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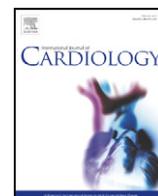
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Severe ischemic cardiomyopathy with mechanical complications: Still a surgical disease



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ABSTRACT

Background: Surgical treatment of ischemic cardiomyopathy (ICM) with mechanical complications has been limited in favor of suboptimal treatments because of the perception of poor outcome.

Methods and results: From May 2009 till June 2014 115 patients with severe ICM (ejection fraction, EF, $\leq 25\%$) and mechanical complications were operated on. Median EF was 24% (19, 24), mean end-systolic volume index (ESVi) was 86 ± 27 ml/m² and all patients had an MR grade of 2 or more. The right ventricle (RV) was hypokinetic in 33 patients. All of them underwent mitral valve surgery. Left ventricular (LV) surgical remodeling was performed in 60 patients (52.2%) and tricuspid surgery in 58 (50.4%). In-hospital mortality was 4.3% (5 patients). Six-year freedom from death any cause and from death any cause and NYHA class III/IV were, respectively, $70.5 \pm 4.9\%$ and $66.4 \pm 4.8\%$. Cox regression analysis showed that risk factors were lower EF (cutpoint $\leq 20\%$) and RV hypokinesia. Eighty-six patients had a follow up echocardiogram after a median of 31 (19, 51) months. EF increased by 60%, from 24 (19, 24) to 35 (27, 46) ($p = 0.00$), and ESVi decreased by 32%, from 87 ± 29 to 59 ± 27 ml/m² ($p = 0.00$). SVi increased by 32%, from 23 ± 7 to 32 ± 12 ml/m². MR grade was ≥ 2 only in 6 patients (7%) and was not severe in any of them.

Conclusions: Surgery for severe ICM with MR can be performed with low surgical risk and good midterm survival. These findings have to be taken into account while abandoning a clear surgical indication in favor of suboptimal alternative therapies.

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1. Introduction

Ischemic cardiomyopathy (ICM) following acute myocardial infarction (AMI) is the most frequent cause of heart failure. Ventricular remodeling frequently causes mitral regurgitation (MR) due to papillary muscles' displacement, which adds complexity to the presence of scars of different extent. Conventional surgery for ICM then includes myocardial revascularization and correction of mechanical complications, as mitral valve surgery and, when necessary, left ventricular surgical remodeling (LVSR). However, surgical possibilities to treat these complex patients are progressively reduced in favor of medical treatment, percutaneous mitral repair or LV assist devices as destination

therapy. On the other side, results of medical treatment alone are poor [1], and the benefit of percutaneous mitral repair, if any, is controversial [2]. Destination therapy is not a solution widely available, mainly due to the high costs [3].

We report our results with conventional surgical treatment of severe ICM and mechanical complications. "Severe" identifies patients with ejection fraction (EF) of 25% or less. The primary objective of this study is to evaluate the surgical outcome and to determine whether assessment of risk factors can help to identify patients who can benefit more from surgical treatment.

2. Material and methods

All elective or urgent patients who underwent surgical treatment of severe ICM due to a previous AMI with mechanical complications in a single institution from May 2009 to June 2014 were included in this study. Mechanical complications are defined as the presence of functional MR and of dyskinetic or akinetic segmental areas of the LV cavity. Patients operated on as an emergency (on inotropic support and/or intra-aortic balloon

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pump [IABP] and/or mechanical ventilation), were not included. Retrospective analysis of our database was approved by the institutional review board, which waived patient consent.

2.1. Echocardiographic evaluation

All echocardiographic measurements were obtained following American Society of Echocardiography (ASE) and European Association of Echocardiographers' (EAE) guidelines [4,5]. Severity of MR and TR was graded in a scale from 1 to 3 (1, mild; 2, moderate; 3, severe). The presence of left ventricular diastolic dysfunction (LVDD) was assessed based on the EAS/ASE recommendations [6] and patients with a ratio $E/e' \geq 15$ were considered to have severe LVDD. Basal right ventricular (RV) dimension was recorded at end-diastole, along with tricuspid annular plane systolic excursion (TAPSE) and/or tissue Doppler imaging. The RV was defined as dilated if basal end-diastolic diameter was >42 mm and hypokinetic if TAPSE was <16 mm and/or S' velocity was <10 cm/s [7] at tissue Doppler imaging. RV dilatation or hypokinesia were included in the analysis as a binary variable. RV systolic pressures were estimated using continuous-wave Doppler data and the simplified Bernoulli equation ($4 \times [\text{peak TR velocity}]^2$) with 10 mm Hg added for the estimated right atrial pressure. The value obtained was considered the systolic pulmonary artery pressure. Pulmonary hypertension (PH), defined as a systolic RV pressure above 55 mm Hg [8], was included in the analysis as a binary, and not as a continuous, variable, as some patients had no TR.

2.2. Surgical indications and techniques

All patients were candidates for MV surgery as all of them had moderate or severe MR. A coaptation depth (CD) of ≤ 10 mm was the limit for MVR. If CD was >10 mm, the anatomy was not considered suitable for repair, and a prosthesis was inserted (MVR) with the preservation of the leaflets and subvalvular apparatus. MVR was achieved by inserting a 40-mm or 50-mm band (Sorin Biomedica, Saluggia, Italy) from trigone to trigone. The LV was surgically remodeled if there were localized dyskinetic or akinetic areas, the exclusion of which could contribute to a decrease in the filling pressure and to an improvement in the efficiency of the cardiac pump. Different techniques were used in case of anteroseptal localization [9], all aimed at reducing the volume maintaining a conical shape. Linear septoexclusion, already described by our group [10], joins the borders of the anterior and the septal scars with interrupted 2/0 U sutures. It is addressed mainly to large hearts (end diastolic volume index, EDVi, >120 ml/m²). Septal reshaping uses, instead of a direct suture, an oval patch [11] and is addressed mainly to hearts with an EDVi <120 ml/m². The septoapical Dor procedure was used only in case of scars that involved the distal portion of the septum, of the anterior wall and of the apex. In case of lateral or inferior scars, an incision was made from the apex to the base of the heart, and the scarred area was excluded by internal plication with interrupted 2/0 Ethibond U sutures. TR was always corrected when ≥ 2 or, if mild, if the systolic dimension of the annulus was >24 mm [12].

2.3. Follow-up

All patients were clinically followed up in our outpatient clinic 3, 6, and 12 months after surgery, and at yearly intervals thereafter. The most recent information was obtained by calling the patient or the referring cardiologists. If the patients were living in places difficult to access or left the country, the last information was included in the analysis. Follow-up ended on April 2016 and was 100% complete. Median follow-up of survivors was 55 (37, 74) months.

2.4. Statistical analysis

Categorical variables are expressed as counts and percentages. Continuous variables are expressed, if normally distributed, as mean \pm standard deviation, if non-normally distributed, as median with the 25th and 75th percentiles. Comparison between groups was performed using unpaired 2-tailed *t*-test for normally distributed continuous variables, Mann-Whitney *U* test for non-normally distributed continuous variables, and Pearson's chi-square test (or Fisher's exact test) for categorical variables. Pre- and postoperative data of each group were compared by paired *t*-test for normally distributed variables or Wilcoxon test for non-normally distributed variables. Repeated categorical variables were compared by the McNemar test if nominal, and the Friedman test if ordinal. Stepwise logistic regression analysis was performed to evaluate independent risk factors for in-hospital mortality. The overall model fit and the Hosmer–Lemeshow test were used to evaluate model predictivity. Survival was evaluated by the Kaplan–Meier method. Results of the Cox proportional hazards regression model were reported as the instantaneous relative risk (hazard ratio, HR), 95% confidence intervals (CI), and *p*-value. All the variables reported in Table 1 were included into the multivariate analyses. Definition of the variables, when not indicated, follows the definition reported in the EuroSCOREII model [8]. Optimal cut-offs were determined by receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) with corresponding 95% CI and *p*-values were reported. Multivariable model was validated in 1000 bootstrap samples. For all tests, a *p*-value <0.05 was considered significant. The SPSS software (SPSS Inc., Chicago, IL, USA) was used.

Table 1

Clinical and echocardiographic preoperative data and surgical characteristics.

Variable (n = 115)	
Age (y)	60 \pm 11
F gender	14 (12.2)
Obesity	21 (18.3)
ESII	8 (5.4, 11.9)
NYHA class	
I	9 (7.8)
II	21 (18.3)
III	73 (63.5)
IV	12 (10.4)
III/IV	85 (73.9)
Angina	71 (61.7)
Recent AMI	34 (29.6)
DM	76 (66.1)
On insulin	27 (23.5)
CrCl	81 \pm 30
<50 ml/min	18 (15.7)
High hs-cTnT	35 (30.4)
High bil (>22 μ mol/l)	11 (9.6)
No SR	5 (4.3)
EF (%)	24 (19, 24)
EDD (mm)	62 \pm 8
ESD (mm)	51 \pm 8
EDVi (ml/m ²)	109 \pm 31
ESVi (ml/m ²)	86 \pm 27
SVI (ml/m ²)	23 \pm 7
SI	0.69 \pm 0.08
sPAP (mm Hg)	45 (30, 60)
PH (>55 mm Hg)	42 (36.5)
LVDD	73 (63.5)
RV dim (mm)	41 \pm 8
RV hypo	33 (28.7)
RV dil	43 (37.4)
MR grade	
2	69 (60)
3	46 (40)
TR grade (0–4)	
0	30 (26.1)
1	46 (40)
2	31 (27)
3	8 (7)
CABG	108 (93.9)
MV repair	76 (77.1)
MVR	39 (33.9)
LVSr	60 (52.2)
SR	41 (68.3)
LSE	9 (15)
SA Dor	6 (10)
lat wall	2 (3.3)
inf wall	2 (3.3)
TV repair	58 (50.4)
CPB time (min)	143 \pm 32
XCl time (min)	113 \pm 27

Values are expressed as mean \pm SD, median (95% confidence interval) or counts (%).

Legend. y, years; F, female; ESII, EuroSCORE II; NYHA, New York Heart Association; AMI, acute myocardial infarction; DM, diabetes mellitus; CrCl, creatinine clearance; hs-cTnT, high sensitivity cardiac troponin T; bil, bilirubin; SR, sinus rhythm; EF, ejection fraction; EDD, end-diastolic diameter; ESD, end-systolic diameter; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; SVI, stroke volume index; SI, sphericity index; sPAP, systolic pulmonary artery pressure; PH, pulmonary hypertension; LVDD, left ventricular diastolic dysfunction; RV, right ventricle; dim, dimension; hypo, hypokinesia; dil, dilatation; MR, mitral regurgitation; TR, tricuspid regurgitation; CABG, coronary artery bypass grafting; MV, mitral valve; MVR, mitral valve replacement; LVSr, left ventricular surgical remodeling; SR, septal reshaping; LSE, linear septoexclusion; SA, septoapical; lat, lateral; inf, inferior; TV, tricuspid valve; CPB, cardiopulmonary bypass; XCl, cross clamping.

3. Results

3.1. Clinical and echocardiographic preoperative characteristics

Surgical treatment of severe ICM with mechanical complications was performed in 115 patients as an elective or urgent procedure. Twelve patients, operated on emergency basis, were excluded. Mean age was 60 ± 11 years. Most patients were in NYHA class III/IV (73.9%), and 29.6% had a recent AMI. High sensitivity cardiac Troponin T (hs-cTnT) was high (>0.014 ng/ml) in 35 patients (30.4%) on the day before surgery. Creatinine clearance was <85 ml/min in 55.6% of the patients. Median EF was 24% (19, 24) and all patients had an MR grade of 2 or more. The RV was dilated in 37.4% of the cases and hypokinetic in 28.7% (Table 1).

3.2. Surgical data

All patients underwent MV surgery, repair (n = 76) or replacement (n = 39) maintaining the whole subvalvular apparatus. LVSR was performed in 60 patients (52.2%), mostly consisting in septal reshaping. Tricuspid valve (TV) repair was performed in one half of the cases. In all patients, myocardial protection was achieved by means of intermittent antegrade warm blood cardioplegia (for dosage calculations see <http://www.sicch.it/index.php/attivita-sicch/e-learning/273-calafiorecardioplegia-dosage-calculations>) (Table 1).

3.3. Early survival and postoperative course

Five patients (4.3%) died while in hospital and 3 within 30 days of surgery (2.6%). All patients needed inotropic support and in 9 an IABP was inserted. In 6 cases (5.2%), the sternum was left open and 4 (3.5%) needed extracorporeal membrane oxygenation (ECMO). One ECMO patient in whom the sternum was left open died (16.7%), and 3 out of 9 patients who needed IABP died (33.3%). At stepwise logistic regression (Table 2), recent AMI and high bilirubin at the moment of surgery (defined as a value >22 µmol/l) were risk factors for early mortality. Mean intensive care unit (ICU) stay was 3 days (1, 6).

Table 2
Multivariate analysis.

Stepwise logistic regression for early mortality						
Variable	OR	95% CI	P-value	Yes	No	P-value
Recent AMI	13.6	1.3–145	0.03	11.8%	1.2%	0.02
High bilirubin	10.8	1.2–96.2	0.01	18.2%	2.9%	0.02
Cox proportional hazards regression						
Variable	HR	95% CI	P-value	Yes ^a	No ^a	P-value
Freedom from death of any cause						
EF	0.91	0.85–0.98	0.01	48.8 ± 10.9 ^b	79.8 ± 5.2 ^c	0.00
RV hypokinesia	1.98	1.26–4.82	0.04	57.8 ± 9.9	75.5 ± 5.5	0.03
Freedom from cardiac death						
EF	0.85	0.78–0.93	0.00	67.5 ± 8.9 ^b	90.4 ± 3.5 ^c	0.00
High hs-cTnT	2.2	1.02–4.7	0.04	72.5 ± 7.8	87.6 ± 3.4	0.03
Freedom from death of any cause and NYHA class III/IV						
EF	0.92	0.86–0.98	0.00	39.7 ± 9.3 ^b	78.5 ± 4.8 ^c	0.00
RV hypokinesia	2.08	1.05–4.13	0.03	49.1 ± 9.7	73.0 ± 5.3	0.00
Freedom from cardiac death and NYHA class III/IV						
EF	0.89	0.83–0.96	0.00	57.6 ± 9.4 ^b	81.4 ± 6.8 ^c	0.00
RV hypokinesia	2.43	1.06–5.66	0.03	78.3 ± 6.5	63.8 ± 9.5	0.02
High hs-cTnT	2.2	1.2–4.8	0.01	67.4 ± 8.8	79.0 ± 6.0	0.01

OR, odd ratio; CI, confidence interval; AMI, acute myocardial infarction; HR, hazard ratio; EF, ejection fraction; RV, right ventricle; hs-cTnT, high sensitivity cardiac troponin T; NYHA, New York Heart Association.

^a Event at 6 years.
^b EF ≤ 20%.
^c EF > 20%.

Thirteen patients (11.3%) were readmitted in the ICU and 2 of them (15.4%) died. Median postoperative in-hospital stay of patients who were discharged was 11.5 days (5, 21). On discharge, all patients received optimal medical treatment (beta-blockers, ACE-inhibitors or angiotensin-receptor blockers, diuretic, aspirin or warfarin or both, statins) (Table 1 supplement).

3.4. Late outcome

After a mean follow-up of 24 ± 17 months, 24 patients died after hospital discharge. Six-year freedom from death of any cause (Fig. 1A) and from cardiac death were 70.5 ± 4.5% and 83.5 ± 3.7%, respectively. Table 2 shows the results of Cox analysis. Lower EF and RV hypokinesia were identified as risk factors for freedom from death any cause (Figs. 1A and 2A supplement) and lower EF and high hs-cTnT were associated to lower freedom from cardiac death. ROC analysis showed that EF ≤ 20% was the cut point associated with a higher incidence of deaths or cardiac deaths (sensitivity 55%, sensibility 80%, AUC 0.63, 95% CI 0.53–0.72, p = 0.03) (Table 1 supplement).

Overall, after a median follow-up of 55.5 (37, 73) months, out of 91 patients who survived, 7 were in NYHA class III/IV and 14 required one or more hospitalization for an episode of heart failure or to optimize medical treatment. In 8 cases an implantable cardioverter defibrillator was implanted, in 6 cases associated with an atrioventricular pacer. Six-year freedom from death of any cause and NYHA class III/IV was 66.4 ± 4.8% (Fig. 1B). Six-year freedom from cardiac death and NYHA class III/IV was 78.0 ± 4.2%. Cox analysis (Table 2) identified lower EF (Fig. 1B supplement) and RV hypokinesia (Fig. 2B supplement) as risk factors in both analyses and high hs-cTnT only for freedom from cardiac death and NYHA class III/IV.

Patients who had EF from 21% to 25% and no RV hypokinesia (n = 60) had higher freedom from all time-dependent events compared to patients who showed both risk factors (n = 13), HR 4.7, 95% CI 1.3, 17.3, p = 0.00, and HR 6.2, 95% CI 1.8, 21, p = 0.00, respectively. Patients with a single risk factor (RV hypokinesia, n = 20 and EF ≤ 20%, n = 22) showed intermediate outcome (Table 2 supplement).

3.5. Echocardiographic outcome

After a median follow-up of 31 (19, 51) months, 86 patients underwent postoperative echocardiographic examination. EF rose by 71% and EDVi and ESVi were reduced by 16% and 30%, respectively. As a consequence, stroke volume index (SVi) increased by 32%. Improvements were higher in patients with EF ≤ 20%, but they remained more dilated with a median EF below 30% (Table 3 supplement). Six patients only (7%) had MR ≥ 2, 5 after MV repair (n = 57, 8.8%) and 1 after MVR (n = 29, 3.4%), p = 0.36. No patient had severe MR. The proportion of patients with RV hypokinesia increased significantly (from 26.7% to 48.8%, p = 0.00), whereas the percentage of patients with RV dilatation did not change significantly. As a result, despite the high incidence of TV surgery, there was no significant reduction in the number of patients with TR ≥ 2, as TR ≥ 2 increased in patients who did not undergo TV surgery (n = 43, from 2.3% to 20.9%, p = 00) and decreased in patients who underwent TV surgery (n = 43) (from 62.8% to 21%, p = 0.00). Most patients with preoperative RV hypokinesia did not improve postoperatively (17/23, 73.9%). On the other hand, out of 63 patients with preoperative RV normokinesia, 25 (39.7%) became hypokinetic. A common denominator of these patients was higher prevalence of dilated RV (22/42 vs 9/44, p = 0.00) (Table 3).

4. Discussion

The benefit of revascularization in patients with severely depressed LV function is well known [13]. As severity of LV dysfunction increases, the potential survival benefit associated with revascularization in patients with myocardial viability also increases. Patients with a

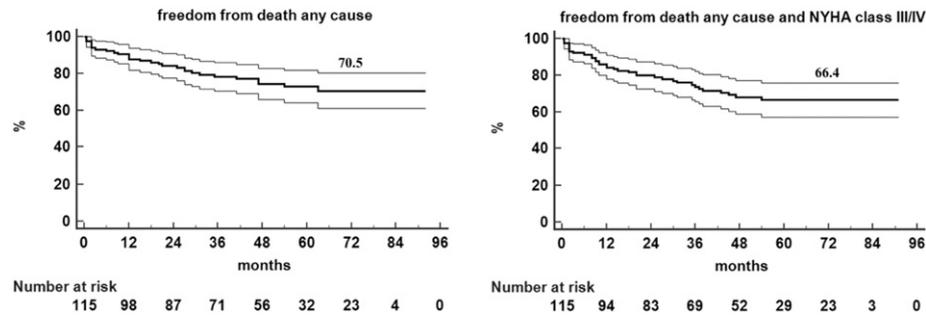


Fig. 1. Freedom from death any cause (A) and from death any cause and NYHA class III/IV (B). NYHA, New York Heart Association.

substantial amount of dysfunctional but viable myocardium may considerably improve EF and prognosis after revascularization. However, in clinical practice, this does not apply to all patients. Lack of recovery in patients with a considerable amount of viable tissue may be related to increased LV volume due to extensive ventricular remodeling. Previous studies demonstrated that $ESV \geq 140$ ml prevents global functional recovery, even in patients with substantial viability [14]. Factors that may induce progressive LV dilatation include the onset of secondary MR and the presence of scars of different extent.

The great majority of patients with severe ICM are treated medically, even if significant mechanical complications exist, but results are poor and less effective than surgical treatment. Samad et al. [1], in patients with similar characteristics to our population, found that MV surgery was associated with higher event-free survival compared with medical therapy alone. There are non-surgical tools used to downgrade, indirectly or directly, secondary MR. Cardiac resynchronization therapy (CRT) is aimed at improving EF and reducing MR in patients with severe ICM. However, reduction of MR after CRT is not the rule [15,16] and MR is more likely to remain unchanged in the presence of extensive LV remodeling [17]. Moreover, survival is not affected by EF improvement if MR does not reduce and in general MR reduces in 30 to 40% of the patients. MitraClip therapy has been applied in patients with secondary MR, but reduction of MR grade appeared to be less effective if compared

to surgery [18–21]. However, even in patients discharged with early optimal procedural results ($MR \leq 1$), MR progression toward higher grades is constant during the first years [22]. Five-year outcome of the EVEREST II trial [23] demonstrated that freedom from death and reoperations was similar in MitraClip and surgical patients starting after 6 months of follow up (most of the reoperations in MitraClip patients occurred during the first 6 months after the procedure). However, the same study demonstrated again that MR reduction was less effective in the MitraClip group. At 5 years, incidence of MR 3+ or 4+ was 2.8% in the surgical group and 18.8% in the MitraClip group ($p = 0.01$). Other interventional procedures are aimed at reducing the grade of MR intervening directly or indirectly on the mitral annulus [24–27], but so far long term results are not available. The presence of transmural scars affects survival [28], but results from the STICH trial found that scar exclusion would not result in a survival benefit compared to patients where revascularization alone was performed [29]. Even if this study has many flaws [30], patients with scars and advanced heart failure may receive a suboptimal treatment because of generalization of results.

Our study included only patients with severe ICM where mechanical complications were predominant. The etiology of MR, ischemic in origin, was related to the presence of transmural AMI, then irresponsive to revascularization alone. In more than half of patients, the extent of scars advised scar exclusion to achieve LV volume reduction to recover a conical shape. However, due to the different positions of scars or to the variable anatomic aspect of the regurgitant mitral valve, it is not possible to apply always the same surgical technique.

In-hospital mortality was lower than expected (4.3% vs 8%) and similar to that reported in patients with depressed LV function by Fedoruk et al. [31] (6.2%) and by Maltais et al. [32] (7%). We found that recent AMI and high bilirubin were risk factors for increased in-hospital mortality. These findings underline how important it is to postpone surgery in patients after AMI to allow a better stabilization of the cardiac lesions and, on the other hand, how a failing liver is often related to high early mortality.

Survival and clinical outcome in this high-risk pathology were satisfying. Although it is not easy to compare different outcomes because of heterogeneity across patients, in the recent era heart transplant survival is around 70% at 5 years [33], a value comparable with that of our study. On the other side our good results are due to the presence of a team of surgeons, anesthesiologists, intensivists and cardiologists dedicated to these difficult and complex patients.

LV systolic function and RV hypokinesia were risk factors for the main time-dependent events. We found that $EF \leq 20\%$ was the cut point for a poorer outcome. The echocardiographic parameters of these patients improved in the follow up, but remained with a lower EF and a bigger LV than in patients with preoperative EF 21 to 25% (Table 3 supplement), at the basis of a worst outcome. The predictive value of RV dysfunction has been emphasized in previous studies. Di Mauro et al. [34], in 111 patients with ischemic or idiopathic dilated cardiomyopathy who had MV annuloplasty with/out CABG, found that RV dysfunction was a predictor of worse survival and survival in NYHA class I/II. Garatti et al. [35], in a population of 324 patients undergoing

Table 3
Echocardiographic changes before and after surgery in 86 patients (mean follow-up 31 (19, 51) months).

Variable	Preoperative	Postoperative	P	%
EF (%)	24 (19, 24)	35 (27, 46)	0.00	+71 (26, 106)
EDD (mm)	63 ± 8	59 ± 8	0.00	
ESD (mm)	51 ± 8	46 ± 9	0.00	
EDVi (ml/m ²)	110 ± 33	92 ± 29	0.00	−16 (−32, 8)
ESVi (ml/m ²)	87 ± 29	59 ± 27	0.00	−30 (−51, −12)
SVi	23 ± 7	32 ± 12	0.00	+32 (0, 91)
SI	0.70 ± 0.08	0.72 ± 0.12	0.20	
PH	24 (27.9)	11 (12.8)	0.00	
RV dim (mm)	40 ± 8	39 ± 6	0.30	
RV dil	29 (33.7)	34 (39.5)	0.63	
RV hypo	22 (25.6)	40 (46.5)	0.00	
MR grade				
0	–	51 (59.3)	0.00	
1	–	29 (33.7)		
2	51 (59.3)	6 (7)		
3	35 (40.7)	–		
MR gradient (mm Hg)	–	4 (3, 5.5)		
TR grade			0.06	
0	24 (27.9)	34 (39.5)		
1	34 (39.5)	34 (39.5)		
2	21 (24.4)	15 (17.4)		
3	7 (8.1)	3 (3.5)		

Values are expressed as mean ± SD, median (95% confidence interval) or counts (%). EF, ejection fraction; EDD, end-diastolic diameter; ESD, end-systolic diameter; EDVi, end-diastolic volume index; ESVi, end-systolic volume index; SI, sphericity index; PH, pulmonary hypertension; RV, right ventricle; dim, dimensions; hypo, hypokinesia; dil, dilatation; MR, mitral regurgitation; TR, tricuspid regurgitation. Bold indicate significance of median and quartiles.

LVSR, showed that long-term survival was strictly related to RV dysfunction. However, lower EF seems to have a stronger prognostic value (Tables 3) than RV hypokinesia. As we could expect, patients who had both risk factors were at high risk for late events. On the other hand, when either risk factor was absent, late prognosis improved dramatically (Table 2 supplement). Our study emphasizes the crucial role of left and right ventricular function in the prognosis of patients who should undergo surgery for severe ICM with mechanical complications, strongly supporting the indication for an earlier surgical intervention to avoid worsening of left or right (or both) ventricular contractility.

Another risk factor, specific for lower freedom from cardiac death and from cardiac death and NYHA class III/IV is higher hs-cTnT immediately before surgery. In our opinion this finding is an indication to postpone surgery. Most likely the surgical procedure interferes with a still ongoing ischemic event and causes local damages which show their effect in the long term.

Follow up echocardiographic data showed an increase in EF along with a decrease in ESVi, higher than the decrease of EDVi. As a consequence there was a real improvement in the SVi, clinically more important as MR grade decreased significantly. TR grade remained similar as TR increased in untreated patients and decreased in patients who underwent TV repair. RV function worsened in survivors, as 46.5% showed RV hypokinesia compared with 25.6% at preoperative assessment. These patients also had larger RV dimensions before surgery and at follow up. We can speculate that persistent or increased RV dilatation may lessen the likelihood of RV function recovery or may cause progressive worsening of RV function in patients with preoperative normal RV function. We have to recognize that the interdependence among the different factors that affect RV function remains to be clearly elucidated.

The main limitation of our study is its retrospective nature and the small number of patients, once we analyze subgroups. Echocardiogram does not give a perfect idea of the systolic function. Nevertheless, the Simpson's method remains the most diffuse way to identify the EF. TAPSE and S' velocity, even if validated, are only imperfect indicators of RV function. However, the complex geometry of the RV makes it difficult to assess its systolic function, and no technique or parameter is exempt from potential criticisms. Nuclear magnetic resonance was, unfortunately, introduced in our Institution only in 2013. On the other hand, the strength of our study is the dedicated experience of the team, which has been working in this field since the last two decades, the completeness of the follow-up, and the high number of postoperative echocardiograms.

There are several surgical options and, due to its variable presentation, severe ICM with MR cannot be treated with a single procedure, either on the MV or, when necessary, on the LV. The infarct site and extension are variable and their effects on the MV tethering can be such to prevent any attempt of repair. On the other side, as the aim of LVSR is to maintain a conical shape, this goal cannot be achieved applying a single technique, due to the variability of the anatomic presentations. Lack of standardization limits the general applicability of surgery, which however remains a valid option for dedicated teams.

In conclusion, severe ICM with mechanical complications is, in our opinion, a disease of surgical interest. While non-surgical options provide often suboptimal results, surgery can be performed with satisfying results and good midterm outcome. The net effect of the SVi improvement goes beyond the crude increase of the percentage, as the huge reduction of MR grade enhances its clinical value. This result is typical of the surgical treatment and is not reproducible with alternate treatments. According to the results of our experience, early surgical results can be improved postponing surgery after 90 days from the AMI. Patients with reduced function of the LV ($\leq 20\%$) or of the RV have to delay surgery in order to try to improve the systolic function of at least one ventricle with an aggressive medical treatment. In general, surgery must never be postponed in patients with an EF $> 20\%$ or with

a normal RV, even if there are limited symptoms, as when the clinical picture worsens and cardiac systolic function worsens as well. Surgical indication should be anticipated not to lose the opportunity of prolonging the life and improving cardiac function of these patients, often without reliable alternatives.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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