Repair or prosthesis insertion in ischemic mitral regurgitation:
Two faces of the same medal

Antonio Maria Calafiore a, Angela Lorena Iàcò a, Daniela Clemente b, Reda Refaie c, Silvio Romano b, Mahmood Asif a, Maria Penco a, Michele Di Mauro b,⁎

a Department of Adult Cardiac Surgery, Prince Sultan Cardiac Center, Riyadh, Saudi Arabia
b Department of Cardiovascular Disease, University of L'Aquila, L'Aquila, Italy
c Department of cardiothoracic surgery, Mansoura university, Mansour, Egypt

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ABSTRACT

Objective: The proper treatment of chronic ischemic mitral regurgitation (CIMR) is still under evaluation. The different role of mitral valve repair (MVR) or mitral valve prosthetic insertion (MVPI) is still not defined.

Methods: From May 2009 to December 2011 167 patients with ejection fraction (EF) ≤40% had MV surgery for CIMR. MVR in 135 (80.8%) and MVPI in 32 (19.2%). Indication to MVPI was a MV coaptation depth >10 mm. EF was lower (26 ± 7 vs 32 ± 6, p = 0.0000) in MVPI, whereas MR grade (3.6 ± 0.8 vs 2.7 ± 0.9, p = 0.0000), left ventricle dimensions (end diastolic, LVEDD, 62 ± 7 vs 57 ± 6 mm, p = 0.0001; end systolic, LVESD, 49 ± 8 vs 44 ± 8 mm, p = 0.0018), systolic pulmonary artery pressure (51 ± 22 vs 41 ± 16 mm Hg, p = 0.0037) and NYHA Class (3.6 ± 0.5 vs 2.8 ± 0.6, p = 0.0000) were higher.

Results: In-hospital mortality was similar (3.1 vs 3.7%) as well as 3-year survival (86 ± 6 vs 88 ± 4) and survival in NYHA Class I/II (80 ± 5 vs 83 ± 4). One hundred thirty nine patients had an echocardiographic evaluation after a minimum of 4 months (13 ± 8). EF rose significantly in both groups (from 26 ± 7% to 30 ± 4%, p = 0.0122, and from 32 ± 6% to 35 ± 8%, p = 0.0018), LVESD reduced significantly in both groups (from 49 ± 8 to 43 ± 9 mm, p = 0.0109, and from 44 ± 8 to 41 ± 7 mm, p = 0.0033). MR grade was significantly lower in patients who had MVPI (0.1 ± 0.2 vs 0.3 ± 0.3, p = 0.0011).

Conclusions: With appropriate indications, MVPI is a safe procedure which provides similar results to MVR with lower MR return, even if addressed to patients with worse preoperative parameters.

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1. Introduction

Surgical treatment of chronic ischemic mitral regurgitation (CIMR) is nowadays more standardized, as its pathophysiology is better understood. Restrictive mitral valve (MV) annuloplasty, proposed by Bolling et al. [1] is the procedure of choice. Other adjunctive procedures, as chordal cutting, papillary muscle repositioning, augmentation of leaflets, have been proposed, but their usefulness is still not well demonstrated. The possibility to insert a MV prosthesis in selected cases, proposed by our group [2], has recently been supported by other studies [3–6], which report mid and long term results similar to those of MV repair with lower grade of late MR. The failure rate of restrictive MV annuloplasty remains one of the weak points of the surgical treatment of CIMR and it is related to lower survival and worse clinical [7] and echocardiographic outcome.

We tried to rationalize MV surgery (repair or prosthetic insertion) for CIMR correction [2,8,9]. We herein report our more recent experience in patients with CIMR and ejection fraction (EF) ≤40% to evaluate if the strict application of that strategy could reproduce and confirm the results of our previous experiences from which it was generated.

2. Material and methods

From May 2009 till December 2011 167 patients with ejection fraction (EF) ≤40% underwent MV surgery for CIMR as first procedure. One hundred thirty five (80.8%) had MV repair (group MVR) and 32 underwent MV prosthetic insertion (group MVPI). Patients in cardiogenic shock were not included. The Institutional Review Board approved the research and waived patients’ consent.

2.1. Definition

CIMR is defined as any MR that is due to excess of tethering of either or both leaflets as a result of misalignment of either or both papillary...
muscles. All the patients in this series had a previous myocardial infarction with regional wall abnormalities.

### 2.2. Preoperative echocardiographic evaluation

MR was graded following the European Society of Echocardiography recommendations [10]. MR was defined mainly according to vena contracta: mild (1+) if <3 mm, moderate (2+) if 3 to <5 mm, moderate to severe (3+) from 5 to <7 mm and severe (4+) if ≥7 mm. Recurrence of MR was defined as postoperative MR ≥2+. All echocardiographic measurements followed American Society of Echocardiography and European Society of Echocardiography guidelines [11]. Table 1 shows some relevant echocardiographic preoperative characteristics. Tissue Doppler Imaging S’ (TDI) was used to assess right ventricular (RV) function. A value of <10 cm/s was the cut point to identify RV dysfunction.

### 2.3. Surgical indications

All patients with CIMR ≥2+ were candidates for MV surgery. CIMR 1+ was never treated, but in 3 cases, where the systolic septolateral distance was severely dilated (>32 mm) and/or the coaptation length was minimal (≤2 mm). A coaptation depth (CD) of 10 mm or less was the limit for MV repair. If the CD was >10, the anatomy was not considered suitable for repair, and a prosthesis was inserted into the MV [2,8,9]. If the anterior leaflet (AL) was short (<25 mm) or excessively tethered, we respectively augmented or cut the second-order chords [9].

### 2.4. Surgical technique

After a median sternotomy, the ascending aorta and both venae cavae were cannulated, the superior vena cava directly. The MV was approached transseptally through a right atriotomy. The mitral annulus was reshaped with the SMB40 (Sorin Biomedica SpA, Saluggia, Italy) in 115 patients and with a Physioring (Edwards Lifescience, Irvine, CA, USA), median #26, in 20 patients. Insertion of a prosthesis inside the MV was reshaped with the SMB40 (Sorin Biomedica SpA, Saluggia, Italy) in 115 patients and with a Physioring (Edwards Lifescience, Irvine, CA, USA), median #26, in 20 patients. Insertion of a prosthesis inside the MV was obtained by cutting only a triangle of the AL with the base at the midpoint of A2. The remainder of the AL was pushed toward the annulus with the prosthetic sutures [8].

### 2.5. Clinical follow-up

Every patient had at least one echocardiographic evaluation at discharge and 139 patients had a control during the follow-up. Time from surgery to the last control was 15 ± 8 months.

### 2.6. Echocardiographic follow-up

All patients were clinically followed up in our outpatient clinic 3, 6, and 12 months after surgery and thereafter at yearly intervals. The most recent information was obtained by telephone interview. Follow-up was 98% complete. As some patient was living outside the country, in case of impossibility to contact him, the information at the last follow-up were considered if it was within the last 6 months, otherwise the patient was considered lost to follow-up. Mean follow-up time was 19 ± 9 months.

### Statistical analysis

Results are expressed as mean ± SD. Categorical variables are reported as counts and percentages. Echocardiographic modifications

| Table 1 | Clinical and echocardiographic data. |
|---------|-------------------------------------|
|         | All (n = 167) | MVr (n = 135) | MVPI (n = 32) | p      |
| Age (y:mean ± SD) | 62 ± 10 | 63 ± 10 | 62 ± 10 | 0.6117 |
| Female gender (n, %) | 39 (23.4) | 34 (25.2) | 5 (15.6) | 0.2504 |
| NYHA Class (mean ± SD) | 29 ± 0.6 | 28 ± 0.6 | 3.6 ± 0.5 | 0.0000 |
| Class II (n, %) | 43 (13.5) | 43 (13.5) | 31.8 | - |
| Class III (n, %) | 97 (66.8) | 86 (63.7) | 11 (34.3) | 0.000 |
| Class IV (n, %) | 30 (17.7) | 9 (6.7) | 21 (65.6) | 0.000 |
| EuroSCORE (mean ± SD) | 7.0 ± 4.9 | 6.1 ± 3.9 | 10.6 ± 6.6 | 0.000 |
| Diabetes mellitus (n, %) | 119 (71.2) | 100 (74.1) | 19 (59.4) | 0.0985 |
| AF (n, %) | 22 (13.2) | 16 (11.8) | 6 (18.8) | 0.2996 |
| Previous AMI | | | | |
| Anterior (n, %) | 55 (32.9) | 40 (29.6) | 15 (46.9) | 0.0000 |
| Lateral (n, %) | 17 (10.2) | 13 (9.6) | 4 (12.5) | 0.1120 |
| Inferior (n, %) | 95 (56.9) | 82 (60.7) | 13 (40.6) | 0.0000 |
| EF (%:mean ± SD) | 51 ± 7 | 57 ± 6 | 62 ± 7 | 0.0001 |
| LVEDD (mm:mean ± SD) | 58 ± 7 | 57 ± 6 | 62 ± 7 | 0.0001 |
| LVESD (mm:mean ± SD) | 45 ± 8 | 44 ± 8 | 49 ± 8 | 0.0018 |
| Coaptation depth (mm) | 7.6 ± 3.1 | 7.3 ± 2.7 | 12.2 ± 3.3 | 0.000 |
| MR grade (1-4:mean ± SD) | 2.9 ± 10 | 2.7 ± 0.9 | 3.6 ± 0.8 | 0.0000 |
| PAPs (mm Hg:mean ± SD) | 43 ± 18 | 41 ± 16 | 51 ± 22 | 0.0037 |
| TDI (cm/s) | 11.6 ± 12 | 11.5 ± 1.1 | 11.9 ± 1.4 | 0.0819 |

Legend. MVr, mitral valve repair; MVPI, mitral valve prosthesis insertion; y, year; SD, standard deviation; NYHA, New York Heart Association; AF, atrial fibrillation; AMI, acute myocardial infarction; EF, ejection fraction; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; MR, mitral regurgitation; PAPs, pulmonary artery pressure systolic; TDI, Tissue Doppler Imaging.
with time were evaluated with ANOVA test for repeated measures. Survival was evaluated by the Kaplan–Meier method. A non-parsimonious multivariate model was developed to estimate propensity scores, which were used as an adjusting variable in the Cox regression models. The optimal cutoff was determined by receiver operating characteristic curve analysis. The SPSS software package (SPSS Inc., an IBM Company, Chicago, Ill) was used.

### 3. Results

Table 1 shows some preoperative characteristics. Patients who underwent MVPI had a lower ejection fraction and larger hearts, with more severe CIMR. Pulmonary pressure was higher, and, by definition, coaptation depth was longer in this group. RV function was similar on both groups, and 10 patients (6.0%), 7 in MVr group and 3 in MVPI group had some grade of RV dysfunction.

Three patients died early after surgery, 2 (1.2%) within and other 4 (2.4%) after 30 days from surgery, but during the same admission, for mechanisms (ring or band or prosthesis dehiscence) or for MR return.

Table 2 shows some surgical details. TV surgery and LV surgical remodeling were more frequent in MVPI. Other procedures on the MV were performed globally in 12 patients (7.6%) in MVr group. Only 4 patients (3 in MVr group and 1 in MVPI group) had no coronary artery bypass grafting. ROC curve analysis showed that the possibility to insert a prosthesis was higher when ejection fraction was 25% or lower or end diastolic diameter was 60 mm or higher.

### 3.1. Survival

Six patients died early after surgery, 2 (1.2%) within and other 4 (2.4%) after 30 days from surgery, but during the same admission, for a global in-hospital mortality of 3.6%, similar in both groups (5 cases, 3.1%. in MVr group and 1 case, 3.1%, in MVPI group, p = 0.8743). Causes of death were low output syndrome, pulmonary infection and sepsis, 2 (1.2%) after 30 days from surgery, but during the same admission, for mechanical problems (ring or band or prosthesis dehiscence) or for MR return.

### 3.2. Functional results

The mean NYHA Class in the survivors was 1.5 ± 0.6, with only 3 patients in NYHA Class III or IV. Possibility to be alive and in NYHA Class I or II was 82 ± 3.2, without differences between groups (83 ± 4 in MVr and 80 ± 5 in MVPI groups, Fig. 2).

MVPI was inserted into a regression Cox model but it was not an independent variable for lower survival, freedom from cardiac death and possibility to be alive and in NYHA Class I or II.

### 3.3. Echocardiographic results

After a minimum of 4 months, 139 patients had an echocardiographic evaluation (mean 13 ± 8), 111 in group MVr and 28 in group MVPI. Table 3 shows the details. EF rose in both groups, whereas PAP, LVEDD and LVESD reduced significantly. MR grade was, in the follow-up echocardiogram, significantly reduced in both groups. MR grade was, however, lower in the MVPI group (0.1 ± 0.2 versus 0.3 ± 0.3 in MVr group, p = 0.0011). RV function improved significantly in the MVr group, whereas it remained unchanged in the MVPI group. RV dysfunction was present in 7 preoperatively and in 9 at the follow-up, with only 2 patients who maintained had RV dysfunction preoperatively and at follow-up.
To avoid the confounding contribution of SVR, Table 1e shows the echocardiographic results of the 119 patients who did not undergo SVR. The results were similar to the global population.

4. Discussion

The main finding of this study is that, with proper indications and a correct surgical technique, MV repair and MVPI are not antagonist, but part of a strategy to treat CIMR. This disease has not a uniform pattern, but can differ from patient to patient. For this reason choosing a single technique for everyone can limit the efficacy of surgical treatment.

The natural history of CIMR is not favorable. The presence of CIMR after myocardial infarction has been demonstrated to be related to lower survival [12,13] and higher incidence of congestive heart failure [14]. The excess mortality was independent of both the EF and the functional status [12]. CIMR left untreated after PCI [15] or when coronary artery bypass grafting was performed has also been shown to be followed by a worse long-term outcome, even if moderate or less [16].

There is general agreement that overreductive MV annuloplasty, proposed by Bolling et al. [1] for ischemic and non-ischemic cardiomyopathies, is the technique of choice to correct CIMR. Even if the same authors [17] were not able to demonstrate any benefit in survival when comparing treated and untreated patients, others [18,19] found, in randomized trials, annuloplasty to improve the clinical status in patients with moderate CIMR. Nevertheless, the evolution of MR after surgical correction is not always favorable. Due to the intrinsic characteristics of the disease, mostly related to ventricular events rather than to MV pathology, residual or recurrent MR is constantly shown in the follow-up of surgical series. CIMR in fact is a ventricular disease, because the mechanism of closure of the MV is affected by displacement of e or both papillary muscles. Consequences of these changes are regurgitation of a different grade and deepening of the CD.

In our opinion, there is a cutoff point, at which conservative techniques do not pay in the mid or long term. Our group [2] proposed a CD > 10 mm as a surrogate for the ventricular modifications that could sustain MR return. In this study, even if patients who underwent MV prosthesis insertion were sicker and showed worse preoperative echocardiographic findings, early mortality was similar than that in the MV repair group, with similar 3-year survival. This finding is coherent with the literature. Studies on this subject, even relatively few [3–6,8,20–22], all report similar early and late survival. The most recent report is the ISTMIR study [5], which included 1006 patients (298 MV replacement and 708 MV repair). In propensity matched patients early mortality was 3.3% in repair vs 5.3% in replacement and 8-year survival was 81.6% ± 2.8% and 79.6% ± 4.8% (p = 0.42). On the other side, different results were reported by De Bonis et al. [23] in a different population, made of 132 patients with dilated cardiomyopathy, mostly ischemic. In the replacement group early mortality was significantly higher (12.7% vs 2.3%, p = 0.03) and the 2.5-year survival was significantly lower (73 ± 7.9% vs 92 ± 3.2%, p = 0.02).

Another important finding in our study is the lower incidence of MR in the MVPI group if compared with the MVr group. This is a common finding in other surgical series as well. Al-Radi et al. [22] reported an incidence of reoperations of 14% in the repair group due to failure of the repair and of 3% in the replacement group (p = 0.003). In the experience of Magne et al. [3], at predischarge examination, incidence of persistent moderate MR was higher in the repair group (18% vs 4%, p = 0.0001). Chan et al. [4] reported that freedom from recurrent MR moderate or more was 85.7 ± 13.2% for replacement and 41.4 ± 14.8% after repair, p = 0.04. Finally, the ISTMIR study [5] reported an actual freedom from valve-related reoperation of 71.3 ± 3.5% versus 85.5 ± 3.9 in MV repair and MV replacement, respectively (p < .001).

In our experience, the grade of persistent/recurrent MR in MV group was low (0.3 ± 0.3), but still higher than in patients in the MVPI group (0.1 ± 0.2, p = 0.018).

It is noteworthy that EF improved in both groups and LVESD reduced as well. Even if our experience includes patients with low mean EF, elimination of the MR was beneficial in terms of improvement of both functional Class and ventricular performance. Even if the concept that CIMR is a ventricular disease is widely accepted, it was not clear if CIMR, as it started when LV function was already compromised, was a variable to cause further worsening or a marker of worsening heart failure. Even if this debate is not over, there are experimental evidences that addition of a moderate MR (created by means of a shunt interposed between the LV and the left atrium) after ligation of the mid LAD in dogs, caused the infarcted hearts to become more dilated with lower EF than the controls, where, after LAD ligation, the shunt was not created [24]. We think that CIMR has its own life and, if corrected, will improve, if not survival, at least the functional Class [18,19].

Surgery on LV scar is an integral part of the treatment of CIMR. In our opinion it is difficult to separate patients where LV surgery is performed by those where LV surgery is not performed. Even if the STICH trial failed to show any benefit in LV surgical remodeling, in our opinion

Table 3

Echocardiographic follow up.

|              | MVr (n = 111) | MVPI (n = 28) |
|--------------|---------------|---------------|
|              | Pre (mean ± SD) | Post (mean ± SD) | p     | Pre (mean ± SD) | Post (mean ± SD) | p     |
| EF (%)       | 32 ± 6        | 35 ± 8        | 0.0018 | 26 ± 7        | 30 ± 4        | 0.0112 |
| LVEDD (mm)   | 57 ± 7        | 53 ± 8        | 0.0001 | 63 ± 7        | 57 ± 9        | 0.0000 |
| LVESD (mm)   | 44 ± 8        | 41 ± 7        | 0.0033 | 49 ± 8        | 43 ± 9        | 0.0109 |
| MR grade     | 2.5 ± 1.1     | 0.3 ± 0.6     | 0.0000 | 3.5 ± 0.9     | 0.1 ± 0.2     | 0.0000 |
| PAPs (mmHg)  | 40 ± 16       | 34 ± 11       | 0.0013 | 51 ± 22       | 33 ± 12       | 0.0004 |
| TDI (cm/s)   | 11.4 ± 1.2    | 11.8 ± 1.5    | 0.0293 | 11.9 ± 1.5    | 12.0 ± 1.2    | 0.7840 |
| Gradient     | 5 ± 3         | 5 ± 3         | 0.0360 |

Legend. MVr, mitral valve repair; MVPI, mitral valve prosthesis insertion; SD, standard deviation; EF, ejection fraction; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; MR, mitral regurgitation; PAPs, pulmonary artery pressure systolic; TDI, tissue doppler imaging.
that trial was addressed to patients with ischemic cardiomyopathy in general, regardless of the presence or not of a scar of surgical interest. On the other hand, other reports [25] underlined how a LV dimension higher than 65 mm was related to a poor outcome. Then very likely there is a limit to what can be done on the MV, at least to reverse symptoms. We think that, to treat correctly CIMR, it is important to have an open mind and not to address only the mitral annulus. Even mitral regurgitation is generated by a ventricular event, there are a variety of anatomic features which can be predominant from time to time, needing different surgical approaches according to the specific findings.

5. Limitations of the study

This was a retrospective study, but it included all the patients who underwent CIMR, independent of the location of the myocardial infarction, as it happens in the real world. The anatomic and functional aspects of the MV were different, just as are the functional consequences of ventricular disease on the pathophysiology of the MV.

The follow-up was relatively short, but most of the adverse outcomes after surgery for functional CIMR are seen in the early follow-up. A large variety of surgical approaches were used on a relatively small number of patients. Although this probably reflects the complexity of this disease process and the lack of consensus regarding its treatment, it also significantly reduces our ability to make scientifically valid conclusions from our data. Myocardial viability was not routinely assessed and this may affect our conclusions on postoperative left ventricular remodeling and functional mitral regurgitation recurrence.

6. Conclusions

CIMR is a complex disease which needs different surgical approaches, as goal of surgery is to eliminate or to reduce the regurgitation, and not to repair the MV. There are many evidences that insertion of a prosthesis, if compared with MV repair, has, at least, the same and, sometimes, a better outcome in terms of MR repair or persistence. Nonetheless, surgeons are reluctant to accept a technique which is considered suboptimal. However, we must be aware that this concept descends from the experience in organic MV diseases and it is not applicable to functional MR. In most of the cases MV can be repaired, adding sometimes other procedures on the MV, but sometimes our choices have to be different to achieve a better long term outcome.

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