Mitral Valve Repair

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Introduction

Congestive heart failure (CHF) has become an international heath care problem and it is one of the world's leading causes of hospitalization and mortality. In the United States alone, 4.9 million people (2.3 % of total population) are suffering from heart failure with 550,000 new cases diagnosed each year. Hospital discharge for CHF increased from 377,000 in 1979 to 970,000 in 2002, an increase of 157 %. Estimated health expenditures amount to $ 25.3 billion in 2005 [1]. In spite of these, only 2,100 of the 53,000 patients who die annually are offered transplantation, which many consider to be the standard treatment for selected patients with severe CHF and end-stage heart disease. Transplantation is severely limited by the paucity of donor availability and enormous cost. The inapplicability in the older patient or those with comorbid medical conditions as well as relatively fixed donor pool suggest that transplantation will likely never have a major epidemiological impact [2]. Treatment with mechanical circulatory support devices dances on the horns of the same dilemma. Consequently, despite improvements with medical management, 1 year, 3 year and 5-year survival after hospitalization from CHF have been reported at approximately 80–60 %, 50 % and 40–20 % respectively, which is worse than that of most cancers [3–7].

In an effort to solve these problems, many alternative surgical and interventional strategies to treat heart failure patients have emerged and evolved over time. Some of them have been evaluated as the first-line approach to heart failure including techniques to restore myocardial perfusion and ventricular synchronization, remodeling ventricular geometry and to eliminate mitral valve regurgitation (MR) in the setting of Ischemic and dilated cardiomyopathy (DCM).

Bolling et al. have been using mitral valve repair techniques from 1993 onwards, to help this patient population based on the assumption that the mitral valve is the geometric functional component of the left ventricle (LV) and that secondary or functional MR occurs in a mitral valve apparatus that is essentially normal and functional. The distorted geometry of the left ventricle is reflected in abnormal coaptation of the mitral valve leaflets leading to mitral regurgitation.

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Secondary or functional MR can be thought of as geometric MR and mitral valve repair of this geometric MR as geometric mitral valve repair in this chapter. Dr Bolling's avid promotion of mitral valve competence in the setting of functional mitral regurgitation has transformed the management of heart failure. In days of cardiological yore, there was a common misconception that addressing mitral regurgitation in failing ventricles got rid of the "pop-off" valve that allowed these patients to survive.

Other methods of mitral valve reconstruction, such as chordal sparing mitral valve replacement, catheter based techniques such as the Mitraclip, etc. are also discussed as possible means of alleviating FMR.

Mitral Valve Structure and Function

In order to address the issues of heart failure and MR, one needs to understand the complex anatomy and functional relationship of the LV and mitral valve. Mitral valve competence depends on the coordinated function and geometry of the components of the mitral valve apparatus: mitral annulus, mitral leaflets, chordae tendinae, papillary muscles, and importantly LV wall [8–10]. The most "efficient" function of LV depends on all the components of the LV and mitral valve apparatus. There is substantial clinical and basic science evidence implicating the importance of preserving mitral valve continuity and geometry in order to preserve the function of the LV [11–13].

The mitral valve is the "inlet" to the LV and can be thought of a "set of French doors". The anterior (septal/aortic) and posterior (mural) leaflets are "nominally" separated near the annulus by the posteromedial and anterolateral commissures. However, it should be noted that leaflet part of mitral valve is entirely continuous within the annulus much like the curtain of a waterfall. The anterior leaflet is semicircular and spans the distance between the two commissures. At the portion of the annulus which serves as "hinge point" of both leaflets, the anterior leaflet is attached to the anterolateral wall of LV in the central region of fibrous skeleton of the heart between right and left fibrous trigone where it is in direct continuity with the left and part of the noncoronary aortic valve leaflets. The posterior leaflet is rectangular in shape, and is divided into three portions by natural clefts in the leaflet. Figure 9.1 shows the relationship of the mitral valve and its components to chords and papillary muscles.

The mitral annulus represents the junction that joins the left atrium and ventricle and consists of fibrous and muscular tissues. The average human mitral annular cross-sectional area is 5–11 cm^2. During systole, the annulus assumes an elliptical shape and is able to contract and decrease in diameter, whereas, in diastole, it assumes a more circular shape. Annular flexibility allows for increased leaflet coaptation during systole and increased annular orifice area during diastole. The anterior aspect of the annulus, which is composed of the fibrous skeleton of the heart and consists of rigid but elastic fibrous tissues, has limited flexibility, whereas the posterior aspect of the annulus, which is in continuity with the fibrous skeleton and consists of a mixture of muscular and gradually tapering fibrous tissues, contributes most of the annular flexibility.

The chordae tendinae are comprised of fibrous connective tissue chords and attach the leaflets to either the papillary muscles or the LV wall directly. The chordae are divided into three groups. The primary chordae attach directly to the free edge of the leaflet, and ensure that the leaflets coapt without prolapse or flail. The secondary chordae, which are more prominent on the anterior leaflet, attach to the leaflet along the line of coaptation, and are important in maintenance of ventricular function [14]. Tertiary chordae are only present on the posterior leaflet, and attach directly to the ventricular wall or to the trabeculae carnae. In addition, there are commissural chordae, which arise directly from either of the papillary muscles and attach to both leaflets.

The anterolateral and posteromedial papillary muscles project into ventricular cavity directly from the apical and mid portion of the ventricular wall, and give rise to chordae tendinae that attach to both leaflets. The anterolateral papillary muscle receives a dual blood supply from the left anterior descending and from either a

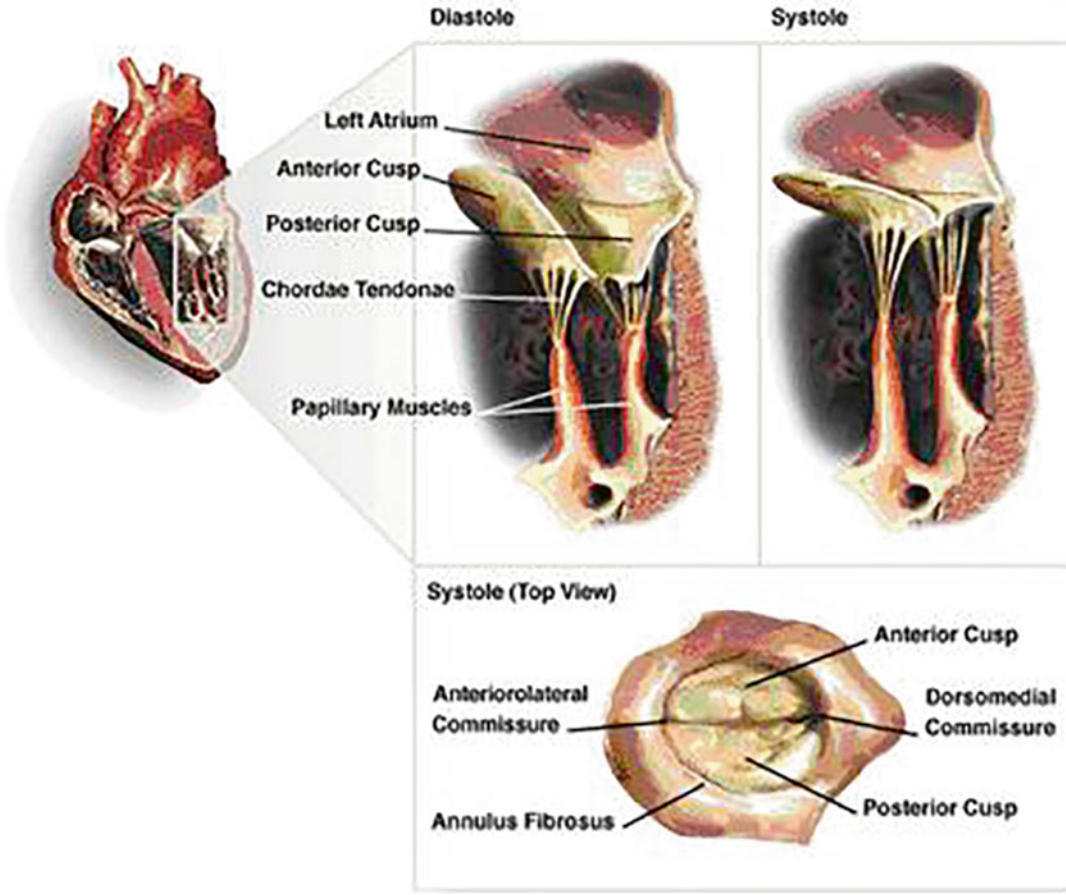

Fig. 9.1 Anatomy – anterior and posterior leaflets of the mitral valve

diagonal or marginal branch of the circumflex artery. In contrast, the posteromedial papillary muscle has a single blood supply, either from the right coronary or the circumflex artery. Therefore, the posteromedial aspect of the LV wall and the papillary muscle is more susceptible to ischemia and infarction and together play a very important role in valvular incompetence and leaflet malcoaptation in the instance of ischemic MR with a variable degree of posterior myocardial infarction.

The most important determinant of mitral valve competency centers on the zone of coaptation. Mitral valve leaflets accommodate high systolic LV pressure and establish competence through the distribution of force that can be likened to the stresses in a Roman arch in order to lessen the stress to the other parts of the ventricle and mitral valve apparatus. To maintain mitral valve competency in a systolic phase, the adequate zone of coaptation needs to be established in a coordinated fashion. To achieve adequate coaptation, both anterior and posterior leaflets should:

1. Be close enough to each other
2. Have enough tissue to cover the length of the zone of coaptation
3. Be guided at the line of coaptation by the leaflet chords at appropriate angle

Pathophysiology of MR

Acute MR vs Chronic MR

In MR, the regurgitant volume that is ejected into the left atrium is dependent upon regurgitant orifice size, ventricular to atrial pressure gradient,

atrial compliance and heart rate. The degree of increase in left atrial pressure, which is associated with congestive symptoms. is significantly affected by the regurgitant volume and the compliance of the left atrium.

The compliance of the left atrium is very different in acute and chronic MR, so it is important to fully recognize and differentiate the chronicity of MR in each patient being evaluated with heart failure.

Acute MR

Causes of acute MR include chordal rupture, endocarditis, blunt chest trauma, or myocardial infarction. The left atrium is of normal size with low compliance. A relatively small amount of acute MR can lead to an acute increase in left atrial pressure and lead to significant pulmonary edema that requires acute treatment. In this setting, symptoms and signs, along with the hemodynamic state dictate the proper timing of surgery. These are patients who benefit from mechanical support of the circulation perioperatively, either with intra-aortic balloon pump (IABP) counterpulsation or extra-corporeal membrane oxygenation (ECMO).

Chronic MR

In chronic MR, there is a gradual increase in regurgitant flow into the left atrium that leads to atrial enlargement and a significant increase in left atrial and pulmonary venous compliance. Therefore, signs and symptoms of pulmonary congestion may not become apparent until much later in the process of the disease in spite of the significant degree of MR and the significant volume overload and pathologic changes in the LV. In this setting, less symptomatic patients are difficult to triage in terms of proper timing of the intervention [15]. In this review, we treat geometric MR, which is chronic MR due to a distortion of the ventricular geometry. This is considered and treated as a different disease entity from acute MR.

Valvular MR vs Geometric MR

To understand the mechanism and the rational treatment of chronic MR, it is very useful to classify MR into primary/anatomic/valvular MR and secondary/functional/geometric MR.

In valvular MR, regurgitation is caused by structural valvular disease. The etiology of structural mitral valve diseases include degenerative (FED or Fibro-Elastic Degeneration, myxomatous disease, Barlow syndrome and fibroelastosis such as Marfan syndrome and connective tissue diseases), rheumatic, endocarditis, trauma, tumor, inflammatory and congenital. In this setting, problems with the components of the mitral valve apparatus cause MR.

Mitral valve repair of this valvular MR is systematically guided by three functional anatomic categories of mitral valve pathology proposed by Dr. Carpentier in 1983 [16];

- Annular dilatation
- Leaflet prolapse with elongated or ruptured chordae
- Leaflet restriction

The treatment of valvular MR aims to establish a zone of coaptation according to the functional anatomy. Mitral valve repair techniques in this setting include annuloplasty, variable degrees of leaflet resection, advancement or "sliding" plasty, chordal transplantation, and PTFE neochordal implantation.

In contrast, secondary or functional MR is defined as MR that is not caused by a structural defect of the components of the mitral valve apparatus but rather is caused by a distorted functional position of the components of the mitral valve apparatus related to LV dilatation. Therefore, functional MR is not a valvular disease but a geometric ventricular disease. Often in this setting, the dilatation of the ventricle may be secondary to an ischemic etiology with inferobasal akinesis or dyskinesis contributing to the MR. Figure 9.2 shows how inferobasal scarring and dyskinesis can contribute to mitral regurgitation. Figure 9.3 shows the stresses placed on the mitral valve leaflets through the connection of the chordae to the

ventricular muscle, suggesting that functional MR is a disease of the ventricle. Figure 9.4 shows that scarring of the muscle around insertion of the posteromedial papillary muscle.

DCM is defined by clinical evidence of chronic and progressive heart failure associated with echocardiographic findings of poor cardiac contractility (reduced LV systolic function reflected in reduced LV ejection fraction) and ventricular dilatation.

According to the primary etiology, DCM is usually classified into ischemic DCM and non-ischemic DCM because ischemic DCM is most prevalent.

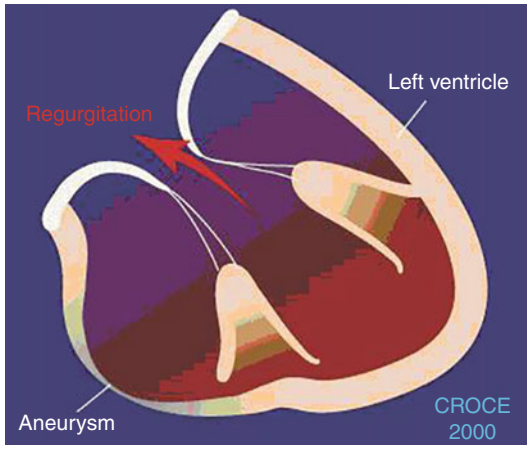

Fig. 9.2 Mechanism of MR with inferobasal scarring of the LV

Non-ischemic DCM can further be classified into idiopathic DCM (ventricular etiology) and valvular DCM (valvular etiology). Figure 9.5 shows the displaced papillary muscles causing central mitral regurgitation. It should be noted that there is a segment of this patient population that have concurrent ischemic heart disease and MR from degenerative mitral valve disease at the same time, commonly seen in elderly patients. This group is distinct from patients with geometric MR with ischemic DCM.

In geometric MR the components of the mitral valve apparatus itself are normal, two of the three functional anatomic categories proposed by Dr. Carpentier hold true;

- Annular dilatation, which may be mild or moderate
- Leaflet restriction: papillary muscle – LV wall displacement

Figure 9.3 shows the components of geometric MR. The treatment aim of geometric MR is to re-establish the zone of coaptation to eliminate regurgitation. To achieve this goal, a flexible complete ring annuloplasty technique was initially used [17]. As surgeons became more comfortable with this technique, more and more aggressive undersizing and overcorrecting ring annuloplasty was used based on the assumption that the most significant determinant of leaflet

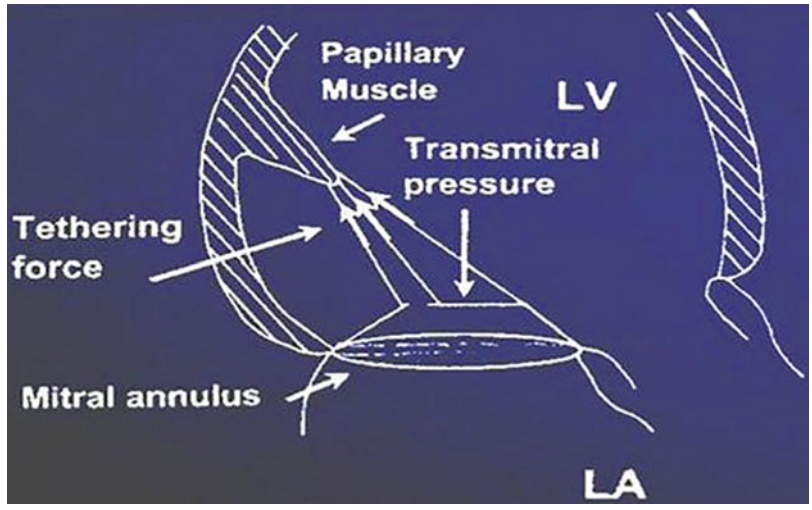

Fig. 9.3 Stresses on mitral valve leaflets and chordae attached to the papillary muscle

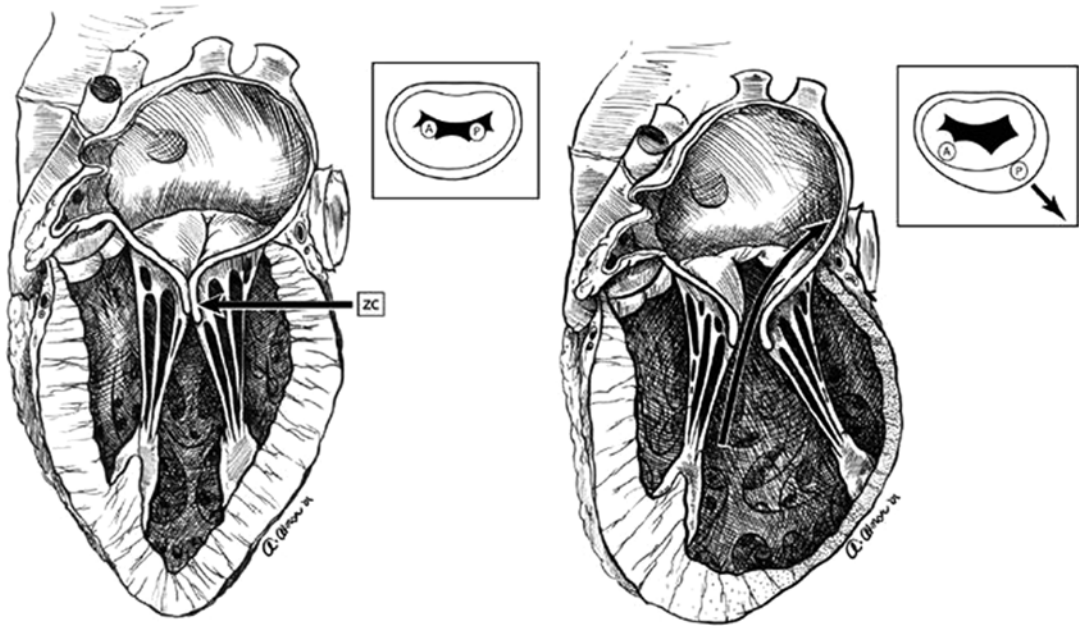

Fig. 9.4 Perturbation of coaptation of the mitral valve leaflets, due to scarring of left ventricle affecting the postero-basal papillary muscle, causing eccentric MR

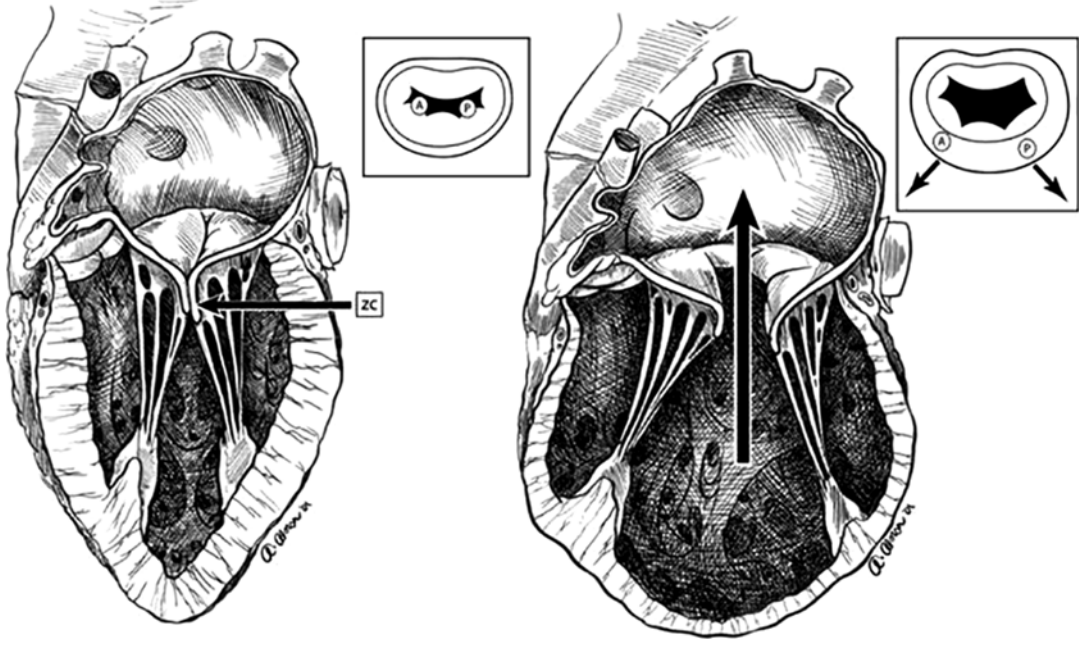

Fig. 9.5 Loss of coaptation of the mitral valve leaflets, due to displacement of both papillary muscles in dilated cardiomyopathy, causing central MR

coaptation in geometric MR is the diameter of the mitral valve annulus and that undersizing/over-correcting the annulus would also help to compensate the widened angle and the septolateral distance of the papillary muscles resulted from LV dilatation. These clinical observations

and acceptable surgical results were correlated with several key echo parameters as well as improvement of symptom and Quality of Life [18–20].

The natural history of chronic degenerative or rheumatic valvular MR can be protracted and long. The progression of the disease may be slow and span several decades. The onset of symptoms are often masked and may present late in the progress of the disease even with elevated left atrial and LV end-diastolic pressures because of a large compliant left atrium and the slow, gradual progression of this process. The presence of MR contributes to this increased back pressure and a decreased forward flow as well. Decreased forward flow is also well compensated with increased total stroke volume that is a combination of regurgitant volume plus effective forward stroke volume and increased heart rate. This leads to increased workload from volume overload to the LV. Short-term or medium-term neurohormonal compensatory mechanism also play a role in maintaining the same effective forward stroke volume in the setting of chronic MR. The normal LV can accommodate a fairly large amount of regurgitant volume and be well compensated before the LV starts to dilate. This is reflected in hyperdynamic wall motion and increased LV ejection fraction. However, once increased volume overload reaches beyond the compensatory adaptation of the LV, the LV is forced to dilate through homeostatic compensation mechanisms according to the Frank-Starling curve. This is reflected in an increased LV end–diastolic and end-systolic volume or dimension producing chronic LV dilatation and increased LV wall tension and stress. The LV reacts by trying to match the increased wall tension/stretch/stress by proportionally increasing LV mass via LV hypertrophy. As LV dilatation progresses, the LV wall tension/stretch/stress increases and coronary flow reserve decreases in addition to increased LV work load by volume overload [20–23]. Increased LV wall stress is the most potent stimulus for progressive heart failure through the mechanism of LV remodeling at a genetic, molecular and neurohormonal level. This chronic energy imbalance of increased workload plus increased wall tension/stretch/stress and decreased coronary flow reserve accelerates the damage to the LV muscle through the loss of LV contractile functional reserve. The poor survival of patients with chronic degenerative MR has been well established. Even though total resistance to the LV is decreased by MR, the total workload to produce the same forward flow is proportionally increased to volume overload with MR. The development of clinical symptoms usually reflects significant LV dysfunction and is a hallmark of reduced life expectancy. In the current setting of low operative mortality and high feasibility of repair, the timing of mitral valve repair can be offered at earlier stages of the disease in hopes of changing the natural history of the disease and before the development of left ventricular dysfunction [15]. A regurgitant volume of ≥60 ml/beat and effective regurgitant orifice area of ≥40 mm^2 are currently recommended as an index of quantitative assessment for the timing of mitral valve repair in asymptomatic patients with degenerative valvular MR [24, 25].

Geometric MR with DCM further contributes to LV dilatation and remodeling through chronic phenotypical changes triggered by increased volume work-load, increased LV wall tension/stretch/stress and decreased coronary flow reserve in addition to originally dysfunctional LV. This LV dilatation and spherical change further increases the magnitude of MR. Therefore, geometric MR sets up a vicious cycle and has been associated with worsened survival even with mild MR and few overt symptoms of heart failure [26–28].

Geometric MR in the setting of Ischemic MR is slightly different. In this instance the remodeling of the LV is predominantly in the region of the inferobasal wall. This area is akinetic, dyskinetic or just lagging the normal systolic function of the left ventricle. As the mitral leaflets try to coapt in systole, the lagging inferobasal wall has an effect on the posterior leaflet of the mitral valve. The downward pull or restriction of the posteromedial posterior leaflet in the P2–P3 area prevents good apposition of the two leaflets. The leads to eccentric mitral regurgitation.

Compared to valvular MR, the natural disease progression of geometric MR is rapid and prognosis remains poor. Geometric MR is a prevalent

complication of end-stage cardiomyopathy and may affect up to 60 % of all heart failure patients as a pre-terminal or terminal event [28–30]. Ischemic MR, that is, geometric MR in ischemic DCM doubles the mortality after myocardial infarction with a graded decrease in survival related to the severity of MR. Figure 9.4 reiterates the ischemic mechanism overlaid on the geometric components. It is reported that in ischemic DCM, the 5-year survival is 60 % without MR, 45–50 % with mild MR and 30–35 % with more than moderate MR [31, 32]. Decreased LV function reflected by a decreased ejection fraction further predicts a worse prognosis [33, 34]. The prognosis of ischemic DCM with MR is generally even worse than idiopathic DCM with MR [28].

However, the appropriate timing of intervention for chronic, geometric MR is still very controversial because of the higher operative risk and poorly defined late outcome measures.

With normal ventricular geometry, the redundant mitral leaflets are responsible for a zone of coaptation that is more than twice the area of the mitral valve orifice [10]. As the failing ventricle dilates, the multifactorial mechanisms of the progressive expansion of the mitral annulus and the dislocation of papillary muscles and LV wall leads to incomplete leaflet coaptation and a regurgitant jet of functional mitral insufficiency.

As more leaflet tissue is utilized for coverage of the enlarging orifice, a critical reduction in leaflet tissue available for coaptation is reached so that leaflet coaptation becomes ineffective and that a central regurgitant jet type of geometric MR develops [8, 35, 36]. In studies of patients with DCM, those with MR have significantly greater mitral leaflet orifice surface area and significantly larger dimensions of the mitral valve annulus than those without MR. However, these changes are minor compared to patients with fibro-elastic degeneration or myxomatous disease. Indeed, in many patients the annulus maybe normal in size. Chordal length and papillary muscle length are not significantly different in patients with cardiomyopathy, with or without MR [8]. It is also reported that pharmacologic reduction in the dynamic MR through the medical treatment of heart failure was through a reduction in the regurgitant orifice area which was related to the decreased mitral annular distention [36].

Therefore, the most significant determinant of leaflet coaptation in geometric MR is the diameter of the mitral valve annulus. This forms the basis of the approach to downsizing, and overcorrecting a complete MV ring annuloplasty. The spatial mis-alignment of the subvalvular mitral valve apparatus, that is papillary muscle – LV wall dislocation, also contributes to inability of leaflet coaptation [9, 37, 38]. As the ventricle dilates, the distance and the angle of the papillary muscles tends to become obtuse rather than acute, forcing the mitral valve leaflet coaptation zone apart. In addition, there is a large apical force that pulls the papillary muscle and chordal apparatus in an inferior and lateral direction and there is a weak closing force of the poorly functioning LV. All of these elements result in the loss of the zone of coaptation and subsequent regurgitation. This is illustrated in Fig. 9.5. The downsized and overcorrected complete ring annuloplasty also has some effect on the of the angle and the distance of de-arranged subvalvular mitral valve apparatus by indirectly providing more leaflet tissue for zone of coaptation and by directly influencing the reduced septal-lateral diameter at the level of papillary muscle through the continuum of papillary muscle-LV wall complex.

Although significant undersizing of a complete ring annuloplasty is performed to increase coaptation, no systolic anterior motion (SAM) of the anterior leaflet, or mitral stenosis was noted in the Bolling series. SAM is not usually seen in the setting of a large aorto-mitral angle and increased LV size, both conditions that are seen in DCM.

In contrast to primary or anatomic MR, geometric MR is also reported to have dilatation along the anterior aspect of the annulus [39]. This could possibly explain why the partial ring annuloplasty, rather than a complete ring annnuloplasty appears unlikely to produce a sustained long term result [40].

With ischemic DCM, geometric MR is furthermore compounded by the dynamic and

regional changes of LV muscle function and geometry. Ischemic papillary muscle dysfunction which is traditionally defined as the cause of geometric MR is a misnomer. It is not an isolated disorder of the contractive function of the papillary muscle, which is often preserved. There is often disturbance in the coordinated geometry of mitral valve complex including the annulus, chordae tendinae, papillary muscles and the LV wall. It is reported that MR cannot be reproduced through direct damage causing fibrosis of papillary muscle and it may actually decrease with papillary muscle ischemia [41, 42]. This is why "papillary muscle – LV wall dislocation "rather than" ischemic papillary muscle dysfunction" has been more recently used to describe this condition [43].

Geometric Mitral Valve Repair (University of Michigan Experience)

In 1993, Dr. Bolling and his group began to use mitral valve repair techniques very cautiously to selected DCM patients with severe MR who were suffering from progressive severe heart failure and were not eligible for transplantation, on the assumption that mitral valve is the geometric functional component of the LV and that geometric MR, in which mitral valve apparatus itself is originally normal, is the functional and geometric problem of the LV [17].

In 1995, a small initial series of patients at the University of Michigan was reported describing the early outcome (1993–1994) of mitral valve reconstruction in 16 consecutive patients with DCM and severe MR, refractory to maximum medical therapy. In that study, 16 patients (11 men and 5 women) ranged in age 44–78 years (64 ± 8 years) underwent mitral valve reconstruction with a simple, undersized, flexible, complete ring annuloplasty. The ejection fraction was 9–25 % (16 ± 5 %). Two patients were listed for transplantation. No postoperative patients required support with an intra-aortic balloon pump. There were no operative or hospital deaths and mean hospital stay was 10 days. There were three intermediate term deaths at 2, 6 and 7 months after procedure, and the 1-year actuarial survival rate was 75 %. At a mean follow-up of 8 months, all remaining patients were in NYHA class 1 or 2, with a mean post-operative ejection fraction of 25 ± 10 % [17].

Historically, while significance of MR in CHF was recognized and attempts were made to treat this surgically with mitral valve replacement, early surgical correction was associated with poor outcomes and surgical teaching evolved to enforce this idea [44–47]. Consequently, these patients were not considered operative candidates due to the prohibitively high morbidity and mortality in this patient population [48–52]. The prevailing surgical thought was that MR provided a "pop-off" effect for these impaired ventricles to function and that by removing the MR and the "pop-off" effect the LV was compromised which led to the high operative mortality. However, the poor outcomes of mitral valve replacement in that era were probably from the adverse consequences of the excision and the disruption of the annular-chordal-papillary muscle continuity, which has significant importance on LV systolic function [11, 53–56]. It has been demonstrated in a number of studies that preservation of the annulus-papillary muscle continuity is of paramount importance to preserve LV function, and this is even more critical in patients with severely compromised LV function [12, 57–62]. Preservation of the mitral valve apparatus and LV in mitral valve repair has been demonstrated to enhance and maintain LV function and geometry with an associated decrease in wall stress [63]. This procedure in degenerative valvular MR has been shown to be safe, with a significant decrease in operative morbidity and mortality, and good long-term outcomes [64–69]. There is no "pop-off" effect seen because the total workload to produce the same forward flow without MR is proportionally decreased compared to the setting of volume overload with MR, even though the total resistance to the LV is decreased by MR [70, 71].

Feasibility of a surgical treatment of geometric MR with DCM had been established through the use of the simple, undersized, flexible complete ring annuloplasty. Pre- and post echocardiography data showed some changes in parameters related to hemodynamic and geometric improvement. The basal angulation of the

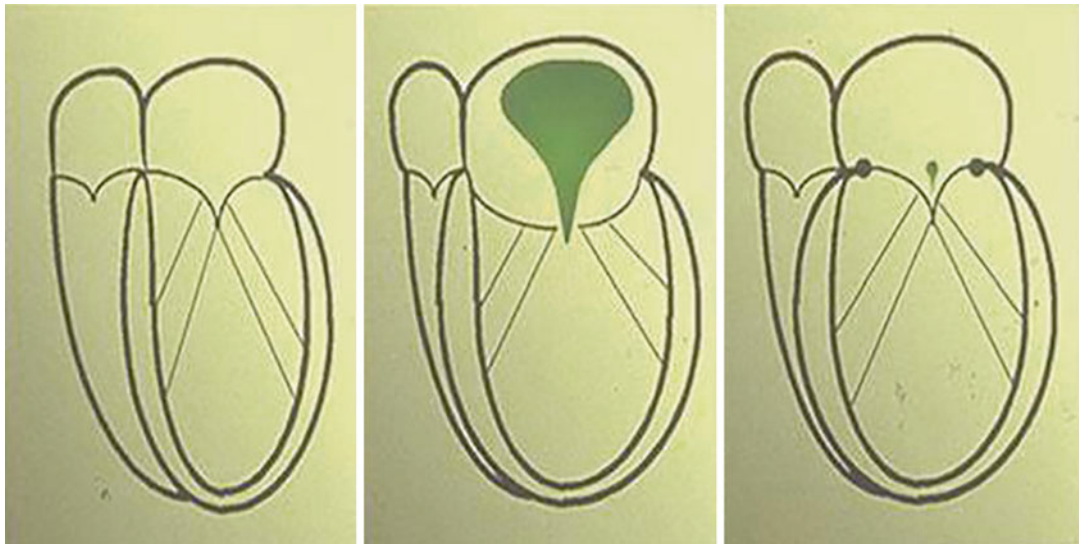

Fig. 9.6 Correction of coaptation by use of an undersized annuloplasty ring

heart was changed by undersizing, overcorrecting the annulus and the elliptical shape of the heart became re-established such that not only was MR acutely obliterated, but the cardiac geometry was also influenced, allowing the subsequent reverse remodeling [17–20]. Figure 9.6 shows schematically how this concept might work.

At the University of Michigan (1993–2003), 215 patients with end-stage cardiomyopathy and refractory MR underwent mitral valve repair with a simple, undersized, complete ring annuloplasty. The range in age was 30–87 years (64 ± 12 years). Ejection fraction was 6–30 % (20.8 ± 6 %). Preoperative NYHA class was 3.1 ± 0.9. A large number of patients (64/215, 30 %) had had a previous open-heart procedure. Thirty-day mortality was 4.7 % (10/215) for all mitral repairs. Postoperative low cardiac output syndrome was 2.3 % (5/215). Complication rates were low with CVA/TIA 2 % (4/215), prolonged ventilation 6 % (14/215), total infection 5 % (11/215), renal failure requiring dialysis 1 % (2/215) and reoperation for bleeding 0.5 % (1/215). Average ICU stay was 2.67 days and average hospital stay was 7.8 days. One and 2 year actuarial survival rates were 80 % and 70 %, respectively.

These techniques and principles have been adopted throughout the surgical community as the contribution of the mitral annulus, chordal structures and LV geometry to LV function were further understood [14, 72–77].

Numerous studies, from the other major surgical institutions, of mitral reconstruction in ischemia and idiopathic DCM, have also noted acceptable low operative mortality and been successful in relieving MR in CHF patients.

Chen from Brigham and Women's Hospital published in 1998 a report of 81 patients undergoing mitral valve surgery for mitral valve regurgitation in dilated cardiomyopathy with 11 % total perioperative mortality. In this series LVEF improved from 24 % to 32 % and there was an improvement in NYHA class from 3.2 to 1.6. Estimated survival in this study was 73 %, 58 %, and 38 % at 1, 3, and 5 years respectively [78].

Bishay and colleagues in Cleveland Clinic Foundation reported in 2000 on 44 patients with isolated mitral valve surgery with LV mean ejection fraction (LVEF) below 35 % with a 2.3 % mortality. In this series LVEF improved from 28 % to 36 % and NYHA functional class decreased from 2.8 to 1.2. Survival was 89 %, 86 %, and 67 % at 1, 2, and 5 years respectively. Furthermore they noted a decrease in the left ventricular chamber sphericity [79].

Bitran in Israel reported in 2001 a decrease in heart failure symptoms and a decrease in

New York Heart Association (NYHA) functional class without any operative mortality in 21 patients with LV mean ejection fraction (LVEF) below 25 % [80].

Rothenburger from Germany in 2002, described 31 patients with isolated mitral valve surgery with LV mean ejection fraction (LVEF) below 30 % with 6.5 % mortality. In this series LVEF improved from 23 % to 36 % and NYHA functional class decreased from 3.3 to 2.1. Survival was 91 %, 84 %, and 77 % at 1, 2, and 5 years respectively. Freedom from readmission for heart failure was 85 %, 79 % and 68 % at 1, 2, and 5 years respectively [81].

More recently Calafiore and associates in Italy published in 2004 a series of mitral repairs in 91 DCM patients (64 ischemic and 27 idiopathic). In this study, mitral valve annuloplasty was performed in 64 patients and 27 underwent a mitral valve replacement. The 30-day mortality rate was 4.4 %. LVEF improved from 27 % to 32 % and NYHA functional class improved from 3.5 to 2.1 in the 69 survivors. Interestingly, the probability of being alive at 5 years was 78 % and was higher in mitral valve repair group (81 %) than in mitral valve replacement group (67 %). The probability of being alive at 5 years with an improvement of at least one NYHA class was 66 % and was higher in the mitral valve repair group (77 %) than in mitral valve replacement group (52 %). Published series have come from numerous other units and countries and now constitute hundreds of cases performed with less than 5 % mortality [82].

The ACORN passive ventricular restraint device has also been studied in this group of patients. In the most recent ACORN series, a prospective, randomized and controlled, multi-institutional, multi-surgeon experience in 193 patients with MR and a mean EF of 23.9 %, LVEDD 69.7 mm, in which most of them underwent undersizing Geometric mitral valve repair, showed that mitral valve surgery in DCM patients with MR could be performed with a 1.6 % 30 day mortality. One-year and 2-year survival was 86.5 % and 85 % respectively. This Acorn trial is also a unique opportunity to assess the long-term efficacy of mitral valve surgery in patients with heart failure. In this report, surgery patients had a significant increase in 6 min walk times immediately after surgery and were associated with significant improvements in two different quality of life measures. Surgery patients were also associated with a remarkable reversal of LV remodeling, as manifested by a decrease in LVEDV and LVESV, an improvement in LVEF and sphericity index, and a reduction in LV mass. MR was effectively reduced and maintained for at least 18 months of follow-up [83]. However, the Acorn CSD has not been approved by the FDA and this is a trial of historic interest.

The latest set of data in mitral valve reconstruction in patients with heart failure have emerged from the NIH sponsored multi-center studies looking at these vexing issues.

One of these was a study involving 301 patients with moderate ischemic mitral regurgitation that were randomized to CABG alone or CABG plus mitral-valve repair (combined procedure). The primary end point was the left ventricular end-systolic volume index (LVESVI), a measure of left ventricular remodeling, at 1 year.

At 1 year, the mean LVESVI among surviving patients was 46.1 ± 22.4 ml per square meter of body-surface area in the CABG-alone group and 49.6 ± 31.5 ml per square meter in the combined-procedure group (mean change from baseline, −9.4 and −9.3 ml per square meter, respectively). The rate of death was 6.7 % in the combined-procedure group and 7.3 % in the CABG-alone group (hazard ratio with mitral-valve repair, 0.90; 95 % confidence interval, 0.38–2.12; $P = 0.81$). The rank-based assessment of LVESVI at 1 year (incorporating deaths) showed no significant between-group difference (z score, 0.50; $P = 0.61$). The addition of mitral-valve repair was associated with a longer bypass time ($P < 0.001$), a longer hospital stay after surgery ($P = 0.002$), and more neurologic events ($P = 0.03$). Moderate or severe mitral regurgitation was less common in the combined-procedure group than in the CABG-alone group (11.2 % vs. 31.0 %, $P < 0.001$). There were no significant between-group differences in major adverse cardiac or cerebrovascular events, deaths, readmissions, functional status, or

Fig. 9.7 Duran ring which is flexible, and can be partial or complete

quality of life at 1 year (ClinicalTrials.gov number, NCT00806988) [84].

An insightful editorial by Sundt into the findings of this article reported that "Entry into this study required multivessel coronary artery disease and a moderate degree of mitral regurgitation without structural valvular abnormalities; a previous myocardial infarction was not a requirement, and indeed only about 65 % of patients had such a history. The inclusion of patients with mitral regurgitation secondary to reversible ischemia may well explain why so many had an improvement in their mitral regurgitation with bypass alone. This may also explain in part why recurrent mitral regurgitation after repair was present in only about 10 % of patients, not the 30 % reported by others. It is possible that the authors set themselves up to show no significant difference between treatment groups" [85].

Many lessons have been learned in these geometric MR patients and further understanding and advances continue to be published in clinical and basic studies. The anterior trigone to trigone distance may enlarge variably in this type of CHF patient and it is not a good or useful guide for ring sizing. Anatomic and laboratory studies have confirmed this dilation of the anterior trigone to trigone distance from ischemia and dilated cardiomyopathy [39, 86, 87].

It has recently been reported that partial ring annuloplasty, not complete ring annnuloplasty is more likely to fail requiring repeat intervention [86]. Furthermore, undersizing or downsizing has been shown to be not only helpful in abolishing MR, but also in remodeling the base of the heart from the "bending" of the mitral annulus. This geometric re-arranging may have helped reestablish an ellipsoid shape to the base of the LV cavity. However, there is also emerging evidence that despite good early results, undersized annuloplasty does not serve all patients well in the short or intermediate term.

Based on the continually evolving understanding of this complex disease process and clinical experience, geometric mitral valve repair by using the simple, undersized, overcorrected, complete ring annuloplasty is safe and effective for improving both symptoms and heart function, in the short term. The durability of this procedure is open to question. It should be underscored that symptom reduction, reduced hospitalization and improvement in QOL should be the treatment targets for these patients in heart failure.

Figures 9.7, 9.8, 9.9, and 9.10 show some of the different types of rings commonly used to repair MR.

Unresolved Issues, Future Perspective

Despite these new insights, residual or recurrent MR and more importantly, limited LV reverse geometric remodeling have also been noted and potentially limit long term improvement [88–90]. LV remodeling is characterized by progressive LV dilatation with a change in the heart from an

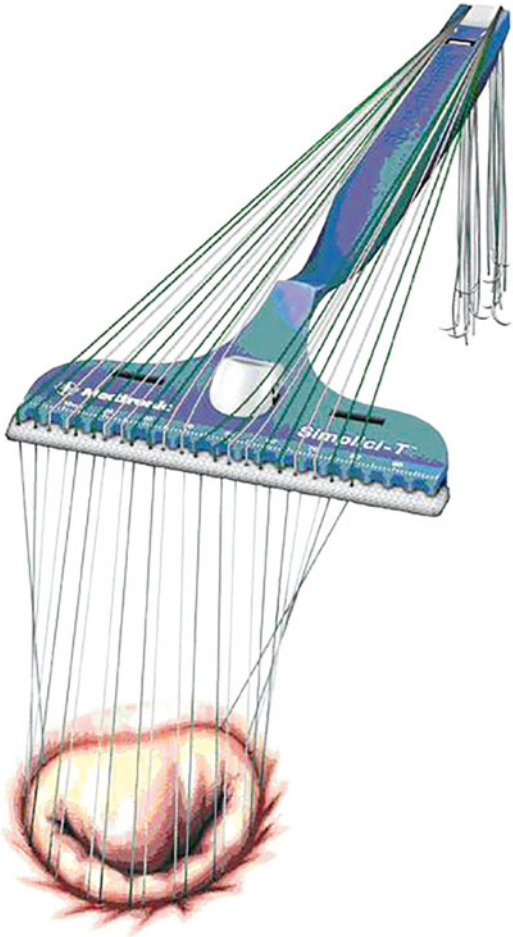

Fig. 9.8 The flexible simplicit band

Fig. 9.9 Semi-rigid band – CG band

ellipse to a more spherical shape and is one of the strongest predictors of mortality in heart failure patients. Despite optimal surgical and/or medical therapy, heart failure is often progressive without

Fig. 9.10 Rigid saddle-shaped ring

reversal of LV remodeling. Surgical CHF treatment must, therefore, be aimed not only at MR, but more importantly, also at LV reverse remodeling [91, 92].

In a recent retrospective analysis from the University of Michigan, the effect of MV repair was compared with medical therapy in heart failure patients with severe MR. Wu et al. examined 293 patients treated medically and 126 treated with MV repair, all with severe CHF, and found that MV repair did not predict a mortality benefit [93]. In this non-randomized, but propensity-matched series, the results showed, qualitative improvement, but that there appeared to be little mortality benefit of MV repair of functional MR in advanced heart failure and severe LV dysfunction over the 10 year period of the review. Indeed, the only predictor of mortality in this study, as in every CHF trial, medical or surgical, was reverse remodeling, which did not correlate well with the abolishment of MR. CHF associated MR from LV geometric distortion does not preclude successful mitral valve repair. However, it may be inferred that reducing MR in these patients may not be "enough", as MR is a late marker for CHF [94, 95]. Interestingly, with further analysis of the same data set, there is favorable trend upon mortality, during the last 5 years of the study, when MVR surgery evolved to include earlier surgical referral for CHF patients, and the use of rigid smaller, remodeling rings. Similarly, the recently presented ACORN trial results also showed quality of life benefit, but did not have a mortality benefit.

In this setting, when recurrent MR might prove to be the final pathway by which a patient decompensates, it might be worthwhile considering alternatives such as mitral valve replacement with complete preservation of chordal supports.

Others have found a group of patients with bad ventricles, especially with very tethered posterior leaflets or very large ventricles to have suboptimal long-term results with tight mitral annuloplasty alone. In these patients, either as a first procedure or at redo surgery, the preference is to reconstruct the mitral valve with a chord preserving prosthetic mitral valve replacement.

Young patients tend to get mechanical mitral valve prosthesis as shown in Fig. 9.11**.**

Older patients (over the age of 60–65 years of age) usually get a porcine bioprosthetic valve with chordal preservation. This is shown in the adjoining Fig. 9.12**.**

A review from the University of Michigan, evaluated the outcome in 289 patients with EF ≤ 30 %, who received an undersized complete mitral ring as their geometric mitral valve repair procedure. Of these, 170 patients had a flexible ring. In follow-up, 16 "flexible" patients (9.5 %) required a repeat procedure for significant recurrent geometric MR and CHF, (ten replacements, three re-repairs, three transplants). In contrast, 119 patients with an EF ≤ 30 % received an undersized non-flexible complete ring. Only one "non-flexible" patient required a repeat mitral valve procedure for recurrent mitral regurgitation secondary to ongoing ventricular remodeling and two patients required a heart transplant (2.5 %). A significant difference in reoperation rates, for recurrent MR, between the groups was noted at $p = 0.012$. There were no differences between groups, in terms of age, ring size, preop EF, LV size, MR grade or NYHA class [40]. From this study, it is concluded that the use of a non-flexible ring appeared to be associated with an increased incidence of recurrent MR and deserves further investigation through a randomized trial.

Recent developments in MV repair have included newer rings aimed at 3D modulation of LV geometry through an annular approach [96]. The GeoForm ring (Edwards Lifesciences, Irving CA) is a unique non-deformable titanium

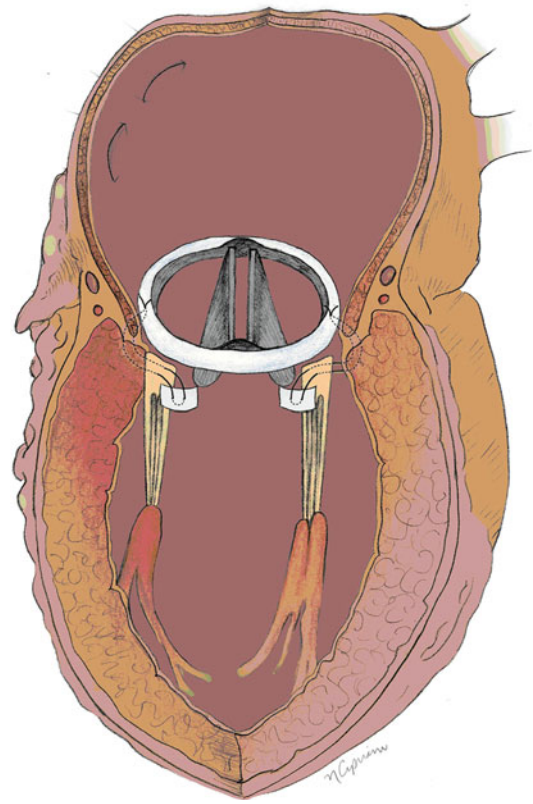

Fig. 9.11 Mechanical mitral valve with preserved chords

3D device aimed not only at abolishing MR, but also at acutely initiating reverse LV geometric remodeling and was developed by Drs Bolling and Alfieri. Figure 9.13 shows this ring. The AP or septal lateral diameter is 40 % reduced compared with standard ring dimensions. This AP reduction has been shown in mathematical computational modeling and in animal studies to dramatically abolish MR. This reduction in AP diameter was more effective than a reduction at P1 or P3 areas of the mitral annulus, even for "asymmetric" MR. While the GeoForm is reduced in AP diameter, the effective orifice area (EOA) of the ring is correspondingly bigger than a same size standard ring, due to the complex 3D orientation of the orifice and mitral stenosis has not been seen.

The 3D nature of the Geoform is directed to altering the geometry of LV. Based on the double toroid or saddle shape of the normal mitral valve during systole, the mid posterior ring is elevated

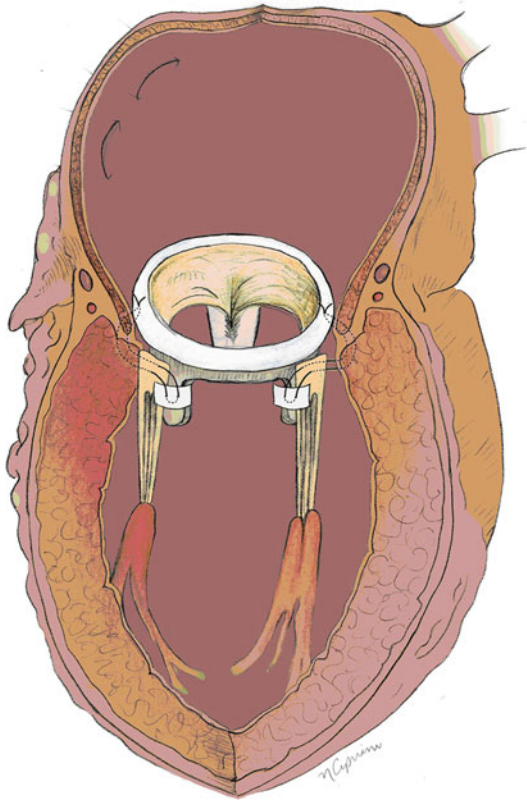

Fig. 9.12 Bioprosthetic mitral valve with preserved chords

Fig. 9.13 Geoform shaped ring

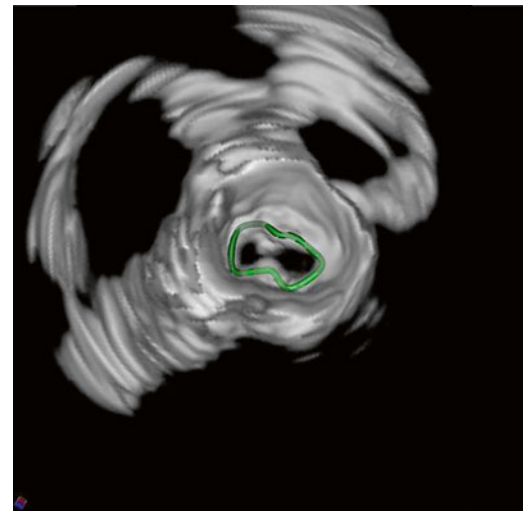

Fig. 9.14 Three dimensional echocardiographic appearance of the geoform ring

6 mm superior and drawn 5 mm anteriorly. Figure 9.13 shows the shape of the ring. From the surgeons viewpoint, this shape in essence, "moves" the LV and mitral annulus upward and forward as a whole to the normal position, directly reversing the trend of the CHF ventricle to "fall" down and outwards. Although coronary alteration is a theoretical concern of this shape, there has been no circumflex bending or resultant ischemia in any implant, animal or human. Additionally, chordal tensioning studies, both by computer modeling and in pulse duplicators, actually demonstrated less chordal tension after Geoform implant, which corrects LV geometry, than in the original state of a large myopathic, round heart. There has not been any chordal rupture following Geoform implant. The three-dimensional echocardiographic picture in Fig. 9.14 shows the ring maintaining the saddle shape of the annulus. Figure 9.15 shows the graphical improvement in LV size with this approach.

Between January and November 2004, in this initial feasibility series, ten consecutive, non-randomized patients at the University of Michigan Medical Center, with ischemia and/or dilated cardiomyopathy and refractory moderately-severe or severe mitral regurgitation, were studied prospectively. Patient ages ranged from 53 to 79 years (mean 73 ± 6). Five patients had nonischemic dilated cardiomyopathy, while five had ischemic disease. No patient was felt to have an acute myopathy. Pre-operatively, six patients had NYHA Class IV congestive heart failure and four had Class II–III. The mean duration of documented cardiomyopathy or symptomatic congestive heart failure was

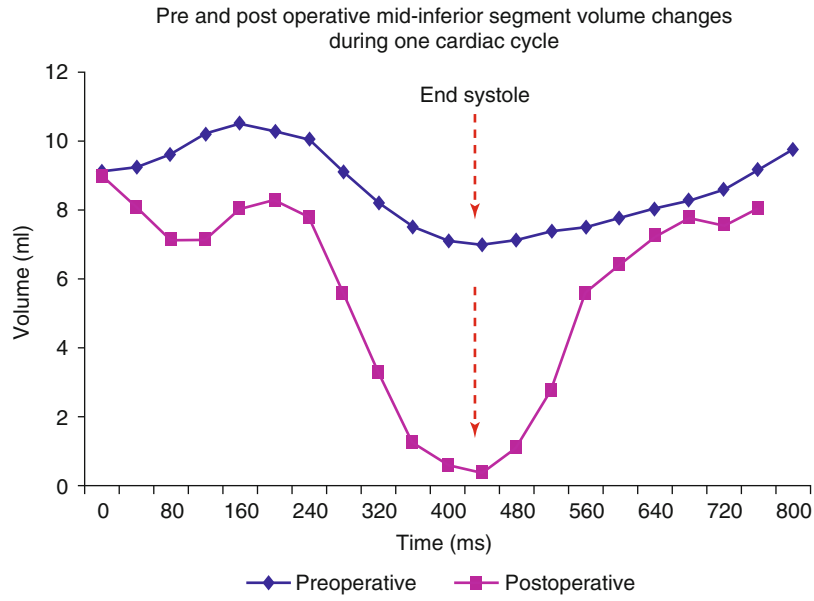

Fig. 9.15 Graph showing reduced left ventricular size with shaped ring

4 ± 6 years. Mean pre-operative ejection was 27 ± 11 (6–41) %.

At the time of surgery, patients underwent mitral reconstruction with a Geoform remodeling annuloplasty ring. Coronary artery bypass grafts (mean – 2.9) were placed in the five patients with coronary artery disease. Additional procedures included tricuspid annuloplasty in seven patients, ASD/PFO closure in four and modified Maze procedure in four patients, where indicated. There were no operative deaths.

There were no in-hospital deaths and the mean duration of hospitalization following surgery was 5.2 days (range 4–23) days. Follow-up was available for all patients. At a mean follow-up of 5 months, all surviving patients are in NYHA class I or II. The NYHA failure class significantly fell for every patient individually from a mean of 3.2 ± 0.4 to 1.4 ± 0.4 for the entire group.

Follow-up echocardiography at 1 week, 3 and 6 months was obtained in all patients. The mean transmitral gradient on follow-up at 1 week was 3 ± 1 (range 1–5) mmHg. All patients had a marked reduction in sphericity, regurgitant volume, regurgitant fraction and significantly improved LV EF, end-diastolic and end systolic volumes. There have been two late deaths, following Geoform mitral valve reconstruction. One late death occurred as a consequence of recurrent ARDS (ECMO supported patient, EF = 6 %) and CHF at 5 months and the other was from acute sudden death at 11 months, while watching television. No patient needed pacemaker or AICD implantation.

Interestingly, these GeoForm patients not only demonstrated immediate clinical improvement, but also showed acute favorable changes in LV geometry as shown by echo at 5 days post-op; decreased LV volumes, sphericity and tenting height with an increase in EF, as opposed to the expected drop in EF when MR is corrected. These types of changes are not dependent on volume loading and are not usually seen acutely with echos following the use of standard rings. These beneficial changes demonstrate potential acute reverse remodeling due to the 3D-shaped GeoForm ring in addition to the slow and chronic reverse remodeling. This favorable trend also appeared to be sustained in these high-risk geometric MR patients in short-term early observation.

The GeoForm ring appears to not only improve MR, but far more importantly for long term patient outcome, also reverses the LV remodeling acutely and chronically associated with CHF. Larger series with longer follow-up will be needed to confirm this novel approach.

As with all rigid structures trying to constrain a dynamic mitral annulus, there maybe excessive tension on the implanting sutures. Despite all the theoretical benefits of septal-lateral cinching of the mitral annulus in animal models, it must be remembered that addressing the annulus alone in patients where the abnormality is in the underlying ventricle may be a solution that does not address the root cause.

This approach has heralded the development of multiple shaped mitral rings by other investigators and companies. Once again, the role of the pioneer may be pathbreaking but laden with a variety of regulatory problems: Despite very encouraging results with the Geoform ring, this annuloplasty device is not being manufactured by Edwards any more.

Patient Selection for Geometric Mitral Valve Repair

Based on the clinical experience, the relative contraindications to mitral valve operations include right ventricular failure, severely enlarged left ventricular diameter and volumes, elevated pulmonary artery pressures, and extremely high norepinephrine levels, TNF, and BNP. All of these are markers of long-term CHF. These were all absolute contraindications early on in our series but we have since relaxed these considerably over time as our experience has grown and newer surgical techniques and patient management strategies have evolved.

Exact patient selection criteria remain to be elucidated, but these criteria may be considered when evaluating high-risk patients for MV repair. It is important to follow these patients closely after their procedures as the role of careful medical management of their heart failure should be emphasized.

It is important to decide which patients would benefit from mitral valve repair and which patients are likely to fail with a mitral ring approach. A recent presentation by Dr Alfieri's group suggested that the causes of positive outcomes in mitral repair in dilated cardiomyopathy were presence of reverse remodeling (>15 % reduction in left ventricular end-systolic volume), resolution of inferior wall ischemia, successful ablation of atrial fibrillation. Conversely, patients without these features tended to have a poor outcome with mitral valve repair.

Another important recent publication from the NIH clinical trials consortium looking at ischemic regurgitation showed superior outcomes with chordal preserving mitral valve replacement, compared to mitral valve repair [97]. While there was no significant difference in mortality, the patients with mitral valve replacement had greater freedom from recurrent MR.

Other Innovative Options to Approach Geometric MR

There are many other innovative surgical and interventional options to approach geometric MR that have been emerging and evolving, including; scar resection with papillary muscle reimplantation, [98] intraventricular papillary muscle imbrication [99], external infarct LV wall plication [100], chordal cutting [101], papillary muscle sling [102], papillary muscle relocation [103], BACE, Myocor, Myosplint, Coapsys: external bands buttressing device [104], localized epicardial balloon patch [105], percutaneous annular reduction by coronary sinus compression, [106] and percutaneous intraluminal edge to edge repair by using clip [107]. Most of these are still in experimental phase. Some are in preliminary clinical trial or small clinical series. The effectiveness, safety and durability of these techniques remain to be studied.

Summary

Considering the increasing incidence and growing population of patients with congestive heart failure, there remains a need for effective medical treatment options, and also effective non-transplant, non-mechanical circulatory support device surgical treatment options. In an effort to solve these problems, many alternative surgical and interventional strategies to treat heart failure have been emerging and evolving. Geometric MV repair is one of these important treatment options and the growing experience with this technique has evolved to the point that the current

excellent results are being tested by a prospective randomized clinical trial [94]. The procedure is safe with operative mortality rates reported from most of the major institutions in the world under 5 %. The most recent ACORN study which included multi-institution and multi-surgeon results reported an operative mortality rate of mitral valve surgery including valve replacement with DCM patients of only 1.6 % [83]. This study also showed that mitral valve surgery was associated with an immediate improvement of QOL and a chronic reversal of LV remodeling. In addition to the benefits of eradicating MR, potential benefits of this conventional surgical therapy should be extended the other patient subgroups not previously considered for surgical intervention. Findings of a future prospective randomized control studies could make new therapeutic options available to millions of patients who suffer from congestive heart failure. It must be remembered that functional and ischemic mitral regurgitation are due to dysfunction of the ventricle and not the annulus. Hence the most effective solutions will incorporate ventricular components while maintaining valvular integrity.

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