

# Myocardial Revascularization on the Beating Heart After Recent Onset of Acute Myocardial Infarction

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## ABSTRACT

**Objective:** Coronary artery bypass grafting (CABG) after the recent onset of acute myocardial infarction (AMI) is associated with high morbidity and mortality. Myocardial revascularization without cardiopulmonary bypass (CPB) has been proposed as an alternative technique to treat these patients in an attempt to decrease the operative risks.

**Methods:** From January 1995 to June 1999, 518 patients underwent CABG after the recent onset of AMI (1-20 days): 421 patients were revascularized on-CPB and 97 patients off-CPB. Preoperative risk factors (redo operations, congestive heart failure, stroke, extensive calcification of the aorta, and dialysis) were significantly higher in the off-CPB group (p-value < 0.05). Preoperative use of intra-aortic balloon pump (IABP) (off-CPB 5.2% versus on-CPB 2.4%, p-value = NS) and emergent operations (off-CPB 5.2% versus on-CPB 2.6%, p-value = NS) were similar in both groups. Mean number of grafts per patient was 3.46 in the on-CPB group versus 1.82 in the off-CPB group (p-value < 0.005).

**Results:** Actual mortality was 2.9% in the on-CPB group versus 6.2% in the off-CPB group (p-value = NS). Morbidity was comparable in the two groups. Multivariate analysis showed that advanced age, preoperative hemodynamic instability, and left ventricular hypertrophy were independent risk factors for death. Global ischemic time and preoperative hypertension were independently related to postoperative AMI. At univariate and multivariate analysis, CPB was not related to mortality or major postoperative complications.

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**Conclusion:** Multivariate analysis demonstrates that CABG can be performed safely with or without CPB in patients with recent AMI. CPB is not independently related to mortality or major adverse outcomes.

## INTRODUCTION

Cardiopulmonary bypass (CPB) is known to be associated with numerous complications [Anderson 1991, Edmunds 1995]. To decrease morbidity, coronary artery bypass grafting (CABG) has been performed without CPB as an alternative to the conventional techniques. The feasibility of this operation has been demonstrated by a number of investigators [Buffolo 1990, Benetti 1991], even in high risk patients [Moshkovitz 1995, Arom 2000]. Off-pump CABG (OPCABG) has recently been proposed as an alternative technique to treat patients with recent acute myocardial infarction (AMI) [Locker 1999, Mohr 1999]. Although perioperative and midterm results are encouraging, the advantages offered by avoidance of CPB in this highly selective group of patients have not been fully delineated. In the last five years, we have performed over 1500 OPCABG, including a large number on high-risk patients. We herein summarize our total experience with CABG performed with and without CPB in the aftermath of recent AMI. Particular emphasis is given to perioperative results in an attempt to better define whether avoidance of CPB can, independently from other preoperative and intraoperative variables, decrease morbidity and mortality in this highly selective population of patients.

## PATIENTS AND METHODS

This retrospective, non-randomized, single-institution review included 518 consecutive patients who underwent CABG after the recent onset of AMI (1 to 20 days). In 421

Table 1a. Myocardial protection protocol in patients operated on with CPB

Induction:	Antegrade 200/300 cc/min. for 2 min. Retrograde 100/150 cc/min. for 2 min.
Maintenance:	Antegrade 200/300 cc/min. for 1 min. Retrograde 100/150 cc/min. for 1 min. After each distal anastomosis, no later than 20 min.
Reperfusion:	No reperfusion protocol, No terminal warm cardioplegia, No aspartate or glutamate

patients, myocardial revascularization was achieved on CPB. The remaining 97 patients underwent OPCABG. Each type of operation was performed by a different group of surgeons who routinely adopt different operative strategies. The patient referral pattern was different for the two groups. Patient selection was based on the prevalence of preoperative risk factors and, at least at the beginning of our experience with OPCABG, on the patient's coronary anatomic condition. Patients at high risk for conventional CABG were referred for OPCABG in an attempt to reduce postoperative complications. Patients with more extensive coronary artery disease were, in the first three years of our experience (1995-1997), preferably referred to conventional CABG, since present-day techniques of coronary exposure and stabilization were not available. Patients undergoing CABG in combination with other cardiac surgical procedures were excluded from this study.

#### **Surgical Technique: CABG with CPB**

Conventional CABG was performed via median sternotomy. Initiation of CPB was obtained after aortic and right atrial cannulations. Mild systemic hypothermia (32°C) was used in the majority of patients. Different techniques of myocardial protection were utilized, including intermittent antegrade-retrograde cold (5-8°C) blood cardioplegia (344 patients, 82%) and continuous warm (37°C) antegrade-retrograde blood cardioplegia (56 patients, 13%). In the remaining cases (21 patients, 5%), CABG was performed on CPB without arresting the heart (beating heart on-CPB). Reperfusion protocols were not used, and aspartate and glutamate were not added to the reperfusate. The infusion protocols and the cardioplegic formula most commonly adopted are reported in Tables 1a (☉) and 1b (☉). This cardioplegia was used in the majority of patients operated on at our institution since the early 1970s. The distal anastomoses were performed using continuous 7-0 polypropylene suture and the proximal anastomoses were constructed with 6-0 polypropylene suture after aortic side-clamping.

#### **Surgical Technique: OPCABG**

Median sternotomy was used in the majority of patients (85 patients, 87.6%) operated on without CPB. Alternative surgical approaches (left anterior small thoracotomy and left posterior thoracotomy) were used in some of the reoperations (12 patients, 12.4%) to achieve revascularization of target vessels, thereby avoiding the risks of

Table 1b. Cardioplegia formula in patients operated on with CPB

1 Crystalloid solution: 4 cold blood at 5-8°C
PH: 7.4
Kcl: 20 mEq/L for induction, 10 mEq/L for maintenance
Methylprednisolone 1 gm/L
Mannitol 20% 60 ml/L
NaHCO <sub>3</sub> 3 mEq/L

sternal reentry and limiting manipulation of the heart, great vessels, and old vein grafts. Techniques of coronary artery exposure and stabilization have evolved since the first OPCABG was performed in 1995. In the beginning of our experience, all distal anastomoses were performed without coronary stabilization. However, since January 1998, coronary artery immobilization was routinely achieved with mechanical stabilization (CTS, Cupertino, CA) after exposing the target vessels by positioning the heart using four deep pericardial sutures and, later in our experience, with a single suture [Bergsland 1999] placed in the oblique sinus of the pericardium. All distal anastomoses were constructed after placement of a proximal coronary snare for hemostasis, performance of an arteriotomy, and insertion of an intracoronary shunt to prevent regional ischemia [Soltoski 1999]. A CO<sub>2</sub> blower was used to improve visualization, maintaining a bloodless operative field [Teoh 1991]. Seven-0 and 6-0 polypropylene sutures were used for distal and proximal anastomoses. Intraoperative graft patency verification via transit time flow measurement (TTFM, Medistim, Oslo, Norway) has been routinely used since June 1996 to confirm patency of the coronary artery grafts performed off-CPB.

#### **Data Collection and Definitions**

All patients' information, including preoperative data and perioperative and postoperative morbidity and mortality rates, was recorded by trained personnel following the directions of the NYS database form (Form DOH 225a). All patients included in the analysis had been preoperatively diagnosed with AMI, occurring from 1 to 20 days prior to surgical intervention. The diagnosis of preoperative AMI was made by conventional electrocardiogram (EKG) and creatine kinase muscle-brain band (CKMB) than 5% of total, confirmed by the presence of an occluded vessel with regional wall motion abnormality at coronary angiography and ventriculography, respectively.

#### **Statistical Analyses**

Data collected for both study groups were statistically analyzed and compared. Differences between variables were considered significant when the p-value was less than 0.05. Discrete and continuous variables were compared using the  $\chi^2$  test and the Student t-test, respectively. Multivariate stepwise logistic regression analysis was done to identify those preoperative and intraoperative variables independently related to perioperative mortality, cere-

Table 2. Preoperative data in 518 patients operated on after recent onset of AMI

	On-CPB (%)	Off-CPB (%)	p-Value
Age (years)	64.1	66.1	NS
Redo	38 (9)	20 (20.6)	0.002
Previous CVA	21 (5)	14 (14.4)	0.002
Calcified AA	16 (3.8)	10 (10.3)	0.017
Aorto-iliac disease	16 (3.8)	9 (9.3)	0.0033
IV-NTG	70 (16.6)	33 (34)	< 0.005
CHF	73 (18.8)	29 (29.9)	0.018
CRF	15 (3.6)	10 (10.3)	0.014
Renal dialysis	3 (0.7)	5 (5.2)	0.007
Preop IABP	10 (2.4)	5 (5.2)	NS
Emergent CABG	11 (2.6)	5 (5.2)	NS
Urgent CABG	263 (62.5)	58 (59.8)	NS
Elective CABG	147 (34.9)	34 (35.0)	NS

CVA = Cerebrovascular accident, AA = Ascending aorta, NTG = Nitroglycerin, CHF = Congestive heart failure, CRF = Chronic renal failure, IABP = Intra-aortic balloon pump

brovascular accident (CVA), and AMI. CPB was considered as one of the variables in the study. Odds ratio (OR) and p-values were evaluated.

## RESULTS

### Clinical Profile and Outcome

Table 2 (●) summarizes the demographics and preoperative risk factors in the two groups. The rates of redo CABG, preoperative CVA, aorto-iliac disease, renal failure and renal dialysis, congestive heart failure (CHF), and recent use of IV nitrates to control angina were all significantly higher (p-value < 0.005) in the OPCABG group. Table 3 (●) summarizes the angiographic data and the graft/patient ratio in the two groups. It is evident that critical disease of the left circumflex coronary artery was more prevalent in the CPB group (CPB 73.9% versus OPCABG 53.6%, p-value < 0.005). A larger number of grafts per patient was performed in the CPB group (CPB 3.46 versus OPCABG 1.82, p-value < 0.005). No conversion to CPB was necessary in the OPCABG group. Postoperative complications, length of hospitalization, and mortality in the two groups are summarized in Table 4 (●). No significant differences were recorded in morbidity and length of stay. When considering perioperative mortality, a trend for a higher actual mortality was found in the OPCABG group (CPB: 2.9% versus OPCABG: 6.2%, p-value = NS). This difference was less evident when calculating the risk adjusted mortality in the two groups (CPB: 2.2% versus OPCABG: 3.1%).

### Univariate and Multivariate Analysis

To identify and select the perioperative and intraoperative variables related to mortality, CVA, and perioperative AMI in both groups, univariate and multivariate analyses

Table 3. Extent of coronary artery disease in 518 patients and graft/patient ratio

	On-CPB (%)	Off-CPB (%)	p-value
LM 50-69%	24 (5.7)	8 (8.2)	NS
LM 70-100%	17 (4.0)	2 (2.1)	0.041
LAD 50-69%	41 (9.7)	3 (3.1)	NS
LAD 70-100%	313 (74.3)	70 (72.2)	NS
RCA 50-69%	30 (7.1)	5 (5.2)	NS
RCA 70-100%	329 (78.1)	72 (74.2)	NS
LCX 50-69%	27 (6.4)	9 (9.3)	NS
LCX 70-100%	311 (73.9)	52 (53.6)	< 0.005
Graft/patient total	3.46	1.82	< 0.005
Graft/patient 1 CAD	2.06	1.2	< 0.005
Graft/patient 2 CAD	2.98	1.55	< 0.005
Graft/patient 3 CAD	3.72	2.82	< 0.05

LM = Left main, LAD = Left anterior descending, RCA = Right coronary artery, LCX = Left circumflex, 1 CAD = 1 vessel disease, 2 CAD = 2 vessel disease, 3 CAD = 3 vessel disease

were conducted in the overall population. At univariate analysis, 11 variables correlated either to mortality, CVA, or AMI (Table 5, ●). At multivariate analysis, only preoperative diagnosis of left ventricular hypertrophy (LVH), hemodynamic instability, and age (older than 65 years) were independently related to mortality (Table 6, ●). Preoperative CVA and aorto-iliac disease were identified as risk factors for perioperative CVA (Table 6, ●). History of arterial hypertension and intraoperative global ischemic time were independently related to perioperative AMI (Table 6, ●). CPB was not related to mortality, CVA, or AMI.

## DISCUSSION

Avoidance of CPB for CABG has been recently proposed as an alternative to traditional methods of myocardial revascularization [Buffolo 1990, Benetti 1991]. Initial results are encouraging, and treatment of patients with high preoperative risk factors has been recently specifically addressed [Moshkovitz 1995, Arom 2000]. Modern techniques of CPB and myocardial protection are remarkably

Table 4. Perioperative results in 518 patients

	On-CPB (%)	Off-CPB (%)	p-value
No complications	351 (83.4)	84 (86.6)	NS
Transmural AMI	9 (2.1)	1 (1.0)	NS
CVA	8 (1.9)	1 (1.0)	NS
Revision for bleeding	12 (2.9)	0 (0)	NS
Post-op IABP	36 (8.5)	7 (7.2)	NS
Actual mortality	12 (2.9)	6 (6.2)	NS
Risk-adjusted mortality	2.2	3.1	

CVA = Cerebrovascular accident, IABP = Intra-aortic balloon pump

Table 5. Univariate analysis in 518 patients

	Mortality p-value	Peri-op CVAp-value	Peri-op AMI p-value
Age (> 65 years)	0.025		
CHF	< 0.005		
Hemodynamic instability	< 0.005		
Surgical priority	0.009		
LVH	0.002		
CVA		0.001	
Aorto-iliac disease		< 0.005	
CRF		0.019	
Global ischemic time			< 0.005
Female sex			0.015
HTN			0.044

CHF = Congestive heart failure, LVH = Left ventricular hypertrophy, CVA = Cerebrovascular accident, CRF = Chronic renal failure, HTN = Hypertension

safe when used in the general population. However, patients with significant preoperative comorbidities may not tolerate the side effects of CPB, and OPCABG has been proposed as an alternative to decrease morbidity and mortality in these patients [Moshkovitz 1995, Arom 2000]. The referral pattern for OPCABG is changing and, in our daily practice, patients with high incidence of comorbidities are being referred to myocardial revascularization. These high-risk patients include those with previous operations, previous stroke, extensive calcification of the ascending aorta, renal failure, congestive heart failure (CHF), and recent AMI. Myocardial infarction is an independent predictor of CABG mortality even after adjustments for other risk factors [Floten 1989, Fremes 1991]. The mortality rate in patients operated on early after recent AMI varies from 3.2% to 16% [Hochberg 1984, Applebaum 1991, Creswell 1995, Every 1996, Lee 1997]. The STS national database (1995-96) indicates a risk-adjusted mortality ranging from 3.88% to 3.94% in this group of patients (prior MI 1-21 days). Avoidance of CPB has been shown to reduce perioperative mortality of patients operated on early after AMI [Locker 1999, Mohr 1999].

In these retrospective studies, the perioperative mortality was 5% in a group of 40 emergent OPCABG patients operated on within 48 hours after an AMI. A significantly

higher mortality rate (24%) was recorded in the on-CPB counterpart. A lower mortality rate (3.9%) was observed by Allen et al. [Allen 1993] in a prospective multicenter study including 156 emergent CABG patients operated upon on-CPB within 24 hours of AMI. Most of the patients in this study were in cardiogenic shock and a meticulous protocol for myocardial protection and reperfusion was proposed to decrease mortality and morbidity [Allen 1993]. Allen suggested five minutes of warm cardioplegic induction with a 37°C substrate enriched (glutamate/aspartate), hyperkalemic (KCl 18-20 mEq/L) blood cardioplegic solution infused in an antegrade and retrograde fashion, followed by an additional three minutes of cold (4-8°C), hypokalemic (KCl 8-10 mEq/L) solution. After completion of each distal anastomosis or no later than 20 minutes thereafter, multidose cold blood cardioplegia was delivered for one minute into the aorta and into each graft, followed by one minute of retrograde perfusion. Before aortic unclamping, warm (37°C), diltiazem-containing, substrate-enriched cardioplegia was given for two minutes. After removal of the aortic clamp, controlled reperfusion of the graft supplying the recently infarcted area was administered for an additional 18 minutes [Allen 1993]. Postoperatively, global and regional wall motion evaluation was assessed with echocardiography and/or radionuclide ventriculography. Regional wall motion recovered significantly in 87% of the treated patients [Allen 1993].

Our retrospective, non-randomized analysis was conducted on a somewhat different cohort of patients with occurrence of AMI ranging from 1 to 20 days prior to surgery. The incidence of preoperative cardiogenic shock was low (0.2% on-CPB, 1% off-CPB) and the majority of the patients were operated upon on-CPB, reflecting the fact that most of the surgeons in our institution do not routinely perform OPCABG. Postoperative evaluation of global and local wall motion abnormalities was not routinely performed. Correct interpretation of our postoperative findings may be difficult considering that the analyses are limited to the univariate comparison between these two very different groups. Due to patient selection, the prevalence of preoperative risk factors was significantly higher in the off-CPB population. This fact could negatively influence mortality and morbidity rates. For this reason, multivariate analysis, using the logistic regression model, was used to determine which of the preoperative and intraoperative variables were

Table 6. Multivariate analysis in 518 patients

	Mortality	Peri-op CVA	Peri-op AMI
LVH	P = 0.017 OR = 7.5		
Hemodynamic instability	P = 0.007 OR = 1.2		
Age (> 65 years)	P = 0.019 OR = 1.1		
Pre-op CVA		P = 0.01 OR = 9.6	
Aorto-iliac disease		P = 0.005 OR = 3.3	
Pre-op HTN			P = 0.04 OR = 8.4
Global ischemic time			P < 0.005 OR = 1.0

OR = Odds ratio, LVH = Left ventricular hypertrophy, CVA = Cerebrovascular accident, HTN = Hypertension

independently related to postoperative mortality and complications (stroke and perioperative AMI). CPB was considered among the variables in the analysis. Our findings at multivariate analysis are similar to other authors' results, in which patient age and hemodynamic instability have been found to be independent risk factors for perioperative mortality of on-CPB CABG after recent onset of AMI [Hochberg 1984, Applebaum 1991, Creswell 1995, Every 1996, Lee 1997]. CPB per se was not related to perioperative mortality. Different results have been reported by other groups using multivariate analysis and risk adjustments [Calafiore unpub., Arom 2000, Puskas 2000] for a less morbid population of CABG patients operated on with and without CPB. When considering the risk of postoperative adverse outcomes, preoperative CVA and aorto-iliac disease were strongly related to postoperative CVA, with an odds ratio of 9.67 and 3.33, respectively. These results are supported by the existing literature [Faggioli 1990, Berens 1992, Wareing 1992]. The difference in neurologic complications between on- and off-CPB remains unclear. Our study shows that, at least in this selected group of patients, CPB is not an independent risk factor for postoperative stroke. In a recent analysis, Calafiore et al. [unpub.] achieved different conclusions, demonstrating a close relationship between the use of CPB and perioperative stroke, with an odds ratio greater than 3. Similar conclusions have been reported by Arom et al. after comparing the incidence of postoperative CVA in high-risk CABG patients operated on with and without CPB [Arom 2000]. In another recent analysis, Taggart et al. have shown no difference in early decline and recovery of neurocognitive function between patients undergoing CABG with and without CPB, suggesting that CPB may not be the major determinant of postoperative cognitive deficits [Taggart 1999].

The rate of postoperative AMI has been proposed to be different for on-CPB versus off-CPB revascularization [Bouchard 1998, Arom 2000]. Univariate analysis showed no significant differences between the two groups in our study (2.1% on-CPB versus 1.0% off-CPB). When logistic regression was applied to the overall population, global ischemic time (i.e., aortic cross-clamp time) was included as one of the variables in the study. A time equal to zero was assigned to the off-CPB patients because intracoronary shunts were routinely used in this group. Cross-clamp time was related to perioperative AMI with an odds ratio of only 1.02. This data should be interpreted cautiously. First, the odds ratio hardly reaches statistical significance. Secondly, the effects of global ischemic time are obviously related to the techniques of myocardial protection, and it is possible that no correlation between the cross-clamp time and AMI would have been observed if the techniques of myocardial reperfusion and cardioplegia enrichment [Beyersdorf 1993, Buckberg 1995] normally suggested for this population of high-risk patients had been used.

Some comments need to be made on the graft/patient ratio noted in the two groups. At univariate analysis, a significant difference between the two groups was noted (3.46 on-CPB versus 1.82 off-CPB,  $p$ -value < 0.005). This difference persisted when regrouping the patients by num-

ber of diseased coronary arteries (Table 3, ⊙). These findings can be explained by the fact that, at least in the first years of our experience with OPCABG, patients with coronary artery disease involving the lateral and posterior surface of the heart were preferably referred to surgical revascularization on-CPB. Recent techniques of stabilization and cardiac positioning [Bergsland 1999, Soltoski 1999] have extended the applicability of OPCABG to all patients. A review of our patients recently referred to OPCABG shows a graft/patient ratio of 2.8. In this study, using multivariate analysis, the number of grafts per patient did not independently correlate either to mortality or to other immediate adverse outcomes. Although the number of grafts performed has no important impact on immediate perioperative results, its effects on long-term outcome may be different. Recent short-term follow-up studies [Gundry 1998, Arom 2000] have shown that, despite comparable actual mortality rates in the on-CPB and OPCABG groups, recurrence of angina and reintervention are more common in the off-CPB population. This could be related to a tendency to perform, at least in the initial phases of the learning curve for OPCABG, incomplete revascularization [Gundry 1998, Arom 2000]. Medium and long-term follow-up studies are necessary before a definitive conclusion can be made. Although our analysis lacks any sort of clinical or angiographic follow-up, intraoperative graft patency verification via transit time flow measurement (TTFM) [D'Ancona 2000 (in press)] was obtained in the majority of the patients operated on without CPB. All grafts performed were patent, at least immediately prior to chest closure.

## LIMITATIONS

This is a retrospective, non-randomized study comparing two cohorts of patients with different preoperative risk factors. There is no clinical or angiographic follow-up. Patients operated upon on-CPB did not receive optimal myocardial protection with the suggested protocols of controlled reperfusion. Patients operated on at the beginning of our OPCABG experience are included in the analysis and, for this reason, the graft/patient ratio may be significantly lower in the off-CPB population, indicating that a certain number of patients were incompletely revascularized. Global and regional wall motion abnormalities were not investigated perioperatively. A multivariate analysis was performed to evaluate the independent correlation between CPB and mortality and/or morbidities. The results of the analysis are derived from experience in a limited subgroup of patients and cannot be applied to the overall population. Furthermore, although the independent risk factors for mortality and morbidity are identified by multivariate analysis, no conclusion can be made regarding the possible interaction between CPB and other preoperative variables. Prospective randomized studies with longitudinal clinical and angiographic follow-up are needed to better define the real advantages and limits of this new surgical strategy in the overall population and in groups of high-risk patients.

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