Percutaneous Intervention for Mitral Regurgitation: What is close to routine clinical use?

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Introduction

Mitral regurgitation (MR) is a significant health problem, with an estimated 4 million people in the US alone having significant MR, and 250,000 new cases diagnosed each year. Moreover, an estimated 15 million people worldwide are afflicted by congestive heart failure (CHF), with a significant proportion of these exhibiting moderate-to-severe MR. MR is associated with poor prognosis due to progressive mitral annular dilatation\(^1\). Whether as a result of functional heart disease or degenerative valve disease, MR is accompanied by a vicious cycle of continuing volume overload, ventricular dilatation, progression of annular dilatation, increased left ventricular (LV) wall tension, and worsening MR and CHF\(^2\).

Treatment of MR involves (1) mitral valve replacement with mechanical or porcine valve, (2) mitral valve repair with various techniques, or (3) LV reduction surgery (in functional MR) with the latter no longer in favour. Furthermore, therapeutic options for patients with functional MR (FMR) are even more limited and medical management is largely ineffective.

Edge-to-Edge Repair Technique and Its Result

The edge-to-edge repair has been used as a surgical technique in open chest, arrested-heart surgery for the treatment of MR since the early 1990s. With this technique, a portion of the anterior leaflet is sutured to the corresponding portion of the posterior leaflet using standard techniques and forceps and suture, creating a point of permanent coaptation ("approximation") of the two leaflets. When the edge-to-edge suture is placed in the middle of the valve, the valve will have a functional double orifice during diastole, hence the alternate name for the procedure: "Double Orifice Repair" (Figure 1). The valve can still open on both sides of the suture, allowing adequate diastolic blood flow through the valve. The suture assures that the two leaflets come together properly, as required, during systole. Tissue approximation is increasingly maintained over time by the healing response that takes place between the approximated leaflets, gradually reducing the need for the mechanical support provided by the suture.

Over 1,500 open surgical procedures using the edge-to-edge technique have now been reported in peer-reviewed literature with follow-up up to 15 years. The reported mortality with this technique is similar to the mortality of the more commonly performed repair techniques\(^3-5,6\). The Alfieri surgical repair has been successfully used with midterm follow-up to treat all of the primary aetiologies of MR. Edge-to-edge repair is infrequently used in open repairs and typically only for a specific subset of patients.

Figure 1: Edge-to-Edge Mitral Valve Repair Technique

A substantial experience of mitral valve repair procedures using the edge-to-edge technique without annuloplasty exists, including published and unpublished experience. However, in the majority of reported procedures where the edge-to-edge technique was used, an annuloplasty was also performed. As with other repair techniques, most surgeons perform annuloplasty at the time of the initial surgical repair procedure to reduce the likelihood of re-operation in the future. It has been suggested that the "edge-to-edge repair, when used alone, preserves the sphincter mechanism of the mitral valve and the systolic performance of the base of the heart. As a consequence, the annulus dilates during diastole, increasing the valve area and avoiding functional mitral stenosis"\(^6\). It has been shown that annuloplasty limits the natural dilation and contraction of the mitral annulus thereby impairing ventricular function\(^6\). In addition, failure of the annuloplasty or complications caused by the annuloplasty itself, have been reported to be causes of re-operations\(^6\).

Percutaneous Intervention for Mitral Regurgitation – MitraClip (Figure 4)

The MitraClip is a catheter-based system that approximates open-heart surgery with the Alfieri Stitch, which provides surgical edge-to-edge repair of the
mitral valve. As a minimally invasive technique, the MitraClip technique involves percutaneous delivery of the clip to collect the anterior and posterior leaflets to create the effect of the Alfieri Stitch. The technique facilitates proper leaflet coaptation, whether for degenerative MR (DMR) or FMR, with the result that it reduces LV volume overload, creates a tissue bridge to limit dilatation of the septal-lateral (anterior-posterior) dimension, and restrains the LV wall, thereby limiting LV dilatation. The MitraClip implant for leaflet repair has been approved for use in Europe and is being applied predominantly to high-risk surgical patients with either FMR or DMR.

Patient selection for MitraClip percutaneous mitral valve repair

In clinical studies and the real world setting, patients considered for MitraClip percutaneous mitral valve repair have symptomatic moderate-to-severe MR or evidence of LV dysfunction in asymptomatic patients. The regurgitant jet should originate from the A2-P2 scallops of the mitral valve. Patients with an ejection fraction of less than 20 to 25% are excluded, as are patients with endocarditis, chronic rheumatic heart disease, and renal insufficiency defined as serum creatinine >2.5 mg/dL. High-risk patient factors that provide evidence of suitability for the procedure include age above 75 years with ejection fraction less than 40%, reoperation with patent grafts, post-radiation mediastinum, two or more prior chest surgeries, FMR with ejection fraction less than 40%, previous mediastinitis, and hepatic cirrhosis. Patients must have sufficient leaflet tissue for mechanical coaptation: this requires a coaptation length of >2 mm, a flail gap of <10 mm, and a flail width of <15 mm.

Clinical outcomes

There is a growing body of clinical evidence to support percutaneous mitral valve repair with the MitraClip system. In the EVEREST (Endovascular Valve Edge-to-Edge REpair Study) II pivotal trial, which enrolled 78 non-randomised high-risk patients and 279 patients who were randomised in a 2:1 ratio to receive either the MitraClip or surgery, the MitraClip procedure was associated with similar efficacy to traditional surgery but with fewer short-term adverse events. In the preliminary cohort of 78 patients in the high-risk registry, Kaplan-Meier freedom from death was 94% at 1 year of follow-up and freedom from MV surgery was 83.2% (Figure 2).

In a 12-month matched pair analysis that included 34 FMR patients and 20 DMR patients, MitraClip therapy resulted in reverse LV remodelling (unpublished data). In this study, both diastolic and systolic volumes were significantly decreased with respect to baseline after MitraClip therapy in patients with FMR (Figure 3). A significant reduction in diastolic volume was also noted in patients with DMR. Furthermore, in FMR patients, MitraClip therapy resulted in significant reductions in both diastolic and systolic septal annular dimension. In the same patient cohort, there was a significant 45% reduction in the rate of re-hospitalisations for CHF. In a cohort of 16 patients requiring explant of the clip, approximately 80% of explants were conducted in DMR patients with recurrent MR being the predominant reason for explant. Subsequent treatment involving valve repair was possible in 63% of cases, while valve replacement was required in 37% of patients.

Conclusions

MitraClip therapy has been shown to produce significant reductions in mitral annual dimensions and LV volumes at one year in high-risk surgical patients with MR. These data demonstrate that high-risk patients with significant FMR particularly benefit from the procedure and significant reverse LV remodelling was noted in patients with DMR. The MitraClip procedure also significantly reduces the rate of re-hospitalisation. Importantly, percutaneous intervention with the MitraClip does not prevent future successful mitral valve surgery or repair.
References