Primary OPCAB as a Strategy for Acute Coronary Syndrome and Acute Myocardial Infarction

(#2003-341043)

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ABSTRACT

Background: Conventional coronary artery bypass graft (CABG) surgery using cardiopulmonary bypass (CPB) carries higher mortality and morbidity for patients undergoing surgery during acute coronary syndrome (ACS). The aim of this retrospective study was to evaluate potential benefits of avoiding CPB by instead performing off-pump CAB (OPCAB) during surgery on patients in ACS.

Methods: Among 624 patients who underwent OPCAB between January 1999 and June 2001, 143 underwent surgery during ACS (group 1). The ACS patients in group 1 were divided into 2 subgroups: 66 underwent surgery during acute myocardial infarction (AMI group) and 77 during unstable angina classified as class III or IV according to the Braumwald classification (unstable coronary artery disease [CAD] group). Group 2 (the elective CAD group) consisted of 481 patients who underwent isolated elective OPCAB during the same time period.

Results: Overall 30-day mortality was 4.9% (n = 7) for the ACS group and 0.83% (n = 4) for the elective CAD group ($P <$ .0001). Differences between groups were found in use of inotropes, intraaortic balloon pump, and subsequent conversion of OPCAB to CPB ($P < .0001$, $P < .01$, and $P < .03$, respectively), as well as use of blood transfusion ($P < .0003$). Multivariate logistic regression analysis for 641 patients revealed ACS ($P < .015$), AMI ($P < .019$), renal failure ($P < .017$), and left ventricle aneurysm ($P < .028$) as independent risk factors for 30-day mortality in ACS reoperation ($P = .02$), whereas in AMI renal failure ($P = .02$) appeared to be an independent risk factor.

Conclusions: OPCAB is a valuable treatment strategy in ACS patients; however, it carries significant mortality and morbidity. Careful preselection and timing of intervention are required in order for patients to fully benefit from the OPCAB strategy.

Presented at the 9th Annual CTT Meeting 2003, Miami Beach, Florida, USA, March 19-22, 2003.

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INTRODUCTION

Coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) carries significant risk for patients undergoing surgery while in acute coronary syndrome (ACS). Any scoring system available at present accounts for unstable angina or recent myocardial infarction (MI) as a severe risk factor. On the basis of STS (Society of Thoracic Surgeons) scoring criteria, CPB is considered an independent risk factor for patients, with a predicted mortality of 10% and more. Therefore the purpose of this study was to evaluate results of CABG without CPB (off-pump CABG [OPCAB]) for patients with one of the major risk factors, ACS. Additionally, early results were compared with regard to different time periods from the occurrence of ACS and MI to the performance of the revascularization procedure. Determinants of patient outcome were evaluated on the basis of multivariate logistic analysis to determine whether evolving MI is a risk factor for CABG surgery without CPB (OPCAB) as it is for conventional CABG surgery with CPB.

METHODS

The early outcome of patients undergoing OPCAB surgery while suffering ACS or acute MI (AMI) was addressed. All patients who underwent OPCAB surgery between 1997 and 2001 were included in this retrospective analysis. There were 143 patients in ACS, including those in evolving MI (group 1, ACS group), and 481 who underwent isolated elective OPCAB in the same time period (group 2, elective coronary artery disease [CAD] group). Group 1 consisted of 2 subsets of patients: patients with AMI (66 patients) and patients with unstable angina (unstable CAD) (77 patients).

Definition of ACS and AMI followed the American College of Cardiology/American Heart Association 2000 guidelines. Patient data were compared for preoperative risk factors, perioperative mortality, and postoperative complications.

Tables 1 and 2 show the patient characteristics and preoperative clinical data of both groups (ACS and elective CAD). Tables 3 and 4 present those data for the 2 subgroups of the ACS group: AMI versus unstable CAD.

Table 1. Patient Characteristics: ACS Group versus Elective CAD Group*

	ACS (n = 143)	Elective CAD (n = 481)	*P*
Age, y	60.6 ± 9.4	57.9 ± 9.3	NS
Sex F/M, n	42/101 (29.4%/70.6%)	118/363 (24.5%/75.5%)	NS
Height, cm	169.1 ± 7.4	169.6 ± 7.35	NS
Weight, kg	78.15 ± 10.3	80.1 ± 11.5	NS
MI	76 (53.1%)	253 (52.3%)	NS
Ejection fraction, %	0.41 ± 0.12	0.45 ± 0.1	NS
Ejection fraction <0.3, n	28 (19.6%)	43 (8.9%)	<.001

*Data are presented as mean ± SD or percent. ACS indicates acute coronary syndrome; CAD, coronary artery disease; MI, myocardial infarction; NS, not significant.

Table 3. ACS Patient Characteristics: AMI Group versus Unstable CAD Group*

	AMI (n = 66)	Unstable CAD (n = 77)	*P*
Age, y	59.93 ± 9.42	61.18 ± 9.97	NS
Sex, F/M	19/47 (28.8%/71.2%)	23/54 (29.9%/70.1%)	NS
Height, cm	169.01 ± 7.54	169.6 ± 5.3	NS
Weight, kg	77.33 ± 9.73	78.9 ± 10.78	NS
Previous MI	37 (56.1%)	39 (50.6%)	NS
Ejection fraction, %	0.4 ± 0.12	0.41 ± 0.12	NS
Ejection fraction ≤0.3%, n	14 (21.2%)	14 (18.2%)	NS

*Data are presented as mean ± SD or percent. AMI indicates acute myocardial infarction; CAD, coronary artery disease; NS, not significant; MI, myocardial infarction.

Perioperative Protocol

To perform OPCAB in the setting of ACS, specific perioperative protocol was established.

A very liberal protocol was followed with regard to preoperative intraaortic balloon pump (IABP) support. In case of hemodynamic instability as assessed by Swann-Ganz measurements, an IABP was inserted.

Our revascularization strategy was to perform the graft of the culprit lesion followed by the left anterior descending artery (LAD) and then other vessels. Arterial grafts and proximal anastomoses were performed first so that blood flow could be reestablished immediately. Exposure was achieved by means of pericardial traction sutures, an epicardial stabilizer (Octopus; Medtronic, Minneapolis, MN, USA), and a heart positioner (Starfish; Medtronic). Verticalization of the heart was achieved with minimal hemodynamic instability. To achieve hemodynamic stabilization a combination of different actions were undertaken: Trendelenburg position and fluid transfusion were used to compensate for preload decrease and inotropes were used to increase coronary flow and stroke volume.

Preconditioning was not routinely performed; however, when subcritical occlusion was present, 3 minutes of preconditioning followed by 3 minutes of reperfusion was performed. This maneuver enabled us to evaluate tolerance to ischemia and to allow continuous perfusion when a shunt had been introduced. Anticoagulation protocol consisted of heparin given as a half-dose regimen, 1.5 mg/kg with an additional 0.3 mg every 30 minutes to achieve an activated clotting time above 300 throughout the procedure. Only half of that dose reversed with protamine. During the early postoperative period, during first hour in the intensive care unit, 150 mg of aspirin was given through the nasogastric tube.

Table 5 shows perioperative and postoperative data for both groups (ACS and elective CAD). Table 6 shows those data for the 2 ACS subgroups (AMI and unstable CAD).

Statistical Analysis

Statistical analysis was performed with the 2-way Fisher exact test and the unpaired Student test, when appropriate, with $P < .05$ considered as statistically significant.

Table 2. Preoperative Data: ACS Group versus Elective CAD Group*

	ACS (n = 143)	Elective CAD (n = 481)	*P*
Atheromathosis	36 (25.2%)	89 (18.5%)	NS
Hypertension	68 (47.6%)	196 (40.7%)	NS
Diabetes mellitus	31 (21.7%)	72 (14.9%)	<.05
Renal failure	9 (6.2%)	33 (6.8%)	NS
COPD	25 (17.5%)	56 (11.6%)	NS
Previous intervention			
PTCA	18 (12.6%)	20 (3.9%)	<.0001
CABG	7 (4.9%)	13 (2.7%)	<.05

*Data are presented as mean ± SD or percent. ACS indicates acute coronary syndrome; CAD, coronary artery disease; NS, not significant; COPD, chronic obstructive pulmonary disease; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft.

Table 4. Preoperative Data: ACS.AMI Group versus Unstable CAD Group*

	AMI (n = 66)	Unstable CAD (n = 77)	*P*
Atheromathosis	15 (22.7%)	21 (27.3%)	NS
Hypertension	36 (54.5%)	32 (41.6%)	NS
Diabetes mellitus	17 (25.8%)	14 (18.2%)	NS
Renal failure	4 (6%)	5 (6.5%)	NS
Chronic obstructive pulmonary disease	12 (18.8%)	13 (16.9%)	NS
Previous interventions			.08
Percutaneous transluminal coronary angioplasty	9 (13.6%)	9 (16.7%)	
Coronary artery bypass graft	1 (1.5%)	6 (7.8%)	

*NS indicates not significant.

Table 5. Perioperative and Postoperative Data: ACS Group versus Elective CAD Group*

	ACS (n = 143)	Elective CAD (n = 481)	*P*
Arterial grafts	98 (68.5%)	441 (91.9%)	<.0001
No. anastomoses per patient	1.87 ± 0.49	2.05 ± 0.59	NS
Inotropes	40 (28%)	88 (18.2%)	<.01
IABP	30 (20.9%)	17 (3.5%)	<.0001
Perioperative MI	3 (2.1%)	6 (1.2%)	NS
Conversion to CPB	4 (2.8%)	3 (0.62%)	<.03
Drainage, mL	549.2 ± 184.2	543.9 ± 211.7	NS
Blood transfusion	45 (31.5%)	84 (17.5%)	<.0003
Intensive care unit time, h	9.3 ± 2.6	9.4 ± 2.4	NS
Hospitalization, d	9.9 ± 3.1	10.04 ± 3.2	NS
Mortality	7 (4.9%)	4 (0.83%)	<.0001

*Data are presented as mean ± SD or percent. ACS indicates acute coronary syndrome; CAD, coronary artery disease; NS, not significant; IABP, intraaortic balloon pump; MI, myocardial infarction.

The statistical software SPSS PC (version 10.0; SPSS, Chicago, IL, USA) was used for final analysis of the data. Data are expressed as frequency distributions and simple percentages. Values of continuous variables are expressed as mean ± SD.

Univariate analysis was performed with 16 preoperative and operative discrete variables (age, sex, ejection fraction [EF], recent MI, AMI within <1 week, AMI within >1 week and <30 days, ACS, Canadian Cardiovascular Society class, New York Heart Association class, hypertension, diabetes mellitus, renal failure, chronic obstructive pulmonary disease, reoperation, atheroscleromathosis, left ventricular aneurysm) were tested, with end-points being 30-day hospital mortality.

Multivariate analysis included data on comorbid conditions found to be associated with increased mortality in the univariate analyses ($P < .15$). These data were entered into multiple stepwise logistic regression models. The level of statistical significance in both univariate and multivariate analysis was defined as $P \leq .05$.

Data including incidence of death for the 3 separate groups were entered into analysis: (*a*) the whole OPCAB group, (*b*) patients in ACS, (*c*) patients in AMI (<30 days).

RESULTS

Overall 30-day mortality was 11 (1.8%) of 624 patients. In the AMI subgroup it was 4 (6.1%) of 66; all deaths were due to low cardiac output syndrome. In the unstable CAD group it was 3 (3.9%) of 77; 2 deaths were due to low cardiac output syndrome and 1 was due to cardiovascular accident (CVA) and stroke. In the elective CAD group, only 1 death of 4 was caused by low cardiac output syndrome related to perioperative MI. Other causes were CVA, multiorgan failure, and pulmonary embolism. Overall mortality was 4.9% (n = 7) for the ACS group and 0.83% (n = 4) for the elective CAD group ($P < .0001$) (Table 5).

Perioperative MI occurred in 3 cases (2.1%) in the ACS group and 6 cases (1.2%) in the elective CAD group (Table 5).

With regard to postoperative complications, differences between groups were found in use of inotropes, IABP, and conversion OPCAB to CPB ($P < .0001$, $P < .01$, $P < .03$, respectively) as well as in use of blood transfusion ($P < .0003$) (Table 5).

In the ACS group the mean postoperative hospital stay was 9.9 ± 3.1 days, and in the elective CAD group it was 10 ± 3.2 days. There were no differences found the AMI and unstable CAD groups were compared (Table 6).

The preoperative risk factors and operative variables were initially evaluated in different models by univariate analysis followed by multivariate analysis. Multivariate logistic regression analysis for 641 patients revealed ACS ($P < .015$), AMI

Table 6. Perioperative and Postoperative Data: AMI Group versus Unstable CAD Group*

	AMI (n = 66)	Unstable CAD (n = 77)	*P*
Arterial grafts	42 (63.6%)	56 (72.7%)	NS
Anastomoses	1.8 (0.67%)	1.9 (0.7%)	NS
Inotropes	20 (30.3%)	20 (26%)	NS
IABP	13 (19.7%)	17 (22.1%)	NS
Perioperative MI	2 (3%)	1 (1.3%)	NS
CPB conversions	2 (3%)	2 (2.6%)	NS
Drainage, mL	538.54 ± 186.3	559 ± 183.3	NS
Transfusions	20 (30.3%)	25 (33%)	NS
Intensive care unit time, h	9.3 ± 2.4	9.23 ± 2.77	NS
Hospitalization	9.89 d (2.72)	10.05 d (3.53)	NS
Mortality	4 (6%)	3 (3.9%)	NS

*Data are presented as mean ± SD or percent. AMI indicates acute myocardial infarction; CAD, coronary artery disease; NS, not significant; IABP, intraaortic balloon pump; MI, myocardial infarction.

Table 7. Logistic Regression Analysis of 30-Day Mortality Associated with Demographic, Clinical, and Procedural Characteristics of OPCAB Patients*

	Adjusted *OR* for 30-d Mortality	95% CI	*P*
OPCAB patients (n = 624)			
ACS	33.7	2-567.6	.015
MI <1 week	8.7	1.4-52.7	.019
Renal failure	56	2.1-1521	.017
Patients with LV aneurysm	360	1.89-7690	.028
ACS group (n = 143)			
Reoperation	5.6	1-579	.02
Acute myocardial infarction group			
Renal failure	8.2	1.3-49.8	.02
Patients with LV Aneurysm	8.7	1.8-94.5	.05

*OPCAB indicates off-pump coronary artery bypass graft; OR, odds ratio; CI, confidence interval; ACS, acute coronary syndrome; MI, myocardial infarction; LV, left ventricle.

($P < .019$), renal failure ($P < .017$), and left ventricular aneurysm ($P < .028$) as independent risk factors for 30-day mortality. Our analysis results for the ACS group and the AMI subgroup of the ACS group indicated that reoperation ($P < .02$) for the first group and renal failure ($P < .02$) as well as left ventricular aneurysm ($P < .05$) for the second group were independent risks factors for 30-day mortality (Table 5).

COMMENT

According to our study, coronary revascularization without CPB (OPCAB) performed on patients in ACS is associated with increased risk, as showed by its influence on mortality and greater use of inotropes and IABP. The strongest influence on perioperative risk was found to occur when the procedure was performed during evolving infarction. The most frequent reason for mortality in the ACS group (6 of 7 cases) was low cardiac output and perioperative infarction, both strongly related to preoperative ACS and evolving infarction. In all 4 cases of death among AMI patients, surgery was performed during the first 6 days of infarct evolution. In contrast to the ACS group, low cardiac output appeared to be responsible for only 1 of 4 deaths in the elective CAD group. However, the rates of overall mortality and frequency of perioperative MI in ACS were low and favorable in our study compared to others [Sintek 1994, Von Segesser 1994, Applebaum 1991, Locker 2000, Lee 2001, Lund 2001, Varghese 2001]. There is a lack of data looking at results of OPCAB in ACS and in particular evolving MI. Varghese et al [2001] recently published data showing satisfactory results of OPCAB in a nonelective setting. Their results were comparable to ours; however, because of the small number of patients, risk analysis could not be performed [Varghese 2001]. Locker et al [2000] compared results after on- and off-pump CABG for AMI and found significant improvement in the off-pump group (5% versus 24%, respectively), a result that corroborates with ours. In another study from Lund et al [2001], surgery during the early "healing phase" of MI was associated with increased risk, similar to our findings. Many published study reports support the concern that CABG surgery performed early after the development of MI carries a significant risk. Sintek et al [1994] and Floten et al [1989] reported higher mortality rates (4% and 7.6%, respectively) in patients in whom CABG was performed within 24 hours of MI. Applebaum et al [1991] reported an increased mortality risk in an elective cohort of patients in whom CABG was performed during 30 days from MI (6.7% versus 1.1%). According to Von Segesser et al [1994], even long-term results are affected. They reported 8-year survival rates of 65% compared to 80 % after elective CABG. Lee and Oz [2001] presented results showing increased mortality up to 3 days after MI in a multiinstitutional study including more than 22,000 patients.

On the other hand, Berg et al [1981] presented exceptionally good results of revascularization during evolving MI, with early mortality of 2%.

One subset of patients is patients in whom angioplasty has failed. We found no mortality if surgery was performed within the short interim of up to 12 hours. However, Borkon et al [1992] and von Segesser et al [1994] reported high mortality rates of 10% to 12% and a high frequency of MI of up to 35% after angioplasty failure. The reason for that high risk is the detrimental role of acutely closed or dissected coronary arteries and the importance of the presence of minimal flow (low-flow phenomenon). In addition, coagulopathy due to aggressive antithrombotic regimens may exaggerate operative risk due to bleeding and its consequences. The improvement in results as shown in our trial may have occurred because OPCAB allows for immediate and straightforward revascularization and thus avoidance of coagulopathy.

Renal failure in our study was found to be an independent overall risk factor for all patients, and in particular it caused significant risk elevation in the ACS group. Severe renal failure is known to be a strong predictor of bad outcome after conventional CABG, and renal function is very likely to deteriorate postoperatively, as reported by Weerasinghe et al [2001]. Although avoiding CPB is supposed to ameliorate this influence, this protection against renal failure was not evident in the subgroup of patients with severe renal dysfunction and a creatinine level of more than 1.5 mg%. The presence of an evolving infarct may be a solitary factor responsible for renal deterioration due to hemodynamic instability and inflammatory mediators released during MI [Weerasinghe 2001]. In our study, the increased use of IABP and inotropes may support this thesis.

We recognized that redo-CABG is a predictor of poor outcome after OPCAB in ACS. Redo-CABG surgery is considered to be 1 of 5 major risk factors for mortality and morbidity, according to a recently published Veterans Preoperative Risk Adjustment Study [Morrison 2001]. Other identified risk factors were surgery within 7 days of MI, EF <35%, age older than 70 years, and treatment with IABP. It was also found that the presence of more than 1 of these factors strongly exaggerated already elevated risk, as was the case in our study [Morrison 2001].

An interesting finding from our analysis was that low EF did not appear to be a risk factor. OPCAB performed for low ejection function can be considered an option according to encouraging reports from studies such as Arom et al [2000]. Patients with severe impairment of left ventricle function poorly tolerate additional loss of cells from already depleted myocardium and also show greater proinflammatory cytokine response, mainly in the form of tumor necrosis factor; both phenomena are related to CPB [Arom 2000]. Surprisingly, the presence of an aneurysm proved to be a significant but weak influence on results in cases of acute infarction, a finding that may reflect development of dyskinetic wall motion early after infarction, a time period that is recognized as not optimal for intervention, precluding salvage of myocardium, because of the high risk of complications [Gott 1995].

Old age did not prove to be a significant risk factor, a result that reflects a trend indicating that off-pump strategy is optimal for older patients because of the significantly low mortality and morbidity rates reported by many investigators [Morrison 2001].

Univariate analysis results alone showed only slightly higher use of IABP and inotropes after OPCAB in the ACS group. This finding is partially related to higher IABP use preoperatively, an approach that is recommended in the literature, in a report that preoperative placement of IABP facilitates safe heart luxation or manipulation [Arom 2000]. The other factor contributing to these findings is likelihood of hemodynamic or electrical instability in these patients. For the same reason there is a higher risk for conversion to CPB, which we encountered as well. Another difference found only in univariate analysis results was in the use of blood transfusion, in spite of similar drainage. This finding may have been caused by inflammatory stimulation and preoperative damage to platelets due to antiplatelet medications. However, these factors are not recognized as independent determinants in our study.

One advantage of the off-pump strategy may be amelioration of inflammatory mechanisms in development of reperfusion injury. It is well documented that complement activation and lysis of myocytes through MAC (membrane attack complex) and activation of neutrophils play an important role. There are studies showing lower postoperative values of MACs together with complement factor C3a and amelioration of complement activation when surgery is performed using an off-pump strategy [Gu 1998]. Another important proinflamatory cytokine released during reperfusion injury is interleukin 8, the release of which is directly related to bypass and reperfusion of ischemic myocardium .

In spite of these advantages, patients are frequently hemodynamically unstable, and revascularisation of posterior arteries may compromise hemodynamics even further. It is not clear whether it is better to protect against superimposed CPB-induced inflammatory damage or to rest the ischemic heart during on-pump revascularisation. Regardless of surgical technique, early reperfusion performed within days of infarction may be too late, missing the window of opportunity for early salvage of myocardium, and may be complicated by dyskinesia and dilation of ventricles, particularly the right ventricle, factors that may contribute to the suboptimal results reported in the literature .

In summary, results of OPCAB surgery for ACS patients are satisfactory and encouraging; however, intervention is associated with increased risk. Therefore appropriate timing of surgical intervention is essential in order to achieve optimal results.

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