

## Chapter 28: Future Transcatheter Mitral Valve Repair / Replacement Technologies

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### **Introduction**

Treatment of mitral valve disease has expanded beyond surgical repair and replacement. In high and prohibitive risk patients, transcatheter options are being considered as alternatives to open and minimally invasive surgery. However, advances in transcatheter mitral therapy have been slow and encountered many challenges. This chapter will discuss these challenges, describe access approaches to transcatheter mitral therapy, and provide a summary of repair and replacement devices that are currently available or in clinical evaluation.

### **Challenges in Transcatheter Mitral Valve Repair / Replacement Designs**

Unlike the aortic valve, the mitral valve is a complex structure with multiple components, e.g. leaflet, annulus, chordae, papillary muscle and left ventricle. Abnormality affecting one or more of these structures can cause mitral regurgitation (MR). Design of transcatheter mitral valve repair (TMVr) and transcatheter mitral valve replacement (TMVR) devices to address MR and in some cases mitral stenosis has been challenging, as discussed in a recent review and editorial [1,2] and highlighted below.

#### Limited Patient Selection

The number of patients clinically eligible for transcatheter mitral therapy is limited as most patients benefit from and are eligible for surgical mitral repair. Surgical mitral repair remains the gold standard in degenerative MR as nearly 100% repair rate is possible with a wide range of pathologies using a variety of techniques [3]. Furthermore, many patients with MR have concomitant tricuspid regurgitation that warrant annuloplasty repair and/or atrial fibrillation that would benefit from a Maze procedure [4-6]. Therefore, unlike TAVR, patients with MR often present with additional considerations that transcatheter mitral therapy alone would not address effectively. In addition, patients with symptomatic severe MR are often younger and have fewer comorbidities that would otherwise preclude them from surgery. Short-term mortality rates of surgical mitral valve repair or replacement are also low. Therefore, the current pool of patients clinically eligible for transcatheter mitral therapy remains limited.

### Mitral Valve Anatomy and Pathology Is Complex

In mitral valve repair, surgeons use a variety of techniques, e.g. leaflet resection or reconstruction, chordal transfer or replacement, and annuloplasty, to address all the contributing lesions. In contrast, TMVr devices thus far only target individual components of mitral valve lesions, e.g. leaflet, annulus or chordae. Several devices (e.g. a MitraClip + Cardioband) may be necessary to optimize TMVr to match the outcomes of surgical repair.

In TMVR, most of the devices are designed for functional MR with a dilated left ventricle. Given the heterogeneity of annular dimensions, subvalvular apparatus and ventricular geometry, a range of sizes is necessary to fit the anatomy in this population. Currently, only the Abbott Tendyne, Medtronic Intrepid, Neovasc Tiara and Caisson TMVR devices have more than one size available. In addition, because the mitral annulus is not a planar structure, and anchoring mechanisms varies among TMVR prostheses, accurate sizing, even using multidetector computed tomography, has been challenging [7].

### Left Ventricular Outflow Tract (LVOT) Obstruction

One of the initially unexpected but most critical complications in TMVR is LVOT obstruction. Because the anterior leaflet is preserved in TMVR, it can swing towards the LVOT after valve implantation. Anatomic risk factors include small aortomitral annular angle, thick septum, and long anterior leaflet. Because many of the TMVR devices have a prominent ventricular profile, LVOT obstruction risk has become a predominant reason for exclusion in clinical studies. A concept of neo-LVOT has been proposed to predict the relative reduction in LVOT area to assess the feasibility of TMVR (Figure 1) [8].

### Valve Thrombosis and Anticoagulation

Leaflet thrombosis has recently emerged as a potentially significant issue in TAVR [9]. In the mitral position, the issue of valve thrombosis and anticoagulation is even more important, given the that the valve frame and cuff are positioned in the left atrium and the lower flow state between the left atrium and left ventricle. Early experience with TMVR has been complicated by early valve thrombosis, and current trials have instituted anticoagulation with warfarin as a standard therapy. Optimal duration of anticoagulation is unknown in both TMVR and TMVr, though anticoagulation requirements for TMVr will likely be less rigorous. Dual antiplatelet therapy is currently used in MitraClip repair but efficacy is not yet known.

### Device Durability

Long-term durability of TMVr and TMVR devices remains unknown, with the exception of MitraClip where the 5-year outcomes are available [10]. The remaining TMVr and TMVR

devices have only been in humans less than 5 years. Given the excellent long-term durability of surgical mitral valve repair and replacement, the future applicability of TMVr and TMVR in younger and lower risk patients remains to be seen.

### **Access Issues**

Transfemoral (TF) approach to the mitral via transseptal access is the least invasive and has been the preferred route for TMVr, such as the MitraClip and Cardioband.

TMVR devices, however, have much larger device and delivery system profiles, and not all devices are amenable to the transfemoral approach. The Edwards Sapien 3 transcatheter valve has been implanted via a TF approach in TMVR in patients with severe mitral annular calcification. However, balloon septostomy and subsequent percutaneous atrial septal defect closure are necessary to deliver the valve to the left atrium and avoid a significant left-to-right shunt afterwards. The Edwards CardiAQ and Caisson transcatheter mitral valve can also be delivered via a TF approach, and a TF version of the Abbott Tendyne and Medtronic Intrepid valve are also under development.

For now, the Tendyne, Intrepid, Tiara and Highlife transcatheter valves are implanted via a transapical (TA) approach. Unlike TA delivery systems in TAVR, these devices range 32-40 French in size, a much larger profile than the current 18 French Edwards Certitude TA system. Previous studies have shown a reduced benefit of the TA compared to TF approach in TAVR. Given a majority of patients with moderate to severe functional MR evaluated for the TMVR trials have reduced left ventricular function, inserting such a large sheath for TMVR may risk further compromising cardiac function and attenuating the benefit of the therapy.

Transatrial approach is also being considered for TMVR (Figure 2). Given the anatomical and technical challenges associated with TF TMVR in severe mitral annular calcification, transatrial approach has been reported with improved anchoring of the Edwards Sapien 3 valve and avoiding LVOT obstruction [11]. However, a transatrial approach, even if performed minimally invasively, still requires thoracotomy and cardiopulmonary bypass.

### **Transcatheter Mitral Repair (TMVr) Devices**

The following 3 categories of TMVr devices are either commercially available or in clinical trials (**Figure 3**).

## MitraClip NT

Greater than 40,000 Mitraclip implants have been performed globally, and >60% of patients who underwent MitraClip repair outside the US were done so for secondary MR. Currently, MitraClip is approved in the US only for symptomatic severe primary MR in prohibitive risk patients. The COAPT trial randomizing patients with secondary MR between MitraClip and optimal medical therapy is ongoing. One-year outcomes of MitraClip repair in the US Transcatheter Valve Therapy Registry were favorable. However, patients with secondary MR, residual moderate-severe or greater MR and TR had worse survival, consistent with outcomes reported in the surgical literature.

## Chordal Replacement

Transapical chordal replacement mimics chordal replacement in surgical mitral repair, but the artificial chordae are secured to the ventricular apex performed on a beating heart under TEE guidance. Currently, the Neochord system is CE-marked and a US clinical trial is underway [12]. The Harpoon system has been used in Europe and a US feasibility study will begin shortly.

## Annuloplasty (Indirect, Direct)

To mimic surgical mitral annuloplasty, transcatheter annuloplasty devices have been developed to reduce the septal-lateral dimension either via the coronary sinus or directly at the annulus. The Carillon is a stent-like device deployed at the coronary sinus whereby cinching leads to annular reduction. The Valtech Cardioband is an annuloplasty band deployed via anchors to the mitral annulus and adjusted under TEE to reduce MR. Both devices are CE-marked and randomized trials will begin soon in the US.

## **Transcatheter Mitral Replacement (TMVR) Devices**

TMVR devices are being used in cases of mitral annular calcification, mitral regurgitation, and mitral valve and valve replacement.

## Mitral Annular Calcification

TMVR in mitral annular calcification has been performed off-label with Edwards Sapien 3 and Boston Scientific Lotus valves, both designed for the aortic position. The Medtronic Melody has also been used, which is designed for the pulmonary position [13-15]. Outcomes from the Global Registry have been variable with a 30-day mortality of 29.7% [13], and LVOT obstruction, paravalvular leak and delayed valve migration are significant limitations to this

approach. A hybrid transatrial approach has also been reported with better success [11], but the longer term outcomes remain uncertain.

### Mitral Regurgitation

A number of TMVR devices to treat severe MR are currently in clinical trials (Figure 4). Tendyne, Intrepid, CardiAQ, Tiara, Caisson and Highlife transcatheter valves all have different features and potential advantages and disadvantages. The Tendyne Global Feasibility Study reported the largest series of TMVR in 30 patients with no cardiovascular mortality or stroke, almost no residual MR, and significant clinical improvement [16]. However, rehospitalization for heart failure was 13.8% and acute renal failure was 17%. As technology evolves in valve design and delivery, outcomes among these procedures will improve.

### Mitral Valve-in-Valve

There has been an expansion in bioprosthetic mitral replacements due to the freedom of anticoagulation. Transcatheter valves for the aortic position can now be used as mitral valve-in-valve replacement for failing bioprosthetic mitral valves in high risk surgical patients (Figure 5). Both transapical and transseptal approaches are available. Transapical access is easy to set up and offers a straight and shorter route to the mitral valve enabling coaxial alignment within the degenerated bioprosthesis, but transseptal approach is less invasive and is particularly suited in those who are high risk for a thoracotomy. This procedure may serve as an appealing alternative to redo operative mitral valve replacement in high-risk patients, however, its efficacy still needs to be determined [17].

### **Summary**

The potential patient population with symptomatic mitral valve disease eligible for treatment has expanded with transcatheter mitral therapy. Technological advances will improve the safety and efficacy of repair and replacement devices. Surgical and transcatheter options to treat mitral valve disease will remain complementary and decision making should be guided by a multidisciplinary heart team.

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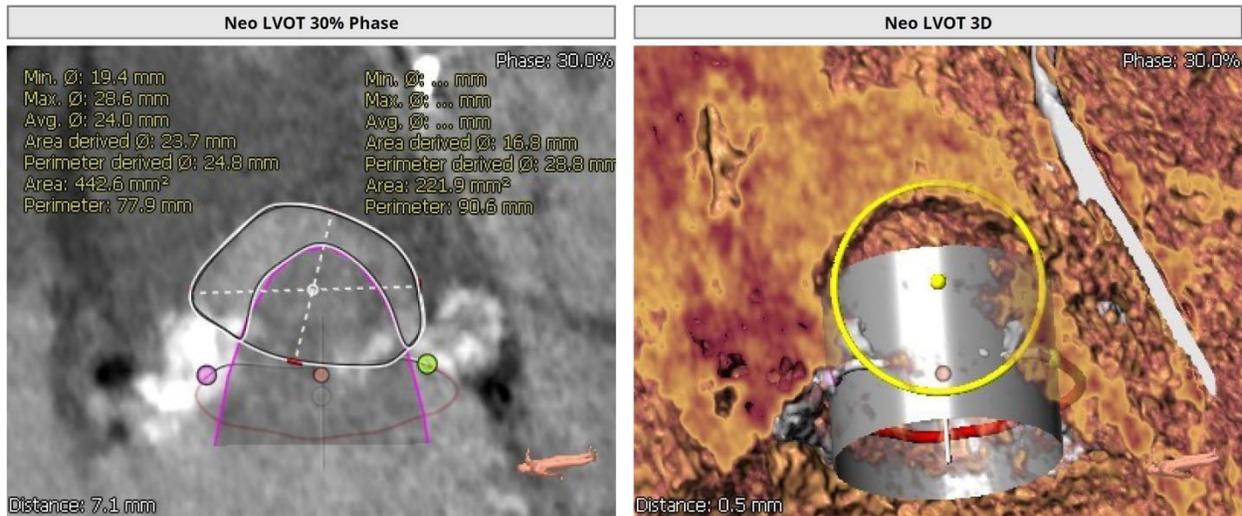
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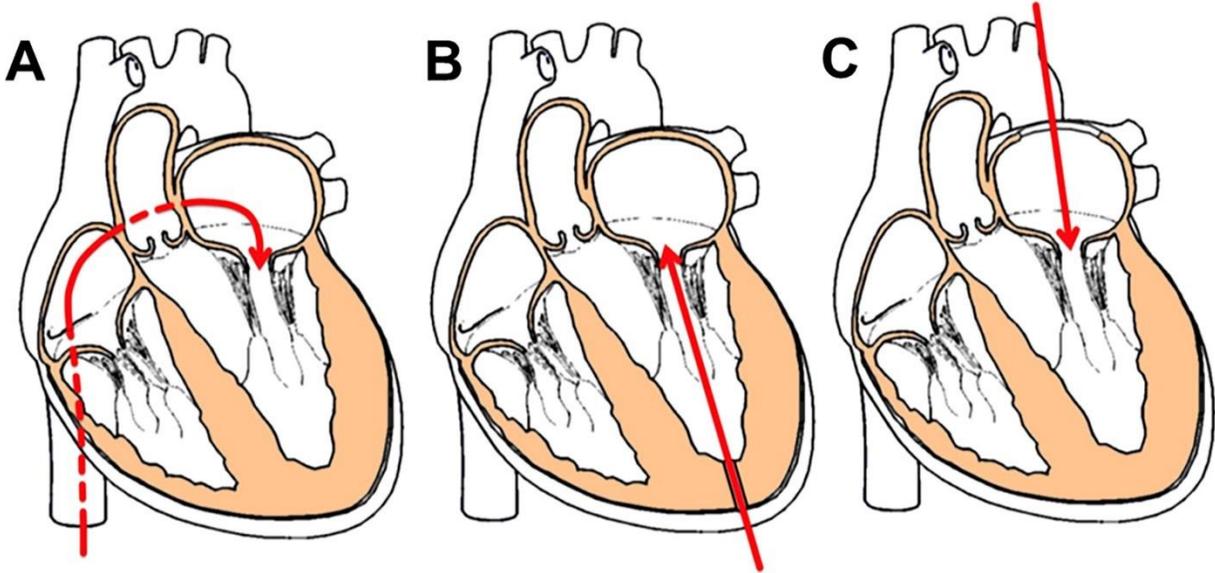
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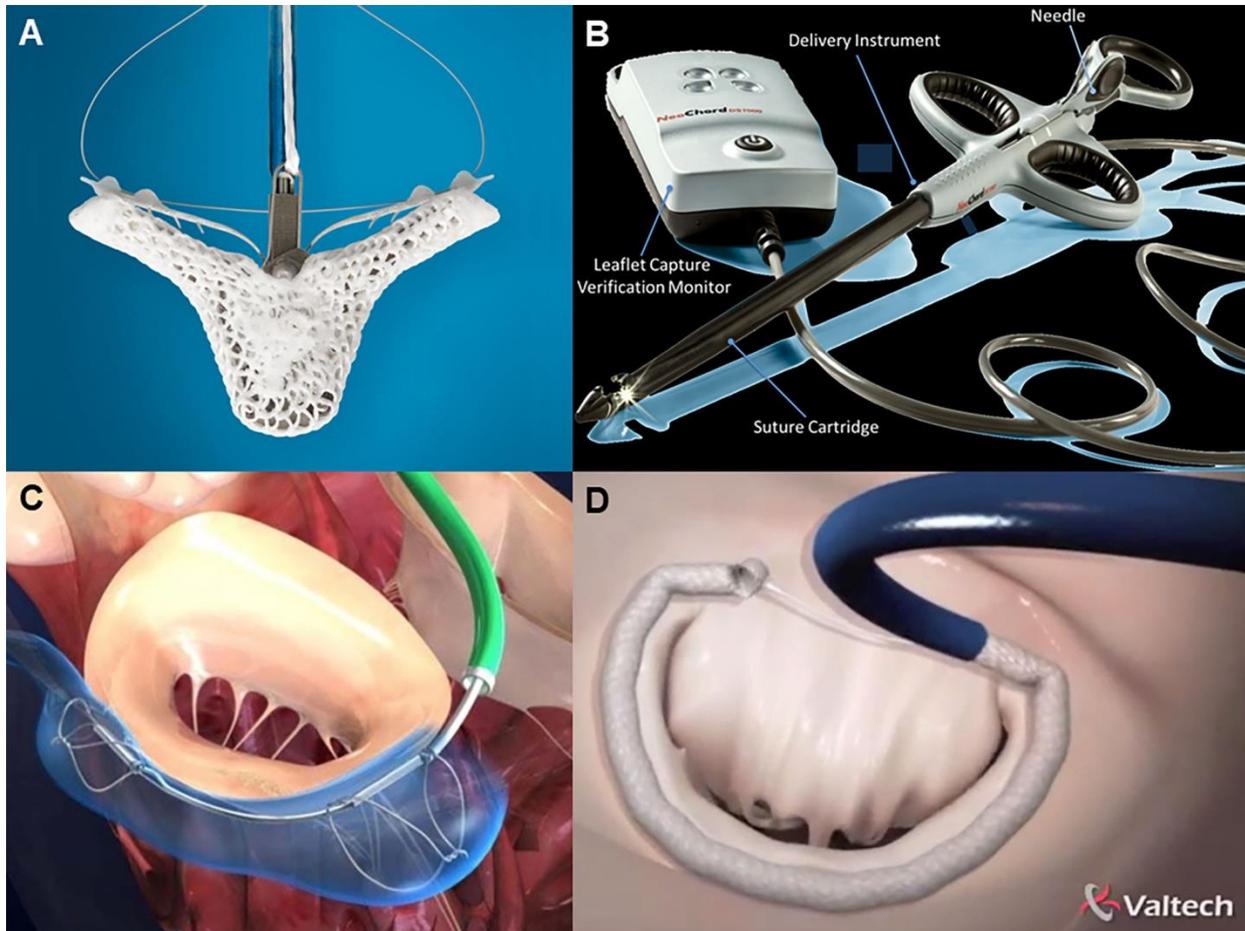
**Figure 1.** The concept of new-LVOT in transcatheter mitral valve replacement. In this patient, the original LVOT area derived from multidetector CT at end-systole is 442.6 mm<sup>2</sup>. After TMVR, the neo-LVOT area is projected to be 221.9 mm<sup>2</sup>, an almost 50% reduction. The risk of LVOT obstruction after valve implantation is therefore very high in this patient, as shown in the 3-dimensional rendering.



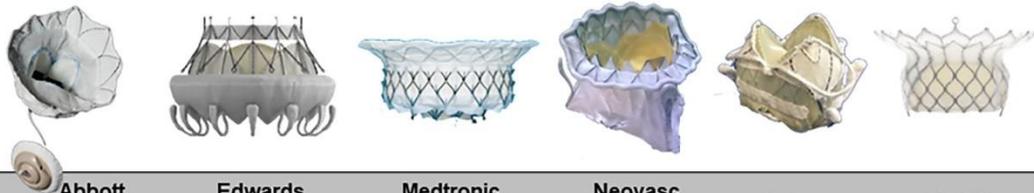
**Figure 2.** Access approaches to the mitral valve in transcatheter therapy: transfemoral / transseptal (A), transapical (B), and transtrial (C).



**Figure 3.** Commercially available or CE-marked transcatheter mitral valve repair devices: MitraClip NT (A), Neochord transapical chordal replacement system (B), Carillon indirect annuloplasty (C) and Valtech Cardioband direct annuloplasty (D).



**Figure 4.** Transcatheter mitral valve replacement devices currently in clinical trials.



	<b>Abbott Tendyne</b>	<b>Edwards CardiAQ</b>	<b>Medtronic Intrepid</b>	<b>Neovasc Tiara</b>	<b>Caisson</b>	<b>Highlife</b>
<b>Implant Shape</b>	D-Shaped	Circular	Circular	D-Shaped	D-Shaped	Circular
<b>Valve Size</b>	Multiple	30 mm	27 mm w/ 3 outer stents (43/46/50)	35, 40 mm	35-40 mm	31 mm
<b>Leaflet</b>	Porcine	Bovine	Bovine	Bovine	Porcine	Bovine
<b>Fixation</b>	Tether	Anchors	Barbs	Anchors	Feet	Ring
<b>Delivery Size OD</b>	32 Fr	33 Fr	35 Fr	32 Fr	31 Fr	Valve: 39 Fr Ring: 18 Fr
<b>Access</b>	T-Apical , T-Septal*	T-Apical, T-Septal	T-Apical, T-Septal*	T-Apical	T-Septal	T-Apical, T-Femoral
<b>Recapture</b>	Fully retrievable	No recapture	Retrievable system soon	No recapture	Fully retrievable	Valve retrievable

\*under development

**Figure 5.** Transcatheter mitral valve-in-valve replacement. Left ventriculogram illustrates an Edwards Sapien 3 valve inside a Medtronic Mosaic mitral bioprosthesis implanted via a transseptal approach.

