



Edge-to-edge repair: will it still be mainstream repair therapy in 2030?

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Introduction

We are only just beginning to address the large number of patients with significant mitral regurgitation (MR), despite guidelines recommending operative repair in our asymptomatic patients with primary MR, and the limitations of medical therapy for secondary MR. Using history as a guide, less invasive therapies, including nonsurgical approaches, will be rapidly adopted once there is some evidence of similar mortality and MR reduction compared to gold standard open surgery.

The past & present

In order to predict the future, one needs to understand the past and the present. Edge-to-edge therapy with MitraClip (Abbott Vascular, Santa Clara, CA, USA) was first designed to be a less invasive approach to repair MR, as initially envisioned by St Goar and colleagues (1). The MitraClip device was delivered via a transvenous, trans-septal approach and used a mechanical clip to oppose the mitral leaflets in the area of regurgitation.

Degenerative MR

In the first ever randomized clinical trial studying MR, the EVEREST II trial demonstrated a significant benefit in terms of safety with MitraClip over open surgical repair, although the outcomes in terms of MR reduction were not equivalent (2). At 5 years follow-up, 97% of surgical patients remained free from grade 3 or 4+ MR versus 81% for MitraClip-treated patients. Interestingly, no differences in

symptoms nor mortality were identified between MitraClip and surgical treatment strategies.

Based on results from a subset of patients in EVEREST II, MitraClip ultimately gained regulatory approval in 2011, with subsequent guideline recommendations for prohibitive surgical risk patients in primary or degenerative MR (3). One criticism of the process was that results from the most experienced mitral valve surgeons were compared with that of MitraClip operators, who were new to the procedure. With greater operator experience, along with improvements in imaging and technological refinement of the MitraClip device, the recent EXPAND study investigated the results of more than 1,000 consecutively enrolled subjects (4). For those with primary MR, treatment by MitraClip resulted in freedom from grade 3–4+ MR in 96% of patients at 12-month follow-up, as adjudicated by an echocardiographic core laboratory.

Coincident with this, another transcatheter edge-to-edge repair device, the Pascal device (Edwards Lifesciences, Irvine, CA, USA), was more recently developed and studies regarding the device were initiated (CLASP study, NCT03706833). The Pascal device also has some potential design advantages over MitraClip, including wider coaptation surfaces, fewer frictional elements to reduce chordal entanglement risks and the use of a spacer element to theoretically optimize MR reduction. Early investigations of the Pascal device in the CLASP study demonstrated a similarly low complication rate and high success rate, with 98% freedom from grade 3–4+ MR at 30-day follow-up (5). If the newer MitraClip NT/XT and the Pascal device can demonstrate surgical-like, long-term durability for primary

MR reduction, these procedures will become mainstream therapy.

Functional MR

In secondary (i.e., functional) MR, the primary therapeutic modality is heart failure medications with cardiac resynchronization therapy in appropriate patients. Surgical intervention has been comparatively limited in its adoption, due to scarce supporting data for improved mortality or heart failure hospitalization benefit and a high rate of late recurrent MR (6). For patients who, despite optimal guideline-directed medical therapy, remain symptomatic with severe functional MR, transcatheter mitral valve repair has recently gained the spotlight. The COAPT trial (i.e., cardiovascular outcomes assessment of the MitraClip percutaneous therapy for heart failure patients with functional mitral regurgitation) demonstrated that patients undergoing repair with MitraClip had significantly improved survival and symptoms, with lower hospitalization rates than the medical therapy arm (7). Remarkably, 95% of patients undergoing MitraClip intervention in the COAPT trial had reductions in MR to lower than grade 3–4+. This in turn has and will continue to cement the role of MitraClip in the treatment of secondary MR in a population that otherwise has a 50% mortality and 90% hospitalization rate over five years (8). Consequentially, the Food and Drug Administration (FDA) approved the use of MitraClip for severe, symptomatic secondary MR refractory to medical treatment last year. Patient selection remains an important component of this therapy in those with secondary MR, as illustrated in the Mitra-FR trial (i.e., percutaneous repair with the MitraClip device for severe functional/secondary mitral regurgitation) (9). The Mitra-FR trial demonstrated a lack of therapeutic benefit in patients with larger left ventricular volumes and lesser degrees of MR. This led to the notion that only patients with MR ‘disproportionate’ to left ventricular dysfunction and size may benefit from the procedure (10).

Although demonstrating gradually improving and near-surgical results without the associated risks and morbidity, percutaneous edge-to-edge repair has its limitations, such as dealing with underlying mitral stenosis pathology and the concern for preservation of future options, including transcatheter mitral valve replacement. There are currently no other mitral valve devices that have the proven safety and results equal to those of percutaneous edge-to-edge repair,

nor with the depth of experience of over 100,000 patients treated worldwide.

Conclusions

Owing to the excellent safety profile, less invasive nature, improving results in MR reduction and mortality benefit, percutaneous edge-to-edge repair will likely still be mainstream therapy in 2030 for patients with degenerative MR at high surgical risk and for patients with functional MR despite medical therapy. Pending the results of trials in lower risk strata of degenerative MR, we anticipate its consideration for a broader range of patients with primary MR. Mitral pathology is often too complex and variable to be treated with a single tool alone. Therefore, percutaneous edge-to-edge repair will likely be one part of the transcatheter toolbox that also includes chordal replacement, annuloplasty and mitral valve replacement. As experience grows with these novel tools, percutaneous edge-to-edge repair will act as the gold standard. Ultimately, many tools will be necessary, but edge-to-edge therapies which continue to evolve and improve in order to remain the primary treatment for many patients with MR.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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