MitraClip Therapy for Mitral Regurgitation

Secondary Mitral Regurgitation

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KEYWORDS

• MitraClip • Mitral regurgitation • COAPT • Functional mitral regurgitation

KEY POINTS

- Both conventional surgery and medical therapy have limited efficacy for patients with functional MR, and surgery has limited application especially in older, high risk patients.
- MitraClip has demonstrated improvements in symptoms, favorable left ventricular remodeling, and reduced heart failure hospitalizations in high risk patients with severe MR in prospective registries.
- The randomized COAPT Trial will compare MitraClip with medical therapy to better define the role of this interventional approach.

Therapy for mitral regurgitation (MR) has been synonymous with mitral valve surgery for several decades. Surgical approaches for primary or degenerative MR have been highly successful. Mitral repair for degenerative MR has been associated with excellent acute and long-term results, with durable repair in a majority of patients. In contrast, surgical correction of secondary MR owing to ischemic or dilated cardiomyopathy has not proven to be as successful (Table 1), and has limited recommended indications in the current valve therapy guidelines (Table 2).[1]

Secondary or functional MR (FMR) represents, as its name suggests, is a secondary disease, related to dilatation or geometric distortion of the left ventricular (LV) chamber. Thus, as a disease of the left ventricle, mitral valve repair or even replacement for secondary MR has had less salutary results than surgery for degenerative MR.

The benefits of decreasing the severity of MR in secondary MR using surgical annuloplasty or valve replacement have been limited.[2] There has not been any clear benefit in mortality associated with reduction of MR in this population. Several studies have showed improvements in symptoms or surrogate measures of benefit, such as favorable LV remodeling, but improvements in these nonclinical endpoints have not translated into benefits in mortality, and in fact for the population of patients with ischemic MR, survival has been poor.

Over the last several years, percutaneous options for therapy for FMR have emerged.[3] The MitraClip device has by far the greatest use in clinical practice. MitraClip is the only percutaneous leaflet therapy available in this category (Fig. 1). Other device approaches including indirect and direct annuloplasty and transcatheter mitral valve replacement have been or are being developed.

The MitraClip device was modeled based on surgical double orifice or edge-to-edge mitral repair.[4] This operative approach was developed by Ottavio Alfieri in the early 1990s.[5] Alfieri used

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Table 1
Therapy options for mitral regurgitation

Surgical risk	Degenerative	Functional
Low	Surgical mitral repair	?
High	Commercial MitraClip	Global practice COAPT

Degenerative MR and low surgical risk candidates are best treated with surgery. MitraClip now offers an option for degenerative etiology patients with high surgical risk. There remains uncertainty regarding surgical treatment for functional MR. High surgical risk patients with functional MR are treated with MitraClip in international practice.

simple sutures to approximate the free edges of the mitral leaflets in patients with mitral prolapse. The methodology of this repair was to obliterate the prolapse segment and reestablish leaflet approximation. Thus, the initial intended use of the MitraClip device was for patients with degenerative MR. It was recognized early during the phase I trial experience that percutaneous MitraClip therapy could be applied to patients with FMR. It is important to remember that the original MitraClip trials were designed when the 1998 valve guidelines were current. The indications for surgical mitral valve intervention at the time did not distinguish between degenerative and functional.

The sequence of trial and registry experience with the MitraClip device has defined the current landscape for use of this therapy both in global practice and in ongoing trials. Ultimately, the MitraClip has come to be used primarily for FMR outside of the United States. In the United States, the MitraClip is commercially approved by the US Food and Drug Administration (FDA) for use in patients with degenerative MR, but remains investigational for use in patients with FMR. The journey to reach this point in current use of the therapy began with the Endovascular Valve Edge-to-Edge Repair (EVEREST) II randomized trial.

The EVEREST II trial was the key step in defining the initial role of the MitraClip device.[6] It was a randomized trial comparing percutaneous repair with conventional surgery for MR. It was designed with the inclusion criteria based on the 1998 valve guidelines. Patients were included if they had moderate to severe or severe MR with symptoms, or in the absence of symptoms had evidence of decreased LV ejection fraction or increased LV end-systolic dimensions. The MR had to originate from malcoaptation of the central portion of the line of coaptation. All of the echocardiographic findings were assessed by a core laboratory. Patients had to be candidates for mitral valve surgery, including cardiopulmonary bypass, and transseptal puncture had to be feasible. The main exclusion criteria were a LV ejection fraction of less than 25%, LV end-systolic dimension of greater than 55 mm, renal insufficiency, or history of endocarditis or rheumatic heart disease. As a result of these inclusion and exclusion criteria, a population composed of predominantly degenerative MR patients (73%) was selected. Despite the predominance of degenerative disease, one-quarter of the patients ultimately included in the trial had FMR. The main findings of the randomized comparison after 1 year, at the time of the primary endpoint assessment, were that surgery is more effective at reducing MR severity and percutaneous repair with the MitraClip device is safer. Importantly, both therapies had similar effectiveness in improving quality-of-life measures and symptoms and both were effective in leading to improved LV chamber dimensions and volumes through favorable remodeling. Subgroup analysis in this trial showed outcomes closest to those of surgery for patients with older age, worse ventricular function, and, most important, a functional etiology for MR.

Table 2
Summary of valve guideline recommendations for chronic severe secondary MR

Recommendation	Class	Level of Evidence
MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing coronary artery bypass grafting or aortic valve replacement	IIa	C
MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)	IIb	B
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	IIb	C

Abbreviations: MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association.