

Transcatheter Mitral Valve Implantation: TMVI Status in 2024

© Gry Dahle

Oslo University Hospital, Department of Cardiothoracic Surgery, Oslo, Norway

Abstract

Today, it is almost 22 years since the first transcatheter aortic valve implant (TAVI) and 11 years since the first transcatheter mitral valve implantation (TMVI) was implanted. TMVI never escalated like TAVI. So far, only one transcatheter mitral valve (TMV) has Conformité Européenne approval and none has Food and Drug Administration approval. This means that no TMV is commercial in the United States. There are several TMVs in clinical studies, but because of anatomical limitations, inclusion is slow. This editorial focuses on the challenges and opportunities in TMVI.

Keywords: Annulus, cardiovascular medicine, heart

Introduction

The mortality rate for untreated severe mitral regurgitation (MR) is up to 50% at a 5-year duration⁽¹⁾, and the incidence in the Western world of such patients is 1-2%, with a prevalence of 10% for patients >75 years⁽²⁾.

Today, it is almost 22 years since A. Cribier performed the “first-in-man” (FIM) transcatheter aortic valve implant (TAVI) procedure April 16, 2002⁽³⁾ and 20 years since “FIM” Mitraclip (Abbott Vascular, Abbott park, IL, United States) was performed in Venezuela 2003 by Dr. Condado and his team (Abbott home page) and received the Conformité Européenne (CE) mark 2008. Almost 10

years later, in 2012, the first transcatheter mitral valve implantation (TMVI) was performed by Søndergaard et al.⁽⁴⁾ using the CardiAQ valve (Edwards Lifesciences, Irvine, United States). TMVI never escalated like TAVI.

Over the last decade, it has become clear that treating the mitral valve represents a much more complex endeavor than TAVI, given the complex saddle-shaped and noncalcified mitral annulus and potential interactions with the left ventricular outflow tract (LVOT). MR is a heterogeneous disease. Repair is generally the preferred surgical treatment option although it is highly dependent on the experience of the center. The question is whether



Address for Correspondence: Gry Dahle, Oslo University Hospital, Department of Cardiothoracic Surgery, Oslo, Norway

e-mail: g_dahle@hotmail.com **ORCID:** orcid.org/0000-0002-6381-6766

Received: 09.02.2024 **Accepted:** 08.04.2024

Cite this article as: Dahle G. Transcatheter Mitral Valve Implantation: TMVI Status in 2024. EJCM 2024;12(2):29-35.

DOI: 10.32596/ejcm.galenos.2024.2024-5-22



©2024 The Author. Published by Galenos Publishing House on behalf of the Heart and Health Foundation of Turkey (HHFT).

This is an open-access article under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License.

the same strategy should be used for catheter treatment. Additional pathologies are common in patients with mitral valve disease, such as aortic stenosis, tricuspid regurgitation, left ventricular dyssynchrony, atrial fibrillation, and heart failure. These must be addressed, in addition to replacement or repair, most often before the mitral procedure, with the exception of tricuspid regurgitation. The durability of bioprosthesis in the mitral position is questionable.

Several TMVI systems are in clinical studies for human implants with different properties and designs. Only one system has CE approval, the Tendyne™ valve from Abbott⁽⁵⁾, and none has Food and Drug Administration approval, which means that there is no commercially available transcatheter mitral valve (TMV) in the US.

For current issues with TMVI, please see Figure 1 for a summary.

Challenges in Patient Selection

To date, TMVI has largely been reserved for patients who are poor candidates for surgery and for whom transcatheter mitral valve repair is unlikely to provide durable MR reduction. The first clinical consideration is

whether the patient can tolerate a transapical intervention and how the patient functions in daily life. To decide between replacement or repair, anatomical suitability and patient frailty should be considered. A frail patient may benefit from the less invasive method even though the result may not be perfect. For patients with restricted leaflets, small annuli, and/or many clefts, replacement may provide the best result.

Patients with HF should receive optimal HF treatment before the procedure, including cardiac rhythm management devices such as implantable cardioverter defibrillator and cardiac resynchronization therapy, if indicated. Other comorbidities to consider are right heart failure, tricuspid regurgitation, aortic stenosis or regurgitation, coronary artery disease, chronic obstructive pulmonary disease, and the ability to tolerate oral anticoagulation.

Computed Tomography Reconstruction must be Performed For

- Prosthesis sizing, see below regarding the challenges in sizing.
- Calcium in the annulus, mitral annular calcification (MAC), evaluation⁽⁶⁾.

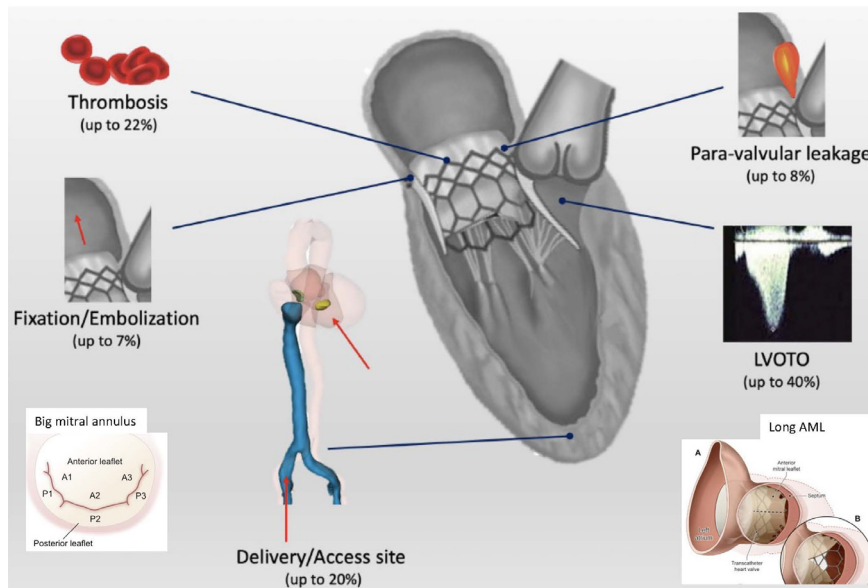


Figure 1. Current issues in TMVI. Fixation/embolization, big annuli, paravalvular leakage, delivery/access, left ventricular outflow tract obstruction including long anterior leaflet, thrombosis. Modified from Russo et al.⁽²⁵⁾

- Evaluation of neo LVOT (aorto-mitral angle, septal bulge, anterior leaflet)⁽⁷⁾.
- Thickness of the myocardium and papillary muscle anatomy.
- Implantation angles for the best coaxiality.
- Chest access.

Several computed tomography (CT) softwares can be used for CT reconstruction: 3Mensio (Pie Medical Imaging, Maastricht, Netherland), Materialize (Loeven, Belgium), and circle CVI (Cadiovascular Imaging Inc., Calgary, Canada). In some cases, CT scan is used for 3D printing. It is of great importance that the CT scan is performed for the entire heart cyclus, is electrocardiography gated, and with thin slices. Multislice CT derived mitral intercommisural dimension and left ventricular endsystolic diameter are easily performed measures that are effective predictors of anatomical suitability or screen failure for TMVI devices⁽⁸⁾.

Figure 2 summarizes preprocedural planning.

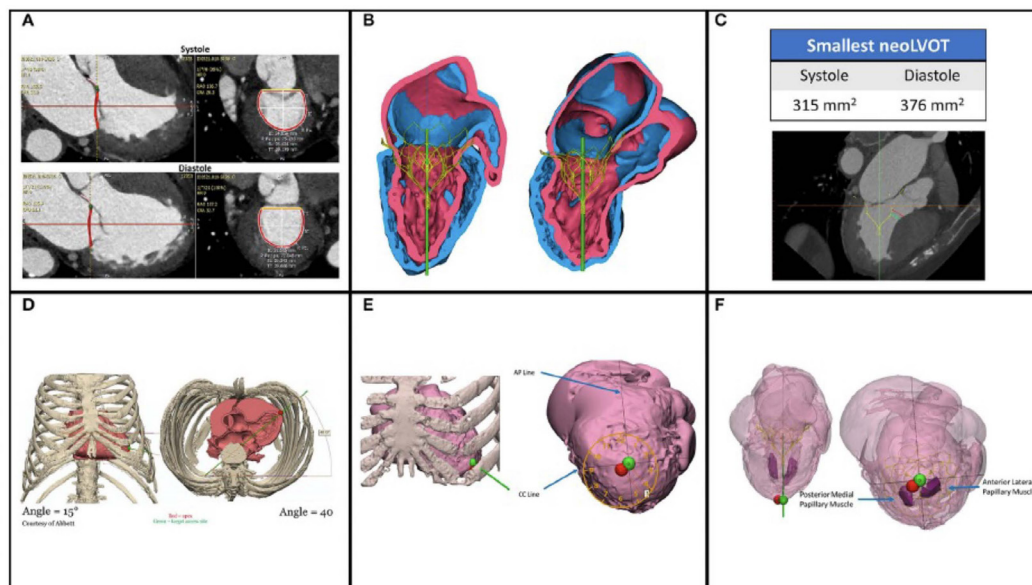


Figure 2. Pre-procedural planning by computed tomography reconstructions. **A)** Measurements for sizing are done both insystole and diastole to calculate for the best fitting. **B)** Simulation of the selected valve to evaluate the neo left ventricular outflow tract (LVOT) and sealing of the valve (here Tendyne™). **C)** Neo LVOT is calculated in systole and diastole. **D)** Calculation of off table angles for delivery sheath. **E)** The best coaxial puncture point (green) is generally slightly different from the anatomical apex. **F)** Papillary muscles are not in the path of the delivery sheath to avoid damage⁽⁵⁾

Anatomical Screen Failures

Size

For noncalcified MR, prosthesis sizing and annular support are crucial. Most valves are in 2-3 sizes and are circular. The Tendyne™ valve is produced in 13 different sizes with a standard profile and low profile frame. It is also oval like the mitral annulus. All prostheses must be somewhat oversized to sit in place and avoid paravalvular leakage (PVL). One must take into account that for the circular prostheses, the transmission of the mitral annulus from an oval shape to a circular shape will change the area.

For patients with MAC, the annulus may be too small for the mitral prosthesis.

Neo LVOT

LVOT is the anatomical region of the left ventricle between the anterior mitral leaflet and the left ventricular septum where blood flows before reaching the aorta through the aortic valve. With the large prosthesis sizes of most TMVI systems, in addition to being anatomically

close to the LVOT, LVOT obstruction is a large design hurdle to overcome. To avoid LVOT obstruction, many factors need to be considered:

- Protrusion of the TMVI into the left ventricle.
- Flaring of the prosthesis created by the anchoring method may extend to the LVOT.
- The angle between the aortic and mitral planes, the aortomitral annular angle, determines the protrusion of the prosthesis into the LVOT and may affect blood flow dynamics.
- Septal bulging can create narrowing of the LVOT in systole.
- Length of the anterior leaflet and potential for obstruction due to systolic anterior motion (SAM). CT reconstruction is performed to calculate the new LVOT area after valve implantation, and an area of 200-250 mm² is recommended as a cut-off⁽⁹⁾. To reduce the septal bulge, it is possible to perform septal ablation, preferably in advance⁽¹⁰⁾.

How to Overcome a Long Anterior Leaflet

Several techniques have been developed to cut the anterior leaflet to avoid LVOT obstruction by a long leaflet:

- Lampon procedure⁽¹¹⁾.
- Direct by endoscopic scissors.
- Shortcut device (Pi Cardia)⁽¹²⁾.
- Placing neochord.

For transapical TMVI, the Shortcut device or just cutting with endoscopic scissors seems to be less complicated.

Challenges in Valve Design

The TMVI prosthesis frame must be able to be crimped down and conform to a low-profile delivery system, and on expanding from the delivery system, the frame “remembers” its shape before crimping. The valve must withstand the dynamic pressure and flow conditions prevailing within the left ventricle during systole and

diastole. The design must additionally have an anchoring system that maintains the valve in place throughout these dynamic conditions after final placement.

Minimizing outflow tract obstruction and allowing for the maximum amount of blood flow through the LVOT is vital for the patient’s heart function.

Proper blood flow washout to avoid flow stagnation is important to prevent thrombosis, especially for mitral prostheses that are larger, resulting in more synthetic material implanted, and partially reside in the atrium with low flow velocities. Proper conformation with optimal sealing prevents PVL and resultant turbulent flow, which can cause thrombus formation or hemolysis. Close matching of the natural shape of the mitral annulus can improve valve performance and reduce PVL. A design that allows the valve to be fully positionable and retrieved during the initial implant procedure allows for optimal valve placement and can mitigate outflow tract obstruction.

Many transcatheter mitral prostheses have an outer (for anchoring) and an inner (housing the valve) frame.

Challenges in Anchoring

The mitral annulus is D-shaped, and during regurgitation, there is little calcium for support. Fixation of the prosthesis may therefore be challenging. Before tissue ingrowth, the prosthesis may dislocate or migrate because of high pressure during the systolic phase when the valve is closed. The prosthesis generally needs to be seated within noncalcified tissue that is both dynamic and D-shaped in one plane and saddle shaped in three dimensions. In some cases, MAC is present and presents distinct challenges due to the heterogeneous mechanical properties and geometry of the annulus. In addition, it may be narrow, and large noncompliant balloons are not available for predilatation. The anchoring systems used by current TMVI systems include the following:

- A tether and epicardial pad to achieve coordination axial forces, Tendyne™ valve (Abbott)⁽¹³⁾.
- Atrial and ventricular flanges to grasp the mitral annulus and leaflets, CardiAQ⁽⁴⁾.

- Native leaflet grasping to fixate the prosthesis in place of the Tiara valve⁽¹⁴⁾.
- Docking systems to allow sufficient radial forces to anchor the valve, High life (Highlife Medical, Irvine, California)⁽¹⁴⁾ and Sapien M3 (Edwards Lifesciences, Irvine, California)⁽¹⁵⁾.
- Subannular hooks that pierce the native mitral valve tissue/annular winglets, NaviGate (NaviGate Cardiac structures, Lake Forest, California)⁽¹⁴⁾.
- Cork-like effects that produce radial forces to aid the anchoring of the prosthesis, Intrepid valve (Medtronic)⁽¹⁴⁾.
- Atrial cage that uses the full anatomy of the left atrium to prevent valve migration, AltaValve, (4C Medical, Marple Grove, Minneapolis, Minnesota)⁽¹⁶⁾.

Delivery Systems

The design of the delivery systems depends on the access route. Till now, apical delivery has been used. The valves are large and difficult to fit in small sheaths. The apical systems range from 32 to 36 Fr. To deliver transfemoral, transseptal sheaths have to be in smaller dimensions.

Pre-Operative Planning

The approved indications or clinical study eligibility criteria must be met for treatment with TMVI. Normally, these criteria include an ejection fraction >30% and left ventricular diastolic diameter <7.0 cm. The regurgitation should be more than 2+, and the patient should be symptomatic to motivate treatment. The advantage of TMVI is that both primary and secondary MR etiologies, including MAC, can be treated.

Echocardiographic evaluation of the severity of MR, length of anterior leaflet, and presence of SAM, resulting in hemodynamic challenges, should be reviewed when selecting patients for TMVI. The function of the non-mitral valves, heart rhythm, and ejection fraction also need to be addressed.

Ongoing Studies

After the first TMVI was performed, several devices were constructed and put into studies. Some devices are mentioned in the section for anchoring, but only one, the Tendyne™ valve, is commercial. Ongoing studies:

1. Tendyne™ EFS trial is published with 2-year follow-up⁽¹⁷⁾ and the resolve MR includes the first patients after commercialization. The Summit trial is also going on in the US comparing Tendyne and MitraClip and has a specific arm for MAC (NCT04940390).

2. Evoque, the first human transeptal replacement, was first described by Webb et al.⁽¹⁸⁾ in 2020 for a series of 14 patients with technical success in 13 of the patients and 7.1% 30-day mortality. Further investigation has to be done, and now it seems like Edwards Lifesciences will further develop this valve for tricuspid implantation in the Triscend II Pivotal trial (NCT04482062)⁽¹⁹⁾.

3. The Encircle trial for the Sapien M3 from Edwards Lifesciences has started both in Europe and the US and plans to include 300 patients (NCT04153292), so far no publication but presented at TCT 2022 by D Daniels.

4. The first Apollo trial was performed transapically to investigate the Intrepid valve (NCT03242642). Later, the Apollo expansion trial started in the US and the Apollo EU trial just started enrolling for transfemoral access, and tricuspid implantation has also been investigated⁽²⁰⁾.

5. The Cephea EFS study is enrolling in the US and Canada introducing the Gen II valve, presented in TCT 2023 J F Granada.

MAC

MAC is a high risk of surgery, both for annular rupture and paravalvular leak. Some case reports and small studies have shown that TMVI may be beneficial in such situations⁽²¹⁾ and that dedicated transcatheter mitral valve replacement therapy may have a future role in these anatomically challenging high-risk patients. There is a specific CT-based MAC score to predict the severity of MAC; the range is from 1 to 10, summarizing the scores for calcium thickness, calcium distribution,

trigone involvement, and leaflet involvement. A score of 7 or more indicates severe MAC⁽⁶⁾ (Figure 3). In the Summit and Apollo trials, there are specific arms for MAC patients, and the results will be published.

Previous AVR and TAVI

For surgical mitral valve replacement, a previous AVR or TAVI may cause difficulties. A series of 11 patients reported TMVI implanted in patients with pre-existing aortic valve replacement. The procedures were performed without complications and did not alter the function of either prosthesis⁽²²⁾, as shown in Figure 4.

Challenges in Anticoagulation Therapy

Because of the large amount of foreign material and risk of blood stagnation and thrombus formation, anticoagulation after TMVI is recommended for at least 3-6 months, but may be lifelong⁽²³⁾.

Challenges in Valve Durability

With regard to surgical mitral valves, the durability of biological valves is an issue. Thus far, it is difficult to perform any valve-in-valve for degenerated TMVIs.

Therefore, the expected lifetime of the patient must be considered before TMVI.

Challenges in Pre-, Peri-, and Postoperative Observation and Treatment

Optimizing heart failure treatment before the procedure is essential. Perioperative dialog between anesthetic and surgical teams is crucial. The patients should be observed in the surgical cardiac intensive care unit first 12-24 hours. Schwann-Ganz monitoring may be useful, particularly in patients with pulmonary hypertension and/or right heart failure. Inotrope support may be better than fluid to maintain acceptable mean arterial pressure. It is important to differentiate between a pure MR patient and a MAC patient regarding strategy⁽²³⁾.

Can TMVI be a Bridge to Transplantation?

To date, there are no publications on TMVI to postpone or bridge to transplant. MitraClip treatment may optimize patient condition and/or postpone heart transplantation. The MitraBridge registry concludes that MitraClip treatment optimizes patient status and provides eligibility for heart transplantation in one-third of patients and no more need for transplantation in 22.5%⁽²⁴⁾. In our center, we postponed heart transplantation in one patient for 8 years and in another 7 months by implanting TendyneTM.

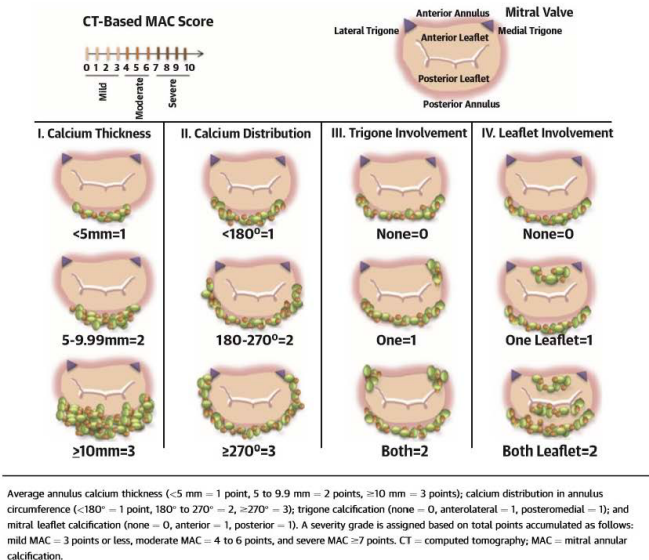


Figure 3. The score for predicting MAC severity from Guerrero et al.⁽⁶⁾

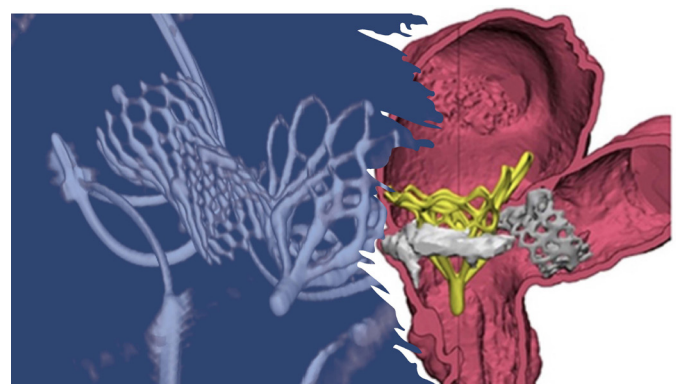


Figure 4. CT reconstruction of TendyneTM implanted in MAC and with pre-existing TAVI⁽²²⁾
CT: Computed tomography, MAC: Mitral annular calcification, TAVI: Transcatheter aortic valve implant

Ethics

Financial Disclosure: This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Mirabel M, Jung B, Baron G, et al. What are the characteristics of patients with severe, symptomatic, mitral regurgitation who are denied surgery? *Eur Heart J* 2007;28:1358-65.
2. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet* 2006;368:1005-11.
3. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. *Circulation* 2002;106:3006-8.
4. Søndergaard L, De Backer O, Franzen OW, et al. First-in-Human Case of Transfemoral CardiAQ Mitral Valve Implantation. *Circ Cardiovasc Interv* 2015;8:e002135.
5. Dahle G. Current Devices in TMVI and Their Limitations: Focus on Tendyne. *Front Cardiovasc Med* 2020;7:592909.
6. Guerrero M, Wang DD, Pursnani A, et al. A Cardiac Computed Tomography-Based Score to Categorize Mitral Annular Calcification Severity and Predict Valve Embolization. *JACC Cardiovasc Imaging* 2020;13:1945-57.
7. Wang DD, Eng M, Greenbaum A, et al. Predicting LVOT Obstruction After TMVR. *JACC Cardiovasc Imaging* 2016;9:1349-52.
8. Blanke P, Modine T, Duncan A, et al. Anatomic suitability for transapical transcatheter mitral valve implantation using a tether-based device. *Catheter Cardiovasc Interv* 2023;102:318-27.
9. Kohli K, Wei ZA, Yoganathan AP, Oshinski JN, Leipsic J, Blanke P. Transcatheter Mitral Valve Planning and the Neo-LVOT: Utilization of Virtual Simulation Models and 3D Printing. *Curr Treat Options Cardiovasc Med* 2018;20:99.
10. Ukaigwe A, Gössl M, Cavalcante J, Olson S, Sorajja P. Neo-Left Ventricular Outflow Tract Modification With Alcohol Septal Ablation Before Tendyne Transcatheter Mitral Valve Replacement. *JACC Cardiovasc Interv* 2020;13:2078-80.
11. Khan JM, Babaliaros VC, Greenbaum AB, et al. Anterior Leaflet Laceration to Prevent Ventricular Outflow Tract Obstruction During Transcatheter Mitral Valve Replacement. *J Am Coll Cardiol* 2019;73:2521-34.
12. Tchétché D, Kodali SK, Dvir D. First dedicated transcatheter leaflet splitting device: the ShortCut device. *EuroIntervention* 2022;18:e428-e9.
13. Muller DWM, Farivar RS, Jansz P, et al. Transcatheter Mitral Valve Replacement for Patients With Symptomatic Mitral Regurgitation: A Global Feasibility Trial. *J Am Coll Cardiol* 2017;69:381-91.
14. Regueiro A, Granada JF, Dagenais F, Rodés-Cabau J. Transcatheter Mitral Valve Replacement: Insights From Early Clinical Experience and Future Challenges. *J Am Coll Cardiol* 2017;69:2175-92.
15. Yasmin F, Najeeb H, Fareed Siddiqui H, et al. Current Practices and Considerations for Transcatheter Mitral Valve Implantation Based on Risk Stratification Among Patients with Mitral Valve Regurgitation. *Curr Probl Cardiol* 2023;48:101413.
16. Nunes Ferreira-Neto A, Dagenais F, Bernier M, Dumont E, Freitas-Ferraz AB, Rodés-Cabau J. Transcatheter Mitral Valve Replacement With a New Supra-Annular Valve: First-in-Human Experience With the AltaValve System. *JACC Cardiovasc Interv* 2019;12:208-9.
17. Muller DWM, Sorajja P, Duncan A, et al. 2-Year Outcomes of Transcatheter Mitral Valve Replacement in Patients With Severe Symptomatic Mitral Regurgitation. *J Am Coll Cardiol* 2021;78:1847-59.
18. Webb J, Hensey M, Fam N, et al. Transcatheter Mitral Valve Replacement With the Transseptal EVOQUE System. *JACC Cardiovasc Interv* 2020;13:2418-26.
19. Fam NP, von Bardeleben RS, Hensey M, et al. Transfemoral Transcatheter Tricuspid Valve Replacement With the EVOQUE System: A Multicenter, Observational, First-in-Human Experience. *JACC Cardiovasc Interv* 2021;14:501-11.
20. Zahr F, Song HK, Chadderdon SM, et al. 30-Day Outcomes Following Transfemoral Transseptal Transcatheter Mitral Valve Replacement: Intrepid TMVR Early Feasibility Study Results. *JACC Cardiovasc Interv* 2022;15:80-9.
21. Gössl M, Thourani V, Babaliaros V, et al. Early outcomes of transcatheter mitral valve replacement with the Tendyne system in severe mitral annular calcification. *EuroIntervention* 2022;17:1523-31.
22. Taramasso M, Sorajja P, Dahle G, et al. Transapical transcatheter mitral valve implantation in patients with prior aortic valve replacement: a feasibility report. *EuroIntervention* 2021;17:257-9.
23. Duncan A, Dahle G, Conradi L, et al. Multicenter Clinical Management Practice to Optimize Outcomes Following Tendyne Transcatheter Mitral Valve Replacement. *Struct Heart* 2022;6:100025.
24. Munafò AR, Scotti A, Estévez-Loureiro R, et al. 2-year outcomes of MitraClip as a bridge to heart transplantation: The international MitraBridge registry. *Int J Cardiol* 2023;390:131139.
25. Russo G, Maisano F, Massaro G, et al. Challenges and Open Issues in Transcatheter Mitral Valve Implantation: Smooth Seas Do Not Make Skillful Sailors. *Front Cardiovasc Med* 2022;8:738756.