# Current and Future Directions for Transcatheter Mitral Valve Intervention

Exploring available technologies, procedural considerations, patient selection, and future directions for transcatheter mitral valve repair and replacement.

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Mitral regurgitation (MR) is one of the most prevalent valvular heart diseases affecting approximately 10% of adults aged > 75 years.[1-3] Severe symptomatic MR carries a poor prognosis with approximately a 50% 5-year mortality if left untreated.[4] Despite high disease burden, up to half of the patients with severe symptomatic MR are never referred for surgical intervention due to high operative risk.[5] This unmet clinical need has driven the development of transcatheter mitral valve interventions as less invasive alternatives to open surgery for high-risk individuals.

Mitral transcatheter edge-to-edge repair (M-TEER), pioneered with the MitraClip system (Abbott), was the first widely adopted catheter-based strategy, receiving FDA approval in 2013 for degenerative MR and subsequently in 2019 for functional MR.[6,7] Clinical trial and registry data have since confirmed procedural safety and efficacy in appropriately selected patients, cementing M-TEER as the standard transcatheter approach in current United States practice.[8]

Although M-TEER has been generally successful, not all patients have favorable anatomy for edge-to-edge repair, the degree of MR reduction is variable and unpredictable, and the long-term durability of repair remains a subject of controversy. Transcatheter mitral valve replacement (TMVR) is being pursued as a complementary strategy that could potentially overcome the anatomic heterogeneity of MR and provide more predictable, uniform correction of MR.[9] Initial clinical experience with TMVR has shown that the procedure is technically feasible and offers a therapeutic option for patients at high or prohibitive operative risk for surgical mitral valve intervention.[10-12]

Transcatheter mitral valve intervention is a rapidly evolving field. This article discusses transcatheter mitral valve repair and replacement technologies, procedural considerations, patient selection, and future directions.

## CURRENT TRANSCATHETER MITRAL VALVE REPAIR AND REPLACEMENT TECHNOLOGIES

### Mitral Transcatheter Edge-to-Edge Repair

Transcatheter edge-to-edge repair mimics the surgical Alfieri stitch by approximating the anterior and posterior mitral leaflets at the regurgitant jet, creating a double orifice.[13] MitraClip initially received FDA approval for high-surgical-risk degenerative MR after the landmark EVEREST II trial results, demonstrating feasibility and improved safety profile compared to conventional surgery.[6] While the primary effectiveness outcome favored surgery at 1 year, beyond 1 year the need for surgery or reoperation, reduction in left ventricular (LV) dimensions, and moderate to severe MR were similar between the groups.[6,14]

FDA approval for MitraClip was later expanded to secondary MR after the COAPT trial showed significant outcome benefits.[7] In the COAPT trial, the addition of M-TEER to guideline-directed medical therapy (GDMT) in patients with heart failure and symptomatic moderate-to-severe or severe functional MR resulted in an approximate 50% reduction in heart failure hospitalizations and a 40% reduction in all-cause mortality compared to GDMT alone.[7]

More recently, the RESHAPE-HF2 trial demonstrated significant clinical benefits of MitraClip in patients with functional MR on GDMT.[15] Contemporary registry data demonstrate the acute procedural success rate of MitraClip to be > 95%, with > 90% of patients achieving MR ≤ 1+ at 30 days and 1 year, with periprocedural complication rates < 2%.[16,17] Additionally, registry data demonstrate persistent improvement in quality of life and functional status at 1 year after implantation.[16]

Durable clinical improvement has also been demonstrated in patients treated with M-TEER. Notably, the 5-year follow-up of the COAPT trial confirmed sustained reduction in heart failure hospitalizations and all-cause mortality in patients treated with MitraClip compared to medical therapy alone, underscoring the long-standing efficacy of M-TEER.[18] M-TEER for functional severe MR was also studied against surgical mitral valve repair or replacement in the recent MATTERHORN trial.[19] In this trial, MitraClip was shown to be noninferior to mitral valve surgery for the composite outcome of death, rehospitalization for heart failure, stroke, reintervention, or implantation of an LV assist device at 1 year.

In September 2022, the Pascal system (Edwards Lifesciences) was the second M-TEER device to be approved in the United States by the FDA for degenerative MR. In the randomized CLASP IID trial, the Pascal system proved noninferior to MitraClip in both safety (30-day major adverse event rate, 3%-5%) and efficacy (approximately 96% of patients in both groups had MR ≤ 2+ at 6 months) in patients with degenerative MR.[20] Design differences of the Pascal device—including broader grasping paddles, an elongatable clasp, and independent leaflet capture—allow for clip placement in anatomically challenging cases.[21] Transcatheter edge-to-edge repair has quickly become a first-line percutaneous therapy for severe MR in patients at high surgical risk, with an extensive evidence base supporting its safety and effectiveness.

**Transcatheter Mitral Valve Replacement**

The allure of complete elimination of MR as well as anatomic challenges precluding M-TEER in some patients has provided the impetus for the development of TMVR devices. In May 2025, the Tendyne valve (Abbott) was the first TMVR device to be approved in the United States by the FDA, and the first commercial implantation was reported on September 10, 2025. Tendyne is approved for high-surgical-risk patients with mitral annular calcification (with MR or stenosis) who cannot be treated with M-TEER. Multiple other dedicated TMVR valves are currently in advanced clinical trial evaluation.

TMVR can be challenging with large, complex, and highly variable mitral valve anatomy. The mitral valve is D-shaped and its dimensions are dependent on hemodynamic status.[22,23] Asymmetric mitral calcification also represents a procedural challenge due to the absence of stable support for prosthetic valve anchoring.[24] Additionally, anatomic proximity to LV outflow tract (LVOT) can sometimes lead to LVOT obstruction by native anterior mitral leaflet post-TMVR, resulting in significant hemodynamic compromise.[25,26] Although TMVR is associated with substantial technical challenges and nontrivial procedural risks, it offers a therapeutic option for patients at prohibitive or high surgical risk and who have anatomy that is unsuitable for M-TEER.

The Tendyne device is an apically implanted system that consists of an outer D-shaped nitinol frame for securement and sealing, an inner nitinol stent that houses the porcine pericardial valve, a tether, and an apical pad. In the early global feasibility study of 100 high-risk patients, Tendyne was successfully implanted in 97% of patients with no intraprocedural deaths and near elimination of MR on echocardiography.[12] Two-year data revealed sustained improvement in MR severity (93.2% with no MR and no patient with greater than mild MR), reduction in heart failure hospitalization rate (62% reduction), symptomatic improvement (81.6% New York Heart Association [NYHA] class I or II), and no structural valve deterioration. The mortality rate was 17.4% at 3 months, predominantly from refractory heart failure and ventricular arrhythmias.[27]

There are distinct disadvantages of the apical approach, as was learned in the early transcatheter aortic valve replacement experience, which include bleeding, apical tear, inadvertent coronary damage, and myocardial injury. Thus, there is substantial interest in transseptal approaches to TMVR. The Intrepid system (Medtronic) demonstrated favorable 30-day results in an early feasibility study, with no periprocedural death or stroke and trace-to-mild MR in all patients with successful implantation.[28] The Intrepid valve is currently being evaluated in the single-arm APOLLO trial (NCT03242642).

There are multiple ongoing investigations of dedicated transseptal TMVR systems. The most notable studies include the AltaValve (4C Medical) early feasibility study (NCT03997305), the ENCIRCLE trial (NCT04153292) for the Sapien M3 (Edwards Lifesciences), and the Cephea (Abbott) early feasibility study (NCT05061004). Collectively, these data highlight both the promise of TMVR as a therapeutic option and the need for continued refinement of devices and techniques to address anatomic challenges and improve long-term outcomes.

## PATIENT SELECTION AND PROCEDURAL DECISIONS

### The Heart Team Approach

The evolution of transcatheter mitral valve interventions has broadened therapeutic options for patients with significant MR. Appropriate patient selection is paramount to optimize outcomes and align procedural choice, whether repair or replacement, with individual patient anatomy, functional status, and surgical risk profile. The heart team model and shared decision-making process is multifactorial, integrating multimodality imaging, anatomic features, clinical comorbidities, and risk stratification tools such as the Society of Thoracic Surgeons Predicted Risk of Mortality score.

### The Importance of Imaging

High-quality transthoracic and transesophageal echocardiography (TEE) is essential for procedural planning, intraprocedural guidance, and postprocedural assessment of both M-TEER and TMVR. Adequate imaging windows are critical for visualizing and determining leaflet anatomy, distribution and density of choral attachments, severity and distribution of mitral annular calcification, MR jet origin and number of jets, annular dimensions, mitral valve area, mitral valve gradients, baseline LVOT gradients, and dynamic interactions during device deployment. Additionally, assessment of left and right ventricular size and function, as well as tricuspid regurgitation, are important considerations in patient selection.

TEE limitations—such as poor esophageal windows in patients with prior esophageal surgery, spinal deformities, or severe obesity—may preclude precise device positioning and increase the risk of suboptimal outcomes. In such cases, alternative imaging strategies or procedural approaches may need to be considered. A limited number of M-TEER procedures have been performed using intracardiac echocardiography guidance; however, this adds significant technical complexity to the procedure.

CTA is a critical imaging technique for patient screening for TMVR. CTA aids in selection of device type and prosthesis sizing (annular perimeter and area, intercommissural distance, septal lateral distance, mitral annular calcification, and relationship of chords, papillary muscles, and basal left ventricle), prediction of LVOT risk (septal bulge, anterior mitral leaflet length, aorto-mitral angle, modeled neo-LVOT), and access planning (transseptal puncture site or chest wall and LV access).

### Transcatheter Mitral Valve Repair

Patients considered for transcatheter mitral valve repair typically present with either primary (degenerative) or secondary (functional) MR. Candidates who are most likely to benefit from repair over replacement generally demonstrate favorable mitral valve anatomy, including:

- A mitral valve orifice area > 4 $cm^2$ to avoid mitral stenosis after repair
- Sufficient leaflet length (typically > 7 mm) and mobility for adequate device grasping
- Absence of significant calcification at the leaflet grasping zones or subvalvular apparatus
- Limited chordal attachments at the grasping zone
- A single central jet with MR location (A2/P2)

These patients often exhibit preserved leaflet and subvalvular anatomy, allowing for effective coaptation through clip deployment without significantly impeding transmitral flow. Functional MR patients with LV dysfunction, particularly those in NYHA class III to IV with LV ejection fraction between 20% and 50%, may benefit from transcatheter repair if symptoms persist despite optimal GDMT.[7] The recent European Society of Cardiology guidelines have elevated M-TEER to class 1a in this patient cohort.[29]

The 2021 American College of Cardiology/American Heart Association guidelines support edge-to-edge repair in symptomatic patients with severe degenerative MR who are at prohibitive surgical risk and meet anatomic criteria for successful device implantation.[30] The ongoing PRIMARY trial—which is randomizing low- and intermediate-risk surgical candidates to surgical mitral valve intervention versus M-TEER—is exploring whether M-TEER is competitive in this non–high-risk cohort.

### Transcatheter Mitral Valve Replacement

TMVR is considered for patients with mitral pathology not amenable to edge-to-edge repair or those in whom repair has failed. Replacement may be preferable to repair in cases of:

- Complex multisegmental prolapse or flail involving both anterior and posterior leaflets
- Multiple MR jets
- Complex commissural jets
- Clefts
- Severe tethering (tenting height > 11 mm) in secondary MR, limiting leaflet coaptation
- Mitral valve area < 3.5 $cm^2$
- Severe leaflet and/or annular calcification
- Failed attempt at M-TEER
- Examples include excessively high gradient or inadequate leaflet length

Given the greater procedural complexity and potential for LVOT obstruction, patient selection for TMVR requires comprehensive preprocedural planning, including advanced imaging such as cardiac CT for annular sizing and neo-LVOT assessment. Patients with a predicted neo-LVOT of < 180 mm$^2$ are at high risk for LVOT obstruction after TMVR. These patients may require adjunctive modification of the anterior mitral leaflet using the electrosurgical LAMPOON technique (laceration of the anterior mitral leaflet to prevent outflow obstruction)[31] and/or modification of the interventricular septum with alcohol septal ablation or SESAME (septal scoring along the midline endocardium).[32,33] Unfortunately, anterior mitral leaflet and septal modification cannot mitigate LVOT obstruction in all patients.

Additionally, TMVR patients require anticoagulation for at least 6 months (and possibly indefinitely) to reduce the risk of valve thrombosis. In an early Tendyne trial, when anticoagulation was not mandated, the risk of valve thrombosis was 17.1%.[34] Therefore, patients who are not candidates for anticoagulation are excluded from TMVR. Another concern is the development of worsening LV systolic dysfunction due to afterload mismatch after the abrupt and complete elimination of MR after TMVR.

## CONCLUSION

M-TEER has emerged as the first-line treatment option for optimally medically treated patients with functional MR and high-risk patients with degenerative MR. In general, it is a safe procedure with good clinical outcomes. However, approximately 15% of patients do not have optimal anatomy for M-TEER, and approximately 10% of patients have greater than mild MR. An alternative approach to predictably eliminate MR, such as TMVR, is intuitively attractive. However, TMVR has a high screen fail rate (~70%), mainly due to annular size and risk of LVOT obstruction.[35,36] Moreover, it seems to carry higher procedural risks (death, bleeding, and vascular trauma),[37] has access site complexities due to large-bore access (> 34 F for transapical access systems and > 30 F for transseptal systems, with the need to manage large iatrogenic atrial septal defect), and requires long-term oral anticoagulation.

The quest to develop TMVR devices has been marked by engineering and clinical challenges, and multiple remaining obstacles need to be overcome if TMVR is to become a widespread treatment option. An ideal TMVR device would be transseptal, lower profile, treat a wide range of annular sizes with low risk of LVOT obstruction, and not require long-term anticoagulation. As the long road of TMVR device development and iteration continues, hopefully there will also be further investigation of choral repair, annuloplasty, and leaflet extension. The future will likely offer a toolbox full of mitral repair and replacement technologies that will be utilized based on patient-specific anatomy and clinical status. ■

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