

## CLINICAL SCIENCE

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### SURGICAL MYOCARDIAL REVASCULARIZATION OF PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND SEVERE LEFT VENTRICULAR DYSFUNCTION

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**OBJECTIVE:** To determine long-term survival, identify preoperative factors predictive of a favorable outcome, and assess functional improvement after coronary artery bypass grafting in patients with advanced left ventricular dysfunction.

**METHODS:** Between 1995 and 2001, 244 patients who underwent coronary artery bypass grafting and had a preoperative left ventricular ejection fraction less than or equal to 35% were included. Left ventricular ejection fraction was determined by uniplanar or biplanar ventriculography during left heart catheterization. Indication for surgery was predominance of tissue viability. Functional improvement was evaluated through echocardiography and gated scintigraphy at exercise/ rest. Survival was determined by Kaplan-Meier analysis.

**RESULTS:** Mean left ventricular ejection fraction was 29±4% (ranged from 9% to 35%). An average of 3.01 coronary bypass grafts per patient were performed. In-hospital mortality was 3.7% (9 patients). The 4-year survival rate was 89.7%. Multivariate correlates of favorable short- and long-term outcome were preoperative New York Heart Association Functional classification for congestive heart failure class I/II, lower PAsP, higher left ventricular ejection fraction and gated left ventricular ejection fraction Ex/Rest ratio >5%. Left ventricular ejection fraction rise from 32±5% to 39±5%,  $p < 0.001$ . Gated left ventricular ejection fraction at exercise/ rest increased markedly after surgery: from 27±8%/ 23±7% to 37±5%/ 31±6%,  $p < 0.001$ .

**CONCLUSIONS:** In selected patients with severe ischemic left ventricular dysfunction and predominance of tissue viability, coronary artery bypass grafting may be capable of implementing preoperative clinical/ functional parameters in predicting outcome as left ventricular ejection fraction and gated left ventricular ejection fraction at exercise/ rest.

**KEYWORDS:** Coronary artery bypass grafting surgery. Left ventricular dysfunction. Myocardial revascularization. Functional improvement. Preoperative predictive factors.

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## INTRODUCTION

Coronary artery bypass grafting (CABG) has achieved a well-established role on the management of patients with coronary artery disease (CAD) and left ventricular dysfunction, providing long-term benefits superior to medical therapy.<sup>1-5</sup> However, when considering patients with severe left ventricular dysfunction (left ventricular ejection fraction [LVEF] <30%), such a success was obtained

very gradually. Provided by the advances on preoperative care stabilization, such as by the prophylactic use of intraaortic balloon pump (IABP),<sup>6-8</sup> on surgical technique by means of new cardioplegic solutions and shorter cross clamp and cardiopulmonary bypass times, associated with the improvement on intensive postoperative care, in-hospital mortality rates decreased about four times<sup>9-19</sup> during the last two decades, which makes the procedure a very suitable implement for the management of these particular population. Nevertheless, a judicious evaluation of preoperative clinical and functional parameters should be undertaken when selecting patients for surgery, especially for those with extremely poor function.

The present retrospective study was performed to determine long-term survival, identify preoperative factors predictive of a favorable outcome, and assess functional improvement after CABG in patients with advanced left ventricular dysfunction.

## MATERIALS AND METHODS

All patients who underwent CABG between 1998 and 2004, and who had a preoperative LVEF $\leq$ 35% were included in this analysis. There were 153 male and 91 female patients. This study was approved by Ethics Committee. The LVEF was estimated by either uniplanar or biplanar ventriculography during left heart catheterization (table 1).

Data were recovered retrospectively from medical records and congestive heart failure class was rated using classification of New York Heart Association.

Indication for surgery was based on predominance of tissue viability, defined as maintained Thallium-201 uptake in more than 50% of dyssynergic segments at rest.

All procedures were performed using cardiopulmonary bypass and hypothermia of 32° Centigrade. Roller pump and membrane oxygenators were used in all of these procedures. Distal anastomoses were performed during cross clamp time and aortic anastomoses were carried out using tangential aortic clamping with empty fibrillating or beating heart. Total number of grafts was 736. Mean number of grafts per patient was 3.01 (77% with internal thoracic artery) and 17% had concomitant mitral valve replacement or repair (table 2). Cold crystalloid cardioplegia (St. Thomas solution) insertion was antegrade and intermittent (into grafts being already constructed).

Patients performed bidimensional echocardiography and gated scintigraphy before surgery and at a median time of 12 months after that, in order to establish functional improvement.

### Statistical methods

All data are presented as proportions or as mean $\pm$ standard

deviation. Comparisons of means as appropriate were determined by using paired t-tests. Difference of proportions was evaluated by using Fisher exact test. Univariate analysis was employed to determine the association between concomitant variables and death. Multivariate analysis was performed by logistic regression analysis. Survival was determined by Kaplan-Meier analysis. Statistical significance was considered with  $p < 0.05$ . All analysis were performed by SPSS 10.0 statistical software package.

## RESULTS

The mean age of patients was 61 $\pm$ 7 years old. Risks for coronary artery disease are shown in table 1. Fifty-nine percent of patients had previous myocardial infarction. Prior revascularization and prior percutaneous transluminal coronary angioplasty were present in 24% and 49%, respectively. Seventy-two percent of patients had angina at the time of operation. Class III or IV of New York Heart Association Functional classification for congestive heart failure (NYHA FCCHF) was present in more than 41% of patients and 87% had multivessel disease. Mean LVEF was 29 $\pm$ 4% (ranged from 9% to 35%) and mean LVDP was 32 $\pm$ 7 mmHg (ranged from 11 to 44 mmHg). Thirty-one patients (12.7%) had LVEF <15%, 140 (57.4%) between 16% and 25%, and 73 (29.9%) between 26% and 35% (table 1). After four years of follow-up, we had 94% of patients included in study.

An average of 3.01 coronary bypass grafts per patient were performed (77% with internal thoracic artery) and 17% had concomitant mitral valve replacement or repair (table 2).

Mean cardiopulmonary bypass time was 65 min (40–92), mean cross clamp time was 42 min (20–51).

Morbidity according to preoperative LVEF are shown in table 3.

In-hospital mortality was 3.7% (9 patients). Causes of death included hemorrhage (4 patients), infection (3 patients) and myocardial infarction (2 patients). The 4-year survival rate was 89.7%. There were 16 (6.5%) cases of stroke in post-operative. In-hospital mortality was as high as 13% for patients with LVEF <15%, 25% for PAsP >70mmHg, and 10% for CHF IV patients. Kaplan-Meier survival curves according to preoperative parameters are shown in figure 1.

Multivariate analysis showed positive correlation between favorable short and long-term outcome and preoperative NYHA FCCHF class I/II ( $p=0,0072$ ), lower PAsP ( $p < 0,0001$ ), higher LVEF ( $p=0,0001$ ), and gated LVEF Ex/Rest ratio >5% ( $p < 0,0001$ ). At a median time of 12 months after surgery, 201 patients repeated bidimensional echocardiography and 173 patients performed radioisotopic evaluation of LVEF. LVEF rose from 32 $\pm$ 5% to 39 $\pm$ 5%,

**Table 1 - Baseline characteristics**

	n = 244
Age, y	61±7
Male sex, %	153 (62.7)
Female sex, %	91 (37.3)
Medical history, %	
Hypertension	75 (30.7)
Hypercholesterolemia	82 (33.6)
Diabetes mellitus	41 (16.8)
Smoking	93 (38.1)
Previous MI	144 (59.0)
Months after MI	5.3±1.6 (2.5-49)
Site of MI, %	
undefined or LBBB	62 (43)
anterior	56 (38.9)
inferior	29 (20.1)
lateral	7 (4.9)
Angina present at surgery, %	175 (71.7)
NYHA FCCHF, %	
I	58 (23.8)
II	85 (34.8)
III	62 (25.4)
IV	39 (16.0)
Cine and hemodynamic data	
Uniarterial, %	32 (13.1)
Biarterial, %	121 (49.6)
Triarterial, %	91 (37.3)
LVEF, %	29±4 (9-35)
SBP, mm Hg	128±21 (91-163)
DBP, mm Hg	77±11 (65-102)
PAsP, mm Hg	57±20 (24-83)
PAAdP, mm Hg	29±21 (13-47)
LVEDP, mm Hg	32±7 (11-44)

Values represent means±SD unless stated otherwise. MI indicates myocardial infarction; LBBB, left bundle branch block; NYHA FCCHF, New York Heart Association Functional classification for cardiac heart failure; LVEF, left ventricular ejection fraction; SBP, systolic blood pressure; DBP, diastolic blood pressure; PasP, pulmonary artery systolic pressure; PadP, pulmonary artery diastolic pressure; and LVEDP, left ventricular end-diastolic pressure

**Table 2 - Surgical treatment**

All grafts	736
Left internal thoracic artery	189
Right internal thoracic artery	81
Radial artery	83
Safena vein	83
Grafts/ patient	3.01
Mitral valve replacement, %	30 (12.3)
Mitral valve repair, %	11 (4.5)

**Table 3 - Morbidity according to preoperative LVEF**

	<15%	16-25%	26-35%	p value*
n of patients	31	140	73	
ICU length-of-stay, days	12±3	7±5	4±4	£0.001
Hospital length-of-stay, days	29±5	18±5	16±3	£0.001
Dob and/or nor use, %	31 (100)	14 (10)	22 (30.1)	£0.001
ARF, %	15 (48.4)	13 (9.3)	8 (11)	£0.001
Infection, %	14 (45.1)	10 (7.1)	5 (6.8)	£0.001
IABP use, %	25 (80.6)	60 (42.8)	8 (11)	£0.001

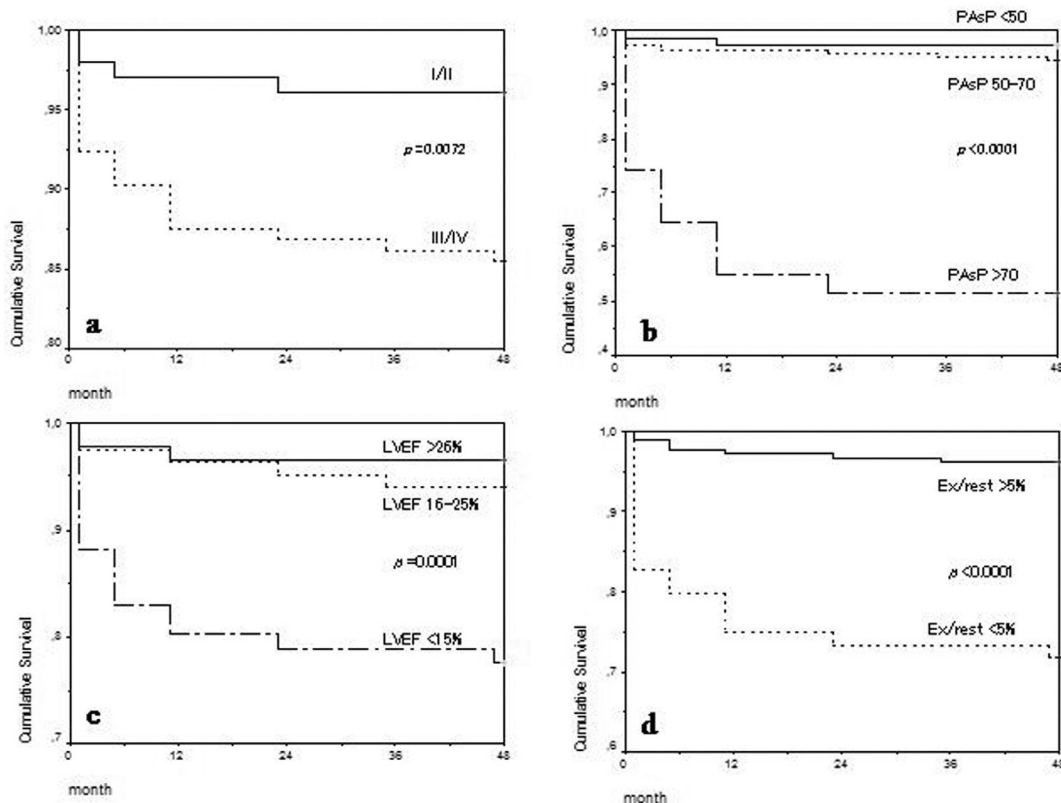
Values represent means±SD unless stated otherwise. Dob indicates dobutamine; nor, norepinephrine; ARF, acute renal failure; IABP, intra-aortic balloon pump. \* For means, p value calculated by ANOVA oneway test; for proportions, Chi-square test. Post-hoc analysis among 3 intervals: for means, p <0.05; for proportions, p <0.001.

p <0.001 (fig. 2). Gated LVEF at exercise/ rest increased markedly after surgery: from 27±8%/ 23±7% to 37±5%/ 31±6%, p <0.001 (figure 2). Class I and II of NYHA FCCHF was present in 30,2% and 41,6% of patients, and Class III and IV in 21,2% and 7,0%, respectively.

**DISCUSSION**

During the last two decades, important advances on the management of patients with severe compromise of left ventricular function have remarkably altered the scenario of grafting as the use of IABP before operation improving survival and reducing hospital stay.<sup>6,20,21</sup> Additionally, advances on myocardial preservation and resuscitation techniques, on surgical procedure by means of shorter cross clamp and cardiopulmonary bypass times, associated with the improvement on intensive postoperative care also collaborated significantly to that changes. Because of all that progress, perioperative mortality rates of 10% to 37%<sup>10,11</sup> was converted to the 2.5% to 8% reported on recent studies.<sup>5,18,19,22-28</sup> In spite of the severe compromise of left ventricular function of our patients (mean LVEF of 29%, ranging from 9% to 35%), we show in-hospital mortality lower than 4% and a 4-year survival close to 90%, in agreement with the current literature. About 49% and 59% of our patients had, respectively, prior percutaneous transluminal coronary angioplasty and myocardial infarction. These data show us one more time the high rate of morbidity in patients included in this study.

In association to such development, careful examination of preoperative clinical and functional parameters also contributes significantly to determine survival, serving as a useful and valuable guide on patient selection for surgery. We observed that some preoperative variables expressively affected outcome. Multivariate analysis showed positive



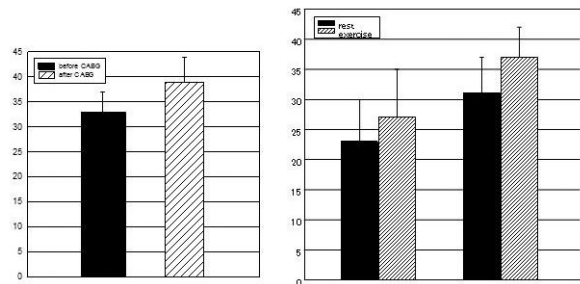
**Figure 1** - Kaplan-Meier cumulative survival curves adjusted for: (a) NYHA FCCHF; (b) PasP (mmHg); (c) LVEF; (d) GATED LVEF exercise/rest

correlation between favorable short and long-term outcome and preoperative NYHA FCCHF class I/II, PA<sub>s</sub>P <50 mm Hg, gated LVEF exercise/ rest ratio >5% and LVEF >16%. Kaplan-Meier curves demonstrate a significant difference in survival when adjusted for each of these variables. Of note, this difference became apparent since the in-hospital period and sustained statistically significant during the 4 years of follow-up (figure 1). On the contrary, when considering the more severely ill patients, in-hospital mortality was as high as 13% for patients with LVEF <15%, 25% for PA<sub>s</sub>P >70mmHg, and 10% for NYHA FCCHF IV patients. Concerning clinical parameters, a report of Trachiotis and colleagues<sup>16</sup> identified older age, female sex, diabetes, and severity of angina class, hypertension, and NYHA FCCHF as predictive of poor survival. Isbir and associates<sup>17</sup> observed a higher mortality for patients with elevated PAP and right ventricular failure, and Milano et al<sup>29</sup> noted depressed cardiac index and elevated LVEDP as important predictors of mortality. Kay and coworkers<sup>30</sup> showed that the probabilities of postoperative complications are 63% and 87% greater for patients with LVEF between 30% and 39% and LVEF <30%, respectively, compared with patients with LVEF >40%. We observed significant higher rates of length of hospitalization, infection, acute renal failure, and IABP and vasoactive drugs use for patients with LVEF <25%. Taken

together, these results raise two provocative issues: if there is a limit for CABG indication and if does exist a situation where it offers no overall benefit over medical therapy. However, they also demonstrate that preoperative clinical, hemodynamic, functional and angiographic parameters are valuable predictors of short- and long-term outcome and capable of interfering with the decision-making process. For the present, it seems reasonable to assess carefully preoperative factors in selection of candidates for surgical treatment, besides different studies have showed that in selected patients with the worst surgical therapy prognosis, medical therapy does not modify the prognosis too.<sup>5,10-12,14</sup>

Another interesting issue refers to the hypothesis of recruitment of the viable muscle (hibernating myocardium), interpreted as the ability to completely revascularize ischemic myocardium. We suppose it is an even more important factor in predicting outcome than the preoperative parameters themselves. Another studies revealed better outcomes for patients who have received a higher number of grafts.<sup>1,3,5,9-14,16,17</sup>

Several studies demonstrate functional improvement after revascularization, either in NYHA or by means of echocardiography results.<sup>10,20,31</sup> Salati and colleagues<sup>32</sup> observed a small but significant global myocardial amelioration, with a 25% rise in LVEF, especially for those



**Figure 2** - Evaluation of myocardial function before and after CABG. (a) echocardiography; (b) GATED at rest/exercise

who underwent complete revascularization and showed a symmetric contraction pattern. We evaluated function through bidimensional echocardiography and, for the first time, gated scintigraphy parameters. We found a mild (12%)

but significant rise in function on echocardiography (figure 2a). Gated LVEF at exercise/ rest increased markedly (27%/26%, respectively) after surgery (figure 2b), which strongly corroborates the feasibility of revascularization.

Our study has limitations because of its retrospective and uncontrolled profile, yet it produces important findings.

## CONCLUSIONS

Our results suggest that in selected patients with severe ischemic left ventricular dysfunction and predominance of tissue viability, CABG may be capable of implement preoperative clinical/ functional parameters in predicting outcome as left ventricular ejection fraction and gated left ventricular ejection fraction at exercise/ rest.

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