Current and Future Application of Transcatheter Mitral Valve Replacement

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KEYWORDS

• Mitral annular calcification • Transcatheter mitral valve replacement • Mitral regurgitation

KEY POINTS

- Transcatheter mitral valve in valve is a safe and effective procedure for most patients with a degenerated bioprosthetic valve.
- Transcatheter mitral valve-in-ring/valve-in-mitral annular calcification outcomes are suboptimal and are reserved for patients at high or extreme surgical risk.
- Laceration of the anterior mitral leaflet to prevent left ventricular outflow tract obstruction and alcohol septal ablation are effective strategies to prevent left ventricular outflow tract obstruction.
- Several transcatheter mitral valve replacement (TMVR) device trials are underway and the ideal device is yet to be found for native TMVR.

INTRODUCTION

Transcatheter device therapy has revolutionized the way valvular heart disease has been managed in the last decade.[1–5] The landscape in transcatheter mitral valve interventions specifically has changed dramatically with randomized trial data showing the safety and efficacy of the MitraClip (Abbott Vascular, Minneapolis, MN) for patients with primary and secondary mitral regurgitation (MR).[3,6,7] However, this technology is not suitable for a large fraction of patients, including those with a failing bioprosthetic mitral valve, recurrent MR after prior ring annuloplasty, and significant mitral annular calcification (MAC) accompanying either MR or mitral stenosis (MS). Often this cohort of patients has comorbid conditions that make them not suitable for cardiac valve surgery. Transcatheter mitral valve replacement (TMVR) may therefore be a reasonable option in patients considered high risk for conventional mitral valve surgery (replacement or repair).

This article highlights various aspects of TMVR, including the evidence, current and upcoming devices, and mitigation strategies for complications post-TMVR.

ANATOMIC CHALLENGES OF THE MITRAL VALVE

The mitral valve annulus is a dynamic, saddlelike structure that is supported by a complex subvalvular apparatus. Wide variations in pathophysiology are seen, including but not limited to MAC, functional/primary MR, MS, and mixed mitral valve disease. The heterogeneous structure of the mitral

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valve poses many challenges, such as device anchoring, delivery, position, and paravalvular regurgitation. Another anatomic challenge is the proximity to the aortic valve, and TMVR can be complicated by severe left ventricular outflow tract (LVOT) obstruction, which can potentially be life threatening.

PREPROCEDURAL IMAGING

Echocardiography

Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) are good initial imaging modalities to evaluate mitral valve pathophysiology. A thorough discussion of the contemporary role of echocardiography in assessing patients with MR is beyond the scope of this article and has been well covered in various state-of-the-art review articles.[8,9] Briefly, they provide valuable information regarding left and right ventricular size and function, pulmonary pressure, mitral valve annulus, annular calcification, subvalvular apparatus, and papillary muscles. Three-dimensional echocardiography is an extremely useful tool providing greater details regarding the mitral valve disorder and pathophysiology, especially when combined with the use of multiplanar reconstruction.

Some of the echocardiographic features that may favor TMVR rather than transcatheter mitral valve repair are commissural MR, broad MR jet across the coaptation line or with a large coaptation gap, mitral valve area less than 3.5 cm^2, multiple prolapsing segments, mixed mitral valve disease with predominant MS, severe calcification at the grasping zone, short (<7 mm) and significantly tethered posterior mitral valve leaflet, and a cleft or perforation. In analyzing patients for valve in valve (ViV) or valve in surgical mitral ring (ViR) TMVR, special consideration should be given to ruling out periprosthetic regurgitation.

Multidetector Cardiac Computed Tomography

Multidetector cardiac computed tomography is imperative for preoperative planning of TMVR. Analysis of the annular size is relevant to prosthetic valve sizing (**Fig. 1**), and understanding the degree and pattern of calcification in the annulus is important concerning procedural technique (**Fig. 2**).[10] Vitally important is the understanding of the remaining LVOT created by the boundaries of the new valve prosthesis/anterior mitral leaflet and the septum, or neo-LVOT; this is discussed in greater detail later. Inadequate space in the neo-LVOT is among the most common reasons for the exclusion of patients for the current TMVR device trials or ViV/ViR/ valve-in-MAC (ViMAC). For those patients undergoing transapical access TMVR, the left ventricular (LV) puncture site target is also chosen based on the most coaxial approach to the mitral valve plane.

The preoperative assessment of neo-LVOT post-TMVR is crucial. This assessment can be performed by careful evaluation of the preprocedural three-dimensional cardiac gated computed tomography scan.[11,12] Multiphase and explicitly early systolic evaluation of the neo-LVOT area is preferred, with an eye toward the narrowest possible dimension.[12,13] This area is measured using a double oblique method by identifying the basalmost insertion points of the mitral leaflets and implanting a virtual valve (typically 20% atrial and 80% ventricular). A neo-LVOT area of less than or equal to 189.4 mm^2 has a sensitivity of 100% and a specificity of 96.8% for foretelling post-TMVR LVOT obstruction.[14] Another study suggested a cutoff of 1.7 cm^2 (sensitivity 96.2% and specificity 92.3%).[15] In addition to the neo-LVOT area, aortomitral angulation closer to 90° and a small left ventricle size are independent predictors of post-TMVR LVOT obstruction.[16]

VALVE IN VALVE/VALVE IN RING/VALVE IN MITRAL ANNULAR CALCIFICATION

ViV/ViR/ViMAC can be performed using the balloon-expandable Edwards SAPIEN 3 TAVR system. The mitral ViV application is extremely helpful for preoperative planning and device choice and is widely available across iPhone and android phone app stores. These procedures are mostly performed antegrade across the interatrial septum. Recently, the contemporary experience with SAPIEN 3 valve for transcatheter mitral ViV replacement was published.[17] The study comprised more than 1500 patients and the procedural success rate was nearly 97%. The 1-year mortality postintervention was nearly 17% and, not surprisingly, the mortality was substantially higher with transapical access compared with transeptal access. Postintervention there was sustained improvement in heart failure symptoms, with an average mitral mean gradient of 7 mm Hg at 1 year.[17]

A global multicenter registry of 116 patients reported a 30-day mortality of 25% and 1-year mortality of 53.7% post-TMVR with balloon-expandable aortic valves in patients with MAC.[18] A systematic review and meta-analysis of 4 studies compared periprocedural outcomes between ViMAC and ViV/ViR cohorts.[19] The periprocedural mortality was higher (ViMAC 31% vs ViV/ViR 7%) and was associated with inferior procedural success rates (ViMAC 64% vs ViV/ViR

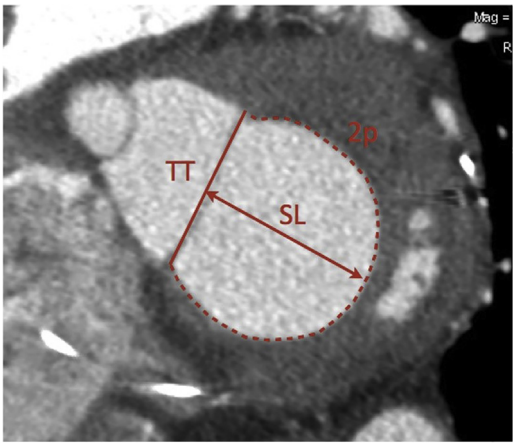

Fig. 1. Mitral annulus measurement using multidetector computed tomography. SL, septal-to-lateral distance; TT, trigone-to-trigone distance; 2p, perimeter. (*From* Faggioni L, Gabelloni M, Accogli S, Angelillis M, Costa G, Spontoni P, et al. Preprocedural planning of transcatheter mitral valve interventions by multidetector CT: What the radiologist needs to know. Eur J Radiol Open. 2018;5:131-40.)

91%) in the ViMAC cohort compared with ViV/ViR cohort.[19] The ViMAC cohort had a higher risk of LVOT obstruction (ViMAC 36% vs ViV/ViR 4%) and surgical conversion (ViMAC 9% vs ViV/ViR 2%) compared with ViV/ViR cohorts.[19] In addition, ViMAC procedures are associated with hemolytic anemia, which can range from mild to transfusion dependent and sometimes is complicated by pigment-induced nephropathy; this is likely caused by paravalvular regurgitation with inadequate annular sealing.[20] The incidence of second valve implantation has been reported to be higher in ViR patients (12.1%) compared with ViMAC (5.2%) and ViV patients (2.5%).[21] ViR cohorts also have a higher risk of greater than or equal to moderate residual MR (ViR 18.4% vs ViMAC 13.8% vs ViV 5.6%) and often require paravalvular leak closure (ViR 7.8% vs ViMAC 0.0% vs ViV 2.2%).

More recently, a combined approach to ViR and ViMAC procedures using laceration of the anterior mitral valve leaflet to prevent LVOT obstruction (LAMPOON) and/or alcohol septal ablation (ASA) to prevent LVOT obstruction has been used. This approach was studied in a cohort of 40 patients that included 28 ViMAC and 12 ViR patients.[22] Using this algorithm, 16 patients underwent LAMPOON and 3 patients underwent ASA before TMVR. The 30-day mortality was 15%, valve embolization or late migration was seen in 5 patients, and technical success was seen in 63% of the patients.[22]

In summary, the literature available thus far strongly supports the role of transcatheter mitral ViV in degenerated bioprosthetic valves. The mortality and complications are higher in patients undergoing transcatheter mitral ViR and ViMAC procedures.[15,18,21,23,24] ViR/ViMAC are more often complicated by paravalvular regurgitation necessitating closure compared with the ViV procedures.[15,18,21,23–28] Further, these patients also show a higher rate of LVOT obstruction and consideration should be given to preemptive

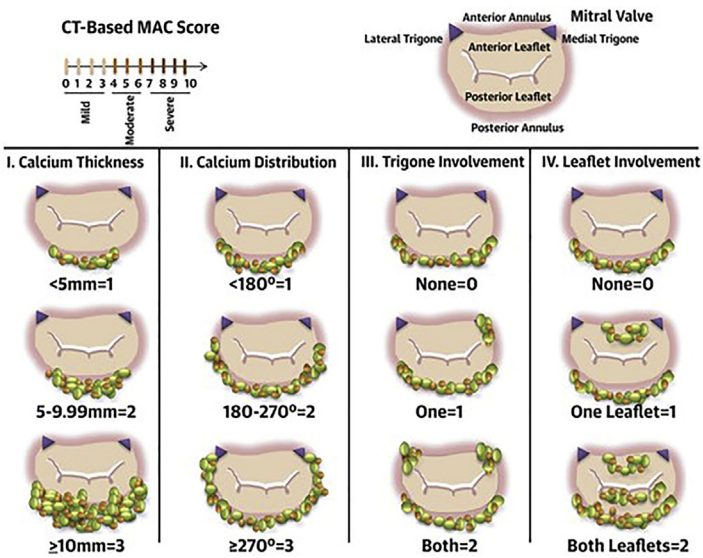

Fig. 2. Multidetector computed tomography scoring system for MAC. (*From* Guerrero M, Wang DD, Pursnani A, Eleid M, Khalique O, Urena M, et al. A Cardiac Computed Tomography-Based Score to Categorize Mitral Annular Calcification Severity and Predict Valve Embolization. JACC Cardiovascular imaging. 2020;13(9):1945-57.)

LAMPOON and/or ASA to mitigate this risk.[15,18,19,21,23,24]

NATIVE VALVE TRANSCATHETER MITRAL VALVE REPLACEMENT DEVICES

There are several valves currently being assessed in clinical trials, although most of the data are limited with regard to the number of patients treated and have been presented at conferences but not yet published in peer-reviewed journals. Therefore, a detailed analysis is not possible, but a summary of the devices and results thus far is provided herein (Fig. 3, Tables 1 and 2).

AltaValve

AltaValve system (4C Medical) is a 32-Fr supra-annular system with a self-expanding spherical nitinol frame that consists of a 27-mm bovine pericardial valve.[29] This valve can be delivered transapically as well as transeptally.[29,30] The first AltaValve implanted via a transapical approach was performed successfully with regard to valve positioning and deployment; however, the procedure was complicated by significant LV bleeding.[29] The patient passed away 5 days later.[29] The procedure performed via the transeptal route was successful in a 77-year-old man who was discharged 9 days later. The patient had good mitral valve function and no LVOT gradient.[30] The supra-annular position of this valve is helpful to minimize LVOT obstruction and prevent valve embolization/migration. The AltaValve early feasibility study is currently underway (NCT03997305).

Cardiovalve (Cardiovalve)

Cardiovalve is a self-expanding platform with a bovine pericardial trileaflet valve with atrial and ventricular frames that is, available in 3 sizes (M, L, XL). This valve is delivered using a 28-Fr transfemoral sheath and is deployed in 3 phases. Initially the mitral leaflets are grasped, followed by the deployment of the atrial flanges, and lastly the final deployment of the valve. This valve is inspired by the surgical mitral prostheses that are designed to provide a low ventricular profile and reduce the risk of LVOT obstruction, with good durability. This valve has been assessed in 5 patients so far with promising procedural results, with 100% implantation rate and 80% of patients had complete resolution of MR. The 30-day mortality was 60%, mostly as a result of access site complications. The AHEAD (European Feasibility Study of High Surgical Risk Patients With Severe MR Treated With the Cardiovalve Transfemoral Mitral Valve System Study) studies (NCT03813524, NCT03339115) in the United States and Europe are currently evaluating the feasibility of the Cardiovalve.

Cephea (Abbott Vascular)

The Cephea valve is a self-expanding transseptal TMVR system with a double-disk design that consists of an outer ring that conforms to the annulus and an inner ring that consists of a trileaflet bovine pericardial valve. They are available in 32-mm, 36-mm, and 40-mm sizes. This system anchors the mitral annulus by axial compression. In 2019, the first-in-human implant of the Cephea system was successfully performed in an 83-year-old woman with degenerative MR.[31] Six months after implantation she had improved clinically (New York Heart Association [NYHA] class I) with good mitral valve function (mean gradient 3 mm Hg), no paravalvular leak, and no LVOT gradient.[31] Further trials are needed to evaluate the safety and feasibility of the device and are underway (NCT03988946).

EVOQUE (Edwards Lifesciences)

EVOQUE is a transseptal nitinol self-expanding system with a bovine pericardial valve. The ventricular segment has 9 anchors that attach to the mitral valve leaflets and chords. The atrial segment has a sealing skirt to prevent paravalvular leak. The device can be delivered via a 28-Fr transfemoral sheath and is available in 2 dimensions (44 and 48 mm). The three-dimensional delivery system allows precise manipulation and tilted deployment of the device at the mitral annulus. The rationale behind the tilted deployment of the device is to reduce the risk of LVOT obstruction. The early experience in 14 patients with moderate to severe MR showed a technical success rate of 92.9%.[32] One patient needed open heart surgery and 2 patients had strokes.[32] Two individuals needed paravalvular leak closure and 1 of them underwent ASA.[32] A reduction to NYHA functional class II was seen in 82% of the individuals. NCT02718001 is an early feasibility study that is currently in progress.

HighLife (HighLife Medical)

This TMVR system uses a ViR model. Initially, a ring (32–48 mm) is deployed across the mitral valve (subannular) in a retrograde fashion via the transfemoral artery. Following this, a 28-mm self-expanding trileaflet valve made of bovine pericardium is deployed either transapically or transseptally inside the mitral ring. This ViR model hypothetically reduces the risk of LVOT obstruction and paravalvular leak. Initial results have been presented among 15 patients. Thirteen patients underwent successful implantation and 2

Fig. 3. TMVR devices in evaluation.

patients needed open heart surgery. The 1-month mortality was 20%. An early feasibility trial (NCT02974881) is recruiting patients to assess this system.

SAPIEN M3 (Edwards Lifesciences)

The M3 system is another device that follows the ViR concept. Unlike the HighLife system, the ring (nitinol dock) is delivered across the atrial septum and deployed in the mitral valve apparatus. The valve is like the SAPIEN S3 and has a knitted polyethylene terephthalate skirt to achieve a tight seal. The initial feasibility study consisting of 35 patients was promising, with a technical success of 88.6% and an all-cause mortality of 2.9%.[33,34] The Encircle trial of this device is in its initial stages (NCT03230747).

Intrepid (Medtronic Inc)

The Intrepid is a transapical, self-expanding, nitinol valve and consists of a dual-stent conformable symmetric model that does not need a rotational alignment. The outer stent frame conforms to the mitral annulus, whereas the inner stent consists of a trileaflet 27-mm valve made from bovine pericardium. The valve anchors to the mitral annulus, left ventricle, with perimeter oversizing, and is delivered using a retrievable 35-Fr transapical system. The early experience with this device in a prospective study consisting of 50 patients at high or extreme risk for conventional mitral valve replacement is feasible. The mean age of the cohort was 73 years, with predominantly secondary MR (84%). The average Society for Thoracic Surgery score of the cohort was 6.4%. The procedural success rate of the device was 96%. The 1-month mortality was 14%, and there was a substantial improvement in functional status and Minnesota Heart Failure Questionnaire scores.[35] The APOLLO TMVR trial (TMVR With the Medtronic Intrepid TMVR System in Patients With Severe Symptomatic Mitral Regurgitation; NCT03242642) is currently enrolling patients with moderate to severe or severe symptomatic MR and will compare TMVR with conventional mitral valve replacement.

Tendyne (Abbott Vascular)

The Tendyne TMVR system is another transapical system that is a fully retrievable and repositionable device, and currently has the largest clinical experience worldwide, with more than 400 valves implanted. This 34-Fr system delivers 2 self-expanding nitinol stents and a trileaflet porcine pericardial valve. It also consists of an apical pad that anchors the valve to the LV apex. This device has gained the CE (Conformité Européenne) mark in Europe.[36,37]

The Global Feasibility Study had a sample size of 100 individuals with primary or secondary MR who had a mean age of more than 75 years. The cohort had a mean Society of Thoracic Surgeons (STS) score of 7.8 and the technical success rate was 96%. The 30-day mortality was 6% and 1-year survival postprocedure was 72%. At 1 year, more than 88% of the individuals who survived had substantial improvements in 6-minute walk distance and quality of life.[37]

This device has been also studied in individuals with severe MAC and MR.[36] There was complete resolution of MR in 9 patients who had a survival rate of 78% at 1 year.[36] The SUMMIT trial (Clinical Trial to Evaluate the Safety and Effectiveness of Using the Tendyne Mitral Valve System for the Treatment of Symptomatic Mitral Regurgitation; NCT03433274) consists of a randomized study, nonrandomized study, and an MAC registry. The

Table 1
Summary of all the transcatheter mitral valve replacement devices and future feasibility studies

Device	AltaValve	Cardiovalve	HighLife	Intrepid	Tiara	SAPIEN M3	Tendyne	Cephea	EVOQUE
Manufacturer	4C Medical Techno-logies	Cardiovalve	HighLife SAS	Medtronic	Neovasc	Edwards Lifesciences	Abbott	Abbott	Edwards Lifesciences
Design	Self-expa-nding, nitinol	NA	Self-expanding, nitinol	Double stent, self-expanding, nitinol	Self-expanding, nitinol	Balloon-expandable, cobalt-chromium frame	Double frame, self-expandable, nitinol	A self-expanding system with a double-disk design	Self-expanding, nitinol
Leaflets	Trileaflet bovine	NA	Trileaflet bovine	Trileaflet bovine	Trileaflet bovine	Trileaflet bovine	Trileaflet porcine	NA	Trileaflet porcine
Anchoring mechanism	Spherical frame shape	NA	Valve in subannular mitral ring; external anchor	Radial force and small cleats on the outer stent engage leaflets	3 ventricular anchoring tabs (on the fibrous trigone and posterior shelf of the annulus)	Nitinol dock system	Apical tether	Mitral annulus double disk	Mitral annulus leaflets/ annulus
Access site	Transapical 32 Fr	Transfemoral-transeptal 28 Fr	Transapical (trans-femoral artery for loop placement) 39 Fr	Transapical 35 Fr	Transapical 32 Fr (35-mm valve) 36 Fr (40-mm valve)	Transfemoral 20 Fr	Transapical 34 Fr	Transeptal	Transeptal 28 Fr
Valve dimensions	27 mm	3 sizes (M, L, XL)	31	27 (with 3 outer stent sizes: 43, 46, and 50 mm)	35 and 40 mm	29 mm	Outer frame 30–43 mm (septal-to-lateral dimension) and 34–50 (IC dimension)	Sizes 32, 36, and 40 mm	44 and 48 mm

Recapturable	Partial	Partial	No	Yes	No	Partial	Yes	Yes	No
Trial	NCT 03997305	AHEAD studies NCT 03813524, NCT 03339115	NCT0 2974881	APOLLO TMVR trial NCT03242642	TIARA-I (NCT02276547) and TIARA-II (NCT03039855)	NCT 03230747	The SUMMIT study (NCT 03433274)	NCT03988946	NCT02718001

Abbreviation: IC, intercommissural; NA, not available.

Table 2
Summary of the early data with upcoming transcatheter mitral valve replacement devices

Valve	Intrepid	Tendyne	EVOQUE	SAPIEN M3	Cardiovalve	HighLife	AltaValve	Tiara	Cephea
Publication Year	2018	2019	2020	2019	2020	2018	2019	2020	2019
Patients Enrolled	50	100	14	15	5	15	2	79	1
Procedural Success (%)	98	96	93	89	100	87	100	92	100
Follow-up (d)	173	416.7	30	30	30	30	9	30	196
Residual MR $\geq$ +2 (%)	0	0	0	2	0	0	0	3	0
Mortality (%)	22	26	7	2	60	21	50	12.3	0

patients in the randomized trial will be randomized to Tendyne or a MitraClip system.

Tiara (NeoVasc Inc)

Tiara has an asymmetric D-shaped design and is composed of a self-expanding nitinol frame, 2 axial anchors (anterior and posterior), and a trileaflet bovine pericardial valve. This device reduces LVOT obstruction because the anterior tab grabs the anterior mitral leaflet and because of its D-shaped design. This transapical device is available in 2 dimensions: 35 mm (32 Fr) and 40 mm (36 Fr). A transeptal delivery system is currently being developed. Feasibility studies TIARA-I (NCT02276547) and TIARA-II (NCT03039855) are yet to be officially published. The procedural success rate was more than 90%, but more than 10% of the patients needed surgical reintervention. The 30-day mortality was 12.3%, with a device migration rate of 7%. None of the patients

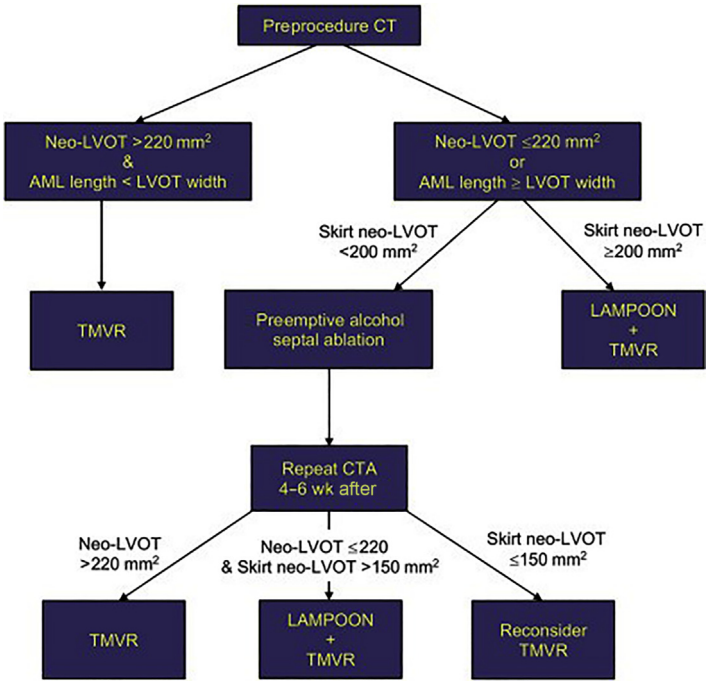

Fig. 4. Algorithmic approach for TMVR. AML, anterior mitral leaflet; CTA, computed tomography angiography. (*From* Tiwana J, Aldea G, Levin DB, Johnson K, Don CW, Dvir D, et al. Contemporary Transcatheter Mitral Valve Replacement for Mitral Annular Calcification or Ring. JACC Cardiovascular interventions. 2020;13(20):2388-98.)

developed LVOT obstruction and, at discharge, 88% of the patients had no or trivial MR.

MITIGATION STRATEGIES TO PREVENT LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

TMVR in ViV procedures, ViR, and MAC is possible; however, these patients are prone to develop severe LVOT obstruction resulting in hemodynamic compromise.[18] The rates of LVOT obstruction resulting in hemodynamic compromise post-TMVR in individuals with MAC are as high as 11%, and the mortality for these patients is substantial.[18,38] Over time, investigators have used several different strategies to circumvent this issue.

Alcohol Septal Ablation

ASA was used as a bailout strategy initially and more recently has been implemented as a preemptive strategy.[22,24,39,40] In the early report of using ASA as a bailout strategy, only 4 of the 6 patients survived post-TMVR.[24] The first-in-human study of 30 patients evaluating ASA as a preemptive strategy before TMVR was recently published.[40] Baseline imaging revealed a median end-diastolic LV septal thickness of 13.5 mm, median baseline neo-LVOT surface area before ASA of 85.1 mm^2, and a baseline median peak LVOT gradient of 5.5 mm Hg.[40] A median increase in the neo-LVOT area by 111.2 mm^2 was observed ($P<.0001$) after a median duration of 40 days post-ASA.[40] Eight patients experienced clinical improvement after ASA and no longer had an indication for TMVR, and 2 patients died after ASA but before TMVR.[40] The pacemaker implantation rate was 16.7%. More encouragingly, this publication reported post-TMVR 30-day mortality of 5.3%, with a TMVR success rate of 100%.[40]

LAMPOON

The LAMPOON procedure was devised to prevent LVOT obstruction. LAMPOON is a catheter-based electrosurgical procedure where the anterior leaflet is lacerated before deployment of the mitral valve. The laceration of the A2 leaflet is performed by first using a 0.36-mm (0.014-inch) stiff guidewire (Astato XS 20, Asahi-Intecc, Nagoya, Japan) to anterogradely puncture the base of the A2 mitral valve scallop via a 145-cm Piggyback Wire Converter (Vascular Solutions, Minneapolis, MN) that has a 0.89-mm (0.035-inch) polymer jacket and provides electrical insulation. The wire is then snared via the ventricle and the leaflet is lacerated from base to tip. In the feasibility study of 30 patients, 30-day survival was 93% with no strokes.[40,41]

In addition to the procedural technique discussed earlier, it is possible in patients with a mitral ring or bioprosthetic to avoid the initial leaflet perforation altogether and instead use the tip-to-base technique.[41–43] For this procedure, the wire is passed antegrade through the mitral valve and snared via a retrograde catheter. The cutting surface is then electrified and pulled from tip to base, and the heart is shielded from further injury by the prosthetic annulus. **Fig. 4** shows the role of a hybrid algorithm in ViMAC/ViR procedures that has a success rate of 63%.[22]

POST–TRANSCATHETER MITRAL VALVE REPLACEMENT ATRIAL SEPTAL CLOSURE

The role of iatrogenic atrial septal closure is controversial post-TMVR.[44] This decision depends on the left atrial, ventricular pressures as well as on the degree of right ventricular failure and volume status. The atrial septum is often closed for the spontaneous right-to-left shunt and/or hypoxia most commonly seen in the presence of severe pulmonary hypertension, right ventricular dysfunction, or concomitant severe tricuspid regurgitation.[44] The MITHRAS trial was a clinical trial that included 80 patients with Qp/Qs of greater than or equal to 1.3 post-TMVR and randomized them to closure using the Occlutech ASD occluder or conservative management at 1-month post-TMVR.[45] Baseline clinical and echocardiographic features were similar across the 2 cohorts. There was no difference in mortality and rehospitalization post-TMVR across the 2 cohorts. The trial was underpowered to assess for differences in special subgroups such as a large defect with spontaneous shunts and the degree of right ventricular failure.[45]

SUMMARY

The future of TMVR seems promising, although the progress in TMVR device technology has been slow. The current evidence is robust for the use of balloon-expandable valves in degenerated bioprosthetic valves. ViR and ViMAC procedures are far more complicated and have inferior outcomes but may present as the only available options for many patients. TMVR for native mitral valve regurgitation is currently reserved for patients with poor anatomy for transcatheter mitral valve repair using the US Food and Drug Administration–approved MitraClip edge-to-edge repair. There are many different transapically and transfemorally delivered TMVR devices in various stages of clinical trials for

native valve disease, primary MR. Most of these trials show excellent procedural success, although further study is needed to establish valve durability and longer-term patient outcomes, and to better understand patient selection.

CLINICS CARE POINTS

- The mitral valve annulus is a dynamic, saddle-shaped structure that is supported by a complex subvalvular apparatus. Wide variations in pathophysiology are seen, including but not limited to MAC, functional MR, primary MR, MS, and mixed mitral valve disease.
- Echocardiographic features favoring TMVR rather than transcatheter mitral valve repair include MR origins that are broad along the coaptation line, large coaptation gap, mitral valve area less than 3.5 cm^2, multiple prolapsing segments, mixed mitral valve disease with predominant MS, severe calcification at the grasping zone, short (<7 mm) and significantly tethered posterior mitral valve leaflet, and a cleft or perforation.
- Cardiac computed tomography is an extremely important tool for preprocedural planning in native TMVR as well as ViV, ViR, and ViMAC procedures to understand the annulus, neo-LVOT dimensions, fluoroscopic angles for valve implantation, and access site assessment.
- Transcatheter mitral ViV is a safe and effective procedure for most patients with a degenerated bioprosthetic valve. In contrast, the outcomes of transcatheter mitral ViR/ViMAC are suboptimal and these procedures are generally reserved for patients at high or extreme surgical risk.
- Intentional laceration of the anterior mitral leaflet and ASA may be effective mitigation strategies in appropriately selected patients to avoid LVOT obstruction in high-risk anatomies of ViR and ViMAC.
- Many devices are currently under investigation, and the ideal device is yet to be established for native TMVR.

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