having intermediate surgical risk and randomized them to undergo TAVI with a second-generation SAPIEN XT balloon-expandable valve or SAVR. Surgical risk was determined by the heart team and patients generally had a 30-day mortality risk of 3% to 7% using the Society of Thoracic Surgeons risk model. There were no significant between-group differences in the primary end point of death from any cause or disabling stroke at 2 years (HR, 0.89 [95% CI, 0.73-1.09] for the TAVI group [$P = .25$]; 19.3% in the TAVI group vs 21.1% in the SAVR group [$P = .33$]).[10] In patients who underwent a transfemoral TAVI, there was a lower rate of death or disabling stroke compared with SAVR. In the long-term follow-up study,[17] there was no significant difference in death or disabling stroke 5 years after the procedure between the TAVI group and the SAVR group (47.9% vs 43.4%, respectively, HR, 1.09 [95% CI, 0.95-1.25], $P = .21$). The Surgical Replacement and Transcatheter Aortic Valve Implantation trial[11] randomized 1660 patients to TAVI with a self-expanding CoreValve or Evolut R valve or to SAVR. Two years after the procedures, TAVI was found to be noninferior to SAVR for the rate of death or disabling stroke (Table 2).

Patients With Low Surgical Risk

The PARTNER 3 trial[12] randomized low-risk patients with severe aortic stenosis to TAVI with a third-generation SAPIEN 3 valve or to SAVR. This trial used a third-generation balloon-expandable valve that had a lower profile delivery system and a sealing skirt around the valve to prevent paravalvular regurgitation after deployment. Earlier-generation TAVI devices had several limitations that negatively affected outcomes (**Table 3**). Because of the large profile of the valves, there was a high incidence of access site bleeding that was associated with increased early mortality.[18,19] Also, without a sealing skirt around the valve, paravalvular aortic regurgitation was often moderate or severe and this was associated with increased rates for late mortality.[20,21] Moderate to severe paravalvular regurgitation was associated with increased late mortality (HR, 2.18 [95% CI, 1.57-3.02]; $P < .0001$).[20] Addressing these limitations along with increased operator experience led to improved short-term and long-term outcomes.

The PARTNER 3 trial[12] enrolled patients with trileaflet aortic stenosis who had been deemed low risk for any surgical intervention. There were 1000 patients enrolled and the primary end point of death, stroke, or rehospitalization was significantly lower in patients in the TAVI group 1 year after the procedure compared with patients in the SAVR group (8.5% vs 15.1%, respectively; absolute between-group difference, −6.6 percentage points [95% CI, −10.8 to −2.5 percentage points], $P < .001$ for noninferiority; HR, 0.54 [95% CI, 0.37 to 0.79], $P = .001$ for superiority; Table 2).[12] Hospital length of stay was significantly shorter and there were lower rates of new-onset atrial fibrillation, lower incidences of acute kidney injury, and improvements in New York Heart Association (NYHA) class, 6-minute walk test distance, and Kansas City Cardiomyopathy Questionnaire score.[12] After long-term follow-up of 2 years, TAVI was found to be superior for the combined primary end point of death, stroke,

Figure 1. Transcatheter Aortic Valve Implantation (TAVI)



and rehospitalization compared with SAVR (11.5% vs 17.4%, respectively; $P = .007$).[22]

The Evolut Surgical Replacement and Transcatheter Aortic Valve Implantation in Low-Risk Patients trial[13] randomized patients with low-risk severe aortic stenosis to a self-expanding TAVI or SAVR device. In this trial, which enrolled 1468 patients, patients in the TAVI group received either a first-generation (CoreValve, 3.6%), second-generation (Evolut R, 74.1%), or third-generation (Evolut PRO, 22.3%) self-expanding bioprosthesis. The second- and third-generation valves were designed to minimize paravalvular regurgitation by adding a sealing skirt around the nitinol frame. The trial demonstrated that the self-expanding TAVI device was noninferior to the SAVR device 2 years after the procedure (5.3% vs 6.7%, respectively; between-group difference, −1.4 percentage points; 95% Bayesian credible interval for difference, −4.9 to 2.1 percentage points; posterior probability of noninferiority, $P > .999$; Table 2).

Current Practice

Based on these trials, the US Food and Drug Administration (FDA) approved TAVI in 2019 for patients with low surgical risk. An online Society of Thoracic Surgeons risk calculator is used to determine 30-day surgical mortality and an estimated mortality rate of less 3%

Box. Frequently Asked Questions About Transcatheter Valve Therapies

Which Patients Should Be Considered for Transcatheter Aortic Valve Implantation?

Patients with severe, symptomatic aortic stenosis should be referred for transcatheter aortic valve implantation (TAVI). Severe aortic stenosis is defined by the following parameters: aortic valve peak velocity of greater than or equal to 4.0 m/s, a mean gradient greater than or equal to 40 mm Hg, or an aortic valve area less than or equal to 1.0 cm^2. At present, patients of all surgical risk categories are eligible to undergo the TAVI procedure. All patients must undergo transthoracic echocardiography, computed tomography, and an assessment by a heart team composed of interventional cardiologists, cardiothoracic surgeons, radiologists, echocardiographers, nurses, and social workers. Patients with bioprosthetic severe, symptomatic aortic stenosis may also be eligible for transcatheter aortic valve-in-valve replacement.

What Are Some Factors That Might Favor Surgical Aortic Valve Replacement Over TAVI?

To determine which patients should undergo the TAVI procedure vs surgical aortic valve replacement (SAVR), a heart team approach is necessary to discuss the risks and benefits of each intervention. Surgical aortic valve replacement should be strongly considered in patients who are of acceptable surgical risk and have certain comorbid conditions. The patients who should undergo SAVR include those with a thoracic aortic aneurysm that meets criteria for surgical repair, those with severe coronary artery disease that meets criteria for surgical revascularization, or those with severe left ventricular outflow tract calcification that may increase the risk of annular rupture with TAVI. Although TAVI is feasible in patients with bicuspid aortic valves, the distribution of calcium on the valve should be determined and the Sievers classification system for bicuspid aortic valves (based on the number of raphes of the native aortic valve [range, 0-2]) should be used when making therapeutic decisions to determine whether TAVI will have favorable results, and if not, SAVR may be a better option for these patients.

Which Patients Should Be Considered for Transcatheter Mitral Valve Repair?

Patients with severe, symptomatic mitral regurgitation who have high surgical risk should be considered for transcatheter mitral valve edge-to-edge repair. The mechanism of mitral regurgitation may be degenerative (due to anatomical defects of the mitral valve) or functional (due to tethering of the mitral valve from left ventricular dysfunction). Patients must be evaluated by a heart team to determine eligibility for transcatheter mitral valve repair.

Which Patients Should Be Considered for Transcatheter Tricuspid Valve Repair or Replacement?

Patients may be eligible for transcatheter tricuspid valve repair or replacement if they have severe, symptomatic tricuspid regurgitation. At present, all transcatheter tricuspid valve therapies are investigational, therefore, patients must qualify for enrollment in clinical trials. Current therapies under investigation include suture annuloplasty and annular reduction techniques as well as transcatheter tricuspid valve replacement.

without comorbidities accounted for in the risk calculator (eg, frailty, porcelain aorta, hepatic disease) is considered low risk. The 2020 ACC/AHA guidelines[2] provided recommendations for patients who should be considered for TAVI. Use of TAVI and SAVR are both class I recommendations (meaning they are recommended as first-line therapies) for any patient with severe, symptomatic aortic stenosis and for those asymptomatic patients with severe aortic stenosis and an ejection fraction of less than 50% regardless of surgical risk. The current guidelines do not distinguish choice of therapy based on the traditional low, intermediate, or high-risk designation. Therefore, it is important to consider that the ultimate recommendation for SAVR or TAVI for each individual takes into account a number of factors, including surgical risk, age, patient frailty, hepatic disease, history of chest radiation therapy, patient anatomy (bicuspid valves, concomitant coronary artery disease, aortopathies), and patient preference (**Table 4**).

One concern regarding TAVI is the durability of the valve compared with surgical bioprosthetic valves. A study that evaluated 241 patients treated with TAVI found excellent durability 5 to 10 years after implantation, with 91% of patients remaining free of structural valve deterioration.[23] Additional long-term follow-up data will be required to fully understand the durability of transcatheter valves, and this is an issue that should be discussed with patients at the time of consultation.

Special Populations of Patients With Aortic Stenosis

Bicuspid Aortic Valves and Concomitant Aortic Diseases

Because patients with bicuspid aortic valves often have unique anatomies, including an elliptical (noncircular) annulus, eccentric valvular calcification, outflow track calcium, and associated aortopathy, compared with those with trileaflet aortic valves, they were excluded from enrollment in the TAVI randomized trials. Bicuspid aortic valves are found in approximately 1% of the population.[24,25] Specifically, patients with bicuspid aortic stenosis tend to present at younger ages than patients with tricuspid aortic stenosis, and therefore, patients with bicuspid aortic stenosis comprise a significant proportion of the low-risk population.[24] Sievers and Schmidtke[26] published a description of a classification system (Sievers classification for bicuspid aortic valves) that is based on the number of raphes (the conjoined area of 2 underdeveloped leaflets that become a malformed commissure between both leaflets) of the native aortic valve (range, 0-2) and this system should be used when making therapeutic decisions for patients with bicuspid aortic stenosis.

Although randomized trials have not specifically addressed bicuspid aortic valves for patients undergoing TAVI, a propensity-matched registry evaluating patients with bicuspid vs tricuspid aortic stenosis demonstrated an increased 30-day risk of stroke and need for pacemaker implantation in the bicuspid aortic stenosis group.[27] There also has been some concern that patients with bicuspid aortic stenosis undergoing TAVI may have higher rates of aortic injury and paravalvular leakage. However, in a subset analysis, these concerns seem specific to patients who received older-generation valves.[28]

Many patients with severe bicuspid aortic stenosis have concomitant thoracic aortopathies, including aortic root aneurysms, that may require concomitant surgical intervention. Current ACC/AHA guidelines[2] have a class 2A recommendation (is reasonable) for replacement of the ascending aorta at the time of bicuspid aortic valve surgery if the diameter of the ascending aorta is greater than or equal to 4.5 cm. Therefore, patients who are candidates for SAVR and have a significant aortopathy based on the ACC/AHA guidelines are better suited for SAVR and aortic root replacement. Patients with

Table 2. Summary of Transcatheter Aortic Valve Implantation (TAVI) Trials

Trial or study name	Dates of trial or study	Surgical risk	Study design	Valve implanted for TAVI	No. of patients	Study duration, y	Primary study end point	Results of primary study end point	Other events and comments
PARTNER 1B[4]	May 2007-Mar 2009	Inoperable	Randomized 1:1 to TAVI or standard therapy	Edwards SAPIEN (balloon-expandable valve)	179 in TAVI group; 179 in standard therapy group	1	Rate of death from any cause	30.7% in TAVI group vs 50.7% in standard therapy group; HR, 0.55 (95% CI, 0.40 to 0.74), $P < .001$	Major stroke: 7.8% in TAVI group vs 3.9% in standard therapy group ($P = .18$)
CoreValve Extreme Risk Pivotal[7]	Feb 2011-Aug 2012	Inoperable	All received TAVI	CoreValve (self-expandable valve)	All 489 in TAVI group (no comparison group)	1	All-cause mortality or major stroke	26.0% vs 43.0% with the prespecified objective performance goal (upper 2-sided 95% CI boundary for 26.0%: 29.9%, $P < .0001$)	Major stroke: 4.3%
PARTNER 1A[8]	May 2007-Aug 28, 2009	High	Randomized 1:1 to TAVI or SAVR	Edwards SAPIEN (balloon-expandable valve)	348 in TAVI group; 351 in SAVR group	1	Rate of death from any cause	24.2% in TAVI group vs 26.8% in SAVR group ($P = .44$); 2-sided 95% CI, −9.3 to 4.1; upper 1-sided 95% CI boundary: 3.0 percentage points ($P = .001$ for noninferiority)	Major stroke: 5.1% in TAVI group vs 2.4% in SAVR group ($P = .07$)
CoreValve High Risk Pivotal[9]	Feb 2011-Sep 2012	High	Randomized 1:1 to TAVI or SAVR	CoreValve (self-expandable valve)	390 in TAVI group; 357 in SAVR group	1	Rate of death from any cause	14.2% in TAVI group vs 19.1% in SAVR group; absolute reduction in risk, 4.9 percentage points; upper 95% CI boundary, −0.4 ($P < .001$ for noninferiority; $P = .04$ for superiority)	Major stroke: 8.8% in TAVI group vs 12.6% in SAVR group ($P = .10$)
PARTNER 2[10]	Dec 2011-Nov 2013	Intermediate	Randomized 1:1 to TAVI or SAVR	SAPIEN XT (balloon-expandable valve)	1011 in TAVI group; 1021 in SAVR group	2	Death from any cause or disabling stroke	No significant between-group difference: HR for the TAVI group, 0.89 (95% CI, 0.73 to 1.09, $P = .25$)	In the transfemoral cohort, the primary end point was lower in the TAVI group than in the SAVR group (HR for the intention-to-treat analysis, 0.79 [95% CI, 0.62 to 1.00], $P = .05$)
SURTAVI[11]	Jun 2012-Jun 2016	Intermediate	Randomized 1:1 to TAVI or SAVR	• CoreValve (84%) • Evolut R (16%) • Both are self-expandable valves	864 in TAVI group; 796 in SAVR group	2	Death from any cause or disabling stroke	12.6% in TAVI group vs 14.0% in SAVR group (95% Bayesian credible interval for difference, −5.2% to 2.3%; posterior probability of noninferiority, $P > .999$)	Higher rates of acute kidney injury and atrial fibrillation in SAVR group; higher rates of aortic regurgitation and pacemaker implantation in TAVI group
PARTNER 3[12]	Mar 2016-Oct 2017	Low	Randomized 1:1 to TAVI or SAVR	SAPIEN 3 (balloon-expandable valve)	503 in TAVI group; 497 in SAVR group	1	Death from any cause, stroke, or rehospitalization	8.5% in TAVI group vs 15.1% in SAVR group; absolute between-group difference, −6.6 percentage points (95% CI, −10.8 to −2.5 percentage points, $P < .001$ for noninferiority); HR, 0.54 (95% CI, 0.37 to 0.79), $P = .001$ for superiority	No significant between-group differences for major vascular complications, pacemaker placement, and moderate to severe paravalvular regurgitation
Evolut Low Risk[13]	Mar 2016-Nov 2018	Low	Randomized 1:1 to TAVI or SAVR	• CoreValve (3.6%) • Evolut R (74.1%) • Evolut PRO (22.3%) • All 3 are self-expandable valves	734 in TAVI group; 734 in SAVR group	2	Death from any cause or disabling stroke	5.3% in TAVI group vs 6.7% in SAVR group (between-group difference, −1.4 percentage points; 95% Bayesian credible interval for difference, −4.9 to 2.1 percentage points; posterior probability of noninferiority $P > .999$)	Prespecified interim analysis: need for permanent pacemaker higher in TAVI group vs SAVR group (17.4% vs 6.1%, respectively; between-group difference, 11.3% [95% CI, 8.0% to 14.7%])

Abbreviations: Evolut Low Risk, Evolut Surgical Replacement and Transcatheter Aortic Valve Implantation in Low-Risk Patients; HR, hazard ratio; PARTNER, Placement of Aortic Transcatheter Valves; SAVR, surgical aortic valve replacement; SURTAVI, Surgical Replacement and Transcatheter Aortic Valve Implantation.

Table 3. Generations of Transcatheter Aortic Valve Implantation (TAVI) Devices

TAVI device						
Manufacturer	Name	Valve type	Sheath size, in F	Size, in mm	Material	Features and limitations
Edwards Lifesciences	SAPIEN	Balloon-expandable	22-24	23, 26	Cobalt-chromium alloy frame with bovine pericardium leaflets	Requires rapid pacing for deployment
	SAPIEN XT	Balloon-expandable	16-20	20, 23, 26, 29	Cobalt-chromium alloy frame with bovine pericardium leaflets	Thinner strut frame, additional valve size, lower profile delivery system, requires rapid pacing for deployment
	SAPIEN 3	Balloon-expandable	14-16	20, 23, 26, 29	Cobalt-chromium alloy frame with bovine pericardium leaflets	Lower profile, lower frame height, requires rapid pacing for deployment, sealing skirt
Medtronic Inc	CoreValve	Self-expandable	18	23, 26, 29, 31	Nitinol frame with porcine pericardial leaflets	Repositionable, does not require rapid pacing for deployment, supra-annular valve
	Evolut R	Self-expandable	Equivalent to 14	23, 26, 29, 34	Nitinol frame with porcine pericardial leaflets	Repositionable, does not require rapid pacing for deployment, supra-annular valve
	Evolut PRO	Self-expandable	Equivalent to 14	23, 26, 29	Nitinol frame with porcine pericardial leaflets	Repositionable, does not require rapid pacing for deployment, supra-annular, improved sealing valve

Table 4. Considerations Regarding Selection of Surgical Aortic Valve Replacement (SAVR) vs Transcatheter Aortic Valve Implantation (TAVI)[a]

	Favors SAVR	Favors TAVI
Patient age	Younger (<60 y)	Any
Valve anatomy	Bicuspid aortic valve	Calcific aortic stenosis of a trileaflet valve
	Subaortic (left ventricular outflow tract) calcification	
Prosthetic valve preference	Mechanical valve	Bioprosthetic valve (favorable ratio of life expectancy to valve durability; TAVI provides larger valve area than same-sized SAVR)
Concurrent cardiac conditions	Aortic root dilation >4.5 cm	Porcelain aorta (a severely calcified aorta)
	Severe coronary artery disease requiring bypass graft surgery	
	Atrial fibrillation that is treatable (vs permanent atrial fibrillation)	
Noncardiac conditions		Severe lung, liver, or kidney disease
		Morbid obesity
Frailty	Not frail or few frailty measures	Frail
Estimated procedural or surgical risk	SAVR risk low	TAVI risk low to medium
	TAVI risk high	SAVR risk high to prohibitive
Procedure-specific impediments	Vascular access does not allow transfemoral TAVI	Previous cardiac surgery with at-risk coronary grafts
	Small annulus	Previous chest irradiation
Patient goals of care, preferences, and values	Accepts longer hospital stay and pain during recovery period	Prefers shorter hospital stay and less procedural pain during recovery period

[a] Adapted from the American College of Cardiology/American Heart Association guidelines.[2]

bicuspid aortic stenosis without aortopathy may require additional studies to determine the best approach.

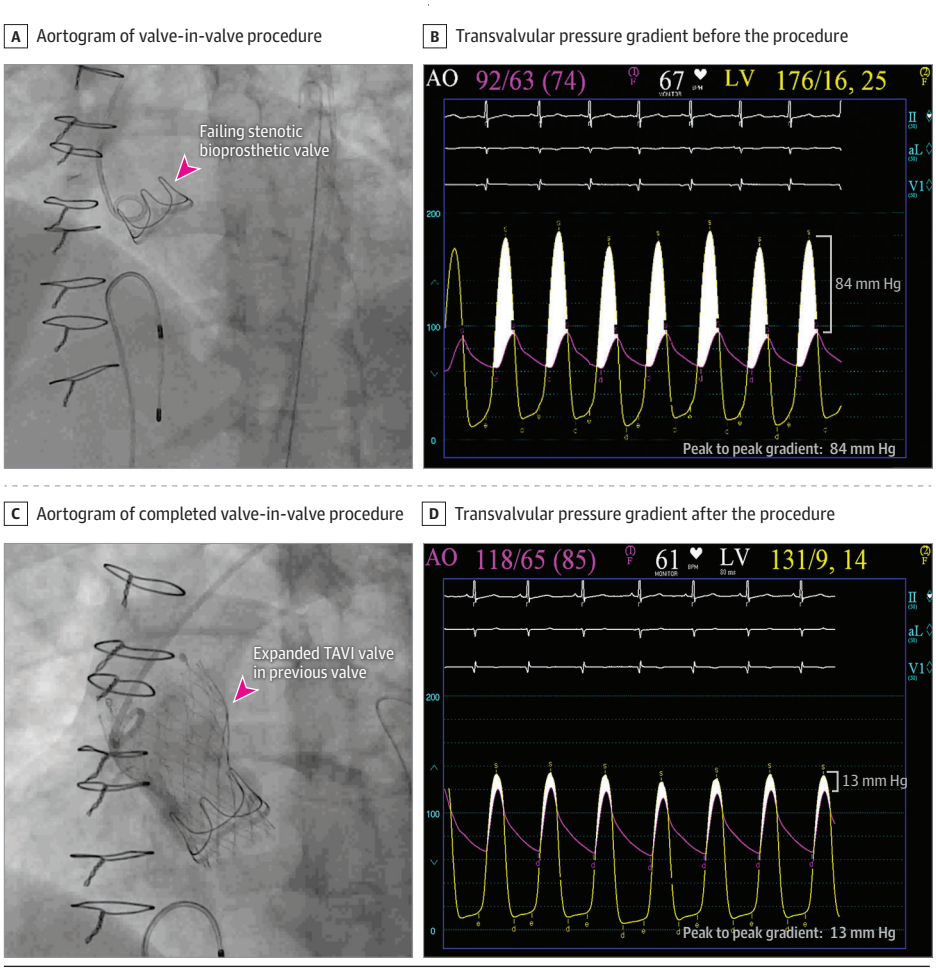
Coronary Artery Disease

Many patients with severe aortic stenosis may have concomitant severe coronary artery disease that is amenable to coronary artery bypass graft surgery or percutaneous coronary intervention. This is a common situation that requires a thorough heart team discussion to determine how to best manage both valvular and coronary artery disease, considering the patient's preferences, surgical risk, and anatomical limitations. In addition, some patients who have nonobstructive coronary artery disease at the time of TAVI may require coronary revascularization in the future. When assessing a patient for TAVI or SAVR, it is important to consider a patient's lifetime risk of requiring coronary revascularization, ability to access the coronary arteries percutaneously following TAVI, and candidacy for coronary artery bypass graft surgery in the future.

Transcatheter Valve-in-Valve Procedures for Bioprosthetic Valve Failure

Transcatheter aortic valve-in-valve procedures are nonsurgical options for patients with bioprosthetic aortic valve failure (**Figure 2** and **Video 2**). Bioprosthetic aortic valve failure occurs in approximately 50% to 60% of patients at 15 years after surgery. In this procedure, a transcatheter aortic valve is implanted inside a bioprosthetic valve, allowing a patient to avoid a second or third sternotomy. Valve-in-valve procedures can only be performed in patients who have previous bioprosthetic valves and are not technically feasible in patients who have previous mechanical valves. The Valve-in-Valve International Data Registry collects data on patients who undergo transcatheter valve-in-valve procedures.[29] Of 459 patients in the registry who underwent aortic valve-in-valve procedures, the 1-year survival rate was 83.2%. Factors associated with worse outcomes

Figure 2. Transcatheter Aortic Valve-in-Valve Procedure



TAVI indicates transcatheter aortic valve implantation.

included patients who presented with bioprosthetic aortic stenosis compared with those who presented with aortic regurgitation and small surgical valves. Similarly, transcatheter mitral valve-in-valve procedures, in which an aortic valve prosthesis is implanted within a failing bioprosthetic mitral valve, have been successfully performed (**Figure 3** and **Video 3**). The procedure uses a transseptal puncture to access the mitral valve, and studies have demonstrated a low complication rate and a low 30-day mortality rate.[30]

One adverse outcome after valve-in-valve procedures is elevated bioprosthetic pressure gradients, especially if the original surgical valve placed is small. This can lead to residual obstruction to outflow, earlier recurrence of symptoms, and potentially lower transcatheter valve durability. A technique referred to as bioprosthetic valve fracture, in which the surgical valve is sometimes used to fracture the surgical valve and improve the effective orifice area of the new prosthesis in patients with small surgical bioprostheses.[31] Overall, the potential for a future valve-in-valve procedure should be considered during the initial decision-making process of choosing a bioprosthetic or a mechanical valve. A mechanical valve has longer-term durability and structural valve deterioration is less common. However, patients with mechanical valves require lifelong anticoagulation that is associated with higher bleeding risk.[32,33] When a younger patient undergoes an aortic valve procedure, it is important to discuss that a valve-in-valve option may be feasible in the future if a bioprosthetic valve is chosen.

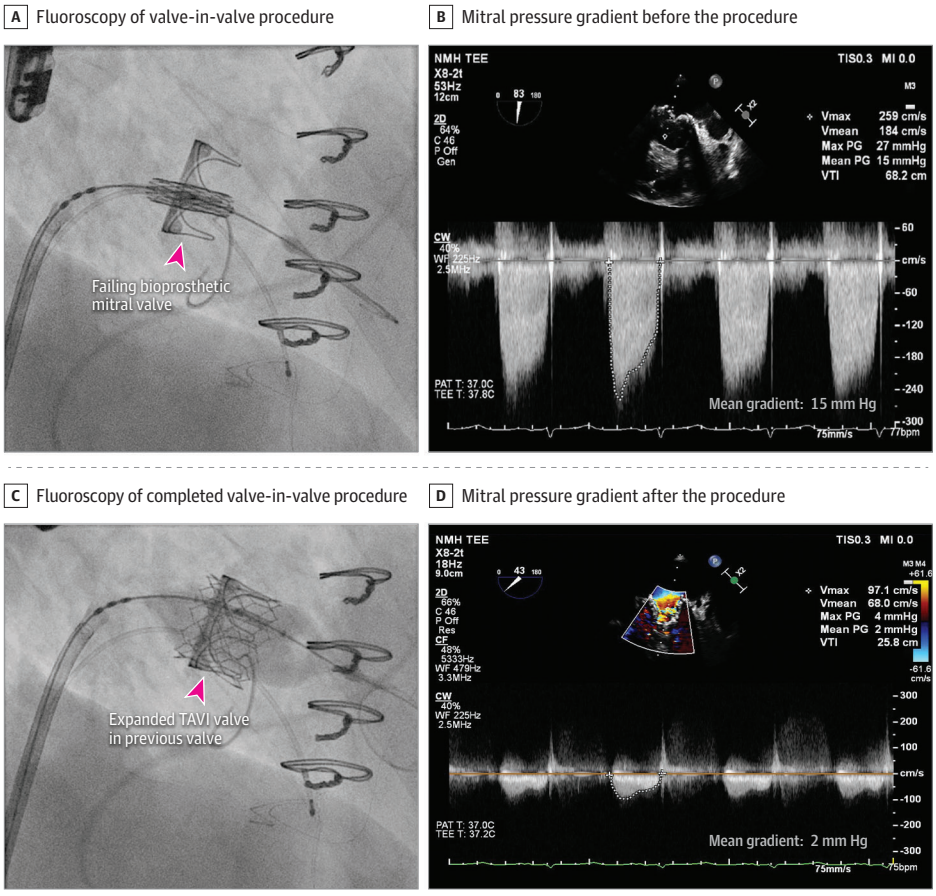
Transcatheter Edge-to-Edge Mitral Valve Repair

Background

There are 2 etiologies of mitral regurgitation that that need to be distinguished to guide treatment decisions for patients. Degenerative (or primary) mitral regurgitation occurs due to an anatomical defect of the mitral valve, which may include mitral valve prolapse or flail mitral leaflets. In contrast, functional (or secondary) mitral regurgitation occurs due to left ventricular dysfunction with annular dilation, which impedes proper leaflet coaptation. Functional mitral regurgitation is a complex disease, which may be the result of intrinsic myocardial disease or severe coronary artery disease with left ventricular dysfunction. The severity of functional mitral regurgitation can improve with medical therapy or interventions directed at improving left ventricular function, but the prognosis without any intervention remains poor.[34-36]

In the current ACC/AHA guidelines[2] regarding degenerative mitral regurgitation, mitral valve surgery is a class I indication (should be performed) for patients with severe, symptomatic

Figure 3. Transcatheter Mitral Valve-in-Valve Procedure



TAVI indicates transcatheter aortic valve implantation.

mitral regurgitation and also for asymptomatic patients with left ventricular ejection fraction less than 60%. At present, mitral valve surgery remains the standard approach for the treatment of degenerative mitral regurgitation in patients with a low or intermediate risk for surgical intervention. However, the MitraClip (Abbott Vascular) is a class 2A treatment option for patients with high or prohibitive risk (per the FDA), degenerative mitral regurgitation, and suitable anatomy.

In patients with severe functional mitral regurgitation, the ACC/AHA guidelines[2] recommend mitral valve surgery as a class 2B recommendation (may be reasonable with a weak level of evidence for the recommendation) only if guideline-directed medical therapy has failed and patients continue with persistent NYHA class III-IV symptoms. Cardiac surgery has not been shown to improve survival for patients with functional mitral regurgitation. The ACC/AHA guidelines[2] now recommend transcatheter edge-to-edge mitral valve repair as a class 2A (is reasonable) indication for patients with severe, symptomatic functional mitral valve and left ventricular ejection fraction of 20% to 50% after guideline-directed medical therapy supervised by a heart failure specialist.

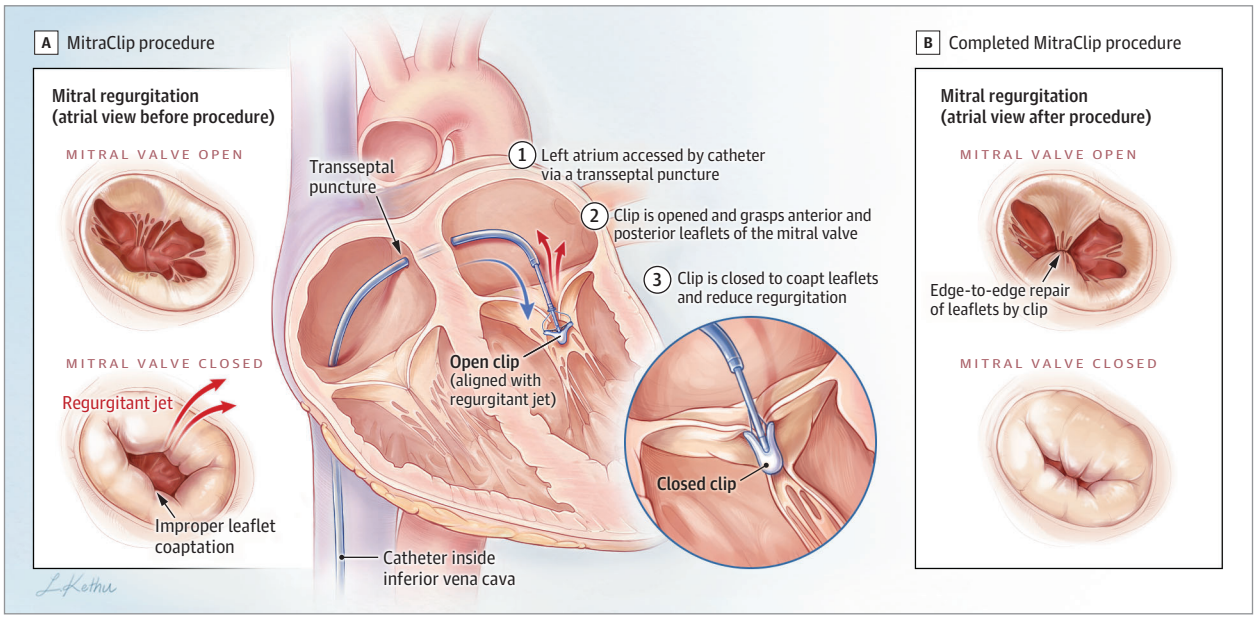
Procedure

Transcatheter mitral valve edge-to-edge repair is performed under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance throughout the procedure. The device is inserted via right femoral venous access and requires a transseptal puncture to access the left atrium (**Figure 4** and Video 4). Under transesophageal echocardiographic guidance, the device is advanced across the mitral valve into the left ventricle and grasps the anterior and posterior leaflet of the mitral valve to approximate the leaflets at the location of the regurgitant jet. During the procedure, the deployment of more than 1 clip is often required to achieve an optimal reduction in mitral regurgitation. The average length of stay following the procedure is 1 to 2 days.

Trials and Current Use

The Endovascular Valve Edge-to-Edge Repair Study[37] evaluated 279 patients with moderately severe or severe mitral regurgitation and randomized them to undergo mitral valve surgery or transcatheter edge-to-edge repair with a MitraClip. At 12 months, patients in the percutaneous repair group had a rate for freedom from death, surgery for mitral valve dysfunction, and moderate to severe or severe mitral regurgitation of 55% compared with 73% in the mitral valve surgical group (P = .007; **Table 5**). The death rate was 6% in both groups. Patients in the percutaneous repair group experienced fewer major adverse events at 30 days (15% vs 48% in the mitral valve surgical group [P < .001] primarily due to blood transfusion >2 units) and similar improvements in left ventricular size, quality of life, and NYHA classification.[37] These data demonstrated the safety and efficacy of transcatheter edge-to-edge repair and led to

Figure 4. Mitral Valve Transcatheter Edge-to-Edge Repair



the initial FDA approval of the technology for degenerative mitral regurgitation therapy in patients with high surgical risk.

However, it remained unknown whether treating patients with functional mitral regurgitation percutaneously would improve clinical outcomes given that functional mitral regurgitation is primarily due to underlying left ventricular dysfunction. Functional mitral regurgitation results from mitral annular dilation and leaflet malcoaptation; it is most commonly from ischemic cardiomyopathy with left ventricular dilation or atrial fibrillation causing atrial dilation. The Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT) trial[38] evaluated transcatheter edge-to-edge repair in patients with functional mitral regurgitation. This was a multicenter, randomized clinical trial that enrolled 614 patients with moderate to severe or severe functional mitral regurgitation who were not eligible for surgical intervention. All patients were assessed by a heart team and were receiving maximal guideline-directed medical therapy prior to enrollment.

The patients were randomized to receive transcatheter edge-to-edge repair and guideline-directed medical therapy or medical therapy alone. The mean left ventricular ejection fraction of enrolled patients was 31%. In the COAPT trial,[38] the annualized rate of all hospitalizations for heart failure was 35.8%/patient-year among patients who underwent transcatheter edge-to-edge repair and received medical therapy compared with 67.9%/patient-year among patients in the medical therapy alone group at 2 years (95% CI, 40%-70%, $P < .001$; Table 5). The data indicated that to prevent 1 heart failure hospitalization within 2 years, 3.1 patients needed to be treated with transcatheter edge-to-edge repair; to prevent 1 death, 5.9 patients need to be treated with transcatheter edge-to-edge repair. Based on the results of the COAPT trial,[38] the FDA approved the MitraClip in March 2019 for the treatment of functional mitral regurgitation.

The Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation (MITRA-FR) randomized trial[39] was conducted in France. Comparing transcatheter edge-to-edge repair with medical therapy in 307 patients (152 in device group vs 155 in medical therapy alone group), this trial showed no difference in all-cause death or rehospitalization at 1 year. However, there were significant distinctions with the MITRA-FR trial[39] compared with the COAPT trial[38] related to the patients having less baseline mitral regurgitation, worse left ventricular size and function, less mitral regurgitation reduction, increased procedural complications, and less intense medical therapy in the MITRA-FR trial.[41] Therefore, the trials are likely not comparable because patients in the MITRA-FR trial had poor left ventricular function that dominated the clinical condition as opposed to patients in the COAPT trial who had mitral regurgitation that was more prominent.

Current Practice

The MitraClip is the only FDA-approved transcatheter mitral valve repair therapy and is limited to patients who are deemed to be high risk for surgery. The most recent ACC/AHA guidelines[2] endorse its use as a 2A recommendation (considered reasonable) for high-risk patients with degenerative mitral regurgitation and as a 2A recommendation for patients with functional mitral regurgitation and low left ventricular ejection fraction and symptoms refractory for medical therapy. There are ongoing clinical trials for mitral regurgitation that compare transcatheter mitral repair and replacement with surgery in intermediate-risk patients. Unlike the aortic valve, which is anatomically somewhat similar from patient to patient, the mitral valve is an extremely complex structure with a diverse pathology that can involve the leaflets, chordae, papillary muscles, or left ventricle. Therefore, choosing the optimal transcatheter intervention for the regurgitant mitral valve is more complex than aortic stenosis. In addition, transesophageal echocardiography is necessary for procedural planning and guidance.

There are several transcatheter technologies for repair or replacement under investigation in ongoing trials. The PASCAL device (Edwards Lifesciences) is another leaflet coaptation technology that

Table 5. Summary of Transcatheter Mitral Valve Edge-to-Edge Repair Trials

Trial or study name	Dates of trial or study	Study design	Transcatheter device	No. of patients	Study duration	Primary study end point	Results of primary study end point	Other events and comments
EVEREST II[37]	Sep 2005-Nov 2008	Randomized 2:1 to percutaneous repair or mitral valve surgery	MitraClip	184 in percutaneous repair group; 95 in mitral valve surgery group	1 y	Freedom from death, surgery for mitral valve dysfunction, and moderate to severe or severe mitral regurgitation	55% in percutaneous repair group vs 73% in mitral valve surgery group (P = .007)	Death rate of 6% in both groups; major adverse events: 15% in percutaneous repair group vs 48% in mitral valve surgery group, P < .001 (primarily due to blood transfusion >2 units in 13% vs 45%, respectively)
COAPT[38]	Dec 2012-Jun 2017	Randomized 1:1 to device and medical therapy or medical therapy alone	MitraClip	302 in device and medical therapy group; 312 in medical therapy alone group	2 y	Annualized rate of all hospitalizations for heart failure	35.8%/patient-year in device group vs 67.9%/patient-year in medical therapy alone group (95% CI, 40%-70%, P < .001)	All-cause mortality rate of 29.1% in device group vs 46.1% in medical therapy alone group (HR, 0.62 [95% CI, 0.46-0.82], P < .001)
MITRA-FR[39]	Dec 2013-Mar 2017	Randomized 1:1 to device and medical therapy or medical therapy alone	MitraClip	152 in device and medical therapy group; 155 in medical therapy alone group	1 y	Death from any cause or unplanned hospitalization for heart failure	54.6% in device and medical therapy group vs 51.3% in medical therapy alone group (OR, 1.16 [95% CI, 0.73-1.84], P = .53)	Death: OR, 1.11 (95% CI, 0.69-1.77); cardiovascular death: OR, 1.09 (95% CI, 0.67-1.78); unplanned hospitalization: OR, 1.13 (95% CI, 0.81-1.56); major adverse cardiovascular events: OR, 1.22 (95% CI, 0.89-1.66)
CLASP[40]	Jun 2017-Sep 2018	Early feasibility study that enrolled patients with functional and degenerative mitral regurgitation	PASCAL	62 patients received device	30 d	Clinical success (procedural success plus reduction in mitral regurgitation to moderate or less [mild, trace, or none] and without major adverse events)	Clinical success rate of 86.9%	Primary safety end point: 6.5% for composite of major adverse events; 1.6% for all-cause mortality

Abbreviations: CLASP, Edwards PASCAL Transcatheter Mitral Valve Repair System Study; COAPT, Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation; EVEREST II, Endovascular Valve Edge-to-Edge Repair Study; HR, hazard ratio; MITRA-FR, Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation; OR, odds ratio.

is in pivotal clinical trials. This leaflet clasping device contains a spacer and 2 paddles to clasp the mitral valve leaflets. The paddles can then be directed to individually grip the anterior and posterior leaflets to improve customization to the patient's anatomy. The initial Edwards PASCAL Transcatheter Mitral Valve Repair System Study[40] (CLASP) reported the experience in 62 patients with moderate to severe mitral regurgitation or with severe functional, degenerative, or both functional and degenerative mitral regurgitation. At 30 days, clinical and procedural success and safety end points were evaluated (Table 5). Among the patients, 85% had NYHA functional class I or II ($P < .001$).[40] There was significant improvement in the 6-minute walk distance, the Kansas City Cardiomyopathy Questionnaire score, and the European Quality of Life–Five Dimensions Questionnaire score.

The ongoing prospective randomized CLASP 2D/2F trial (NCT03706833) compares the PASCAL device with the MitraClip in patients with high-risk degenerative mitral regurgitation and in those with functional mitral regurgitation. To evaluate whether these transcatheter mitral valve interventions will have expanded indications for patients who are at intermediate risk for surgery is under investigation in the ongoing Percutaneous MitraClip Device or Surgical Mitral Valve Repair in Patients With Primary Mitral Regurgitation Who Are Candidates for Surgery trial (NCT04198870) comparing the MitraClip with surgical mitral valve repair.

There are several clinical trials for transcatheter mitral valve replacement, which may serve as an alternative therapy for patients with an anatomy that is not suitable for transcatheter mitral valve repair.[42] This may include patients with large annular sizes and leaflets that are severely diseased with poor coaptation, which makes repair technically challenging. These valves are designed to be implanted from the left ventricular apex or transfemoral venous access using a transseptal puncture to access the left atrium.

Transcatheter Tricuspid Valve Interventions

Background

Tricuspid regurgitation is an often underrecognized and undertreated condition that is associated with significant mortality. The 1-year survival rate for patients with severe tricuspid regurgitation is approximately 64%.[43] This resembles the mortality of patients with severe, symptomatic aortic stenosis. Most surgical interventions for severe tricuspid regurgitation occur in conjunction with another already planned left-sided cardiac surgery. It is uncommon for a patient with isolated severe tricuspid regurgitation to undergo surgery; there are only about 250 isolated surgeries performed each year in the US.[44] Mortality for isolated tricuspid valve surgery approaches 20% and major morbidity approaches 50% at 30 days.[45] As a result, options for patients with this devastating disease are quite limited, but transcatheter tricuspid valve therapies have the potential to expand treatment options.

The ACC/AHA guidelines[2] state that isolated tricuspid valve repair or replacement is a 2b recommendation for patients with previous left-sided surgery with severe, symptomatic tricuspid regurgitation without signs of right ventricular dysfunction or pulmonary hypertension. There is also a 2b recommendation for patients with asymptomatic, severe tricuspid regurgitation with progressive right ventricular dilation or dysfunction.[2] Cardiac surgery has a 2a recommendation (considered reasonable) for isolated, severe, symptomatic secondary tricuspid regurgitation poorly responsive to medical therapy without pulmonary hypertension or left-sided disease.[2] Medical therapy has a limited role in the treatment of patients with tricuspid regurgitation, including the use of diuretics (such as furosemide or bumetanide), and in the treatment of patients with pulmonary hypertension. However, there is a paucity of data supporting the use of medical therapy to improve long-term outcomes for these patients. Commercially available transcatheter tricuspid valve therapies have been approved in the European Union and are being investigated in several ongoing trials throughout the US.

Procedures

All transcatheter tricuspid valve procedures are performed under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance and occasionally intracardiac echocardiographic guidance throughout the procedure. Imaging of the tricuspid valve can be challenging due to the varying number of leaflets, its anterior location, dynamic coaptation based on volume status, and distortion of imaging due to previous left-sided valve procedures.[46] Preparation for the procedure typically involves transesophageal echocardiography. Cardiac computed tomography is needed for transcatheter annular repair and valve replacement to determine valve or annulus sizing, coronary proximity, and anatomical feasibility for these devices.

Repair Trials

There are 2 categories of transcatheter tricuspid valve repair devices: coaptation and annuloplasty (**Table 6**). Coaptation devices function similarly to the devices used on the mitral valve and approximate the leaflets of the tricuspid valve at the location of the regurgitant jet to reduce the severity of regurgitation. In contrast, annuloplasty devices mimic a surgical annuloplasty ring to reduce the regurgitant orifice area of the tricuspid regurgitation.

The Evaluation of Treatment With Abbott Transcatheter Clip Repair System in Patients With Moderate or Greater Tricuspid Regurgitation (TRILUMINATE) study[47] evaluated the TriClip device (Abbott Structural Heart) in 85 European patients. Tricuspid regurgitation was reduced by at least 1 grade in 86% of patients, indicating a high safety signal; there were 2 deaths unrelated to the device and no cases of stroke, myocardial infarction, or device embolization. Based on these data, the TriClip device received European approval. Currently, the TRILUMINATE prospective randomized trial comparing the TriClip device with medical therapy is ongoing in the US (NCT03904147).

The PASCAL device, which was originally developed for the treatment of mitral regurgitation, has been approved for use in the European Union and is also being evaluated in a prospective randomized trial comparing the device with medical therapy for patients with severe, symptomatic tricuspid regurgitation (NCT04097145). In a series of 34 patients in the CLASP TR study[48] who received the device, the procedural success rate was 85% with a significant improvement in 6-minute walk test distance and quality of life ($P < .001$), and a reduction in tricuspid regurgitation (grade $\geq$1 in 85% of patients). For patients with a large tricuspid annulus with large leaflet coaptation gaps and tethered leaflets, transcatheter valve replacement or an annuloplasty device is a better alternative.

The Cardioband tricuspid valve reconstruction system (Edwards Lifesciences) is a transfemoral direct annuloplasty device that

Table 6. Summary of Transcatheter Tricuspid Valve Trials

Trial or study name	Type of procedure	Study design	Transcatheter device	No. of patients	Study duration	Primary study end point	Results of primary study end point	Other events and comments
TRILUMINATE[47]	Transcatheter edge-to-edge repair	EU registry	TriClip	85	1 y	Major adverse cardiovascular events and all-cause mortality, cardiovascular mortality, stoke, tricuspid valve surgery, and new-onset kidney failure	Major adverse cardiovascular events and all-cause mortality in 7.1%, cardiovascular mortality in 4.8%, and new-onset kidney failure in 1.2%	Single leaflet detachment rate of 7.7% and major bleeding rate of 11.9%
CLASP TR[48]	Transcatheter edge-to-edge repair	Early feasibility study	PASCAL	34	30 d	Safety and efficacy	Reduction of tricuspid regurgitation ≥1 grade in 85% ($P < .001$); major adverse event rate of 5.9%; improved NYHA class, KCCQ score, and 6-minute walk test distance ($P < .001$); no mortality	Severe bleeding rate of 5.9%; single leaflet detachment rate of 2.9%
TRI-REPAIR[49]	Annuloplasty device	EU registry	Cardioband	30	6 mo	Safety and performance	Improved NYHA class, KCCQ score, and 6-minute walk test distance ($P < .01$); technical success rate of 100%; all-cause death rate of 10% at 6 mo by Kaplan-Meier method	Severe bleeding rate of 13.3%; significant reduction in tricuspid regurgitation ($P < .01$) and septolateral annular dimension ($P < .01$)
Cardioband TR EFS[50]	Annuloplasty device	Early feasibility trial	Cardioband	30	30 d	Safety and performance	Device success rate of 93%; improved NYHA class and KCCQ score ($P < .001$); no mortality	Severe bleeding rate of 23.3%; significant reduction in tricuspid regurgitation ($P < .001$) and septolateral annular dimension ($P < .001$)
EVOQUE Compassionate Use[51]	Valve replacement	Compassionate use	EVOQUE	25	30 d	Safety and performance	Technical success rate of 92%; grade reduction of >2 for tricuspid regurgitation in 96% of patients; mean gradient of 3 mm Hg; no mortality	No major bleeding, reintervention, or conversion to surgery

Abbreviations: CLASP TR, Edwards PASCAL Transcatheter Mitral Valve Repair System Tricuspid Regurgitation Study; EU, European Union; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA, New York Heart Association; TRILUMINATE, Evaluation of Treatment With Abbott Transcatheter Clip Repair System in Patients With Moderate or Greater Tricuspid Regurgitation; TRI-REPAIR, Tricuspid Regurgitation Repair With Cardioband Transcatheter System.

functions similarly to a surgical annuloplasty repair. The Tricuspid Regurgitation Repair With Cardioband Transcatheter System registry study[49] has shown positive 6-month outcomes in patients with moderate or greater functional tricuspid regurgitation after treatment with the Cardioband tricuspid system and supported the first therapy approved in the European Union for the treatment of functional tricuspid regurgitation. There was 100% technical success in 30 patients. Technical success is defined as successful access achieved, deployment of the device, implant positioning, and annulus size reduction. Between 6 months and baseline, transthoracic echocardiography showed an average reduction of annular septolateral diameter of 9% (42 mm vs 38 mm; $P < .01$) and improvements in tricuspid regurgitation ($P < .01$), NYHA class, 6-minute walk test, and quality of life (Table 6). The Edwards Cardioband Tricuspid Valve Reconstruction System Early Feasibility Study is ongoing in the US (NCT03382457).[50] There were no deaths by 30 days and the device success rate was 93%.

There are several transcatheter tricuspid valve replacement trials that are in the early feasibility stage of clinical trial enrollment. The EVOQUE device (Edwards Lifesciences), which is a transcatheter tricuspid valve replacement, was recently evaluated in a compassionate use trial[51] including 25 patients and was found to have high technical success, 0% mortality at 30 days, and improvements in functional status and tricuspid regurgitation grade. These technologies have promise for patients with advanced tricuspid regurgitation whose anatomy is unsuitable for repair.

Limitations

This review has some limitations. First, although TAVI is an established technology and technique, transcatheter valve repair and replacement is an evolving field with technology that is constantly advancing. Second, this review is limited to the literature currently available but is not necessarily inclusive of every investigational device. Third, the data for transcatheter therapies for valvular heart disease does not have as long-term outcomes as surgical therapies for valvular heart disease. Fourth, conclusions about the durability and longer-term outcomes of these procedures are limited compared with the surgical literature.

Conclusions

Approximately 78 000 TAVI procedures and 10 000 mitral valve repairs take place yearly in the US to treat patients with severe, symptomatic aortic stenosis and mitral regurgitation, respectively. Transcatheter valve therapies have expanded therapeutic options for patients, including for those who previously had no viable surgical options.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Mary McGrae McDermott, MD, at mdm608@northwestern.edu.

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