What Is the Next Generation of Transcatheter Mitral Valve Repair Devices?

Mi Chen¹,² and Lizhong Sun¹*

¹ Department of Cardiac Surgery, Beijing Anzhen Hospital, Capital Medical University, Beijing, China, ² Department of Cardiac Surgery, University Hospital of Zurich, University of Zurich, Zurich, Switzerland

In the evolving scenario of the transcatheter mitral valve repair (TMVr), TMVr devices constitute a rapidly expanding field. The standard classification includes edge-to-edge repair, direct annuloplasty, indirect annuloplasty, chordal/papillary muscular repair, and the others. However, the unknowns and uncertainties to innovate a high-performing device are addressed. In this viewpoint, the authors discuss the potential future of the next generation and the challenges of TMVr devices.

Keywords: transcatheter mitral valve repair, transcatheter mitral valve intervention, transcatheter device, mitral regurgitation, functional mitral regurgitation

INTRODUCTION

Mitral regurgitation (MR) affects 9.3% of people older than 75 years, while 2.5% for aortic stenosis (1). However, transcatheter mitral intervention devices have been developed to address an unmet clinical need for inoperable patients with symptomatic severe MR. Given the more catastrophic and less forgiving complications of transcatheter mitral valve replacement, transcatheter mitral valve repair (TMVr) may be associated with a superior safety profile. Various TMVr devices are classified based on the surgical technique (Table 1), including edge-to-edge repair, direct annuloplasty, indirect annuloplasty, chordal/papillary muscular repair, and the others (2–10). Transcatheter edge-to-edge repair devices are based on Alfieri surgical technique by anchoring the free edge of the mitral leaflets and produce a double orifice. Transcatheter direct annuloplasty devices obtain reduced mitral annular dimension by anchoring mitral annulus directly, whereas, transcatheter indirect annuloplasty devices accomplish repair through adherent anatomies, such as the coronary sinus (CS) and left ventricle. Acknowledging the lack of scientific evidence to date, it is difficult to predict what the ultimate future TMVr devices will be. The purpose of this viewpoint is to address the potential future scenarios considering four aspects: safety, learning curve, the variability of disease and anatomy, and long-term outcomes.

FAVORABLE SAFETY PROFILE

Given the complexity and the heterogeneity of mitral valve anatomy and pathology, an excellent safety profile is mandatory as a permit to be available commercially. The safety of the device is first supported by its less invasive approach. It remains an increasing and strong interest to move from a transapical procedure toward a transfemoral and transeptal procedure shown by NeoChord DS 1000 (NeoChord, Inc., St. Louis Park, MN) via transapical approach and Pipeline (Gore Medical, USA) via transfemoral approach. Second, the less interference of the mitral valve apparatus and its adjacent anatomy, the safer it is. To
TABLE 1 | Classification of transcatheter mitral valve repair devices.

| Edge-to-edge repair | Direct annuloplasty | Indirect annuloplasty | Chordal/papillary muscular repair | Others |
|---------------------|--------------------|-----------------------|-------------------------------|--------|
| Transfemoral        |                    |                       |                               |        |
| Transapical         |                    |                       |                               |        |
| Others              |                    |                       |                               |        |

*In patients.
†CE mark approval.
‡FDA approval.

TABLE 2 | CE mark approval devices.

| Device      | Year of CE mark approval | No. of patients in trials | Variability of disease | Anatomical variations | Procedure duration |
|-------------|---------------------------|---------------------------|------------------------|----------------------|--------------------|
| MitraClip   | 2008                      | In total: 4,232           | FMR                    | ++ + +               | ++ + +             |
| PASCAL      | 2019                      | First-in-man: 23          | FMR                    | + + + +              | ++ + +             |
| CardioBand  | 2015                      | Early feasibility study: 31 CE trial: 61 | FMR | + + + + + + | + + + + + + + |
| Carillon    | 2009                      | AMADEUS: 48 TITAN: 36 TITAN II:36 REDUCE FMR:87 | FMR | + + + | + + + + + + + |
| Mitralign   | 2015                      | Early feasibility study: 71 | FMR | + + + | + + + + + + |
| Neochord    | 2012                      | TACT:30 TOP-MINI:49       | DMR                    | +                  | + + +             |

+, +++, +++++, ++++++ symbols represents the intensity from weak to strong.

date, the most common TMVr device is the MitraClip (Abbott, Abbott Park, IL, USA) with more than 100,000 implants based on the Alfieri edge-to-edge technique with only interference of mitral leaflets. COAPT registry illustrated high freedom from device-related complications of 96.6% (11). The Carillon (Cardiac Dimension Inc., Kirkland, WA, USA) is delivered through the CS to achieve indirect mitral annuloplasty with a relatively quick procedure. However, because of the contiguity of the circumflex artery with CS, 17% of cases due to coronary artery compression were reported in the TITAN II trial (12). Additionally, its safety to reproduce the surgical technique has been confirmed as the standard therapy. Cardioband system (Edwards Lifesciences, Irvine, CA, USA) is a surgical-like direct annuloplasty applied as an isolated or adjunctive approach, waiving the possibility of increasing the severity of MR. Meanwhile, because of the pure anatomical implant, Cardioband leaves the door open to further potential transcatheter mitral valve intervention (13). Finally, post-procedural safety matters. An ideal TMVr device does not require anticoagulation. A promising concept of transcatheter papillary muscular repair commenced, named Mitral Butterfly (AVVie, Vienna, Austria), but the thrombogenic potential of the device has not been studied clearly (14). Therefore, only CE marker–approved devices deemed with safety profiles are pooled in our further discussion (Table 2, Figure 1).

STEEPER LEARNING CURVE

Burt et al. (15) reported that the learning curve determined the operative efficiency and long-term outcomes of surgical mitral valve repair. The impact of the operator and institutional experience can be more determinant in TMVr procedures, which were initially studied by Chhatriwalla et al. (16) in the review of the TCT Registry of 12,334 MitraClip procedures. Visual inflection points in the learning curves for acceptable

**Abbreviations:** TMVr, transcatheter mitral valve repair; MR, mitral regurgitation; DMR, degenerative mitral regurgitation; FMR, functional mitral regurgitation.
procedural success were evident after ~50 cases, whereas optimal procedural success was observed in up to 200 cases. In the future, TMVr is to be considered as an alternative to surgery in eligible patients: operator experience may play a crucial role to achieve trace residual MR. With the gain of experience, the optimal procedural success and a wider spectrum of anatomical variations can increase not only in MitraClip but also in other TMVr techniques. A steep learning curve of the TMVr technique illustrates the outcomes to be less predictable in the early stage, which may prevent the promotion of the devices. Because of the lack of evidence of the learning curve for each TMVr device, the authors compared the procedure duration as the reference of the learning curve roughly (Table 2) (12, 17, 18).

**VARIABILITY OF DISEASE AND ANATOMICAL VARIATIONS**

MitraClip was initially approved for organic MR and has subsequently been approved for functional MR (FMR) with a satisfactory variability of the disease. However, with the discordant clinical outcomes between COAPT and MITRA-FR trials, a notable concept of proportionate vs. disproportionate FMR offered us a deeper perspective to estimate the efficacy of MitraClip. (2) The 1-year follow-up reveals the efficacy of the TMVr device. In COAPT and MITRA-FR trials, 1-year mortalities of MitraClip were 18.8 and 24.3%, respectively (11, 19), but the clinical outcomes are discordant when comparing with the controlled cohort. Nevertheless, the concept of proportionate vs. disproportionate FMR provided a comparison when comparing with the controlled cohort. However, with the discordant clinical outcomes between COAPT and MITRA-FR trials, a notable concept of proportionate vs. disproportionate FMR offered us a deeper perspective to estimate the efficacy of MitraClip. (3) The 5-year follow-up ensures the durability of the TMVr device. In 5-year outcomes of the EVEREST II trial, the rates of surgery for MV dysfunction between 1- and 5-year follow-up are comparably low in either TMVr or surgical therapy, whereas the MitraClip cohort more commonly required surgery for residual MR during the 1-year follow-up (22). These outcomes convinced us of the durability of MitraClip if it is a reliable implant during the first year. Only if a device is evaluated by the staged outcomes of 30-day, 1-year, and 5-year follow-up can a satisfactory spectrum of the safety and feasibility, efficacy, and durability ensure survival.

**DISCUSSION**

We provide an overview of four elements that should be taken into consideration for the next generation of TMVr devices (Table 2, Figure 1) and offer a comparison between the CE mark–approved devices. A safety profile always takes the first position for a new device. A shorter learning curve with a wider spectrum of disease and anatomy ensures the device's feasibility. Last not least, satisfactory long-term outcomes make the TMVr device survive for a long time.

**DATA AVAILABILITY STATEMENT**

The original contributions presented in the study are included in the article/supplementary
material, further inquiries can be directed to the corresponding author.

**AUTHOR CONTRIBUTIONS**

MC: concept, design, clinical studies, and manuscript preparation. LS: manuscript review.

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**Conflict of Interest:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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