

Clinical Outcomes and Angiographic Patency in 125 Consecutive Off-Pump Coronary Bypass Patients



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ABSTRACT

Background: This study compared clinical outcomes, length of stay, and hospital costs in patients having off-pump coronary bypass (OPCAB) versus conventional bypass surgery (CABG).

Methods: From November 1996 through April 9, 1999, OPCAB was performed for 125 consecutive patients and compared with a contemporaneous, matched control group of 625 CABG patients. Patients were matched according to age, gender, incidence of renal failure, diabetes, pulmonary disease, stroke (CVA), hypertension, peripheral vascular disease, and previous myocardial infarction. Follow-up in the OPCAB patients was 100% and averaged 15 months.

Results: An average of 2.0 grafts per patient were performed in the OPCAB group (range 1-5). Ninety-four OPCAB patients (75.2%) had a total of 179 grafts assessed angiographically prior to hospital discharge. All but 4/179 grafts (2.2%) were patent, including 94 of 94 IMA grafts (100%). There were no in-hospital deaths in the OPCAB group compared to a mortality rate of 1.4% in the CABG group. OPCAB reduced postoperative hospital stay from 5.5 days in the traditional CABG group to 3.3 days ($p=.002$), with a decrease in hospital cost of 24% ($p=.01$). In addition, there was a significant reduction in the rate of transfusion in the OPCAB group (29.6%) compared to the CABG group (56.5%, $p=.0001$). Two OPCAB patients required postoperative intervention to improve graft patency during the follow-up period. No internal mammary grafts required revision. There was

one perioperative CVA and one myocardial infarction in the OPCAB group.

Conclusions: OPCAB surgery reduces hospital cost, postoperative length of stay, and transfusion rate compared to CABG. OPCAB is safe, cost effective, and associated with excellent graft patency and clinical outcomes.

INTRODUCTION

In an attempt to avoid the deleterious effects of cardiopulmonary bypass (CPB), off-pump coronary bypass surgery has recently been rediscovered and refined. Coronary artery bypass graft surgery was first performed without the use of extracorporeal circulation in the late 1960s [Kirklin 1983]. This technique was largely abandoned after the use of CPB and cardioplegic arrest became routine [Buffolo 1996].

Blood contact with artificial surfaces on the CPB circuit produces a well-documented diffuse inflammatory response that affects multiple organ systems. Specific deleterious effects of the inflammatory response have been documented in the heart, lungs, central nervous system, kidneys, and gastrointestinal tract. Virtually all detrimental effects of this diffuse inflammatory response increase with increased duration of CPB [Edmunds 1997]. Also associated with increased CPB time are increased hospital costs and length of stay [Puskas 1998].

Multiple previous authors have reported series of off-pump CABG [Benetti 1995, Buffolo 1996, Calafiore 1996, Calafiore 1998, Bergsland 1999, Hart 1999]. While these authors have reported excellent mortality rates, concern has been raised of a decrement in graft patency rates [Subramanian 1997]. We previously described the early evolution of the off-pump coronary bypass operation at our institution, and reported outcomes in 51 off-pump patients to determine the safety and efficacy of off-pump coronary surgery [Puskas 1998]. The present study reports clinical outcomes and angiographic patency in 125 consecutive off-pump patients and compares these results to a computer-matched control group having CABG on cardiopulmonary bypass.

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Table 1. Preoperative Characteristics of the Groups

Variable	Off-pump	Control	p Value
Age (years)	61.0	61.4	NS
Gender (male, %)	69	72.5	NS
Hypertension (%)	68	72.3	NS
Renal insufficiency (%)	8	7.2	NS
Previous myocardial infarction (%)	38.4	49.8	NS
Previous stroke (%)	10.4	11.4	NS
Diabetes (%)	25.6	24.5	NS
Peripheral vascular disease (%)	19.2	22.6	NS
Chronic obstructive pulmonary disease (%)	25.6	20	.04

No significant difference in preoperative characteristics was found between groups.

MATERIALS AND METHODS

The off-pump group included 125 patients who presented from November 1996 through April 9, 1999 and underwent OPCAB by a single surgeon at Crawford Long Hospital of Emory University. The comparison group was a computer-matched control group derived from the Emory University Cardiac Surgical Database. For each off-pump patient, the computer generated five control patients matched for age, gender, and pre-existing disease, having primary coronary bypass surgery by the authors at the same institution during the same time period. Pre-existing disease variables included history of hypertension, diabetes, renal insufficiency (creatinine greater than 2.0 mg/dl), previous stroke, chronic obstructive pulmonary disease, peripheral vascular disease, and previous myocardial infarction.

During the first few months of the study period, the procedure was accomplished via minithoracotomy (MID-CAB; N = 9 patients) as previously described [Puskas 1998]. The surgical technique then evolved from a minithoracotomy to a median sternotomy incision. This was prompted by concern about precision and safety with the limited exposure afforded by minithoracotomy and by the very limited number of patients referred for surgical management of single-vessel disease at our institution. The remaining 116 patients underwent the off-pump operation through a median sternotomy incision. The internal mammary artery (IMA, right or left) was harvested under direct vision. Heparin administration has also evolved and now consists of a full pump dose of 400 units/kg administered prior to division of the internal mammary artery. This is partially reversed with a half dose of protamine (typically 1mg/kg) after completion of the last anastomosis. One of several commercially available mechanical stabilizing devices was used for stabilization of the coronary target(s) on the beating heart (United States Surgical, Norwalk CT; Cardiothoracic Systems, Cupertino CA; Medtronic Octopus II, Minneapolis MN; Genzyme, Boston MA). The target coronary arteries were occluded proximally with a silastic vessel loop, and retrograde bleeding was controlled with a sterile, humidified carbon dioxide blower. Distal anasto-

moses were constructed with 7-0 or 8-0 monofilament suture. Proximal anastomoses were sewn to the aorta under a partial occlusion clamp with 5-0 or 6-0 suture. Intraoperative epiaortic ultrasound was performed to rule out significant atherosclerosis of the ascending aorta prior to application of the clamp. Evidence of significant atherosclerosis (Grade III or higher) prompted alternative construction of proximal anastomoses on the LIMA pedicle.

Data reflecting intraoperative and postoperative variables were collected for comparisons. These data included the number of distal grafts, use of the internal mammary artery as a conduit, intra-aortic balloon pump, inotropic support for more than 48 hours postoperatively, intubation for greater than 48 hours following surgery, postoperative myocardial infarction, stroke, sternal wound infection, leg wound infection, renal failure, re-exploration for bleeding, transfusion requirements, atrial and ventricular arrhythmias, postoperative length of stay, and hospital costs associated with the operation.

In the early experience, any patient with a postoperative complaint remotely suggestive of angina underwent angiography. Later, all OPCAB patients were requested to consent to postoperative angiography under our institutional quality assurance protocol. Patients with preoperative renal insufficiency or severe calcification/atherosclerosis of the ascending aorta were excluded from postoperative angiography. In several other cases, patients or referring cardiologists refused postoperative catheterization. A total of 94 of the off-pump patients (75.2%) had coronary angiography to document graft patency prior to hospital discharge. None of the control patients had postoperative angiography.

Measures of central tendency, inferential, and multivariate statistics were used for the data analysis. The frequency, mean, and standard deviation were calculated for the independent and dependent variables. The Student's t-test was used for two-group comparisons with continuous variables. Chi-Square was used for comparisons with categorical variables. Comparisons between the two groups were made by using logistic regression for the dichotomous dependent variables. Multiple regression was used as a means to identify independent predictors of length of stay and hospital charges. An alpha level of .05 was used to determine significance [Bailar 1992].

RESULTS

All off-pump patients (thoracotomy and sternotomy approaches) were grouped together and compared with control patients having CABG on CPB. The off-pump group consisted of 125 patients, and the control group included 625 patients for a total sample of 750 patients. The two groups were compared on the basis of age, gender, and all seven comorbidities listed above to ensure that the two groups were appropriately matched (see Table 1). The mean age was 61.0 years (31% female and 69% male) for the off-pump group and 61.4 years for the control group (27.5% female and 72.5% male; $p=.4$). The groups differed only in preoperative chronic obstruc-

Table 2. Clinical Outcomes

Variable	Off-pump	Control	p Value
In-hospital mortality (%)	0	1.4	NS
Number of grafts	2.0 (range 1–5)	3.6 (range 2–7)	0.001
Stroke (%)	0.8	1.8	NS
Myocardial infarction (%)	0.8	0.5	NS
Re-entry for bleeding (%)	1.6	2.2	NS

No significant difference in mortality between groups. There were no in-hospital deaths in the off-pump group.

tive pulmonary disease (COPD) (25.6% OPCAB vs 20% traditional CABG; $p = .04$).

Table 2 (●) compares clinical outcomes between the two groups. No patient in the off-pump group had to be converted to CPB during the procedure. The mean number of distal anastomoses was significantly higher in the control group (3.6 grafts per patient) when compared with the OPCAB group (2.0 grafts per patient; $p = .001$).

There were no hospital deaths in the OPCAB group (0%) while there were nine in the control group (0.64%). These results did not reach statistical significance. Postoperative complications are presented in Table 3 (●). There was only one myocardial infarction in the OPCAB patients (0.8%) as compared with an incidence of 0.5% in those receiving traditional CABG (NS). A completed stroke occurred in 0.8% of the off-pump group versus 1.8% of patients with traditional CABG with CPB. There was also a significant reduction in postoperative inotropic support and intra-aortic balloon pump use in the off-pump group. Interestingly, there was no difference in the incidence of atrial fibrillation between groups, despite the absence of atrial sutures, cannulation, and extracorporeal circulation in the off-pump group. Both groups received a similar postoperative regimen of tapering beta-blockade for prophylaxis against atrial fibrillation.

A striking difference was found between groups in the incidence of postoperative transfusion requirements (see Table 4 ●). While more than half of the patients in the control group required transfusion of some blood

Table 3. Postoperative Complications

Variable	Off-pump	Control	p Value
IABP (%)	0.8	4.2	0.04
Inotropic support (%)	0.8	3.7	0.04
Prolonged intubation (%)	0	3.0	NS
Renal failure (%)	0.8	2.2	NS
Ventricular arrhythmia (%)	0	0.8	NS
Atrial arrhythmia (%)	14	13.9	NS
Sternal infection (%)	0	0.2	NS
Leg infection (%)	0.8	0.3	NS

Note that there was no significant difference in the incidence of atrial arrhythmia between groups.

Table 4. Transfusion Requirements

Variable	Off-pump	Control	p Value
Transfusion	29.6	56.5	0.0001
PRBC (units)	0.6	1.7	0.0001
Platelets (units pooled)	0.02	0.25	0.0001
Fresh frozen plasma (units)	0.03	0.26	0.0001
Cryoprecipitate (units)	0	0.19	0.0001

Less than one-third of the off-pump group had any transfusion requirement.

product(s) during their hospitalization, less than one-third of the off-pump group received any blood products ($p < .0001$).

Ninety-four of the off-pump patients (75.2%) had repeat coronary angiography prior to discharge: 175/179 grafts (97.7%) were widely patent, 3/179 were totally occluded (1.6%; all vein grafts to diagonal targets), and 1/179 anastomoses was narrowed $>50\%$ (0.5%; one vein graft to a posterior descending artery). All 94 internal mammary graft anastomoses were widely patent (100%; see Table 5 ●). One patient had asymptomatic occlusion of a vein graft to a diagonal target, with a widely patent LIMA-left anterior descending coronary artery (LAD) graft. One patient with undiagnosed protein C and S deficiencies had uneventful three-vessel OPCAB complicated by acute thrombosis of two vein grafts to diagonal coronary targets and suffered a perioperative anterior myocardial infarction (MI). An IABP was placed and she had urgent reoperation on CPB, with replacement of her vein grafts. Subsequent repeat postoperative catheterization documented patency of her original LIMA and both reoperative vein grafts. She was discharged home on aspirin and warfarin under the care of a hematologist. One patient had asymptomatic stenosis of a vein graft to a small posterior descending coronary artery. All other graft anastomoses were widely patent on postoperative catheterization.

Dramatic differences in total postoperative length of stay and hospital costs were found between groups (see Table 6 ●). Length of stay was reduced by 40%, while hospital costs fell by 24% for the off-pump group. CPB was found to be an independent predictor of increased hospital cost and increased postoperative length of stay.

The multiple regression model for length of stay had a multiple R of 0.49, R squared of 0.24, $F = 17.73$, $p = .00001$.

Table 5. Angiography Results

Number of grafts	Widely patent	$>50\%$ stenosis	Totally occluded
94 IMA grafts	100%	0%	0%
82 SVG grafts	95.1%	1.2%	3.7%
3 RA grafts	100%	0%	0%
179 total grafts	97.8%	0.6%	1.7%

All IMA grafts were patent, with 97.8% patency rate for all grafts studied before hospital discharge.

Table 6. Length of Stay and Hospital Costs

Variable	Off-pump	Control	p Value
Hospital costs (\$)	15,033	19,644	0.013
Postop length of stay (days)	3.3	5.5	0.002

There was a significant reduction in cost and length of stay associated with the off-pump group.

Significant variables which contributed to the model of length of stay were CPB, atrial arrhythmia, prolonged intubation, inotropic support greater than 48 hours, sternal wound infection, and transfusion requirement. Additional variables analyzed which were not independently significant included re-exploration for bleeding, postoperative renal failure, postoperative stroke, and postoperative MI. When mortality was included in the length of stay model, death was a significant independent predictor (see Table 7 ●).

The following variables contributed to a significant model predicting hospital cost: CPB, postoperative renal failure, transfusion, prolonged intubation and inotropic support, intra-aortic balloon pump, pre-existing COPD, and the presence of any complication. Variables entered into the regression equation that were not independently significant included the number of grafts, postoperative stroke, and postoperative MI. The multiple R was 0.62, R squared was 0.38, F = 19.9, p = .00001 for the cost model (see Table 8 ●).

Follow-up was 100% complete for the 125 OPCAB patients. (The conventional CABG patients matched from the database served as controls for comparisons of perioperative events. There was no follow-up of these control patients after hospital discharge.) All OPCAB patients were telephoned and questioned regarding any recurrent angina, myocardial infarction, cardiac reintervention, hospital readmission, wound complications, infections, etc. Follow-up ranged from one month to 29 months, with a mean of 15 months.

Two patients developed recurrent angina in the OPCAB group. A 67-year-old smoker with oxygen-dependent COPD and bilateral carotid occlusions had an uneventful three-vessel OPCAB and was readmitted to hospital with chest pain 12 months postoperatively. Car-

Table 7. Multiple Regression Model of Hospital Length of Stay

Variable	p Value
Cardiopulmonary bypass	0.0032
Atrial arrhythmia	0.0003
Prolonged intubation	0.0001
Sternal wound infection	0.03
Transfusion	0.03
Intra-aortic balloon pump	NS
Re-exploration for bleeding	NS
Postoperative renal failure	NS
Postoperative stroke	NS
Postoperative myocardial infarction	NS

CPB and atrial arrhythmia are independent predictors of length of stay.

Table 8. Multiple Regression Model of Hospital Cost

Variable	p Value
Cardiopulmonary bypass	0.0001
Transfusion	0.0001
Postoperative renal failure	0.0009
Intra-aortic balloon pump	0.003
Prolonged inotropic support	0.0008
Prolonged intubation	0.0001
COPD	0.07
Any complication	0.05
Postoperative stroke	NS
Postoperative myocardial infarction	NS
Atrial arrhythmia	NS
Re-exploration for bleeding	NS
Number of distal grafts	NS

CPB and atrial arrhythmia are independent predictors of hospital cost.

diac catheterization revealed a LIMA string sign and occlusion of the saphenous vein graft to the right coronary artery. The diagonal vein graft was widely patent, and the patient was managed medically. Another patient very early in our experience had an OPCAB single vessel vein graft to an intramyocardial ramus intermedius target. Early angiography demonstrated that the graft was patent, but had been misplaced to a small branch of the intended vessel. This graft closed six weeks after discharge, and PTCA was performed to the ramus intermedius, with resolution of angina symptoms.

There was one death after hospital discharge in the OPCAB group. This 81-year-old woman with COPD (oxygen-dependent, FEV₁ = 0.48 L), a porcelain aorta, moderate mitral regurgitation, and a 90% ostial left main lesion had a single vessel OPCAB with LIMA-LAD. She was discharged on postoperative day six and expired at home less than 30 days after hospital discharge. All other OPCAB patients are alive and well without angina at mean follow-up 15 months.

DISCUSSION

Pioneered by Benetti and Buffolo in South America almost twenty years ago, CABG without CPB has been recently rediscovered and continues to be refined. Off-pump CABG via sternotomy can now be performed for lesions in virtually any coronary artery with presently available instrumentation and a high degree of patient safety and surgeon comfort. Clinical and angiographic results described above support this statement. No patient in the off-pump group had to be converted to CPB during the procedure. Surgical management of lesions in the left circumflex territory formerly required cardiopulmonary bypass at this institution and limited the proportion of coronary cases which could be performed off-pump to less than 20%. We have considered complete revascularization to be the “gold standard” for coronary bypass surgery irrespective of the surgeon’s choice of incision or use of cardiopulmonary bypass, and still hold this belief. Incremen-

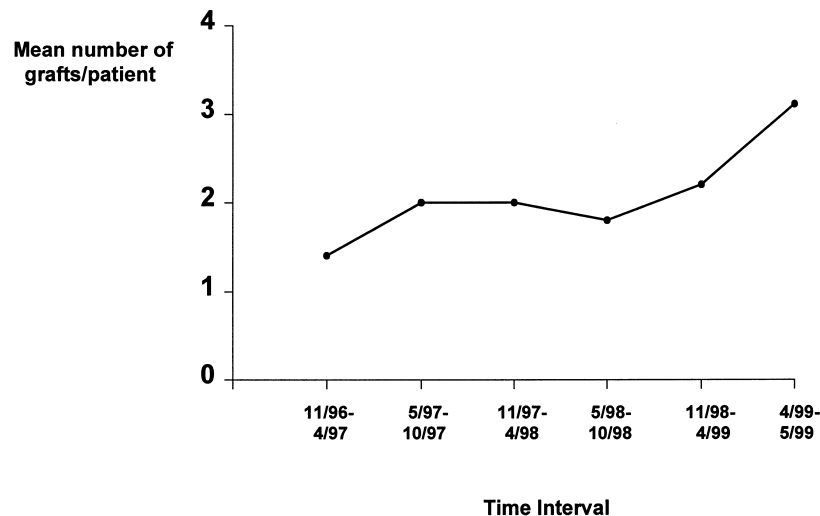


Figure 1. Number of grafts per patient during five time intervals. Note the dramatic increase in recent months as improved technique and stabilizers allowed routine access to the obtuse marginal coronary arteries.

tal improvements in surgical technique, including the routine use of wide bilateral transverse diaphragmatic pericardiotomies, multiple deep pericardial traction sutures and rotation of the heart into the right pleural space have recently allowed visualization of obtuse marginal coronary targets in a high proportion of patients. This has led to a recent sharp increase in the number of grafts per patient in the OPCAB group (see Figure 1). The very recent commercial introduction of improved mechanical stabilizer devices has also contributed significantly to a fundamental shift towards OPCAB (see Figure 2). Presently, over 80% of all CABG cases may be safely done off-pump by an experienced OPCAB surgeon, including those requiring grafts to the obtuse marginal branches of the left circumflex artery.

The preoperative differences between the OPCAB and CABG groups (see Table 1) reflect the evolving bimodal pattern of patients referred specifically for OPCAB. The first is a small group of young, healthy patients who have failed PTCA for single or double vessel disease and the second, a growing number of older, sicker patients with relative or absolute contraindications to cardiopulmonary bypass. This latter group has multiple severe comorbidities, often including pre-dialysis renal failure, oxygen-dependent COPD, and morbid peripheral vascular disease including unilateral or bilateral carotid occlusion. These patients often have been refused CABG in the past. Thus, the incidence of severe COPD in the OPCAB group was so high compared to patients undergoing conventional

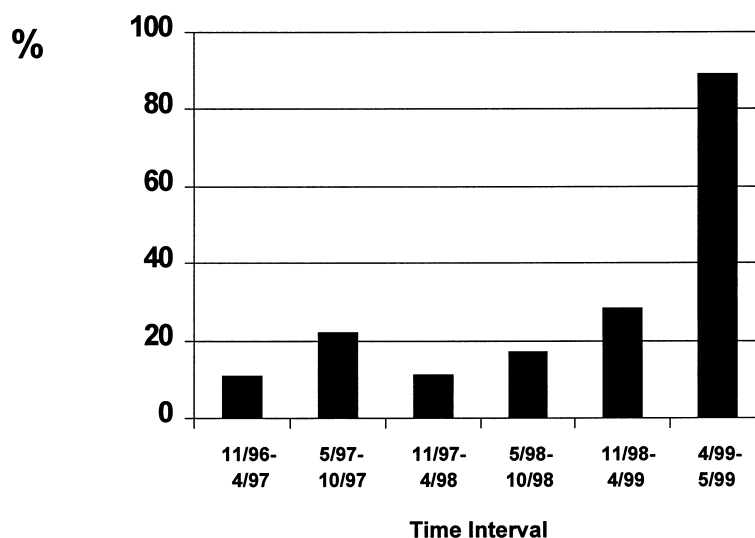


Figure 2. Percentage of cases performed without cardiopulmonary bypass. Note the dramatic increase in recent months. This increase is due to important improvements in surgical technique along with significant advances in stabilization devices, allowing routine access to the obtuse marginal branches of the left circumflex artery.

CABG that the Emory University Cardiac Surgical Database could not match completely for this variable, given the other constraints imposed in the matching program. This resulted in the observed preoperative difference between groups with respect to incidence of COPD.

The emphasis of minimally invasive cardiac surgery is on less invasive techniques which may decrease cost, length of hospital stay, and the overall morbidity associated with cardiac surgery. As older, sicker patients are referred for coronary bypass surgery, an increasing proportion of patients may have relative contraindications to CPB. The present study demonstrated that CPB is a statistically significant independent predictor of hospital cost and length of stay.

The early angiographic patency rates presented here equal or exceed all published series for coronary bypass on CPB, and are encouraging relative to many earlier series of MIDCAB and OPCAB results [Mack 1998]. All 94 internal mammary anastomoses and all but 4 of 179 total grafts studied prior to hospital discharge were widely patent. This is clear evidence that careful technique and use of advanced mechanical stabilizer devices permit reproducible, precise construction of coronary bypass anastomoses on the beating heart. All routine conduits (LIMA, RIMA, radial artery, saphenous vein) were used in this series to bypass all named coronary targets, including the obtuse marginal branches of the left circumflex coronary artery. Clinical outcomes during a mean 15 months of follow-up strongly suggest that these excellent early outcomes in the OPCAB group are maintained over time. Nonetheless, the conclusions from this series are weakened by its short period of follow-up and its retrospective and non-randomized nature, despite the use of a computer-generated contemporaneous control group matched for multiple indices of perioperative risk. Only a large, prospective, randomized, longitudinal comparison of graft patency and clinical outcomes after coronary bypass surgery performed with and without the use of cardiopulmonary bypass can ultimately validate the safety, efficacy, and superiority of the off-pump approach.

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