Clinical Outcomes of Coronary Revascularization without Cardiopulmonary Bypass

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ABSTRACT

Objective: Coronary artery bypass without cardiopulmonary bypass (OPCAB) eliminates the complications related to cardiopulmonary bypass. However, the long-term outcomes of this procedure are largely unknown.

Methods: We sought to investigate the rates of late mortality, stroke, acute myocardial infarction, and target vessel reintervention after OPCAB in a consecutive series of 857 patients who underwent OPCAB between May 1987 and March 1999.

Results: Long-term follow-up was obtained for 86% of eligible patients. Actuarial and event-free survival was 89% and 76%, respectively, for a median follow-up period of 2.2 years (range, 0-13.3 years). Risk factors for late mortality were identified with Cox regression analysis. In the multivariate analysis, patient age >75 years (odds ratio, 1.1; 95% confidence interval, 1.0-1.1; *P* = .01) and an ejection fraction <35% (odds ratio, 2.7; 95% confidence interval, 1.2-6.2; *P* = .02) emerged as independent predictors of late mortality.

Conclusion: OPCAB is associated with a low mortality and clinical event rate. Advanced age and depressed ejection fraction may increase mortality after OPCAB.

INTRODUCTION

Minimally invasive techniques without cardiopulmonary bypass for coronary revascularization (OPCAB) have gained wide acceptance as an alternative to the conventional on–cardiopulmonary bypass approach [Subramanian 1999]. Encouraging early clinical reports on coronary revascularization without cardiopulmonary bypass, which demonstrated excellent early patency rates, low morbidity and mortality, and shortened hospital stays, have stimulated worldwide interest in these techniques [Stanbridge 1997]. Elimination of cardiopulmonary bypass is desirable, because extracorporeal circulation elicits a series of physiologic derangements, including the activation of a systemic inflammatory response as well as detrimental hematologic effects that hinder normal hemostasis [Lancey 2001, Puskas 1998, Stamou 2001]. Compared with on-pump techniques, OPCAB has been associated with decreased foreign surface/blood interactions and shear response [Allen 1997], lower stroke rates, and improved perioperative outcomes [BhaskerRao 1998, Stamou 2000]. OPCAB may also be of particular benefit to patients at high risk for coronary artery bypass graft (CABG) surgery (ie, octogenarians, patients with atherosclerosis of the ascending aorta, patients undergoing reoperations, or patients with impaired left ventricular function) [Cernaianu 1995].

Early outcome findings of OPCAB have been encouraging [Puskas 1998], but few long-term outcome studies have yet been published. The purpose of the present study was to investigate clinical outcomes after OPCAB for a consecutive series of patients who were followed for periods up to 13 years following the procedure.

METHODS

Patients

A total of 926 patients underwent OPCAB at the Washington Hospital Center since the introduction of the technique in May 1987 until March 1999. Fifty-six of these patients refused consent for this study, and 13 resided out of the country. Thus, 857 patients were eligible for inclusion in the study.

Selection Criteria

Indications for OPCAB included high risk for on-pump CABG because of medical comorbid conditions such as renal failure, diffuse cerebrovascular and peripheral vascular disease, aortic atherosclerosis, chronic obstructive pulmonary disease, and religious convictions that precluded blood transfusions [Stamou 2000].

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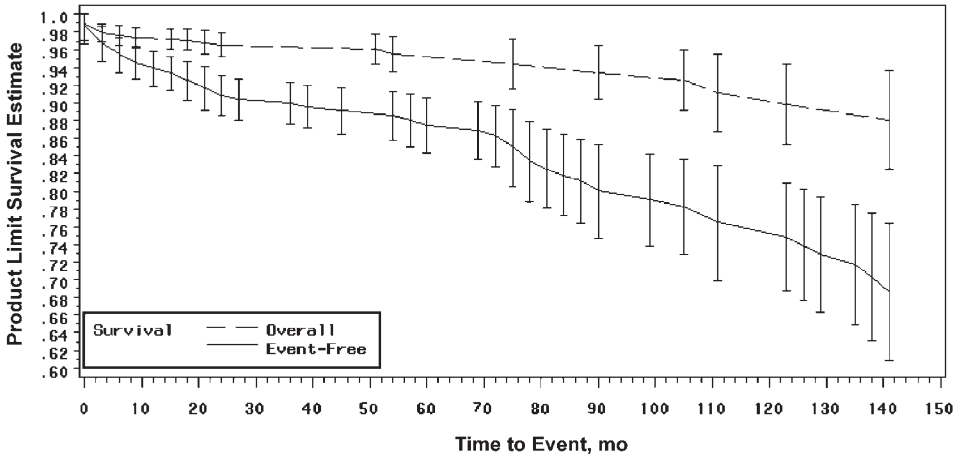

Actuarial and event-free survival of patients who had off-pump coronary artery bypass surgery.

Surgical Techniques

OPCAB was performed with 1 of 3 surgical approaches: median sternotomy (n = 589; 69%) and anterior (n = 245; 28%) or lateral (n = 23; 3%) minimally invasive direct coronary artery bypass (MIDCAB). A median sternotomy approach was favored in the grafting of the right coronary artery or the posterior descending branch. Main indications for anterior MIDCAB included isolated proximal disease of the left anterior descending or first diagonal artery, and the principal indication for lateral MIDCAB was regrafting of the circumflex system. Surgical techniques and the selection criteria in this group of patients have been described elsewhere [Stamou 2000].

Follow-up

Baseline demographics, procedural data, and perioperative outcomes were recorded at the time of the procedure and entered prospectively in a computerized database by a dedicated data-coordinating center. All hospital adverse events were source documented and were entered with standardized criteria in a computerized database by research nurses (exclusive of the nurses who performed the data collection). A separate team of research assistants prospectively collected follow-up clinical data via telephone questionnaire (patients were contacted between March 1999 and June 2000) after the patient hospital discharge, and events were similarly reconciled after reviewing the original source documents (medical records, electrocardiograms, laboratory reports, and catheterization sheets). Event-free survival was defined as the period of freedom from hospitalized myocardial infarction, stroke requiring hospitalization, death, or reinterventions (percutaneous transcatheter interventions or reoperative CABG), whichever occurred first.

Statistical Analysis

Descriptive statistics are reported for preoperative, operative, and postoperative characteristics. The Fisher exact test was used to compare categorical variables. The Wilcoxon test was used to compare continuous variables that were not normally distributed. Event-free survival was computed with Kaplan-Meier survival curves. Cox proportional hazards multivariate regression analysis was used to determine the independent predictors of mortality (excluding operative or 30-day mortality) and of major adverse cardiac events (myocardial infarction requiring hospitalization, stroke requiring hospitalization, death, or reinterventions). Likelihood with 95% confidence intervals are reported. Model fit was evaluated with residual analysis techniques. P values <.05 were considered statistically significant.

RESULTS

Follow-up information was obtained for 735 (86%) of the 857 eligible patients. The patients lost to follow-up were distributed evenly among the years (62 patients had surgery before 1995, and 60 patients had surgery after 1995). The median follow-up period was 2.2 years (range, 0-13.3 years) (Figure). Baseline clinical characteristics are summarized in Table 1.

Table 1. Preoperative Patient Characteristics (N = 857)*

Age, y	64 ± 11.7
Female sex, n	282 (33.1%)
Diabetes, n	181 (21.1%)
Hypertension, n	504 (58.8%)
Renal failure (creatinine >2.0 mg/dL), n	36 (4.2%)
Ejection fraction <35%, n	153 (17.8%)
Congestive heart failure, n	50 (5.8%)
Prior myocardial infarction, n	388 (45.3%)
Preoperative IABP, n	9 (1.0%)
Reoperative CABG, n	144 (16.8%)
Cerebrovascular accident, n	57 (6.6%)
COPD, n	43 (5.0%)
Carotid artery disease, n	24 (2.8%)

*Ages are expressed as the mean ± SD. IABP indicates intra-aortic balloon counterpulsation; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease.

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Table 2. Operative Characteristics and Postoperative Morbidity (N = 857)*

Operative	
Surgical approach	
Median sternotomy, n	589 (68.7%)
Anterior MIDCAB, n	245 (28.5%)
Lateral MIDCAB, n	23 (2.6%)
No. of grafts, median (range)	2 (1-8)
Postoperative	
Postoperative transfusions, n	104 (12.1%)
Atrial fibrillation, n	184 (21.4%)
Renal failure, n	36 (4.2%)
Reoperation, bleeding, n	9 (1.0%)
Prolonged ventilation, n	12 (1.4%)
Pulmonary edema, n	10 (1.2%)
Hemodialysis, n	5 (0.6%)
Reoperation, cardiac, n	3 (0.3%)
Myocardial infarction, n	3 (0.3%)
Median length of stay (range), d	6 (1-85)

*MIDCAB indicates minimally invasive direct coronary artery bypass.

Hospital Outcome

Hospital results are presented in Table 2. Postoperative new-onset atrial fibrillation was the most common complication and occurred in 21.4% of patients. The 30-day (operative) mortality rate was 2.1% (n = 18). Angiograms for persistent postoperative chest pain were performed in 3 patients (0.3%) and showed patent FitzGibbon grade A anastomoses [FitzGibbon 1978]. Length of hospital stay was significantly longer in the first half of the study period than in the second half. The median stay was 6 days (range, 4-29 days) for the first half versus 4 days (range, 1-85 days) for the second half ($P < .001$, Wilcoxon rank sum test).

Long-term Clinical Outcome

In the year following surgery, 33 patients (4%) underwent angiography (Table 3). Of these patients, 1 (3%) underwent CABG, 17 (52%) underwent transcatheter cardiovascular therapy, and the remaining 15 (45%) were managed medically. At the end of 5 years, 78 patients (9%) had angiograms, 1 (1%) underwent CABG, 32 (41%) underwent transcatheter cardiovascular therapy, and the remaining 45 (58%) were managed medically. At the end of 10 years, 94 patients (11%) underwent angiography, 1 (1%) underwent CABG, 39 (42%) underwent transcatheter cardiovascular therapy, and the remaining 54 (57%) were medically managed (Table 4). The Figure illustrates the actuarial and event-free survival of patients who had OPCAB. Causes of death were cardiovascular for 35% of patients (6 of 17 late deaths; data not shown).

Table 4 demonstrates the angiographic findings in target vessels (grafted) and nontarget (nongrafted) vessels. Significant stenosis was defined as >50% decrease in diameter.

Multivariate Analysis

Because of sample size limitations, variables were screened with a forward selection procedure for inclusion in the regression model. In the Cox regression analysis, a patient age >75 years and an ejection fraction < 35% emerged as independent predictors of late mortality (Table 5). Peripheral vascular disease, diabetes, and hypertension emerged as independent predictors of late major cardiac events (Table 5). Renal failure could not be included in the first model, and prior acute myocardial infarction could not be included in the first and the second models because the cell sizes were too small to permit a good model fit.

DISCUSSION

The concept of employing OPCAB for coronary revascularization proposes that patient morbidity and potentially mortality can ultimately be reduced without compromising the excellent results of the conventional on–cardiopulmonary bypass approach. Compared with on-pump CABG, OPCAB has been associated with decreased foreign surface/blood interactions and shear response [Allen 1997], lower rates of atrial fibrillation [Allen 1997, Stamou 2000] and stroke [BhaskerRao 1998], and improved perioperative outcomes [Stamou 2001]. The decreased incidence of organ dysfunction obtained with OPCAB has been largely ascribed to the avoidance of the systemic inflammatory response elicited by the cardiopulmonary bypass circuit that may account for the increased morbidity and mortality observed after conventional CABG [Magee 2002].

Despite encouraging early reports [Subramanian 1999], OPCAB surgery has raised concerns about its technical limitations and the accuracy/durability of the anastomosis [Lytle 1996, Ullyot 1996]. Inappropriate patient selection (ie, those with small, calcified, or intramyocardial vessels) and inadequate exposure or stabilization of the anastomotic site are

Table 3. Late Clinical Events*

	30 Days (n = 857)		1 Year (n = 728)		5 Years (n = 703)		10 Years (n = 164)	
	Survival	No. of Events	Survival	No. of Events	Survival	No. of events	Survival	No. of Events
Event-free survival	.97 (.99-.96)	20	.93 (.95-.91)	54	.87 (.90-.84)	81	.76 (.81-.70)	97
Actuarial survival	.98 (.99-.97)	15	.97 (.98-.95)	26	.94 (.96-.91)	36	.89 (.94-.85)	42
AMI-free	.99 (1.0-.99)	2	.99 (1.0-.99)	6	.98 (.99-.96)	11	.95 (.99-.93)	14
Stroke-free	.99 (1.0-.99)	3	.99 (1.0-.99)	5	.98 (1.0-.97)	8	.96 (.99-.94)	11
Revascularization-free	1.0 (—)	0	.97 (.99-.96)	18	.89 (.93-.85)	33	.87 (.92-.82)	40

*Data are presented as the product limit survival estimate (95% confidence interval, with the upper limit first). AMI indicates acute myocardial infarction.

Table 4. Patients with Angiographic Findings and Treatment*

	1 Year, n (%)	5 Years, n (%)	10 Years, n (%)
Angiograms	33 (4)	78 (9)	94 (11)
New TV stenosis (>50%)	9 (27)	14 (18)	17 (18)
Non-TV stenosis (>50%)	18 (54)	45 (58)	56 (60)
<50% Stenosis	6 (19)	19 (24)	21 (22)
TCT	17 (52)	32 (41)	39 (42)
CABG	1 (3)	1 (1)	1 (1)
Medical management	15 (45)	45 (58)	54 (57)

*TV indicates target vessel; TCT, transcatheter cardiovascular therapy; CABG, coronary artery bypass graft.

major causes of suboptimal results. Gundry and colleagues [Gundry 1998] in their initial experience with off-pump CABG found that twice as many off-pump patients required recatheterization (20% off-pump versus 7% on-pump) and attributed this difference to the limited revascularization obtained during the initial period of employing off-pump CABG. In our initial experience with 274 off-pump patients who had MIDCAB, most of whom received 1 or 2 grafts, the reintervention rate (redo CABG or percutaneous transcatheter intervention) was 4% for the first year after surgery [Mehran 2000]. The learning curve of this technically demanding novel approach may account for this rate of graft failure [Mehran 2000]. In the present study, we present 10-year follow-up results after OPCAB. The clinical event rate was low, and there was a slight tendency toward improvement with accumulated technical experience. Length of hospital stay was also abbreviated during the course of the study.

Perioperative Outcome

Despite the absence of angiographic follow-up, the event-free 30-day recovery of 97% of the entire cohort appears encouraging for OPCAB. This result mirrors the reported 98% in-hospital patency rate (with possible obstructive stenosis) of anastomoses of the left internal mammary artery to the left anterior descending coronary artery after conventional on-pump CABG [Berger 1999].

Table 5. Predictors of Mortality and Major Adverse Cardiac Events*

	Odds Ratio	95% Confidence Intervals	*P*
Mortality			
Age >75 y	1.1	1.0-1.1	.01
Ejection fraction <35%	2.7	1.2-6.2	.02
Major adverse cardiac events			
Diabetes	1.8	1.1-3.1	.03
Peripheral vascular disease	2.0	1.1-3.7	.02
Hypertension	1.7	1.0-2.7	.03

*Cardiac events are death, acute myocardial infarction, stroke, and revascularization (transcatheter cardiovascular therapy or coronary artery bypass graft surgery).

Long-term Clinical Outcome

The low rate of repeat revascularization documented in our study supports the safety of OPCAB as a surgical option for the treatment of coronary artery disease. The 1-, 5-, and 10-year reintervention rates of 3%, 11%, and 13%, as well as the respective actuarial survival rates of 97%, 94%, and 89%, are promising and emphasize the efficacy of OPCAB versus the conventional on-pump approach. Length of stay was abbreviated during the course of the study, reflecting the improvements in surgical techniques and in patient management as more experience was acquired through the study period.

Predictors of Late Mortality

Only age and depressed ejection fraction were statistically significant predictors of mortality after OPCAB, results echoing previous reports on conventional CABG [Herlitz 2000]. Statistically significant predictors of major acute cardiac events following OPCAB included diabetes, peripheral vascular disease, and hypertension.

Clinical Implications

The relatively low rate of acute myocardial infarction and stroke after OPCAB suggests that OPCAB is a safe alternative to conventional on-pump CABG for coronary revascularization. The heightened stroke and acute myocardial infarction rates documented after on-pump CABG may be related to the postoperative organ dysfunction triggered by the cardiopulmonary bypass and the systemic inflammatory response associated with it, the so-called postpump syndrome. Elimination of cardiopulmonary bypass may benefit patients who are at high risk for stroke and acute myocardial infarction, even many years after the procedure.

Study Limitations

The limitations of our study include the retrospective single-institution methodology and the lack of angiographic follow-up. However, all data elements were prospectively recorded according to prespecified definitions. Although the rates of mortality and loss to follow-up remained constant over the study period, there were changes in the diagnosis and treatment of cardiac disease over that time that cannot be accounted for in the statistical analysis. In addition, more patients were entered in the latter part of the study period than in the beginning.

Conclusions

Excellent clinical results can be achieved with OPCAB 10 years following the completion of procedure. OPCAB is a safe alternative to the conventional on–cardiopulmonary bypass approach and offers decreased cardiac event rates and relatively low late mortality.

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