

REVIEW

Solving the Puzzle of Chronic Ischemic Mitral Regurgitation

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Chronic ischemic mitral regurgitation is a prevalent problem among patients following a myocardial infarction. Until recently, the pathophysiology was poorly understood, resulting in surgical strategies with suboptimal results and limited durability. The surgical approach has evolved from revascularization alone to an additional mitral valve procedure, replacement, or repair. When the valve was repaired, isolated annuloplasty was performed. The dilemma that surgeons had when repairing a mitral valve was which type of ring to use and what size. In all series with annuloplasty alone, the results were poor with very high recurrence rates. The primary feature of ischemic mitral regurgitation is a prolapse of the anterior leaflet at $A3 \pm A2$. This prolapse can be caused by fibrotic elongation of the papillary muscle supporting $A3 \pm A2$ or tethering of $P3$ by a ballooning posterior left ventricular wall. Using a technique that corrects this prolapse with Gore-Tex neochords, we have achieved excellent results with effective and durable correction of the ischemic mitral regurgitation.

INTRODUCTION

Ischemic mitral regurgitation (IMR[†]) is present in 10 percent to 20 percent of patients with coronary artery disease (CAD), with a conservatively estimated prevalence of 1.6 million to 2.9 million patients in the United States alone [1]. Other authors believe this to be a gross underestimate and have calculated that more than 5 million Americans are afflicted with this condition [2]. In spite of these numbers, relatively little progress has been made toward effectively treating this complicated condition.

There are no randomized trials addressing IMR, and there is a lack of a unifying definition throughout the literature. Many authors have drawn conclusions regarding IMR based upon studies that included patients with myxomatous MR and incidental CAD.

One aspect of IMR that is well documented is the grave prognosis it portends. Data from the Survival and Ventricular Enlargement (SAVE) Study has shown that patients who develop MR following a myocardial infarction (MI) demonstrated a significantly worse overall prognosis than

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[†]Abbreviations: IMR, ischemic mitral regurgitation; CAD, coronary artery disease; SAVE, Survival and Ventricular Enlargement Study; MI, myocardial infarction; CABG, coronary artery bypass grafting surgery; PM, papillary muscles.

Table 1. Modified Carpentier Classification of Mitral Regurgitation

Type	Leaflet Motion	Description
Ia	Normal	Annular dilation only
Ib		Leaflet perforation
IIa	Excessive	Chordal elongation
IIb		Chordal rupture
IIc		PM infarction/elongation
IId		PM rupture
IIIa	Restricted	Commisural or chordal fusion
IIIb		Leaflet tethering by left ventricular dysfunction or aneurysm

did patients without MR for all clinical end points tested (MR vs. no MR: cardiovascular mortality, 29 percent vs. 12 percent, $p < 0.001$; severe heart failure, 24 percent vs. 16 percent, $p = 0.0153$; and the combined end point of cardiovascular mortality, severe heart failure, or recurrent myocardial infarction, 47 percent vs. 29 percent, $p < 0.0001$) [3]. A study of 11,748 cardiac catheterization patients showed a one-year mortality rate in patients with severe IMR of 40 percent, moderate IMR 17 percent, and mild IMR 10 percent [4]. The one-year mortality rate was 6 percent in patients without IMR.

Finding a treatment modality for IMR that significantly improves survival in a durable fashion has eluded physicians for decades. There is considerable disagreement within the literature as to what approach should be taken in this difficult patient population. Many authors have shown that revascularization alone is sufficient [5,6], whereas others favor surgically addressing the valve itself in addition to revascularization [7]. If the surgeon decides to perform a valve-directed procedure at the time of coronary artery bypass grafting surgery (CABG), should the valve be replaced or repaired? Two recent large-scale studies have tackled this question, and the data supports repair of the mitral valve when possible [8,9]. The final question remaining is how to recon-

struct a valve that appears morphologically intact. Dr. L. Henry Edmunds, Jr. has written of IMR: "Most often the entire valve appears normal ... There is little to fix, yet the valve leaks. ... the valve is structurally normal; it need not be replaced, but currently we do not know how to fix it. ..." [10].

The purpose of this paper is to review the mechanisms of chronic IMR, the surgical techniques being utilized, and our own surgical approach to this problem.

DEFINITIONS AND MECHANISMS OF CHRONIC IMR

Borger et al. proposed the definition as MR occurring more than one week after an MI with (1) one or more left ventricular segmental wall motion abnormalities; (2) significant coronary disease in the territory supplying the wall motion abnormality; and (3) structurally normal MV leaflets and chordae tendinae [1]. Other authors have used less specific criteria. Grossi et al. considered ischemic mitral insufficiency to be the presence of severe mitral incompetence (by echocardiography or angiography) arising from an ischemic process confirmed by the intraoperative pathologic evaluation of the valve [8]. The definition put forth by the Toronto group, on the other hand, is extremely specific and includes mechanistic

schemes for the regurgitation. They defined chronic IMR as occurring in patients with CAD and resulting from PM infarction, scarring, dysfunction, or a delayed presentation due to partial rupture of a PM head (types IIc, IIId, and IV, Table 1) or leaflet tethering by left ventricular dysfunction (type IIIb). Annular dilation alone (type Ia) was included only in the absence of other features of degenerative valve disease [11]. The authors categorize the various forms of IMR according to the Modified Carpentier Classification (Table 1) that is based upon normal, excessive, or restricted leaflet motion.

When discussing chronic IMR in the literature and attaching that label to a patient's condition, one should use a definition that is as specific as possible in order to ensure the exclusion of other etiologies for mitral regurgitation (myxomatous, rheumatic, infectious, or congenital).

The pathophysiology leading to chronic IMR is a myocardial infarction that distorts the papillary muscles. This usually occurs with occlusion of the right or left dominant circumflex coronary arteries, causing an infarction involving the posterior ventricular wall and posterior PM [12]. The involvement of the anterior PM is less common because of its dual blood supply from both the left anterior descending coronary artery and a diagonal or obtuse marginal coronary artery.

Following an MI, mitral regurgitation has been documented by Doppler in up to 39 percent of patients [13]. Competency of the mitral valve is dependent upon the coordinated interaction between the leaflets, the annulus, chordae tendinae, and the papillary muscles (PM) [1]. A consistent finding at surgery for IMR is the observation that there is an overriding $A3 \pm A2$ over the opposite leaflet, whether it is due to fibrotic elongation of a PM or to leaflet tethering by a ballooning infarcted wall. Therefore, the common functional pathology in IMR is prolapse of $A3 \pm A2$. The mitral regurgitation increases the left ventricular volume and size. This dilates the annulus and increases the regurgitant volume, and a vicious cycle begins. Not only does the mitral annu-

lus dilate with ischemia, but its distinctive saddle shape is flattened. This ischemia-induced annular modulation was elegantly demonstrated by Gorman et al. in a sheep model using sonomicrometry array localization that measured the three-dimensional geometry of the mitral annulus. The authors found an accentuation of the saddle shape annulus during systole in normal subjects, but during ischemia that caused mitral regurgitation, this accentuation was eliminated [14]. Neither isolated PM dysfunction nor annular dilation alone cause significant IMR [1].

SURGICAL OPTIONS FOR CHRONIC IMR

The first question when considering surgical treatment for chronic IMR is to determine if the etiology of the regurgitation is ischemic. Transthoracic echocardiography represents the most useful tool in establishing the diagnosis. The presence of left ventricular wall abnormalities or absence of myxomatous or rheumatic leaflet pathology leads to a high probability that ischemia is the cause of the mitral regurgitation. The decision to treat IMR should be based on preoperative transthoracic echocardiography rather than intraoperative transesophageal echocardiography because of the afterload reduction induced by anesthesia [1,15]. Borger et al. have proposed lowering established echocardiographic criteria for MR when dealing with ischemic regurgitation because of the associated worse long-term prognosis. Specifically, they recommend considering an effective regurgitant orifice of more than 20 mm² as severe in patients with chronic IMR, as opposed to the classic 40 mm² in organic mitral disease [1].

Once the diagnosis is established and a decision made for operative revascularization, the question becomes whether revascularization alone is sufficient to treat the IMR. Tolis et al. recently described clinical and echocardiographic outcomes examined after isolated CABG in 49 patients with ischemic cardiomyopathy and 1+ to 3+ MR undergoing surgical revascularization. The authors



Figure 1. Transesophageal echocardiogram showing a complex regurgitant jet in a patient with IMR.

showed a significant improvement in ejection fraction (22.0 percent to 31.5 percent, $p < 0.05$), New York Heart Association congestive heart failure class (3.3 to 1.8, $p < 0.05$), and degree of MR (1.73 to 0.54, $p < 0.05$) with 50 percent five-year survival [5]. One limitation of the study was the relatively high percentage of patients falling into the 1+ MR category (37 percent) and low percentage in the 3+ MR category (10 percent). It is generally agreed that patients undergoing CABG with moderate-to-severe IMR (3+ to 4+) also should have a mitral valve-directed procedure as part of the operation [1]. The controversy lies in patients with mild to moderate MR (1+ or 2+). Multiple studies have shown a progression of mitral regurgitation and worse overall prognosis in this patient population when CABG alone was performed [16,7]. Exercise cardiography is very helpful to determine the significance of IMR in patients with 1+ to 2+ regurgitation on a resting echocardiogram.

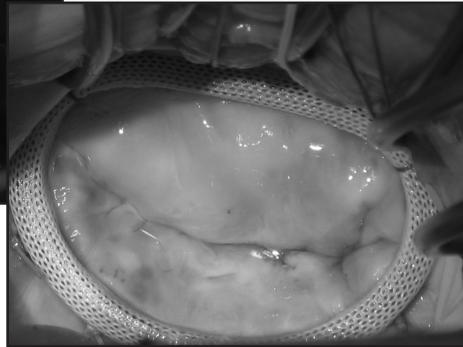
If preoperative echocardiography suggests that the mitral valve will have to be ad-

ressed directly, the surgeon must decide whether to repair or replace the valve. Mitral valve replacement had been the preferred approach to chronic IMR prior to the pioneering work in mitral valve repair of Alain Carpentier. Historically, mitral valve replacement involved complete excision of the valve leaflets together with the subvalvular apparatus. Such methods were shown to compromise left ventricular function [17]. Currently, preservation of the entire subvalvular apparatus is the preferred technique [18]. Additional disadvantages of mitral valve replacement include the requirement for life-long anticoagulation if a mechanical valve is used and poor durability of tissue prostheses. The advantages of replacement are primarily reliability and reproducibility and should be considered in patients with chronic IMR who have multiple comorbidities, complex regurgitant jets, or severe tethering of both mitral valve leaflets [1].

Two large studies from respected mitral valve surgery centers, New York University Medical Center and the Cleveland Clinic Foundation, compared the results of mitral



Figure 2. At left: Mitral valve after insertion of annuloplasty ring demonstrating a Gore-tex neochord to A3 portion of anterior leaflet in a patient with IMR. Below: Mitral valve following completion of ring annuloplasty and neochord to A3 showing even coaptation plane without prolapse.



repair vs. replacement for IMR. The results in both studies have shown a perioperative survival advantage in patients who have had mitral valve repair. Nevertheless, the five-year survival with either technique was only 50 percent [8,9]. Additionally, any perioperative advantage was lost in the most high-risk patients [9]. The overwhelming majority of mitral valve repair patients in both series consisted of isolated ring annuloplasty. The underlying concept of ring annuloplasty is to undersize the ring to achieve leaflet coaptation during systole. This concept was promoted by Bolling et al. in the treatment of severe MR associated with end-stage cardiomyopathy [19]. In those patients, satisfactory results were obtained, but unlike the patients with cardiomyopathy who have intact papillary muscles, patients with IMR have infarcted papillary muscles and left ventricular walls. This causes distortion of the geometric relation between the papillary muscles and, therefore, suboptimal leaflet coaptation. In most patients, ring annuloplasty reduces the MR grade back to the level it was in the early stages after the myocardial infarction, before the vicious cycle produces left ventricular dilation. This explains why there is frequent recurrence of MR following ring annuloplasty that initially produced good results in the early postoperative period.

In another study from the Cleveland Clinic Foundation, 585 patients with IMR were treated with ring annuloplasty alone, and the authors found that 28 percent of

those patients had redeveloped 3+ or 4+ MR only six months after the operation [20]. Roshanali et al. [21] found a similar failure rate of 24.4 percent following ring annuloplasty alone. They identified by multivariate analysis that an interpapillary muscle distance of greater than 20 mm as measured on preoperative echocardiography predicted failure of annuloplasty alone and concluded that this could be used as an index for determining whether MR might recur after simple annuloplasty. They proposed adding a complementary procedure to the annuloplasty if the interpapillary muscle distance is greater than 20 mm. A meticulous echocardiography examination can, in most cases, reveal that in addition to a central regurgitant jet, there is a posteriorly directed jet (Figure 1).

Cutting secondary chordae and relocation of the posterior papillary muscle are two adjunctive techniques to ring annuloplasty. Cutting secondary chordae removes the chordae that are primarily responsible for leaflet restriction in IMR [22]. Surgical relocation of the posterior papillary muscle was developed by Kron and associates [23] at the University of Virginia. This relatively simple procedure involves passing a 3-0 prolene suture twice through the fibrous portion of the posterior papillary muscle tip and then up through the adjacent mitral annulus just

posterior to the right fibrous trigone. As the prolene suture is tied, the posterior papillary muscle tip is drawn closer to the annulus with the final position determined by the point at which leaflet coaptation occurs in the plane of the mitral annulus.

In 1983, Dr. Alain Carpentier revolutionized the treatment of mitral regurgitation by introducing repair techniques that addressed the function of the valve regardless of etiology [24]. The proposed techniques, such as leaflet resection and leaflet transposition, addressed the pathology of the mitral valve when it involved excess leaflet tissue. This was very successful in the treatment of rheumatic and myxomatous valves. He also proposed ring annuloplasty in all cases of mitral regurgitation. In chronic IMR, there is no excess tissue, and only ring annuloplasty could be applied. This operation was widely used, but led to frequent recurrence of mitral regurgitation. The underlying pathology in IMR is anterior leaflet prolapse without excess tissue. The recent application of Gore-Tex neochords for myxomatous valve disease was very well suited to the treatment of chronic IMR, but was not applied. In our institution, we have extensive experience with the Gore-Tex neochord and have adopted its use in IMR (Figure 2). In IMR, the dysfunction present is a prolapse of $A3 \pm A2$, regardless of the pathophysiology of the myocardial infarction. Our experience with neochords in the treatment of IMR dates back to the year 2000. We analyzed our results with 14 patients who had moderate to severe IMR and who underwent this type of repair with CABG. The surgeries were performed by the senior author (SWH). Follow-up included echocardiography in all patients. Thirteen of the 14 patients were alive at a mean interval of 3.03 years from surgery. The one death occurred at nine months due to complications from pre-existing end-stage renal failure. Mitral regurgitation was minimal or absent in all patients except one (moderate), with no patients requiring reoperation. There was a statistically significant improvement in mitral regurgitation grade, NYHA grade, and

ejection fraction following the operation. These results compare favorably with recurrence rate and survival data quoted in the literature [8,9,20,21].

CONCLUSIONS

Chronic IMR is a relatively common condition among patients with CAD and has a dismal prognosis. The medical treatment of IMR is associated with a high mortality rate, and traditional surgical techniques have failed to improve upon the natural history of the disease. Only recently has an increased awareness emerged that the correction of IMR should address the muscular pathology, including the papillary muscle and left ventricle. Our surgical approach addresses the functional pathology of the valve and has led to a significant improvement in the treatment of this disease.

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