

## CLINICAL SCIENCE

# Off-pump coronary artery bypass surgery in selected patients is superior to the conventional approach for patients with severely depressed left ventricular function

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**OBJECTIVES:** Patients with coronary artery disease and left ventricular dysfunction have high mortality when kept in clinical treatment. Coronary artery bypass grafting can improve survival and the quality of life. Recently, revascularization without cardiopulmonary bypass has been presented as a viable alternative. The aim of this study is to compare patients with left ventricular ejection fractions of less than 20% who underwent coronary artery bypass graft with or without cardiopulmonary bypass.

**METHODS:** From January 2001 to December 2005, 217 nonrandomized, consecutive, and nonselected patients with an ejection fraction less than or equal to 20% underwent coronary artery bypass graft surgery with (112) or without (off-pump) (105) the use of cardiopulmonary bypass. We studied demographic, operative, and postoperative data.

**RESULTS:** There were no demographic differences between groups. The outcome variables showed similar graft numbers in both groups. Mortality was 12.5% in the cardiopulmonary bypass group and 3.8% in the off-pump group. Postoperative complications were statistically different (cardiopulmonary bypass versus off-pump): total length of hospital stay (days)—11.3 vs. 7.2, length of ICU stay (days)—3.7 vs. 2.1, pulmonary complications—10.7% vs. 2.8%, intubation time (hours)—22 vs. 10, postoperative bleeding (mL)—654 vs. 440, acute renal failure—8.9% vs. 1.9% and left-ventricle ejection fraction before discharge—22% vs. 29%.

**CONCLUSION:** Coronary artery bypass grafting without cardiopulmonary bypass in selected patients with severe left ventricular dysfunction is valid and safe and promotes less mortality and morbidity compared with conventional operations.

**KEYWORDS:** Coronary artery bypass; cardiopulmonary bypass; off-pump surgery, ejection fraction, cardiac dysfunction.

Caputti GM, Palma JH, Gaia DF, Buffolo E. Off-pump coronary artery bypass surgery in selected patients is superior to the conventional approach for patients with severely depressed left ventricular function. *Clinics*. 2011;66(12):2049-2053.

Received for publication on July 12, 2011; First review completed on July 21, 2011; Accepted for publication August 23, 2011

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## INTRODUCTION

Despite several advances in the treatment of coronary artery disease, many patients, especially those with multivessel disease and complex anatomies, benefit greatly when subjected to surgical treatment. In the presence of ventricular dysfunction, the difference between medical treatment or angioplasty compared with surgical intervention is even more impressive.<sup>1</sup>

Coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) and cardioplegic arrest is considered the gold standard in intervention with well-documented

and consistent outcomes. Nevertheless, it is known that the use of cardiopulmonary bypass has major drawbacks, such as the inflammatory reaction and the potential induction of multiple-organ dysfunction.<sup>2-5</sup>

However, there are a number of advantages of using the technique of myocardial revascularization without cardiopulmonary bypass (off-pump); myocardial ischemia is regional rather than global and the technique is performed only in the area of the coronary artery that is being grafted, which possibly reduces injury to the myocardium and contributes to better results.

In this context, myocardial revascularization without the use of cardiopulmonary bypass was investigated and has demonstrated reduced complications related to cardiopulmonary bypass.<sup>4,6</sup> Furthermore, there is doubt as to the effectiveness of the off-pump procedure, which may be relevant for only certain groups of patients, especially those at high risk.

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No potential conflict of interest was reported.

The presence of severe left ventricular dysfunction is an additional risk factor for CABG, but it has been demonstrated that even in this group of patients, both revascularization techniques may be safe.<sup>7-9</sup>

The aim of this study is to assess the safety and efficacy of myocardial revascularization without cardiopulmonary bypass in patients with markedly depressed ventricular function (<20%) by comparing the results with a series of patients operated upon in the conventional manner.

## METHODS AND PATIENTS

Between January 2001 and December 2005, 217 nonrandomized, consecutive and unselected patients with an ejection fraction less than 0.20 underwent CABG as an isolated procedure; 112 who had undergone operations (the CPB group) and 105 without cardiopulmonary bypass (off-pump group). The inclusion criteria were all patients with an echocardiographic ejection fraction below 20% undergoing CABG in one hospital and operated upon by the same surgical team.

Operating with or without cardiopulmonary bypass was left to the surgeon's discretion. The decision was made during the preoperative evaluation based primarily on the coronary anatomy (mainly position and diameter of the target vessel). Decreased vessel diameter and more diffuse disease were observed in the pump group.

The protocol was approved by the institutional ethics committee (0369/02).

The demographic data collected are shown in Table 1.

Hospital mortality was defined as death during the same hospital stay. Stroke was defined as a new focal deficit or a comatose state lasting more than 24 hours. Acute myocardial infarction was defined as elevated serum CK-MB>30 IU/L, the presence of new electrocardiographic changes indicative of necrosis, or new akinetic segments revealed by echocardiography. Acute renal failure was defined as a postoperative creatinine level greater than 2.0 mg/dL (with a history of prior normal renal function).

## Operative Technique

The decision about whether to perform cardiopulmonary bypass was a personal decision made by the surgical team. Once the decision had been made, standard protocols were followed, including the administration of heparin at a dose of 4 mg/kg. Cardiopulmonary bypass was established through a cannula inserted in the ascending aorta and right atrium, with nonpulsatile blood flow of approximately 2.4 L/min/m<sup>2</sup> associated with moderate hypothermia (28°C) and a membrane oxygenator. Myocardial protection was achieved by antegrade blood perfusion at systemic temperature, with a hyperkalemic cardioplegia infusion, repeated during 3 minutes every 15 minutes to maintain an average pressure above 70 mmHg at the aortic root. Continuous 7-0 polypropylene monofilament sutures were placed. Proximal saphenous vein anastomoses were created in the aorta with a cross clamp during the cardiopulmonary bypass.

In the patients who underwent revascularization without cardiopulmonary bypass, compression or suction stabilizers as well as intracoronary shunts were used at the discretion of the surgical team. Heparin was administered at a dose of 2 mg/kg. Additional maneuvers were used during cardiac exposure in order to maintain cardiac output, including the

**Table 1 - Demographic data in CPB and off-pump groups.**

Variable	CPB		Off-pump		p-value
	n	%	N	%	
Number	112	100	105	100	
Age (median)	67±2		71±3		NS
Sex Female	23	20.5	27	25.7	0.36
Reoperative	11	9.8	18	17.1	0.11
Tobacco Use	29	25.9	26	24.8	0.84
Diabetes	38	33.9	31	29.5	0.48
Chronic Renal Failure	10	8.9	12	11.4	0.54
Hemodialysis	7	6.25	8	7.6	0.69
Body Mass Index > 40	8	7.1	9	8.1	0.69
Emergency Procedure	7	6.25	4	3.8	0.41
Heart Failure (NYHA>3) admission	12	10.7	23	21.9	0.55
Heart Failure (NYHA>3) previous	13	11.6	16	15.2	0.43
Previous Myocardial Infarction	40	35.7	42	40	0.51
Unstable Angina	81	72.3	75	71.4	0.88
Hypertension	59	52.7	70	66.7	0.05
COPD	13	11.6	14	13.3	0.7
Dyslipidemia	48	42.8	40	38	0.47
Atrial Fibrillation	13	11.6	12	11.4	0.96
CVA	8	7.1	4	3.8	0.28
Peripheral Artery Disease	14	12.5	16	15.2	0.55
Left Ventricle Ejection Fraction (%)	17±2		16±3		0.55

NYHA: New York Heart Association.

COPD: Chronic Obstructive Pulmonary Disease.

CVA: Cerebrovascular Accident.

NS: Nonsignificant.

opening of the right pleural space and the use of a deep pericardial traction suture. Continuous 7-0 polypropylene monofilament sutures were placed. The visualization of target vessels was aided by intermittent instillation of saline with a syringe. Proximal anastomoses were performed using a partial occlusion clamp. Site selection was performed by ascending aorta palpation to avoid plaques. No additional methods, such as an epiaortic scan, were used.

The left internal thoracic artery was used in all cases (unless it had been used before or presented with inadequate flow after dissection) for connection to the anterior descending artery. The remaining targets received saphenous vein grafts.

Statistical Analysis was performed using the EPI-INFO of the World Health Organization (WHO), public domain, version 3.3.2, February 2005. The chi-square test was used for nominal variables, and the Mann-Whitney U test was used when appropriate.

## RESULTS

The mortality of patients undergoing intervention with CPB was 12.5% (14/112) versus 3.8% (4/105) in the off-pump group ( $p=0.008$ ). There were no statistically significant differences in the following postoperative complications: acute myocardial infarction — three patients (2.7%) in the CPB group and four (3.8%) in the off-pump group; reoperation for graft occlusion — one patient (0.9%) in the CPB group and one patient (0.95%) in the off-pump group; and congestive heart failure — nine cases (8%) in the CPB group and six (5.7%) in the off-pump group. The other

**Table 2 - Postoperative variables.**

	CPB		Off-pump		p-value
	n	%	n	%	
Grafts	2.6	-	2.15	-	0.06-
LIMA-LAD	105	-	100	-	0.62
ICU stay (days)	3.76	-	2.12	-	0.004
Length of Stay (days)	11.3	-	7.2	-	0.001
IABP use	5	4.5	0	0	0.028
Mechanical Ventilation (hours)	22.3	-	10.2	-	0.02
Pneumonia	12	10.7	3	2.8	0.022
Perioperative Myocardial Infarction	3	2.7	4	3.8	0.95
Acute Renal Failure	10	8.9	2	1.9	0.023
Hemodialysis	4	3.6	1	0.95	0.19
Reoperation (graft occlusion)	1	0.9	1	0.95	0.96
AF (postoperative)	13	11.6	10	9.5	0.62
Bleeding (mL)	654	-	440	-	0.022
Packed Red Blood Cells (units)	3	0.8	2	0.2	0.01
Cardiac Failure	9	8	6	5.7	0.90
Pulmonary Edema	9	8	6	5.7	0.9
LVEF (postoperative) (%)	22	-	29	-	0.02
Mortality	14	12.5	4	3.8	0.008
Stroke	3	2.7	1	0.95	0.34
Reoperation – Bleeding	3	2.7	1	0.9	0.205

LIMA-LAD: Left Internal Mammary Artery to Left Anterior Descending Artery.

ICU – Intensive Care Unit.

IABP – Intra-Aortic Balloon Pump.

AF – Atrial Fibrillation.

LVEF – Left-Ventricle Ejection Fraction.

variables presented significant differences, as described in Table 2, with significant reduction of mortality and morbidity in patients undergoing CABG without cardiopulmonary bypass.

There was no incomplete revascularization in any group and no conversions (cross-over). The descending anterior artery territory was revascularized in all patients. The remaining territories (lateral and right) did not reveal any statistically significant differences between the CPB and off-pump groups.

## DISCUSSION

One of the persistent challenges in coronary disease treatment is treating patients with ventricular dysfunction. It is known that the clinical treatment yields poor results with high mortality.<sup>10</sup> CABG in these patients is challenging, with reduced ventricular function directly reflecting procedure risk and representing an independent risk factor for morbidity and mortality.<sup>11,12</sup> Interestingly, these are the patients who benefit most from surgical treatment.<sup>13</sup>

Although operation with CPB is considered the gold standard, several strategies have been recently used in order to decrease the complications related to its use and to improve outcomes.<sup>14</sup> The nonuse of cardiopulmonary bypass has been shown to be safe and effective, even superior to conventional operations,<sup>7,8</sup> even in patients with left ventricular dysfunction.<sup>15</sup>

This finding would lead to more complications and postoperative mortality in patients with ventricular dysfunction who underwent the procedure with cardiopulmonary bypass. In our study, we observed that the mortality rate, intubation time, ICU and total stay were significantly greater in the group with CPB use. The significantly lower incidence of complications in the off-pump group applied to postoperative bleeding, transfusion

requirements, reoperation for bleeding, acute renal failure, hemodialysis, and stroke. This trend was also observed in the literature.<sup>4</sup>

Criticisms of the procedure without cardiopulmonary bypass addressed the incomplete revascularization, possibly reduced graft patency and long-term results. A common finding in the literature is a reduced number of grafts in the procedures performed without cardiopulmonary bypass, which raises questions about revascularization completeness.

The mortality rate of our sample (12.5% CPB and 3.8% off-pump) is comparable to findings in other series of patients with left ventricular dysfunction operated upon with and without cardiopulmonary bypass. However, most of those series involved an ejection fraction above the average found in our series.<sup>16-18</sup>

Most CABG studies in patients with ventricular dysfunction include patients with an ejection fraction below 35%, which promotes averages well above 20%,<sup>8,19</sup> representing the focus of our study. There is a significant hemodynamics difference between patients with ejection fractions of 20% and 35%.

Survival studies in patients with severe left ventricular dysfunction (EF 18%) after coronary artery bypass grafting in 86 patients demonstrated a mortality rate of 11%, and those who survived showed improvement of left ventricular contraction resulting from a significant decrease in left ventricle diastolic diameter and an increase in left ventricular ejection fraction, with a median survival of 59% at five years and significant improvement in NYHA functional class.<sup>20</sup> These findings are similar to the data recorded for the CPB group of this study.

A large retrospective series comparing patients with ventricular dysfunction who underwent operation with and without cardiopulmonary bypass failed to show

differences between the two groups, even when paired, suggesting that the off-pump procedure is safe and possibly leads to fewer complications in spite of the lack of statistically significant findings.<sup>21</sup>

Admitting that a low ejection fraction is synonymous with a bad ventricle is controversial. There are patients with low ejection fractions who have good functional capacity for years and others with comparable ejection fractions that require high doses of medications and even a heart transplant.<sup>22</sup> Thus, other ways of quantifying the functional cardiac reserve should be used in order to stratify these patients more effectively.<sup>23</sup> That finding may partly explain the differences found in several studies.

The finding of lower complication incidence in the group operated upon without extracorporeal circulation is consistent with the literature, even in patients with markedly reduced ejection fractions. Factors such as shorter duration of intubation and fewer pulmonary complications can be explained by the possibility of cardiopulmonary bypass inducing pulmonary dysfunction secondary to complement activation, neutrophil sequestration in pulmonary microcirculation and an increase in pulmonary capillary permeability, and interstitial pulmonary edema.<sup>24</sup>

The incidence of neurological complications in our sample was low and, although suggested to be lower in the off-pump group, did not reach statistical significance. A larger sample size might be able to more clearly document this difference. However, it is consistent with published findings (1%–5%) showing that most accidents are related to embolic events occurring during cannulation, cardiopulmonary bypass, and aortic surgical manipulation.<sup>25,26</sup>

The observation of minor renal failure in the CPB group is also compatible with literature findings demonstrating that patients undergoing CABG with CPB have a higher risk of developing acute renal failure because of decreased perfusion, the absence of pulsatile flow, excessive hemolysis, embolization of platelet aggregates, and fibrin.<sup>4</sup>

Another interesting finding is the fact that the applicability of the technique is very heterogeneous among different groups, showing that certain groups achieve unsatisfactory results with the off-pump technique.<sup>27</sup> This demonstrates that the procedure is often highly dependent on the skill of the surgical team in performing beating-heart CABG in technically challenging scenarios, such as the presence of severe ventricular dysfunction.

A recent meta-analysis demonstrated higher mortality in patients operated upon without cardiopulmonary bypass, possibly because of higher graft occlusion and a higher rate of incomplete revascularization.<sup>28</sup> Unfortunately, these figures were heavily influenced by the Rooby Trial results, which yielded highly unsatisfactory results and demonstrated several methodological biases.<sup>27</sup>

Finally, studies comparing CABG with and without cardiopulmonary bypass often fail to demonstrate significant differences, especially because of the failure to include patients with multiple risk factors or very low ejection fractions. Recently, the ongoing CORONARY Trial has randomized patients with multiple and significant risk factors for revascularization with and without CPB in order to determine the possible benefits and disadvantages associated with both techniques.

Several limitations are inherent to this study design, such as the fact that there is no randomization. Randomized studies in patients with severe ventricular dysfunction are

unlikely to be conducted, given the diversity of the technical limitations of off-pump CABG, especially in circumflex artery territory in patients with severe dysfunction. Another bias is the selection procedure, based on the surgeon's selection of intraoperative clinical conditions, his or her personal experience, vessel diameter, the position and presence of diffuse disease, and whether or not the procedure was performed using CPB.

A smaller number of grafts in the group without extracorporeal circulation also contributes to the imbalance between the groups (despite not being statistically different), but the fact that complete revascularization rate and risk factors are similar contributes to a more adequate comparison between groups.

This sample follow-up includes only the in-hospital phase; studies of medium- and long-term effects must be conducted in order to determine the durability of this initial advantage in terms of comparative survival, such as hospital readmission, reintervention, and quality of life. Currently the long-term results are under review as part of a separate submission. Another concern is the retrospective analysis, which lacked randomization. Despite this fact, similarity between groups could reduce the selection bias.

Few studies have evaluated patients with severe ventricular dysfunction. Our data show that, even in this group, the morbidity and mortality of the procedure is acceptable and favors the group operated upon without cardiopulmonary bypass.

In this context, the use of cardiopulmonary bypass should be considered in assigning risk scores as well as contribute to the choice of surgical strategy in patients with ejection fractions below 20%. Coronary artery bypass surgery today is safe, efficient and low risk, but poor left-ventricular function still represents a significant risk factor.

## AUTHOR CONTRIBUTIONS

Caputti GM was one of the operating surgeon, also responsible for the research conduction, data collection, and revision and writing of the manuscript. Palma JH was one of the operating surgeon, also responsible for the revision and writing of the manuscript. Gaia DF was responsible for the data collection, revision and writing of the manuscript. Buffolo E was one of the operating surgeon, also responsible for the research conduction and revision of the manuscript.

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