

Chronic Ischemic Mitral Regurgitation: More Treatment Could Mean Better Treatment

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Chronic ischemic mitral regurgitation (CIMR) is a frequent complication after acute myocardial infarction (AMI), appearing in approximately 20% of cases, and is far more frequent in inferior AMI (38%) than in anterior AMI (10%).

The standard treatment of severe CIMR is coronary surgery combined with mitral valve replacement or repair. Historically, this procedure is associated with a high hospital mortality of around 15% in series and registries published in the first half of the 1990s. In the light of this, we understand the attitude of many surgical teams who only perform combined surgery in cases of strictly severe mitral regurgitation (MR) and trust that — in cases of moderate or moderate-severe regurgitation — myocardial revascularization will alleviate valvular dysfunction. This approach is currently followed by many cardiology teams who minimize the clinical importance of CIMR in favor of an isolated percutaneous coronary angioplasty procedure. This involves less risk but, like surgery alone, does not modify the clinical manifestations and prognosis of many patients.

In view of this important clinical problem, during the last decade, many relevant clinical and experimental studies have been conducted leading to advances in our knowledge of the pathophysiology of CIMR, in particular its natural history, which has led many teams to completely change their approach toward managing this condition. Innovative therapeutic changes have been implemented, but new questions have also arisen and old ones exacerbated.

In the context of these changes that are currently being assessed, this issue of *Revista Española de Cardiología* offers us the opportunity of furthering our knowledge and analyzing the short-term and medium-term outcomes of the treatment of CIMR through valvular repair using

a ring especially designed for this ischemic dysfunction: the Carpentier-McCarthy-Adams Etlogix prosthetic ring (Edwards Lifesciences, Irvine, Calif., USA). This article, presented by Filsoufi et al,¹ who belong to the Mount Sinai Medical Center team in New York, is one of the broadest series published by a single center using the technique under study. This team has the added value of having participated in the design of and experimental work with this ring, and includes Alain Carpentier, the grandmaster of this pathology, as a collaborator.

Ischemic Mitral Regurgitation: A Trilogy (Vessels, Ventricle, and Valve)

The pathophysiological mechanism of CIMR, after AMI, involves local myocardial remodeling (usually in the lower wall) with thinning of the necrotic wall and apical and posterior displacement of the papillary muscles (usually the posterior). This displacement involves the corresponding chordae tendinae, which tether the valve leaflets, and progressively reduces their area of coaptation (Carpentier type-IIIb mitral regurgitation). Thus, mitral regurgitation appears initially at segments A3-P3 of the mitral valve — areas which are exclusively supported by the posterior papillary muscle — and sometimes extends toward segments A2-P2,² depending on the patient. The ventricular volume overload that accompanies mitral regurgitation and ventricular dysfunction then causes mitral ring dilatation and a loss of coaptation over the entire surface of the mitral leaflets. Thus, in more advanced stages of severe CIMR, there is leakage over almost the entire contact area, mild annular dilatation, and restricted mitral leaflet motion (especially in the posterior leaflet), with loss of contact and coaptation area below the plane of the mitral ring (increase in tenting area) due to tethering of the subvalvular apparatus on the leaflets. At this stage, we would be facing Carpentier type-I + type-IIIb CIMR (annular dilatation + restricted systolic leaflet motion).^{3,4}

What Degree of Mitral Regurgitation Changes the Natural History of a Patient and Therefore Should Be Considered Severe and Treated?

Together with other studies published in the 1990s (SAVE study), the work of Grigioni et al,⁵ published

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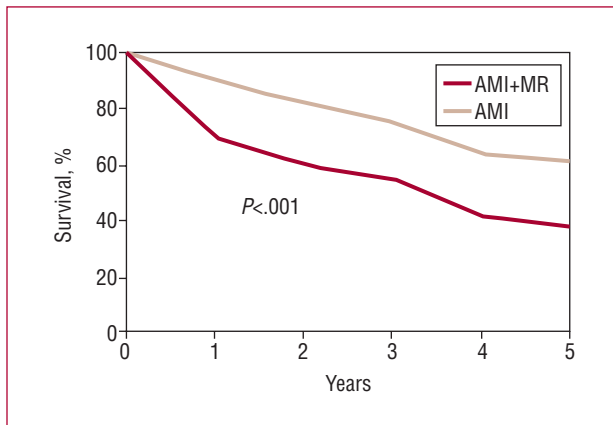


Figure 1. Decreased survival after diagnosis of acute myocardial infarction (AMI) according to presence or absence of mitral regurgitation (MR). Modified from Grigioni et al.⁵

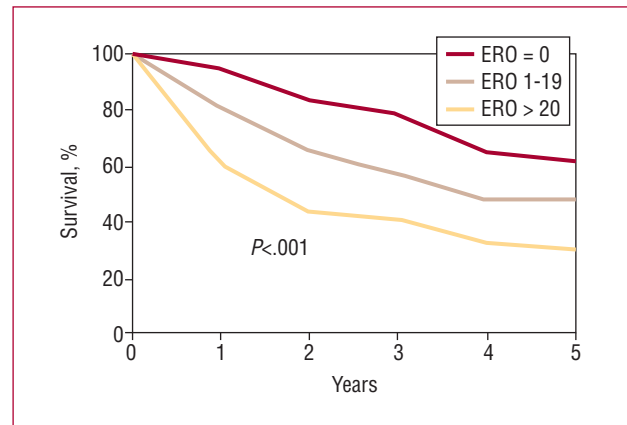


Figure 2. Decreased survival after acute myocardial infarction according to quantification of ischemic mitral regurgitation by an effective regurgitant orifice (ERO) ≥ 20 mm² or < 20 mm². Modified from Grigioni et al.⁵

in CIRCULATION in 2001 (Figure 1), has been of great relevance. This team showed that patients with CIMR have higher mortality (due to increased cardiac mortality) at 5 years than patients of equal age, sex, and ejection fraction who do not present MR after infarction. An effective regurgitant orifice (ERO) area greater than ≥ 20 mm² or a regurgitant volume (RVol) ≥ 30 mL, which implies moderate grade (+2) MR, is significantly associated with increased mortality (Figure 2). These data highlight the importance of detecting CIMR and quantifying it, and that we should assume that moderate CIMR (ERO ≥ 20 mm², grade 2+) is indicative of poor prognosis in the chronic stage of an AMI, comparable to a severe grade 4+ (ERO ≥ 40 mm²) in MR of other etiology (degenerative, rheumatic, etc).

These new considerations have led different authors,⁶ expert in this issue, to quantify CIMR with ERO ≥ 20 mm² as severe and to establish indications for mitral valve surgery in this etiology (Table 1).

Can We Predict in Which Patients Mitral Regurgitation Will Be Reduced by Revascularization Alone?

Revascularization alone could lead to improvements in patients who present viable myocardial segments (using low-dose dobutamine or positron emission tomography (PET)) which have attached papillary muscles. Exercise echocardiography may predict improvement if there is a demonstrated reduction in MR with improvement in inferobasal region motion induced by the exercise.⁷

TABLE 1. Indications for Mitral Valve Surgery Due to Chronic Ischemic Mitral Regurgitation^a

Decision for Mitral Valve Surgery	
Coronary artery bypass graft surgery indicated by angina	
Severe MR (ERO ≥ 20 mm ²)	Yes
Mild-to-moderate MR (ERO < 20 mm ²)	Possible yes
Minimal MR	No
Coronary artery bypass graft surgery not indicated by angina but possible	
Severe MR (ERO ≥ 20 mm ²)	Yes
Mild-to-moderate MR (ERO < 20 mm ²) at NYHA grade III with viable myocardium	Possible yes
Minimal MR	No
Coronary artery bypass graft surgery not possible	
Severe MR (ERO ≥ 20 mm ²)	Yes
RVol > 50 mL and EF $> 30\%$	Uncertain
RVol < 50 mL or EF $< 30\%$	No
High comorbidity	No
Mild-to-moderate MR (ERO < 20 mm ²)	No
Minimal MR	No

ERO indicates effective regurgitant orifice; EF, ejection fraction; MR, mitral regurgitation; RVol, regurgitant volume. Taken and modified from Enriquez Sarano.⁶

Does Residual Moderate (Grade 2+) CIMR Have an Impact on Ventricular Remodeling, Functional Capacity, or Patient Survival?

Mitral regurgitation caused by alterations in left ventricular geometry and function after AMI can in itself induce more ventricular remodeling and lead to a vicious circle whereby AMI generates more AMI.

Although different articles published in the 1980s and 1990s suggested that coronary surgery alone did not affect the survival of patients with residual moderate MR, a deeper analysis of this information shows vast heterogeneity in the groups of patients, 25% of whom had MR due to non-ischemic causes. Recent studies by Grossi et al⁸ and Lam et al,⁹ both using multivariate analysis and statistical techniques which compare groups using propensity-scores, found that moderate (grade 2+) CIMR that was not corrected during coronary surgery is an independent predictor of short-term and medium-term mortality. Similar reductions have been reported regarding early survival among patients with CIMR after coronary angioplasty.¹⁰

What is the Current Operative Risk and Success Rate of a Combined Mitral Valve Procedure in Patients With at Least Moderate CIMR?

The surgical management of CIMR has evolved significantly. The first valve replacement techniques were performed with little understanding of the adverse effect that interrupted ventricular-wall/papillary-muscle/mitral-ring continuity had on ventricular function. Consequently, patients undergoing combined mitral valve replacement and coronary surgery had high early and late mortality rates (10%-15%). In recent years, better knowledge of the pathophysiological mechanisms of CIMR has led to wider adoption of different mitral valve repair techniques. Compared to replacement, mitral valve repair involves a lower rate of complications, especially thromboembolism and hemorrhage due to chronic oral anticoagulant therapy, and higher survival rates.

Most teams have reported important reductions in hospital mortality for combined surgery, around 4%-6% since 2000, due to valve repair and intervention in patients with less disease progression. In this issue of *Revista Española de Cardiología*, Filsoufi et al¹ report a hospital mortality of 2.5%; the same team has recently reported a mortality of around 4% using combined coronary surgery and mitral repair in patients with moderate CIMR.¹¹

Although, as pointed out in the following section, the outcomes of mitral valve competence in the short-term and long-term are highly dependent on the surgical technique used, the team's experience, and the degree of left ventricular remodeling found during surgery, we can

expect that around 15%-30% of patients will have residual MR throughout their evolution.¹²

Should the Mitral Valve Be Repaired or Replaced in Patients With CIMR?

Although distinguished authors such as Enríquez-Sarano¹³ have reported that there are no differences in survival rates between patients with CIMR undergoing combination surgery either with mitral valve repair or replacement, the beneficial effects on ventricular function, the reduction in morbidity and mortality due to avoiding chronic anticoagulation therapy, and the data indicating improved survival in other series¹⁴ make mitral valve repair the surgical technique of choice for CIMR.

Almost all cases of Carpentier type-IIIb and type-I + type-IIIb CIMR can be corrected by annuloplasty. When the mitral ring size is reduced there is an increase in the surface of coaptation of the valve leaflets impaired by subvalvular apparatus tethering, thus reestablishing mitral valve competence. Different outcomes have been obtained with different annuloplasty techniques depending on the era and the preferences of the surgical teams. Flexible, rigid, and complete rings have been used as well as posterior leaflet half-rings, partial pericardial annuloplasty, etc.

The fundamental aim of mitral repair in any etiology is achieving a good surface of coaptation between the 2 mitral leaflets which strongly correlates with good early outcomes and excellent long-term durability. This surface area, which has been established at ≥ 8 mm, should also have a homogeneous contact surface. This broad coaptation surface area guarantees normal valve function even in the event of mild-moderate increases in ventricular remodeling and, thus, increases in tethering forces.

Based on experience obtained from the surgical treatment of CIMR, we can state that the greater the degree of left ventricular remodeling the greater the difficulty in obtaining a good surface of coaptation after repair. Such remodeling is calculated by the severity of mitral valve regurgitation, and especially echocardiographic data, such as tenting height or displaced closure of the mitral valve (distance in a straight line from the point of coaptation of the leaflets to the theoretical height of the mitral ring) and the tethering area (surface area formed by the theoretical plane of the mitral ring and the surface of both leaflets when closed). Bolling et al¹⁵ introduced the increasingly popular practice of implanting rings 1 or 2 sizes smaller than the intertrigonal distance. Although high recurrence rates of MR have been reported of up to 35% have been reported using partial pericardial annuloplasty, rates of up to 15%-20% have been reported using complete rigid rings. Given that in ring annuloplasty there is anterior displacement of the posterior ring, increased tethering on the posterior leaflet can occur, whereby

anterior displacement may even decrease. Successful repair should be obtained at the expense of the mitral valve becoming a monocuspid valve, from a functional point of view, with a posterior leaflet with restricted motion becoming a surface of coaptation for the anterior leaflet. This is the rationale underlying early surgery, when there is less ventricular remodeling, leading to successful and durable repair. For the same reasons, some authors prefer valve replacement in more advanced cases as the technique that better guarantees competent mitral valve function.

To obtain a good homogeneous coaptation area (≥ 8 mm) in a patient with CIMR, we should perform a repair that affects the entire surface of the mitral ring (complete ring) and that compensates for the displacement of the papillary muscles. This decreases the anteroposterior distance of the mitral ring more than normal techniques (undersized ring) given that in the cases of degenerative MR the leaflets are more redundant and there is no subvalvular apparatus tethering.

Currently, no echocardiographic values for subvalvular apparatus tethering are available to determine whether repair is impossible, because the new annuloplasty devices and leaflet repair techniques, as well as deeper understanding of the subvalvular apparatus itself, have modified the results of previous publications. Recent publications¹⁶ have indicated that a preoperative posterior leaflet angle (in relation to the annular plane) $\geq 45^\circ$ correlates with worse clinical outcome at 3 years and more recurrence of mitral valve regurgitation. If a patient presents these characteristics, the authors recommend combined repair techniques, such as posterior leaflet extension with a pericardial patch.

What New Alternative Techniques Are Available for Ischemic Mitral Valve Repair?

New technical alternatives and modifications related to annuloplasty are constantly being described, with greater impact on the subvalvular apparatus, and thus involving greater technical complexity and yielding variable outcomes. Among these we may mention infarction lesion resection and papillary muscle repositioning (ventricular restoration techniques¹⁷), suture plication of the inferior infarction area, which causes anterior displacement of the inferior papillary muscle (the same effect is attempted by placement of an epicardial inflatable patch-balloon with saline serum), the double-ring approach to both papillary muscles,¹⁸ sectioning the basal chordae tendinae that insert into the leaflet body, and external containment or compression devices, such as the Coapsys annuloplasty system or Acorn mesh device, to reduce or prevent ventricular remodeling.

Parallel to these developments, new rings have been designed for type-IIIb CIMR, specifically, the Carpentier-McCarthy-Adams ETlogix annuloplasty ring (Edwards Lifesciences, Irvine, Calif., USA), which is the subject

of the article by Filsoufi et al.¹ This offers the great advantage of being simple and technically reproducible compared to the alternatives mentioned, but its short-term and long-term outcome remain to be demonstrated. The article presents the advantages of the new design compared to classic rings: it is rigid, complete, has a smaller anteroposterior diameter and 3-dimensional morphology, and has an indentation toward the P3 apex to compensate for displacement of the posterior papillary muscle. The early results in their first 40 patients with preoperative grade 3+ and 4+ CIMR are excellent, with a hospital mortality of 2.5%; follow-up (15 to 36 months) is also very promising with grade 1+ MR recurrence of 36% and grade 2+ recurrence of 3%. A reduction in tenting height and a reduction in subvalvular apparatus tethering area has been demonstrated. These results agree with those reported by Daimon et al.¹⁹ in a multicenter study using the same device in 59 patients with preoperative grade $\geq 2+$ CIMR. In our modest experience (oral communication at the XIII Congress of the Catalan Society of Heart Surgery, April 2007), there was no hospital mortality in the first 14 patients with preoperative grade $\geq 2+$ CIMR who underwent implantation with the CMA ETlogix annuloplasty ring, whereas there was a significant 50% reduction in tenting height and tethering area values. In any case, these results should be confirmed at 3 years and 5 years, at least in a given subgroup of patients, in order to consider it the treatment of choice.

Conclusions

Chronic mitral valve regurgitation after AMI should be detected and quantified, as it is an indicator of poor prognosis regarding patient survival. Chronic ischemic mitral regurgitation with an ERO ≥ 20 mm², although classified as moderate, should be considered severe and treated, due to its negative impact on the natural history of the patients. Early surgery, which involves working with less ventricular remodeling, and innovations in the arsenal of devices and surgical techniques will enable successful and durable correction with low hospital mortality.

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