

Impact of Incomplete Revascularization Following OPCAB Surgery

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ABSTRACT ***Background and aim of the study:* The aim of this study was to evaluate the early and mid-term off-pump coronary artery bypass surgery (OPCAB) results in a single surgical unit, assessing the impact of completeness of revascularization. *Methods:* Three hundred and twelve patients underwent OPCAB between August 2000 and January 2005. In-hospital data were collected prospectively for all patients undergoing OPCAB. Complete revascularization (CR) was derived by comparing significantly stenotic vessels at cardiac catheterization with surgically grafted coronary vessels. Grafting of all the significantly stenotic coronary vessels was considered CR. In-hospital outcomes were compared between patients with CR and incomplete revascularization (IR). A multivariate analysis based on the Cox proportional hazards regression model was performed. *Results:* Patients receiving IR (105 patients, 43.7%) presented a worse preoperative risk profile then those having CR (mean Euroscore 6.8 ± 2.9 vs. 4.3 ± 2.8, p < 0.0001). IR was not associated with a higher incidence of early adverse events. Five-year freedom from death and major adverse cardiac events (MACE) were 0.88 (0.02 SE) and 0.86 (0.03 SE), respectively. Complete revascularization was protective for mid-term unstable angina recurrence [heart rate (HR) = 0.24, 95% confidence interval (CI) 0.10 to 0.58], acute myocardial infarction (HR = 0.25, 95% CI 0.09 to 0.73), all-cause repeat revascularization (HR = 0.35, 95% CI 0.13 to 0.90), and MACE (HR = 0.2, 95% CI 0.1 to 0.5). *Conclusion:* Our study suggests that, although incomplete revascularization may not result in increased short-term morbidity and mortality, it increases the incidence of mid-term MACE.** doi: 10.1111/j.1540-8191.2009.00881.x *(J Card Surg 2009;24:650-656)*

Incomplete revascularization (IR) was shown to affect outcome after coronary artery bypass surgery (CABG).[1-4]

This issue appears to be very important in deciding whether to adopt off-pump coronary artery bypass surgery (OPCAB), as a number of studies comparing OPCAB with conventional CABG have shown a higher incomplete revascularization rate, or lower mean number of bypass grafts, associated with off-pump surgery,[5-12] suggesting a potential detriment related to OPCAB application.

IR can derive from a surgical strategy of "target vessel revascularization" in high-risk patients, where the impact of surgery is minimized to reduce perioperative mortality and morbidity.[13] But IR can reflect the technical complexity of OPCAB. The perception of higher technical difficulties and the fear of deleterious effects on patient health can lead some operators to reduce the extension of revascularization during OPCAB, aimed at achieving the best feasible "safe" revascularization.

IR after OPCAB does not seem to affect perioperative morbidity,[7,13] but it is has been reported as a risk factor for survival in the first four to six months after surgery.[11]

The aim of this study is to assess the impact of completeness of revascularization on the short- and mid-term outcomes in patients undergoing OPCAB surgery in a single center.

MATERIALS AND METHODS

The data of the study came from five sources: (1) an institutional database of preoperative characteristics, surgical information, and in-hospital outcomes, including complications and adverse events, collected prospectively on all OPCAB surgery patients treated in our unit; (2) death registrations from hospital databases; (3) information about cardiac-related events from a postal questionnaire or telephone calls to patients and to their family physicians; (4) clinical assessments in hospital outpatient clinics; and (5) institutional cardiac catheter laboratory database.

This study was approved by the Institutional Ethics Committee on May 22, 2007. Informed consent was obtained from each patient included in the study.

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Patient population, indication criteria, and data definitions

From June 2000 to February 2005, 1,183 patients underwent isolated CABG surgery at the Cardiac Surgery Unit of Santa Croce Hospital, Cuneo, Italy. Of these patients, 312 (26%) were scheduled for OPCAB. Indications for OPCAB were based on surgeons' preference. Contraindications to OPCAB were[1]: unfavorable anatomy (intramyocardial vessels or vessels with distal calcification)[2]; and electrical and/or mechanical instability.

Complete revascularization (CR) was derived by comparing significantly stenotic vessels at cardiac catheterization with surgically grafted coronary vessels. Grafting of all the significantly stenotic coronary vessels was considered CR. Coronary vessels whose angiographic diameter was ≥1.5 mm were considered amenable for grafting.

An analysis based on the initial treatment intent was performed on the 312-patient cohort.

Early outcomes

Postoperative mortality included any death occurring during the same hospital admission for surgery or within 30 days of surgery.

Postoperative cardiac mortality included any death from cardiac causes. Postoperative Q-wave acute myocardial infarction included peak level of creatine kinase MB greater than 10% of total creatine kinase associated with new Q-wave or new left-bundle block.

Postoperative non-Q-wave acute myocardial infarction (AMI) was defined as greater than or equal to a five-fold increase of creatine kinase MB in the first postoperative week. Any AMI included postoperative Q-wave and non-Q-wave infarction. Perioperative low-output syndrome (LOS) included all conditions with a cardiac index <1.8 L/min requiring inotropes.

The diagnosis of stroke was established according to neurological medical records and included any new postoperative central neurological deficit persisting more than 24 hours and confirmed by computed tomography scans.

Postoperative acute renal failure (ARF) was defined as abnormal values of creatinine (>1.2 mmL/L) in patients with normal preoperative values and at least a 50% increase in postoperative serum creatinine concentration in patients with preoperative chronic renal failure or mild renal dysfunction.

Follow-up outcomes

Mortality included death from any cause. Cardiac mortality included any death from cardiac causes, sudden death, and death from unknown causes. Major adverse cardiac events (MACE) were defined as the composite end point of cardiac death, unstable angina, acute myocardial infarction, hospitalization for cardiac heart failure, and all-cause repeat revascularization, with patients included only once.

Target vessel repeat revascularization (TVR) included all procedures on grafts or grafted native vessels, more or less associated with the revascularization of vessels that were stenotic but not grafted, at surgery (incomplete surgical revascularization). OPCAB failure repeat revascularization (OFR) included TVR and all procedures needed exclusively for incomplete surgical revascularization. All causes of repeat revascularization included OFR and all procedures needed exclusively for new lesions of the native vessels.

Anesthetic, surgical technique, and postoperative management

The surgical and anesthetic techniques adopted have been previously described in literature.[14,15] Briefly, cardiovascular monitoring was performed with Swan-Ganz pulmonary artery catheter [when ejection fraction (EF) <30% a fiber-optic pulmonary artery catheter for continuous monitoring was used] and transesophageal echocardiography (TOE). Target artery stabilization was achieved with disposable suction devices (Medtronic Octopus, Medtronic Inc., Minneapolis, MN, USA). Traction sutures were always placed in the posterior pericardium to obtain heart verticalization. From January 2003, apical suction devices (Medtronic Starfish) were routinely used to optimize heart displacement. When an atheromatous ascending aorta wall was detected with TOE, the procedure was performed avoiding any aortic manipulation ("no-touch" technique). Silicon intracoronary shunts have been routinely used in performing distal anastomosis. After surgery, patients were transferred to the intensive therapy unit and managed according to a "fast-track" protocol.[15]

FOLLOW-UP

Cross-sectional follow-up data were collected through telephone interviews and clinical checkups in our outpatient clinic three months after surgery and thereafter at yearly intervals. Patients who underwent a telephone interview were asked to transmit their clinical reports, including all postoperative invasive and noninvasive diagnostic tests and revascularization procedures, to the investigators. Cardiology labs provided descriptions of provocative tests, angiographic studies, and revascularization procedures. Thirty-three patients (10.5%) underwent coronary angiography. Five patients (1.6%) were lost for follow-up.

Statistical analysis

Results were expressed as mean value and range unless otherwise indicated. All data were analyzed with the SAS System 9.1.3 statistical package (SAS Institute, Cary, NC, USA).[16] A statistical analysis comparing two groups was performed with unpaired 2-tailed *t*-testing for the means or chi-square test (or Fisher's exact test) for categorical variables. Survival curves were obtained according to the Kaplan-Meier method.[17] The association between clinical prognostic factors and the survival function was assessed by the log-rank test.[18] To check for potential confounders, a multivariate analysis based on the Cox proportional hazards regression model[19] was performed. The

TABLE 1
Prognostic Factors among Patients Receiving Complete and Incomplete Revascularization

Preoperative Data	Total Patients (n = 312)	CR (n = 207)	IR (n = 105)	p value
Mean age	68.7 (41–87)	66.4 (±9.1)	73.2 (±7.2)	$p < 0.0001$**
Sex female	82 (26.3)	54 (26.1)	28 (26.7)	$p = 0.91$*
One-vessel disease	28 (9.0)	22	6	
Two-vessel disease	84 (26.9)	62	22	$p = 0.06$*
Three-vessel disease	200 (64.1)	124	76	
EF < 30%	23 (7.4)	9 (4.4)	11 (10.5)	$p = 0.04$*
Extracardiac arteriopathy	94 (30.1)	48 (23.2)	46 (43.8)	$p = 0.002$*
COPD	57 (18.3)	28 (13.5)	29 (27.6)	$p = 0.002$*
Chronic renal failure	35 (11.2)	15 (7.3)	20 (19.1)	$p = 0.002$*
Insulin-treated diabetes mellitus	38 (12.2)	28 (13.5)	10 (9.5)	$p = 0.31$*
Obesity	35 (11.2)	18 (8.7)	17 (16.2)	$p = 0.048$*
Neurological dysfunction	18 (5.8)	9 (4.4)	9 (8.6)	$p = 0.13$*
Mean Euroscore	5.2 (0–15)	4.3 (±2.8)	6.8 (±2.9)	$p < 0.0001$**
Unstable angina	191 (61.2)	124 (59.9)	67 (63.8)	$p = 0.50$*

EF = left ventricle ejection fraction; COPD = chronic obstructive pulmonary disease.
Ranges and percentages are in brackets.
*Chi-square test.
***t*- test.

variables analyzed included all the factors that were found to be significant in the univariate analysis. For each variable, the proportional hazards assumption was tested graphically. The exponentiation of the coefficients estimated from the regression model can be assumed as the hazard ratio of disease progression in the exposed category of each variable, compared with the reference category, after allowing for the other factors entered in the model. Several Cox regression models were fitted. The goodness-of-fit of each model was assessed with the D statistic = –2 the likelihood ratio and the comparison between two models, when feasible, was tested calculating the likelihood ratio test.[20] The limit of significance for all analyses was defined as a p-value of 0.05. All statistical tests were 2-sided. Variables utilized for statistical analysis are listed in the Appendix.

RESULTS

Operative data

The on-pump conversion rate was 3.8% (12/312). Causes of on-pump conversion were: (1) electrical and/or mechanical instability (seven cases); (2) unsatisfactory quality of anastomosis (two cases); (3) ischemia following anastomosis (one case); (4) asymmetric sternotomy with impossibility of adequate lateral wall exposition (one case); and (5) unfavorable anatomy (one case). CR was achieved in 207 patients (66%). Patients receiving IR (105 patients, 34%) had a higher incidence of chronic obstructive pulmonary disease, extracardiac arteriopathy, chronic renal failure, severely depressed left ventricular function, and obesity and showed a higher mean age and Euroscore (Table 1). IR was associated with a lower arterial graft usage. The operative data are reported in Table 2.

Early results

Four patients (1.3%) died during hospitalization or within 30 days. Two patients died of massive pulmonary embolism, one due to sepsis, and one due to mesenteric ischemia following perioperative low-output syndrome. The incidence of AMI, stroke, LOS, and ARF were 4.5%, 0.6%, 5.1%, and 15.1%, respectively. Univariate analysis did not show any difference

TABLE 2
Operative Data

Operative Variables	Total Patients (n = 312)	CR (n = 207)	IR (n = 105)	p value
On-pump conversion	12 (3.8)	9 (4.3)	3 (2.9)	$p = 0.74$*
N. graft/patient	2.7 (1–5)	3.0 (1–5)	2.2 (1–4)	$p < 0.001$**
Two IMA	98 (31.4)	83 (40.1)	15 (14.3)	$p < 0.001$*
Radial artery usage	124 (39.7)	98 (47.3)	26 (24.8)	$p < 0.001$*
Sequential grafts	78 (25.0)	68 (32.9)	10 (9.5)	$p < 0.001$*
Composite grafts	91 (29.2)	68 (32.9)	23 (21.9)	$p = 0.06$*
Carotid endoarterectomy	21 (6.7)	11 (5.3)	10 (9.5)	$p = 0.25$*

*Chi-square test.
***t*- test.
Ranges and percentages are in brackets.
IMA = internal mammary artery; CR = complete revascularization; IR = incomplete revascularization.

TABLE 3
Hospital/30-Day Results

	CR		IR		
	OPC (n = 9)	Total Group (n = 207)	OPC (n = 3)	Total Group (n = 105)	p value
Death	0	3 (1.4)	0	1 (1.0)	0.87*
Cardiac death	0	1 (0.5)	0	1 (1.0)	0.80*
QAMI	0	1 (0.5)	0	2 (1.9)	0.55*
Non-QAMI	1 (11.1)	5 (2.4)	2 (66.7)	6 (5.7)	0.24*
AMI	1 (11.1)	6 (2.9)	2 (66.7)	8 (7.6)	0.11*
Stroke	0	2 (1.0)	0	0	0.80*
LOS	1 (11.1)	8 (3.9)	1 (33.3)	8 (7.6)	0.25**
ARF	2 (22.2)	29 (14.0)	2 (66.7)	18 (17.1)	0.57**

Percentages are in brackets.
OPC = on-pump conversion; QAMI = Q-wave acute myocardial infarction; Non-QAMI = non-Q-wave acute myocardial infarction; AMI = acute myocardial infarction; LOS = postoperative low-output syndrome; ARF = postoperative acute renal failure.
*Fisher's exact test.
**Chi-square test.

in early outcome between the patients receiving CR and those having IR (Table 3).

Mid-term results

Follow-up ranged from 8.9 to 72.3 months (mean 42) and was complete in 98% of patients. The cumulative patient survival at five years, taking into account also operative mortality, was 0.88 [0.02 SE (27 events)].

Five-year freedom from MACE was 0.86 [0.03 SE (30 events)].

Fifteen patients underwent TVR for graft failure [0.94 (0.02 SE) five-year freedom]. In all these cases the target vessel lesion was recognized to be the culprit lesion. One patient received PCI on both graft and stenotic vessels not grafted at surgery.

Among the patients receiving TVR, nine had stenotic vessels left behind at surgery, which were considered unsuitable for PCI because of chronic occlusion (five point) or diffuse disease (four point).

Five-year freedom from OFR was 0.93 [0.02 SE (16 events)]; only one repeat revascularization was performed to treat exclusively stenotic vessels not grafted at surgery.

Five-year freedom from all-cause repeat revascularization was 0.91 [0.02 SE (18 events)]; two patients underwent PCI exclusively for disease progression on the nongrafted native vessels.

Among the patients who underwent repeat revascularization, 11 (61%) had IR at surgery. All repeat revascularizations were PCI. After repeat revascularization, 17 patients remained asymptomatic and only one had a further PCI for stent occlusion at follow-up.

Five-year survival was influenced by postoperative acute renal failure [heart rate (HR) = 4.0, 95% confidence interval (CI) 1.8 to 8.9], extracardiac arteriopathy (HR = 3.7, 95% CI 1.4 to 9.9), chronic obstructive pulmonary disease (HR = 3.7, 95% CI 1.6 to 8.8), insulin-treated diabetes mellitus (HR = 3.4, 95% CI 1.3 to 8.9), and preoperative chronic renal failure (HR = 2.4, 95% CI 1.1 to 5.5).

CR was shown to be protective for MACE (HR = 0.2, 95% CI 0.1 to 0.5) (Fig. 1). In analyzing the predictors of the single factors of MACE, the Cox hazard model showed CR to be the only determinant for unstable angina (22 events, HR = 0.24, 95% CI 0.10 to 0.58), acute myocardial infarction (18 events, HR = 0.25, 95% CI 0.09 to 0.73), and all-cause repeat revascularization (HR = 0.35, 95% CI 0.13 to 0.90). Cardiac death (six events) was predicted by preoperative chronic renal failure (HR = 8.7, 95% CI 1.7 to 42.9). There were only two new admissions for cardiac failure and this number appeared too small to justify statistical analysis.

A positive effect of CR was also shown on OFR (HR = 0.32, 95% CI 0.12 to 0.88) and TVR (HR = 0.35, 95% CI 0.12 to 0.99).

CONCLUSIONS

We adopted an anatomic definition of completeness of revascularization, conditional for vessel diameter,[21] in order to avoid an underestimation of the rate of patients receiving IR.

The influence of IR on early outcome appears a controversial issue, as several studies report no differences in early morbidity and mortality between patients having CR and IR[7,13,22,23] while other experiences suggest a negative effect of IR on early survival,[11] especially in elderly patients.[24] Within the limits of our descriptive analysis, patients who had IR presented a worse preoperative risk profile then patients having CR and did not show higher early mortality and morbidity.

Although IR was shown to be an independent risk factor for mid- and long-term survival in several experiences,[2-4,11,22,25,26] this effect was not observed in our study. Only the preoperative conditions of the patients and postoperative acute renal failure, according to several experiences reported in literature,[27-32] represented the risk factors for reduced mid-term survival. Conversely, IR was shown to be a strong determinant of mid-term MACE.

The influence of IR on mid-term MACE appears related to a higher incidence of unstable angina, acute myocardial infarction, and new revascularization. It is

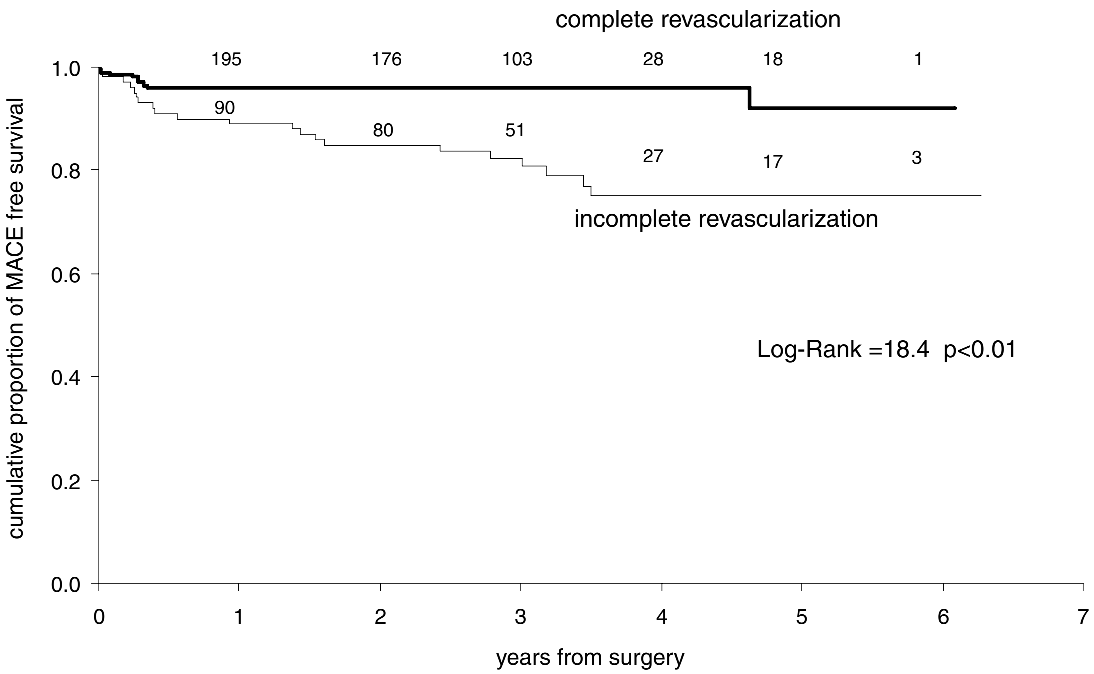

Figure 1. *Kaplan-Meier's estimates of MACE-free survival distribution by level of complete revascularization (312 patients). Residual numbers of patient at risk are reported for each year of follow-up.*

worth noting that, although 61% of patients receiving repeat revascularization had IR at surgery, most of the new PCI (83%) were performed to treat graft failure, which was identified as being responsible for the onset of symptoms. IR was identifiable as the only cause of repeat revascularization in a single case. Only three procedures were performed on stenotic vessels left behind at surgery and in two cases they were associated with TVR. Most of the patients who underwent repeat revascularization after IR did not receive a revascularization of the stenotic vessels not grafted at surgery, without further recurrence of symptoms.

This finding suggests that the influence of IR on repeat revascularization may not be related to the need for revascularization of the stenotic vessels left behind at surgery.

A role of IR in facilitating the onset of unstable angina and AMI in the cases of graft stenosis or occlusion could be hypothesized. The ischemic areas residual to the incomplete revascularization, when added to other ischemic areas due to graft failure, could concur to determine large amounts of ischemic myocardium, influencing the onset of clinical instability, the need for repeat revascularization, and, consequently, the hard end point of MACE.

We conclude that anatomic complete revascularization, although it may not influence short-term morbidity and mortality, may represent a protective factor for mid-term event-free survival.

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APPENDIX

List and definitions of the variables

Preoperative	
Age	Continuous (years)
Gender	Dichotomous
Extracardiac arteriopathy	Any or more of the following: claudication, carotid occlusion or >50% stenosis, previous or planned intervention on the abdominal aorta, limb arteries or carotids[33]
Carotid disease	Any degree of stenosis
Obesity	BMI > 30%
COPD	FEV1/FVC < 70% or chronic medical treatment
Chronic renal failure	Creatinine ≥ 2 micromol/l[33]
Mild renal dysfunction	Creatinine level between 1.3 and 1.9 micromol/l
Extra renal depuration	Any dialytic treatment
Any renal dysfunction	Dichotomous
Treated diabetes	Medical treatment for hyperglicemia
IT diabetes	Insulin-dependent diabetes
OT diabetes	Diabetes on oral treatment
Treated malignancy	Malignancy <5 years from the beginning of the therapy
Active malignancy	Malignancy diagnosed and not yet treated
Neurological dysfunction	Severely affecting ambulation or day-to-day functioning[33]
Chronic heart failure	Diagnosis in the history or at the admission, with specific drug treatment
Preoperative critical state	Any or more of the following: tachycardia or fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before arrival in the anaesthetic room, preoperative inotropic support, intra-aortic balloon counter-pulsation or preoperative acute renal failure[33]
Recent myocardial infarction	< 90 days[33]
Unstable angina	ACC/AHA guidelines criteria[34]
Euroscore unstable angina	Rest angina requiring iv nitrates until arrival in the anaesthetic room[33]
Number of stenotic vessels	Continuous
Left main stem stenosis	Stenosis ≥ 50%
Ejection fraction	Continuous
Poor left ventricular dysfunction	LVEF < 30%[33]
Additive EuroSCORE	Continuous
Operative	
Number of anastomoses	Continuous
"No touch" procedures	Operations performed without manipulation of ascending aorta
Associated carotid endoarterectomy	Performed in the same operation, before CAB
CR	See text
Bilateral mammary artery usage	In situ or free-graft
No mammary artery usage	Safenous vein or radial artery usage only
Surgeon	First operator
Postoperative	
Acute renal failure	See text
Low-output syndrome	See text
Q-wave acute myocardial infarction	See text
Non Q-wave acute myocardial infarction	See text
Any acute myocardial infarction	See text
Stroke	See text