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REVIEW

The MitraClip Experience and Future Percutaneous Mitral Valve Therapies

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Mitral regurgitation is the most common valve abnormality worldwide and its prevalence is expected to increase in the future due to aging of the population. Percutaneous mitral valve repair therapies may offer an opportunity to treat severe MR in the elderly or other high-risk groups who would otherwise be ineligible for surgery. The MitraClip system uses edge-to-edge coaptation of the mitral leaflets to create a double-orifice valve and reduce MR. It has been performed in over 10 000 patients to date, and as experience has improved, procedural times have shortened from over 200 minutes to less than 100 minutes, with increasing numbers of patients being left with ≤ grade 2+ MR. This review will focus on the literature available on MitraClip and other novel percutaneous techniques that are being developed for the treatment of severe MR.

Keywords Mitral regurgitation • Valve disease • Percutaneous therapies • Heart failure

Introduction

Mitral regurgitation (MR) is the most commonly occurring valve abnormality worldwide with a quarter of a million cases of severe MR being diagnosed in the US each year [1]. Since the prevalence of MR increases with age, the burden of mitral regurgitation is likely to increase significantly in the future [1]. Severe MR leads to left ventricular (LV) dilatation and failure, pulmonary hypertension, atrial fibrillation, stroke, and sudden death. The risk of death in subjects aged ≥70 years old with moderate/severe MR has been shown to be more than four-fold higher than that of age and sex matched subjects with absent/mild MR [2]. For surgically eligible patients, the current preferred strategy is surgical valve repair rather than valve replacement whenever possible [3,4]. Valve repair is associated with a lower surgical risk, improved survival and LV function, excellent long-term durability, and absence of risks associated with long-term anticoagulation. However, 30-50% of patients with severe MR are denied surgery, being deemed to be at prohibitively high risk because of advanced age, impaired left ventricular function or the presence of comorbidities [5].

A very common reason for denial of surgery is advanced age. Although mitral valve repair in the elderly is feasible, reasons for the lower uptake of the procedure in this population may include the higher prevalence of mitral annular calcification (which limits the use of ring annuloplasty), the presence of anterior or bileaflet degenerative MV disease, and a higher prevalence of Carpentier class IIIb "functional" MR [6]. Alternative percutaneous methods of treating severe MR are currently being evaluated and aim to offer comparable outcomes to conventional surgery in the elderly and in other high-risk groups.

The Mitral Valve

The MV is a complex anatomical structure consisting of two leaflets, each of which is segmented into three scallops. The larger anterior leaflet lies adjacent to the aorta, and the

Abbreviations: CI, Cardiac Index; CS, Coronary Sinus; DMR, Degenerative Mitral Regurgitation; FMR, Functional Mitral Regurgitation; LV, Left Ventricular; LVEDP, Left ventricular end-diastolic pressure; LVEF, Left ventricular ejection fraction; MR, Mitral regurgitation; NYHA, New York Heart Association

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narrower posterior leaflet lies posterolaterally, in relation to the left atrial free wall. The leaflets are anchored to the left ventricle by chords (chordae tendinae) running from the edge (primary chordae) and ventricular surface (secondary chordae) of the leaflets to two papillary muscles. The leaflets are attached to the mitral annulus, an ovoid, saddle-shaped structure that changes shape and diameter during the cardiac cycle. In contrast to the aortic annulus, the mitral annulus plays an important role in myocardial contraction and left ventricular function [7].

Mitral regurgitation arises when pathological changes in the mitral leaflets or in the annulus result in a failure of leaflet coaptation or apposition. Degenerative mitral valve disease refers to abnormal thickening, redundancy, or perforation of the leaflets, or elongation or rupture of the support structures including the chords and papillary muscles. This commonly leads to severe eccentric MR. A spectrum of disease from simple chordal elongation of one segment with relatively normal leaflets (fibro-elastic deficiency), to severely redundant, myxomatous degeneration of all leaflets (Barlow's disease) has been well described [8].

Functional mitral valve regurgitation arises as a consequence of left atrial or ventricular dysfunction. Dilatation of the ventricle and/or atrium, as occurs in dilated cardiomyopathies, myocardial infarction, and longstanding atrial fibrillation, prevents leaflet apposition leading to central mitral regurgitation. Myocardial ischaemic injury may also lead to chordal shortening and leaflet retraction, which aggravates the coaptation defect.

The variable pathogenesis of MR has led to multiple approaches to surgical valve repair. For example, functional MR due to LV dilatation in which anatomically normal leaflets fail to coapt adequately, is treated using one of several surgical annuloplasty techniques. Ischaemic MR causing papillary muscle displacement and leaflet tethering, with ischaemic LV remodelling and dilatation is typically treated by a combination of coronary revascularisation and annuloplasty procedures. Chordal lengthening may also be considered. In contrast, degenerative MR is treated by restoring leaflet coaptation by leaflet plication or resection with or without chordal reconstruction combined with an annuloplasty ring [8].

The asymmetric and variable shape of the mitral annulus makes the development of percutaneous devices challenging. In contrast to aortic valve implantation, a simple balloon expandable, or self-expanding device cannot be positioned easily and reliably in the mitral annulus as the annulus is typically not calcified, thus making it difficult to anchor a percutaneously deployed prosthesis. To date, the most successful percutaneous treatment has been edge-to-edge leaflet repair using the MitraClip device. This review will focus on the literature available on MitraClip and other novel percutaneous techniques that are being developed.

The MitraClip Device

The MitraClip procedure is based on a surgical technique, originally reported by Alfieri and colleagues [9], that has been used with a high degree of success to treat functional and degenerative MR. In this procedure, the middle scallops of the mitral valve leaflets are sutured together to create a double-barrel opening thus reducing MR while avoiding mitral stenosis (Fig. 1). Valve suturing is commonly combined with an annuloplasty ring to optimise control of the mitral regurgitation. It is an effective but simple method to reduce MR, with patients having an overall survival of 92 $\pm$ 3.1% at 6 years and 95 $\pm$ 4.8% freedom from reoperation [9].

The MitraClip device consists of a steerable guide catheter, a clip delivery system and an implantable clip. The procedure is typically performed under general anaesthesia using fluoroscopy and transoesophageal echocardiographic guidance. After gaining venous access via the femoral vein, access to the left side of the heart is achieved by trans-septal puncture. The guide catheter is 24Fr at the level of the groin and 22Fr at the atrial septum. The MitraClip device itself is a cobalt/chromium implant consisting of two arms and two ''grippers'' (Fig. 2). The clip is aligned above the MV perpendicular to the line of coaptation and advanced across the mitral orifice before grasping and coapting the leaflets. When an appropriate grasp is obtained, the grippers are lowered, the clip arms are closed and valve function is assessed. If there is a suitable reduction in MR, the clip is deployed (Fig. 3). However, if the degree of MR is unacceptable, the clip can be re-opened, re-positioned, and redeployed. Alternatively, additional clips can be deployed to achieve an optimum result.

The elimination of MR using MitraClip results in an acute reduction in left ventricular end-diastolic pressure (LVEDP) [(10,11] and a significant reduction in mean pulmonary artery pressure. In patients with left ventricular dysfunction,

Figure 1 Double Orifice Surgical MV Repair With Suture Illustration depicts a double-orifice mitral valve (MV) surgical repair. The MV is viewed from the left atrial side. The middle scallops of the anterior and posterior leaflets have been sutured together, which creates a double orifice. (Adapted with permssion from Feldman et al, *J Am Coll Cardiol*. 2009;54(8):686-694.