The early outcome in patients undergoing off-pump coronary artery bypass grafting: our experience

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Background. **Many studies confirm that beating heart surgery is an alternative to on-pump myocardial revascularization. However, the clinical conditions of patients are currently considered as a major landmark in the indication for beating heart surgery. This retrospective non-randomized study was carried out to evaluate the efficacy and the advantages of this surgical technique when anatomical criteria are used to choose the surgical strategy.**

Methods. **From February to December 2003, 222 consecutive patients underwent isolated myocardial revascularization: 76 (34%) with an off-pump coronary artery bypass (OPCAB) and 146 (66%) with an on-pump coronary artery bypass (ONCAB) procedure. Selection for surgical treatment was based on coronary anatomy. All patients were stratified for mortality risk class according to the EuroSCORE system. Operative and postoperative data were analyzed.**

Results. **Morbidity and mortality did not differ significantly between the two groups but the release of creatine kinase-MB fraction was significantly higher in the ONCAB group (48.7 ± 55.3 vs 20.8 ± 16.6 U/ml, $p < 0.001$). Patients at high surgical risk were dealt with a more complicated clinical outcome; logistic regression analysis showed that this class was an independent risk factor for postoperative complications in both groups.**

Conclusions. **We did not find any statistical difference in hospital mortality and morbidity either using ONCAB or OPCAB; however a lower release of creatine kinase-MB in beating heart revascularization group suggests that OPCAB reduces myocardial injury and preserves cardiac function when anatomical criteria are considered for patient selection.**

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Introduction

Off-pump coronary artery surgery revascularization has recently been introduced in surgical practice with encouraging results[1-4].

The first experience with this technique was limited to single-vessel disease and for young patients with a good left ventricular function; with developing of stabilization and exposure devices, the application of this technique has been dramatically increasing. Nevertheless, the tendency of indications for beating heart surgery considers the clinical status of the patient rather than the anatomy of his coronary disease[5-7]. The advantages of using the off-pump procedure was documented in high-risk patients[8]. Several studies have shown a better outcome in patients with chronic pulmonary disease[9], advanced age[10,11] and severe left ventricular dysfunction[12] using off-pump over on-pump myocardial revascularization.

However some comparative analyses did not show homogeneous results in terms of clinical outcome in either the intensive care unit or hospital stays with cost reduction[10,11,13-15].

This retrospective non-randomized study reports our first experience with beating heart revascularization; its aim was to test clinical results, following only anatomical criteria to determine the strategy of operation, in order to evaluate efficacy and advantages of this surgical technique. In-hospital outcome and early results are reported.

Methods

Patient selection. From February to December 2003, 222 consecutive patients underwent primary isolated coronary artery bypass grafting (CABG). All operations were performed by a single experienced surgeon.

In each patient a coronary angiogram was carefully analyzed and according to anatomical criteria and number of grafts required, patients were divided into two groups: 146 patients (66%) underwent an on-pump coronary artery bypass (ONCAB) procedure and 76 (34%) an off-pump coronary artery bypass (OPCAB) procedure.

Inclusion criteria for ONCAB were multivessel disease, severe left main stenosis, presence of stenosis of the distal lateral wall arteries, coronary artery disease with heavily calcified arteries, diffusely atheromatous and intramyocardial coronary vessels.

Inclusion criteria for OPCAB were lesions ≥ 70% in the left anterior descending coronary artery, isolated or associated with lesions in the right coronary artery.

Young patients needed a total artery revascularization and were routinely operated on ONCAB to perform a high-quality anastomosis particularly on the distal and smaller coronary artery. In 18 patients, a total artery revascularization was performed with only bilateral descending mammary and right gastroepiploic arteries. Exclusion criteria for right gastroepiploic artery harvesting were a previous upper abdominal operation (excluding laparoscopic procedure), previous gastrectomy, active gastritis, severe obesity, coronary lesions < 90%[16].

Patients with concomitant heart valve disease, ventricular aneurysm, other associated surgical procedures, reoperation or hybrid procedure (percutaneous transluminal coronary angioplasty + surgery) were excluded from the study.

The EuroSCORE was used for risk stratification and patients were divided into three classes: EuroSCORE class 1 (low operative mortality risk patients); EuroSCORE class 2 (medium-risk patients) and EuroSCORE class 3 (high-risk patients)[17].

All patients continued their preoperative drugs until the morning of the operation. Antiplatelet drugs were ceased 5 days prior to the scheduled date of surgery.

Operative technique. In the ONCAB group, anesthesia was induced with propofol 1-2 mg/kg, fentanyl 10-15 μg/kg and pancuronium 0.1 mg/kg and maintained with a propofol infusion.

In the OPCAB group, anesthesia induction was obtained with midazolam 0.1-0.2 mg/kg, fentanyl 15-20 μg/kg and norcuron 0.1 mg/kg and was maintained by midazolam infusion.

In all patients a median sternotomy was performed. Arterial and venous conduits were harvested simultaneously.

ONCAB patients received heparin at a dosage of 3 mg/kg with a target activated clotting time > 400 s. Pump flow was maintained at 2.4 l/min/m^2. Minimal rectal temperature was 34°C. A cold intermittent antegrade/retrograde 4:1 blood cardioplegic solution was routinely administered for myocardial protection according to the Buckberg's protocol[18] and warm induction was only used in patients with unstable angina, ejection fraction < 40%, cardiogenic shock and acute myocardial infarction.

In OPCAB patients heparin was administered at a dosage of 1.5 mg/kg. The target activated clotting time was > 250 s. The exposure of lateral and right coronary branches was achieved by a sling fixed with a tourniquet in the pericardium between the left inferior pulmonary vein and the inferior vena cava as proposed by Lima[19]. Mechanical stability of coronary arteries was achieved with Octopus (Medtronic Inc., Minneapolis, MN, USA) or CTS stabilizer (OPCAB-System-CTS, Inc., Cupertino, CA USA). Trendelenburg position was used to gain a good lateral and inferior left ventricular wall exposure, maintaining a stable hemodynamic.

Proximal occlusion of the target vessel was performed with an encircling 3-0 polypropylene suture with pledget and tourniquet. Whenever necessary a flow-shunt was introduced in the coronary artery providing a better visualization at the anastomotic site. Left anterior descending coronary artery was revascularized first to minimize the effect of heart manipulation. Distal coronary anastomosis was performed using an 8-0 polypropylene suture for internal mammary artery and a 7-0 polypropylene suture for saphenous vein grafts. Proximal vein anastomoses were carried out with a 6-0 polypropylene suture under partial aortic occlusion clamp. In 10 patients (22%) we used the St. Jude Medical aortic connector for proximal anastomosis, avoiding aorta manipulation. The proximal anastomoses were always performed before the distal anastomosis.

Clinical data collection, monitoring and definitions. After surgery the following data were measured: serum creatine kinase (CK) MB isoenzyme peak level within the first 24 hours (Creatine Kinase Liquid, Roche/Hitachi), inotropic drug requirement for a period > 12 hours, new myocardial infarction, incidence of atrial fibrillation and malignant arrhythmia, reoperation, prolonged intensive care unit stay (> 24 hours), time to extubation and hospitalization length.

Early mortality included all in-hospital deaths among patients who were not discharged after surgery.

Postoperative blood loss was defined as total chest tube drainage during the first 12 hours.

Two classes of complications were considered: *major complications* which include incidence of death, cerebrovascular accidents, acute myocardial infarction, acute renal failure, intra-aortic balloon pump and malignant arrhythmia events, and *total complications* which include the incidence of all postoperative complications i.e., major complications plus the use of inotropic drugs and all arrhythmic events occurring during the intensive care unit stay.

Postoperative renal function was assessed as creatinine peak release; complications included acute renal failure, defined as the requirement of hemodialysis or an elevated creatinine level (> 2 mg/dl).

Neurological complications included permanent and transient strokes.

Statistical analysis. Preoperative clinical data, operative and postoperative data were reported as mean ± SD. The χ^2 test was used to compare categorical variables. Unpaired Student's t-test was used for continuous variables between the groups. A p value < 0.05 was considered statistically significant. Univariate comparisons between two independent groups were made by means of the analysis of variance (ANOVA).

Multivariate analysis of surgical treatment, EuroSCORE risk classes and postoperative complications (major and total) were performed using a stepwise logistic regression analysis. Statistical analysis was performed using SAS software for Windows.

Results

There was no conversion from OPCAB into ONCAB operation.

Baseline characteristics and distribution in EuroSCORE risk class (p = 0.11) were well balanced across the two groups (Tables I and II). Patients in the ONCAB group had more extensive coronary artery disease and received more grafts than those in the OPCAB group (Table III).

Thirty-five patients (15.7%) received a completely arterial conduit revascularization by means of ONCAB procedure.

Hospital mortality. Four (2.7%) ONCAB group patients died; no death occurred in the OPCAB group (p = 0.14). One female patient with Horton disease died on postoperative day 4 of sudden death; 2 male patients with ejection fraction < 0.30 died of heart failure on postoperative days 2 and 4, respectively; 1 female patient experienced a ventricular fibrillation 2 hours after surgery. She was promptly assisted with extracorporeal membrane oxygenation, but she died on postoperative day 6 due to multiorgan failure.

Hospital morbidity. Detailed data on postoperative period are presented in table IV.

No statistically significant differences were found as regard ventilation time (9.3 ± 6.9 hours ONCAB vs 8.5 ± 4 hours OPCAB, p = 0.26) in surviving patients. Four OPCAB patients (5.3%) required a prolonged intensive care unit stay after surgery, compared with 17 (11.6%) ONCAB patients (p = 0.12). Similarly, no statistically significant differences were found as for bleeding (494 ± 377 ml ONCAB vs 429 ± 204 ml OPCAB, p = 0.09), postoperative atrial fibrillation rate (24.7% ONCAB vs 15.8% OPCAB, p = 0.13) or hospitalization length (4.9 ± 1.6 days ONCAB vs 4.8 ± 1.3 days OPCAB, p = 0.61).

Table I. Preoperative data.

	ONCAB (n=146)	OPCAB (n=76)	Total (n=222)	p
Age (years)	62.3 ± 8.6	62.7 ± 8.5	62.4 ± 8.6	0.710
Sex (M/F)	128/18	65/11	193/29	0.653
Previous AMI	69 (47.3%)	36 (47.4%)	105 (47.3%)	0.988
EF (%)	55.3 ± 8.8	54.8 ± 8.4	55.1 ± 8.4	0.712
EF ≤ 40% (%)	34.6	35	34.7	0.334
EF ≤ 40%	13 (8.9%)	4 (5.3%)	7 (7.7%)	0.333
Emergency	6 (4.1%)	1 (1.3%)	7 (3.1%)	0.259
Diabetes	42 (28.8%)	18 (23.7%)	62 (28%)	0.362
COPD	21 (14.4%)	19 (25%)	40 (18%)	0.71
Creatinine peak release ≥ 2 mg/dl	6 (8.8%)	5 (3.8%)	11 (5%)	0.422

AMI = acute myocardial infarction; COPD = chronic obstructive pulmonary disease; EF = ejection fraction; ONCAB = on-pump coronary artery bypass; OPCAB = off-pump coronary artery bypass.

Table II. EuroSCORE risk class.

	Low risk (EuroSCORE 1)	Medium risk (EuroSCORE 2)	High risk (EuroSCORE 3)
ONCAB	63 (43.1%)	59 (40.4%)	24 (16.4%)
OPCAB	45 (59.2%)	19 (25%)	12 (15.8%)
Total	108 (48.6%)	78 (35.1%)	36 (16.2%)

ONCAB = on-pump coronary artery bypass; OPCAB = off-pump coronary artery bypass. All p = 0.110.

Table III. Operative data.

	ONCAB (n=146)	OPCAB (n=76)
1 graft (LIMA-LAD)	–	54
2 grafts (LIMA + venous)	41	22
2 grafts (BIMA)	17	–
3 grafts (BIMA + RGEA)	18	–
3-4 or more grafts	70	–

BIMA = bilateral internal mammary artery; LAD = left anterior descending artery; LIMA = left internal mammary artery; ONCAB = on-pump coronary artery bypass; OPCAB = off-pump coronary artery bypass; RGEA = right gastroepiploic artery; Venous = saphenous graft.

Three patients (2.1%) in the ONCAB group and only 1 (1.3%) in OPCAB group (p = 0.69) required reoperation due to bleeding; comparable results were found also for prolonged use of inotropes (8.2% ONCAB vs 3.9% OPCAB, p = 0.23), incidence of perioperative acute myocardial infarction (2.7% ONCAB vs 1.3% OPCAB, p = 0.5), cerebrovascular accidents (0.69% ONCAB vs 1.3% OPCAB, p = 0.64). Major and total complications were not significant (p = 0.38 and p = 0.06, respectively).

OPCAB was associated with lower serum CK levels (313.7 ± 182.5 U/ml OPCAB vs 769.9 ± 986.8 U/ml ONCAB, p ≤ 0.001) and CK-MB peak release (20.8 ± 16.6 U/ml OPCAB vs 48.7 ± 55.3 U/ml ONCAB, p < 0.001).

Outcome among EuroSCORE risk classes. The distribution of postoperative variables for patients' EuroSCORE risk classes are shown in table V.

Postoperative malignant arrhythmia events, rate of prolonged use of inotropes, time of extubation, intensive care unit stay, atrial fibrillation and total event score increased significantly with increasing of the EuroSCORE risk class.

Predicted risk was measured using a logistic regression equation (Table VI).

There were no statistically significant differences in predicted arrhythmia, total complications, major complications and intensive care unit stay between the OPCAB and the ONCAB group. The prevalence of predicted arrhythmia and total complications was significantly lower in low-risk patients than in medium- and high-risk patients (predicted arrhythmia: odds ratio-OR 2.5 and 6.2; predicted total event score: OR 2.9). Also the prevalence of major complications and intensive care unit stay was lower and not statistically significant in low-risk than in high-risk patients.

There were no statistically significant differences in ventilation time between the OPCAB and the ONCAB group. Ventilation time was statistically longer in medium-risk than in low-risk patients (p = 0.0018). Postoperative major complications and renal failure increased ventilation time requirement, but the same does not hold true for arrhythmic complications and serum creatinine elevation.

Discussion

There is increasing evidence that cardiopulmonary bypass (CPB) may be responsible for the systemic inflammatory response that occurs after CABG and may contribute to multiple organ dysfunction and postoperative complications[2,20-24].

The avoidance of CPB during CABG is believed to reduce the inflammatory response; for this reason the OPCAB procedure is thought to have significantly decreased the complications due to the use of extracorporeal circulation.

Table IV. Postoperative data.

	ONCAB (n=146)	OPCAB (n=76)	Total (n=222)	p
Ventilation time (hours)	9.3 ± 6.9	8.5 ± 4	9 ± 6.1	0.267
Prolonged ICU stay*	17 (11.6%)	4 (5.3%)	21 (9.5%)	0.123
Bleeding (ml)	494.7 ± 377.5	429.2 ± 204.5	472.3 ± 329.7	0.097
Atrial fibrillation	36 (24.7%)	12 (15.8%)	48 (21.6%)	0.128
Hospital stay (days)	4.9 ± 1.6	4.8 ± 1.3	4.9 ± 1.5	0.609
Inotropes > 12 hours	12 (8.2%)	3 (3.9%)	15 (6.8%)	0.229
Perioperative AMI	4 (2.7%)	1 (1.3%)	5 (2.2%)	0.498
Reoperation	3 (2.1%)	1 (1.3%)	4 (1.8%)	0.694
CVA	1 (0.69%)	1 (1.3%)	2 (0.9%)	0.637
Death	4 (2.7%)	0	4 (1.8%)	0.145
Major complications	10 (6.8%)	3 (3.9%)	13 (5.9%)	0.382
Total complications	37 (25.3%)	11 (14.5%)	48 (21.6%)	0.062
CPK (U/ml)	769.9 ± 986.8	313.7 ± 182.5	613.7 ± 835	< 0.001
CPK-MB (U/ml)	48.7 ± 55.3	20.8 ± 16.6	39.1 ± 47.7	< 0.001

AMI = acute myocardial infarction; CPK= creatine phosphokinase; CVA = cerebrovascular accidents; ICU = intensive care unit; ONCAB = on-pump coronary artery bypass; OPCAB = off-pump coronary artery bypass. * number of patients who stay > 1 day in the ICU.

Table V. Postoperative data for preoperative patient risk class.

	EuroSCORE 1 (n=108)	EuroSCORE 2 (n=78)	EuroSCORE 3 (n=36)	Total (n=222)	p
Ventilation time (hours)	7.8 ± 3	10.7 ± 8.6	8.9 ± 5.4	9 ± 6	0.005
Prolonged ICU stay*	6 (5.6%)	9 (11.5%)	6 (16.7%)	21 (9.5%)	0.035
Bleeding (ml)	491.5 ± 390.8	457.6 ± 247.2	446.5 ± 287.3	472.3 ± 329.7	0.691
Atrial fibrillation	12 (11.1%)	20 (25.6%)	16 (44.4%)	48 (21.6%)	< 0.001
Hospital stay (days)	4.9 ± 1.4	4.9 ± 1.8	5.1 ± 1.3	4.9 ± 1.5	0.73
Inotropes > 12 hours	4 (3.7%)	6 (7.7%)	5 (13.9%)	15 (6.8%)	0.034
Perioperative AMI	2 (1.8%)	2 (2.6%)	1 (2.8%)	5 (2.2%)	0.704
Reoperation	2 (1.8%)	2 (2.6%)	0	4 (1.8%)	0.631
Death	1 (0.9%)	1 (1.3%)	2 (5.6%)	4 (1.8%)	0.117
Major complications	5 (4.63%)	5 (6.4%)	3 (8.3%)	13 (5.9%)	0.391
Total complications	17 (15.7%)	18 (23.1%)	13 (36.1%)	48 (21.6%)	0.011
CPK (U/ml)	611.1 ± 975.5	622.4 ± 697.6	603.1 ± 650.4	613.7 ± 835	0.992
CPK-MB(U/ml)	37.5 ± 52.1	38.1 ± 34.8	46.3 ± 57.7	39.1 ± 47.7	0.617

AMI = acute myocardial infarction; CPK = creatine phosphokinase; CVA = cerebrovascular accidents; ICU = intensive care unit. * number of patients who stay > 1 day in the ICU.

Table VI. Logistic regression model.

Endpoints	No. events	OR (95% CI)		
		OPCAB vs ONCAB	Medium vs low risk	High vs low risk
Arrhythmia	48	0.633 (0.30-1.35)	2.57 (1.16-5.70)	6.261 (2.56-15.31)
Major complications	13	0.582 (0.15-2.21)	1.297 (0.36-4.71)	1.8 (0.41-7.98)
Total complications	48	0.52 (0.24-1.11)	1.45 (0.69-3.08)	2.925 (1.23-6.93)
ICU stay > 1 day	21	0.461 (0.15-1.45)	1.983 (0.67-5.89)	3.247 (0.97-10.89)

CI = confidence interval; ONCAB = on-pump coronary artery bypass; OPCAB = off-pump coronary artery bypass; OR = odds ratio.

In a study by Matata et al.[2] comparing ONCAB with OPCAB, there were lower levels of oxidative stress, as measured by blood levels of lipid hydroperoxidase, protein carbonyls, and nitrotyrosine and less systemic inflammatory response among OPCAB patients.

Brasil et al.[23] affirm that the systemic inflammatory syndrome is not peculiar to CPB but the degree of inflammation may increase with the use of CPB.

Several clinical trials comparing OPCAB with ONCAB have been published but often the results observed are heterogeneous. Many papers have reported that the prevalence of complications without the use of CPB is lower, but their clinical relevance is unclear[24-26].

In a randomized study, Khan et al.[27] showed that OPCAB caused a less myocardial damage and was as safe as ONCAB, but it resulted in lower graft-patency rates after 3 months, which may influence long-term outcomes. In a randomized single-center trial, carried out on 300 patients requiring CABG, Legare et al.[28] were unable to demonstrate any advantage with OPCAB in terms of patient morbidity, transfusion, perioperative myocardial infarction, stroke, new atrial fibrillation, sternal wound infection, or length of hospitalization. Similar conclusions were obtained by Gerola et al.[13]

In our study, there were no differences between the two groups in terms of incidence of main morbidity and hospital mortality; however it did document a significantly lower CK-MB release in the OPCAB group although there was no difference in the prevalence of myocardial infarction in both groups.

The reduction in postoperative CK-MB release suggests that avoiding CPB can reduce the degree of myocardial necrosis. The entity of local ischemia during coronary artery occlusion that occurs in beating heart surgery is less harmful than myocardial ischemia during cardioplegic arrest. This reduction in CK-MB release confirms the results reported by other studies[29,30] that investigate the level of markers of myocardial ischemia and the role of "minor myocardial damage" related to the use of CPB. Ischemic myocardial arrest leads to a postoperative increase in troponin I and T and CK-MB with regard to patients operated on with beating heart surgery, even if myocardial protection technique is optimal, although the clinical relevance of these findings is still unclear. However, Califf et al.[31] found that higher CK-MB levels after balloon angioplasty are associated with worse long-term outcomes with regard to both mortality and cardiac events. These results suggest that OPCAB technique could be better for very unstable ischemic patients who need a better myocardial preservation. The limit of our observation is the difference between the two groups in terms of disease extension and number of grafts performed; only a prospective randomized study could validate or contradict our data.

In this study we observed the impact of the patient preoperative clinical status in the postoperative course. From our experience it can be argued that postoperative complications were not related to the CPB use but to compromised clinical conditions of the patients.

Higher CK-MB release was not related to EuroSCORE high-risk class, and this finding did not increase intensive care unit stay, ventilation time and total complications for the ONCAB group. On the other hand we found that prolonged intensive care unit stay, ventilation time and total complications were increased in high-risk patients. Even the prevalence of atrial fibrillation was significantly increased in high-risk patients, suggesting an important correlation between postoperative arrhythmias and other complications with preoperative status regardless of the surgical technique adopted.

Harvesting of multiple arterial grafts is commonly associated with prolonged surgery times and increased trauma in complete CABG. In accordance with our surgical strategy, complete arterial revascularization and multivessel diseased patients were operated on with CPB. In this group significant differences were not found for clinical postoperative results compared with the OPCAB group; this seems to underline that even if CPB is the primary cause of systemic inflammatory response, the avoidance of extracorporeal circulation is not sufficient to achieve a clear clinical advantage.

Proximal anastomoses in ONCAB patients were performed during cross-clamping and in the OPCAB group, to avoid aortic tangential clamping, a mechanical aortic connector was used for the last 10 patients. In this way we reduced the risks associated with aortic tangential clamping such as aortic dissection, trauma, atheromasic embolism. Aortic connector could be a good alternative to overcome these problems but its performance in terms of long-term patency need to be further investigated.

In conclusion, in our study we did not find any advantage between the two techniques in terms of early clinical outcome; off-pump CABG is safe and yields a short-term cardiac outcome comparable with on-pump CABG. The lower CK-MB release suggests that the avoidance of CPB could be better in terms of myocardial preservation. Therefore high-risk patients could benefit more than others from off-pump revascularization. Long term follow-up is now necessary to assess the clinical relevance of that opinion.

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