BRIEF REPORT

Variables Associated with Improved Left Ventricular Function after Myocardial Revascularization

Variables asociadas con la mejoría de la función ventricular luego de la revascularización miocárdica

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ABSTRACT

Background: Myocardial revascularization is the treatment of choice in patients with ischemic systolic dysfunction. Left ventricular ejection fraction (LVEF) constitutes a prognostic factor in these patients, so it is of interest to identify the variables related with left ventricular function improvement.
Objective: The aim of this study is to determine the variables associated with improvement of LVEF in patients with ischemic systolic dysfunction undergoing myocardial revascularization.
Methods: Patients with LVEF <50% undergoing surgical myocardial revascularization with echocardiographic monitoring ≥6 months were included in the study. The variables associated with LVEF improvement >5% were analyzed.
Results: The cohort consisted of 95 patients; 91.6% were men, mean age was 63 years, 40% were diabetic, 27% had previous myocardial infarction and LVEF was 36%±6%. Viability was assessed in 78% of cases. During the immediate postoperative period, 12.6% of patients presented ischemia and 28% low cardiac output. Multivariate analysis revealed that myocardial viability and lack of perioperative ischemia were independent predictors of LVEF improvement.
Conclusions: Myocardial viability and absence of perioperative ischemia were associated with improved LVEF during long-term follow-up.

Key words: Myocardial revascularization - Ventricular dysfunction - Myocardial ischemia.

RESUMEN

Introducción: La revascularización miocárdica es el tratamiento de elección en pacientes con disfunción sistólica isquémica. La fracción de eyección del ventrículo izquierdo (FEVI) constituye un factor pronóstico en estos pacientes, por lo que resulta de interés identificar las variables relacionadas con la mejoría de la función ventricular.
Objetivo: Determinar las variables asociadas con el restablecimiento de la FEVI en pacientes con disfunción ventricular isquémica sometidos a revascularización miocárdica.
Material y métodos: Se evaluaron pacientes con FEVI < 50% sometidos a revascularización quirúrgica y con seguimiento ecocardiográfico ≥6 meses. Se analizaron variables relacionadas con la mejoría de la FEVI (> 5%).
Resultados: Se incluyeron 95 pacientes, 91,6% de sexo masculino, edad media de 63 años, 40% diabéticos, 27% con infarto previo y FEVI del 36% ± 6%. Se evaluó viabilidad en el 78%. Durante el posoperatorio, el 12% presentaron isquemia perioperatoria y el 28%, bajo gasto cardíaco. Tras análisis multivariado, la viabilidad y la ausencia de isquemia perioperatoria fueron predictores independientes de la mejoría de la FEVI.
Conclusiones: La viabilidad y la falta de isquemia durante el perioperatorio se asociaron con mejoría de la FEVI durante posoperatorio alejado.

Palabras clave: Revascularización miocárdica - Disfunción ventricular izquierda - Isquemia miocárdica

Abbreviations

ECG	Electrocardiogram	**MR**	Myocardial revascularization
HF	Heart failure	**SD**	Systolic dysfunction
LVEF	Left ventricular ejection fraction	**SPECT**	Single photon emission computed tomography
MV	Myocardial viability		

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INTRODUCTION

Coronary artery disease (CAD) is the most common cause of heart failure (HF) and different strategies are available for its treatment. (1) Myocardial revascularization (MR) has demonstrated acceptable outcomes in patients with systolic dysfunction (SD), particularly in the presence of viable myocardial tissue. (2)

Left ventricular ejection fraction (LVEF) constitutes a prognostic factor in these patients, (3) which could be improved by MR in selected cases.

A substudy of the STICH trial (4, 5) evaluated the usefulness of early detection of myocardial viability (MV) in patients with SD due to myocardial ischemia. The results of the study indicate that the presence of MV is not decisive to predict LVEF improvement. This conclusion has been challenging, since the presence of MV has been historically considered essential.

In turn, other variables have been related with LVEF improvement, as the presence of angina, R waves in the electrocardiogram (ECG) (6) and complete revascularization. On the other hand, HF, electrocardiographic signs of fibrosis (Q waves) (7) and evidence of ventricular remodeling have been identified with absence of LVEF recovery.

The aim of this study was to analyze the variables associated with LVEF improvement in patients with CAD and SD undergoing surgical MR.

METHODS

We analyzed a database which included consecutive patients with ischemic-necrotic cardiomyopathy and SD (LVEF <50% measured by transthoracic echocardiography) who underwent MR surgery. Patients with associated primary valvular heart disease were excluded as SD could be attributed to this condition, and patients with follow-up <6 months after surgery were also excluded (Figure 1) as this time period was considered insufficient to evaluate the adaptation of the myocardium to revascularization.

In areas with high suspicion of necrosis, MV was defined as:

- SPECT perfusion imaging: presence of reversible perfusion defects with at least 50% of tracer uptake compared with a normal segment, greater uptake after nitrate administration or preserved wall thickness on gated images;
- Stress echocardiography: presence of biphasic response after administration of intravenous dob utamine (increased contractility in altered segments at low dose and worsening at high dose).
- Cardiac magnetic resonance imaging: presence of late gadolinium enhancement <50% of wall thickness.

All patients underwent transthoracic echocardiography to evaluate LVEF before and at least 6 months after surgery, thus minimizing myocardial stunning and adaptation to revascularization. Left ventricular ejection fraction improvement after revascularization was defined as an increase of LVEF ≥5%, estimated by Simpson's rule, compared to preoperative values (8-10). Both studies were performed by one of the two staff members of the echocardiography laboratory who were blind to the clinical variables of the patients.

Perioperative variables were defined according to the 2012 SAC Consensus Statement on Cardiovascular Recovery (11), considering:

- Perioperative ischemia: transient ST-T changes, elevated CK-MB levels above the expected values or new wall motion abnormalities.
- Low cardiac output: hypotension, oliguria, cardiac index <2 L/min/m2 or inotropic drug requirement.

Statistical analysis

All the statistical calculations were performed using SPSS 19.0 statistical package. Results are expressed as mean, median or range. Continuous variables were analyzed using Student's t test and the chi square test to analyze discrete variables. A p value < 0.05 was considered statistically significant. A binary logistic regression analysis was performed to establish the relationship between the variables and LVEF improvement.

Ethical considerations

The study protocol was revised and approved by the Institutional Bioethics Committe. An informed consent was not requested as it was a retrospective study based on a historical record.

RESULTS

The cohort consisted of 95 patients; 91.6% were men and mean age was 63±10.2 years. Hypertension was the most prevalent risk factor (72.6%), followed by smoking habits (63.1%) and diabetes (40%). A history of myocardial infarction was present in 27.4% of patients and 15.8% had undergone percutaneous revascularization. Only 5.3% had been hospitalized due to HF. Angina was the most prevalent symptom in 67.4% of cases and 20% of patients had signs of pump failure

Q waves were present in 41% of patients: 53.8% in the anterior wall and 21.1% had absence of R waves in precordial leads.

The echocardiogram showed the following results: left ventricular diastolic dimension was 58.5±7.2 mm; mean LVEF was 36.9 ±6.4% (range 20-49%), and 43.2% presented severe left ventricular dysfunction (<35%): 56.8% presented akinetic segments and 5.3% had dyskinesia.

Seventy-one patients (74.7%) underwent evaluation of MV before surgery. Myocardial perfusion SPECT scan was used in 57.9% of cases, and identified MV in 81.8%. The remaining patients were evaluated using stress echocardiography and cardiac magnetic resonance imaging. Myocardial viability was identified in 78.8% of the patients evaluated.

The mean number of affected vessels with significant stenosis was 2.75 ± 0.5. The left anterior descending coronary artery presented significant stenosis in 95.8% of cases and the left main coronary artery was affected in 58.9%.

Cardiopulmonary bypass was used in 85.3% of MR surgeries. The mean percentage of graft implantation was 3.3 ± 0.9 and complete revascularization was accomplished in 86.3% of patients. During the immediate postoperative period, 12.6% presented perioperative ischemia and 28.4% low cardiac output.

Treatment at discharge included beta blockers (80%), angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (62.1%) and aldosterone receptor antagonists (41%).

Echocardiogram was performed during a mean follow-up of 16.8 ± 9.7 months. Significant improvement of LVEF was observed (36.9±6.4% vs. 43.3±10.6%; p=0.002): 26.3% presented normal systolic function and only 25.3% had severe left ventricular dysfunction (Figure 2). Left ventricular ejection fraction improvement was seen in 58 of 95 patients, resulting in 61.1% prevalence of transient LV dysfunction.

Univariate analysis to evaluate LVEF improvement after revascularization (Group I: no improvement; Group II: LVEF improvement ≥5%) was performed on variables of clinical relevance, those associated with the presence of fibrosis or preoperative ventricular remodeling and those related with surgery. Presence of previous angina, lack of signs of necrosis, presence of MV, complete MR and low rate of perioperative complications (ischemia and low cardiac output) were significantly higher in Group II (Table 1). All the variables with a p value ≤0.1 at univariate analysis and with prevalence >2% underwent multivariate analysis to determine the independent predictors of LVEF improvement after MR (Table 2). The presence of documented preoperative MV was the most significant predictor of LVEF improvement (OR 1.818; 95% CI 1.422-1.943; p=0.004), followed by the absence of postoperative ischemia.

Table 1. Univariate analysis

LVEF improvement	Goup I (n=37) No impovement	Group II (n=58) LVEF impovement	p
Age	62.9±9.7	62.9±9.7	0.7
Male sex	91.9%	91.9%	0.9
Diabetes mellitus	43.2%	43.2%	0.6
Previous AMI	29.7%	29.7%	0.6
Previous HF	5.4%	5.4%	0.9
Angina	54.1%	54.1%	0.02
CHF	24.3%	24.3%	0.4
Presence of Q waves	54.1%	54.1%	0.04
Absence of R waves	32.4%	32.4%	0.03
Preoperative LVEF	38.1±5.7	38.1±5.7	0.1
LVDD >70 mm	13.5%	13.5%	0.15
Akinesia	62.2%	62.2%	0.4
Dyskinesia	8.1%	8.1%	0.3
Myocardial viability	37.8%	37.8%	0.003
Complete revascularization	75.5%	75.5%	0.016
Absence of perioperative ischemia	27%	27%	0.001
Low postoperative cardiac output	40.5%	40.5%	0.036

AMI: Acute myocardial infarction. HF: Heart failure. CHF: Congestive heart failure. LVEF: Left ventricular ejection fraction. LVDD: Left ventricular diastolic diameter.

DISCUSSION

Heart failure is the leading cause of disability and cardiovascular death affecting millions of people. (12, 13) Myocardial revascularization is an adequate therapeutic option with potential benefit in adequately selected patients, as the risk of the procedure is high. (14) Therefore, many authors have postulated the importance of detecting MV to differentiate patients with predominant fibrosis and ventricular remodeling from those with hibernating or stunned myocardium who could obtain LVEF improvement after revascularization. (15) In our series, the prevalence of transient left ventricular dysfunction was 61%.

The substudy of the STICH trial (4) published in 2011 analyzed the impact of MV on the revascularization outcome of patients with LVEF <35%. They analyzed MV in 601 patients included in the initial study by stress echocardiography or SPECT scan. Univariate analysis revealed that patients with viable myocardium had higher overall survival (HR 0.64; 95% CI, 0.48 to 0.96), higher cardiovascular survival (HR, 0.61; 95% CI, 0.44 to 0.84) and higher survival from a composite of death and hospitalization for cardiovascular causes (HR, 0.59; 95% CI, 0.47 to 0.74) After adjusting for prognostic values, multivariate analysis showed that the relationship between MV and primary and secondary outcomes was not significant.

The main limitations of this substudy are due to the fact that only 19% of patients had viable myocardium. This could have influenced subsequent clinical decision making as there was a non-significant trend toward greater rates of revascularization in those patients who had undergone MV assessment. Despite this methodological limitation could generate uncertainty about this perspective, data from this study question the importance of MV to predict events. In our study, multivariate analysis identified the presence of MV as the only preoperative variable to predict events.

Left ventricular ejection fraction improvement after MR not only depends on the surgical procedure (skill, complete revascularization, cardiopulmonary

Table 2. Multivariate analysis

Variable	OR	95% CI	p
Angina	1.516	0.350 – 1.858	0.246
Presence of Q waves	1.578	0.755 – 1.857	0.118
Absence of R waves	1.721	0.739 – 1.938	0.097
Preoperative LVEF	1.104	0.996 – 1.200	0.058
Myocardial viability	1.818	1.422 – 1.943	**0.004**
Complete revascularization	1.638	0.270 – 1.924	0.362
Absence of perioperative ischemia	1.908	1.328 – 1.988	**0.019**
Low postoperative cardiac output	1.289	0.120 – 1.825	0.633

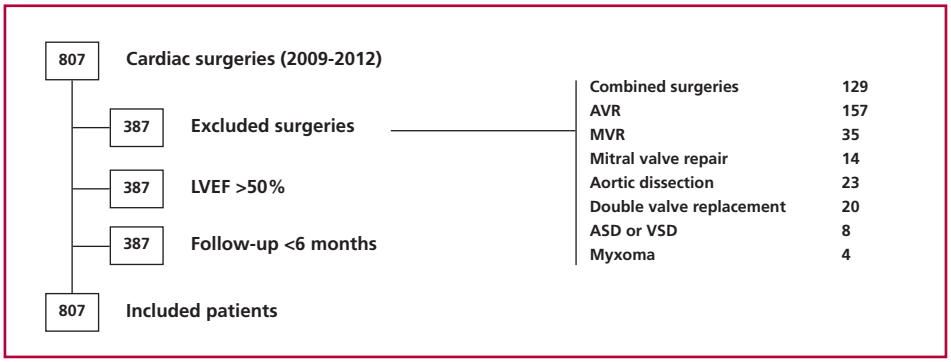

Fig. 1. Patient selection

LVEF: left ventricular ejection fraction. AVR: aortic valve replacement. MVR: Mitral valve replacement ASD: atrial septal defect. VSD: ventricular septal defect

bypass, ischemic time or type of myocardial protection) but also on other postoperative variables as drug therapy. Perioperative ischemia is a potential complication in this group of patients which can influence the long-term outcome. We demonstrated that postoperative ischemia had a significant association with lack of long-term LVEF improvement, even in patients with documented MV. The use of pharmacological agents could have influenced LVEF improvement.

Study limitations

Our study is a descriptive analysis performed in a single center of a young adult population with moderate left ventricular dysfunction, predominant manifestation of angina, high prevalence of left main coronary artery disease and low prevalence of HF. These characteristics could be associated with a high prevalence of MV.

The 5% cut-off point to determine LVEF improvement could also be considered low. Although this value was chosen based on multiple previous publications, it should be pointed out that the variability of Simpson's rule, estimated in up to 4%, is very close to the value used.

CONCLUSIONS

The detection of preoperative MV in the study population was independently associated with LVEF improvement 6 months after revascularization. The presence of ischemia during the immediate postoperative period was an independent variable associated with lack of improved SD.

Conflicts of interest

None declared. (See author´s conflicts of interest forms in the web / Supplementary Material)

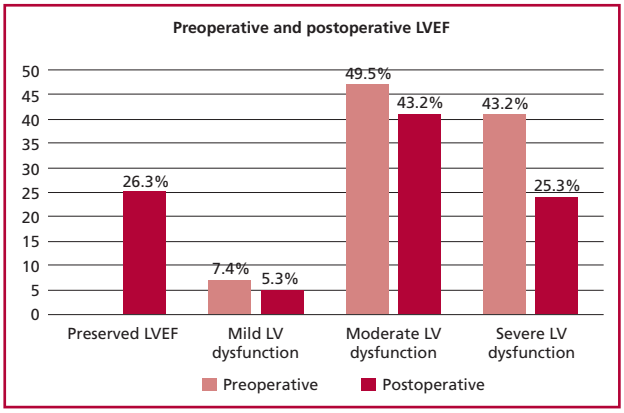

Fig. 2. Echocardiographic follow-up

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