Background—Off-pump coronary artery bypass surgery (OPCAB) is currently used as an alternative to conventional “on-pump” surgery, but there are very little data available on long-term follow-up. The aim of this study was to review our long-term experience with the use of systematic OPCAB.

Methods and Results—1000 consecutive OPCAB surgeries were systematically performed between 1996 and 2004, representing 95% of all coronary revascularization during that same time frame, with a 97% complete follow-up. Average age of the patients was 64 ± 10 years (778 men and 222 women). Seventy-three percent had triple-vessel disease. Operative 30-day mortality was 1.6%. Overall survival at 96 months was 74 ± 3.5% and cardiac survival was 94 ± 1.3%. By Cox regression analysis, age (odds ratio [OR], 1.07), congestive heart failure (CHF) (OR, 1.90), peripheral vascular disease (OR, 1.74), chronic renal insufficiency (OR, 2.04), previous myocardial infarction (MI) (OR, 1.60), and New York Heart Association functional class (OR, 1.60) were risk factors for long-term mortality. Survival free of any cardiac events (cardiac death, MI, unstable angina, heart failure, or reintervention) was 80 ± 3.4%. Survival free of any type of reintervention alone was 90 ± 3%. By Cox regression analysis, mitral regurgitation (OR, 2.3), peripheral vascular disease (OR, 2.1), and diffuse coronary disease (OR, 2.3) were significant predictors of recurrent cardiac events. Conversion to “on-pump” (OR, 14.3) was predictor of long-term need for repeat revascularization.

Conclusion—In this series, systematic OPCAB surgery was shown to be an acceptable alternative to conventional “on-pump” coronary artery bypass graft for the treatment of coronary artery disease. (Circulation. 2006;114[suppl I]: I-486–I-491.)

Key Words: coronary disease ■ surgery ■ survival

The safety of off-pump coronary artery bypass (OPCAB) has been clearly established by many groups with immediate and short-term results comparable to conventional coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB).1–3 However, the long-term results after OPCAB are scarce in the literature. Nevertheless, if long-term results are proven satisfying, this technique can be established as a definite alternative to on-pump CABG.

Use of CPB with cardiac arrest provides a bloodless field and a perfectly still heart to perform distal anastomoses. However, CPB is associated with activation of the inflammatory cascade and is a major determinant of perioperative morbidities, hospital length of stay,4,5 and costs.6,7 With the use of improved cardiac stabilizers, refinements in the surgical technique,8 increasing surgical experience, and close collaboration from the anesthesiology team, OPCAB surgery becomes possible in almost all cases. Although completeness of revascularization was a major concern in the early era of beating heart surgery, most recent series have shown the absence of any such disparity between OPCAB and conventional on-pump CABG.5 Despite uncertain benefit of OPCAB surgery in the short- and medium-term according to some reports,8–11 it is generally accepted that OPCAB represents a safe alternative to conventional on-pump CABG in most patients. However, long-term results are few in the literature. Therefore, the objective of this study was to analyze the long-term (up to 8 years) clinical results after OPCAB and to identify factors predictive of poor long-term outcomes.

Materials and Methods

Study Design

This is a retrospective analysis of prospectively gathered data over an 8-year period (mean: 42 ± 26 months) of patients systematically undergoing OPCAB surgery by a single surgeon (R.C.) at the Montreal Heart Institute. From January 1997 to December 2004, 1000 OPCAB surgeries were performed, representing the surgeon’s total OPCAB experience. Figure 1A and 1B shows the progression of OPCAB procedures compared with on-pump CABG through the years, exceeding 97% after 1998. Follow-up of the patients was 97% complete and was performed using phone and chart reviews.
Heparin was administered at a half dose of 150 KIU/kg. Patients with hemodynamic instability, deep myocardial left anterior descending artery (LAD), and moderate to severe (3+) mitral regurgitation were excluded from undergoing OPCAB surgery. Absolute contraindications to OPCAB surgery were: preoperative angiography hardly justifiable. Therefore, only patients who presented adverse cardiac events (recurrent angina, MI, or CHF) or those whose symptoms were doubtful enough to warrant invasive imaging angiography before discharge from the hospital to assess the safety and patency of the constructed grafts. The first 12 patients in this series underwent systematic coronary angiography before discharge from the hospital to assess the safety and patency of the constructed grafts.12 The results are included in the final analysis, although they do not reflect long-term follow-up.

Clinical Follow-Up
All preoperative, intraoperative, and early postoperative data were prospectively gathered. Perioperative myocardial infarction (MI) was defined as a new Q wave on ECG (EKG) by Minnesota code criteria or myocardium specific creatine kinase (CK-MB) levels >100 ng/mL after surgery. Clinical follow-up thereafter was completed through several means: Patients were seen for regular postoperative visits. All patients were followed-up by telephone by the attending surgeon and chart reviews were reviewed whenever applicable in case of visits to the emergency or hospitalizations. If patients visited a different hospital, the attending physician was consulted for the consultation motive and subsequent findings. All data were systematically entered into the database.

Adverse cardiac events on follow-up were defined as: cardiac death or death of unknown cause, MI, recurrent angina, hospitalization for congestive heart failure (CHF), or repeat revascularization (surgery or percutaneous coronary intervention [PCI]).

Angiographic Follow-Up
The first 12 patients in this series underwent systematic coronary angiography before discharge from the hospital to assess the safety and patency of the constructed grafts.12 The results are included in the final analysis, although they do not reflect long-term follow-up. No systematic long-term angiographic evaluation was performed because of the inherent risks of this procedure, which makes routine angiography hardly justifiable. Therefore, only patients who presented adverse cardiac events (recurrent angina, MI, or CHF) or those whose symptoms were doubtful enough to warrant invasive imaging were referred for angiography. Grafts were graded according to the Fitchgibbon classification as follows: A (excellent), B (fair), and O (occluded).13 Completeness of revascularization was defined according to the original Coronary Artery Surgery Study (CASS) trial definition14 as all 3 major vessels receiving a bypass graft in patients with triple-vessel disease.

Statistical Analysis
Statistical analyses were performed using SPSS software (SPSS Inc, Chicago, Ill). Results are expressed as mean values±standard deviation. Univariate analysis was performed to evaluate the impact of patients’ characteristics and risk factors as defined in Table 1 on long-term outcomes. Multivariate analysis using Cox logistic regression analysis was performed on all clinically relevant variable with P<0.10. All patients were considered as “intention to treat.” No more than 1 variable for 10 events was considered for multivariate analysis purposes. For long-term endpoints, independent risk factors analysis excluded patients that died within 30 days of the surgery. Results are presented as odds ratio (OR) with a 95% confidence interval (CI). Actuarial survival was obtained using the Kaplan-Meier method. P<0.05 was considered statistically significant.

Statement of Responsibility
The authors had full access to the data and take full responsibility for their integrity. All authors have read and agree to the manuscript as written.
Results

Patient Demographics and Risk Factors

Table 1 shows the demographic characteristics of the entire cohort of patients undergoing OPCAB surgery during the study period. Average age of the patients was 64±10 years (78% male, 22% female). Seventy-three percent had triple-vessel disease and 30% had left main disease (stenosis >55%). Mean ejection fraction was 53±13%. Unstable angina was the indication in 69% and 5.3% were operated on emergently (<24 hours after diagnostic procedure). Twenty percent of the patients had experienced a recent MI (<30 days). Seven percent of the cases were reoperations (n = 69).

Operative Data

Table 2 depicts operative data regarding the patients in the cohort. The average number of total anastomoses per patient was 3.2±0.9 (1.2±0.3 grafts/territory). Complete revascularization was achieved in 95% of cases. Both internal thoracic artery (ITA) were used in 32% of patients and the left ITA was used for sequential bypasses in 17% of patients (mostly on the diagonal and LAD). Systematic skeletonization of both ITAs has greatly enhanced the rate of sequential bypasses in the more recent time period. Conversion to CPB was necessary in 4 cases (0.4%), 1 patient had an acute dissection of the aorta on side-clamping requiring CPB for completion of the bypasses and replacement of the aorta, another had an ischemic triggered ventricular fibrillation, and 2 showed severe hemodynamic compromise during mobilization precluding the access to the circumflex territory. All converted patients survived the procedure and were discharged from the hospital.

Early Clinical Outcome

Overall operative mortality (30 days) was 1.6% (Table 3). Three percent of patients had a perioperative MI (ST segment elevation: 2% and non-ST segment elevation: 1.3%). Mean levels of troponin I (48 hours) and CK-MB (24 hours) were, respectively, 0.3±0.9 ng/mL and 17±42 ng/mL. Transfusion of blood or blood-related products was necessary in 28% of patients (mean, 1.3 U/transfused patient). Atrial fibrillation was observed in 27% of patients. Eight patients (<1%) had a cerebrovascular accident. Mean hospital stay was 6.5±5.3 days.

Clinical predictors (Table 3) or operative mortality on logistic regression analysis were age (OR, 1.23; P = 0.002), chronic obstructive pulmonary disease (OR, 3.70; P = 0.02), diffuse coronary disease (OR, 4.04; P = 0.01), and chronic renal failure (OR, 3.67; P = 0.04).

Late Clinical Outcome

Actuarial Survival

Overall actuarial survival at 1, 5, and 8 years is 96±1%, 88±1.5%, and 72±3%, respectively (Figure 2). “Cardiac” survival is depicted in Figure 3 and stands at 98±0.5%, 96±1%, 95±1.5% at 1, 5, and 8 years, respectively. Cardiac death included all patients with cardiac-related deaths or deaths of unknown causes.

Event-Free Survival

Figure 3 shows long-term survival free of cardiac events after OPCAB surgery including cardiac death, MI, recurrent angina, heart failure, or repeat revascularization. At 1 year, event-free survival was 96±0.6%, at 5 years, 89±1%, and decreased to 80±4% at 8 years.

TABLE 1. Demographics and Preoperative Risk Factors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>28%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>54%</td>
</tr>
<tr>
<td>Tobacco</td>
<td>29%</td>
</tr>
<tr>
<td>COPD</td>
<td>12%</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>4%</td>
</tr>
<tr>
<td>PVD</td>
<td>18%</td>
</tr>
<tr>
<td>CVA/TIA</td>
<td>8%</td>
</tr>
<tr>
<td>Left main</td>
<td>30%</td>
</tr>
<tr>
<td>Obesity</td>
<td>11%</td>
</tr>
</tbody>
</table>

**Note:** CHF indicates coronary heart failure; CRI, chronic renal insufficiency; CVA/TIA, cerebrovascular accident/transient ischemic attack; IABP, intra-aortic balloon pump; IMI, ischemic mitral insufficiency; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PVD, peripheral vascular disease.

**CHF:** indicates type I and type II diabetes.

**Hypertension:** patients using drug therapy for blood pressure control.

**Tobacco:** tobacco use (>10 cigarettes/day) in the year before surgery.

**PVD:** patients with history of claudication, decreases peripheral pulses, or previous peripheral vascular surgery.

**Obesity:** body mass index >30.

**CRI:** creatinine level >177 mmol/L.

**CHF:** history of cardiac heart failure before surgery.

TABLE 2. Perioperative Data

<table>
<thead>
<tr>
<th>Variable</th>
<th>1.6%</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative MI</td>
<td>3.3%</td>
<td>79%</td>
</tr>
<tr>
<td>STEMI</td>
<td>2.0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Non-STEMI</td>
<td>1.3%</td>
<td>95%</td>
</tr>
<tr>
<td>Grafts</td>
<td>3.2±0.9</td>
<td>65±61</td>
</tr>
<tr>
<td>Grafts/territory</td>
<td>1.2±0.3</td>
<td>18±33</td>
</tr>
<tr>
<td>ITA grafts</td>
<td>97%</td>
<td>6.5±5.3</td>
</tr>
<tr>
<td>Bilateral grafts</td>
<td>32%</td>
<td>17±42</td>
</tr>
<tr>
<td>Sequential grafts</td>
<td>17%</td>
<td>0.3±0.9</td>
</tr>
<tr>
<td>Vein grafts</td>
<td>84%</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** CKMB indicates creatine kinase myocardium specific; CPB, cardiopulmonary bypass; ICU, intensive care unit; ITA, internal thoracic artery; MI, myocardial infarction; STEMI, ST elevation myocardial infarction.

**CKMB:** indicates level of troponin I (48 hours) and CK-MB (24 hours) were, respectively, 0.3±0.9 ng/mL and 17±42 ng/mL. Transfusion of blood or blood-related products was necessary in 28% of patients (mean, 1.3 U/transfused patient). Atrial fibrillation was observed in 27% of patients. Eight patients (<1%) had a cerebrovascular accident. Mean hospital stay was 6.5±5.3 days.

**Clinical predictors (Table 3)** or operative mortality on logistic regression analysis were age (OR, 1.23; P = 0.002), chronic obstructive pulmonary disease (OR, 3.70; P = 0.02), diffuse coronary disease (OR, 4.04; P = 0.01), and chronic renal failure (OR, 3.67; P = 0.04).

**Late Clinical Outcome**

**Actuarial Survival**

Overall actuarial survival at 1, 5, and 8 years is 96±1%, 88±1.5%, and 74±3%, respectively (Figure 2). “Cardiac” survival is depicted in Figure 3 and stands at 98±0.5%, 96±1%, 95±1.5% at 1, 5, and 8 years, respectively. Cardiac death included all patients with cardiac-related deaths or deaths of unknown causes.

**Event-Free Survival**

Figure 3 shows long-term survival free of cardiac events after OPCAB surgery including cardiac death, MI, recurrent angina, heart failure, or repeat revascularization. At 1 year, event-free survival was 96±0.6%, at 5 years, 89±1%, and decreased to 80±4% at 8 years.

**TABLE 3. Clinical Predictors of Operative Mortality**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Stepwise Logistic Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.002 1.23 1.05–1.21</td>
</tr>
<tr>
<td>Diffuse disease</td>
<td>0.01 4.04 1.43–11.52</td>
</tr>
<tr>
<td>COPD</td>
<td>0.02 3.70 1.20–11.70</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>0.04 3.67 1.03–12.92</td>
</tr>
<tr>
<td>Cerebral vascular disease</td>
<td>0.09 2.50 0.87–7.33</td>
</tr>
</tbody>
</table>

**Note:** CI indicates confidence interval; COPD, chronic obstructive pulmonary disease; OR, indicates odd ratio.
Freedom From Cardiac Reintervention (Surgery or PCI)

Figure 3 reveals the long-term freedom from repeat revascularization by surgical or percutaneous (PCI) approaches. Freedom from reintervention stands at 99±0.5%, 95±1%, and 90±3% at 1, 5, and 8 years, respectively.

Clinical Predictors of Long-Term Poor Outcome

Adverse predictors of long-term survival are shown in Table 4. Predictors were selected out of risk factors and demographics depicted in Table 1. A history of CHF (OR, 1.90; 95% CI, 1.08 to 3.31), peripheral vascular disease (OR, 1.74; 95% CI, 1.10 to 2.84), New York Heart Association class (OR, 1.66; 95% CI, 1.07 to 2.57), previous MI (OR, 1.60; 95% CI, 1.02 to 2.50), chronic renal insufficiency (OR, 2.04; 95% CI, 1.01 to 4.30), and age (OR, 1.06; 95% CI, 1.04 to 1.09) were all predictors of poor long-term clinical outcome. Specific predictors of cardiac death were left ventricular ejection fraction and cerebrovascular disease (Table 5).

Angiographic Outcome

Angiographic studies were mainly performed in patients with adverse cardiac events (recurrent angina, MI, or CHF). One hundred eight patients underwent angiography over the follow-up period. Overall, 310 grafts were assessed (96 LAD, 94 circumflex arteries, 49 posterior descending arteries, 42 diagonals, and 29 right coronaries). Figure 4 shows the angiographic patency of various bypass grafts according to target vessels using the Fitzgibbon classification.13 Left ITA (LITA) to LAD grafts were graded A or B in 90% and 3% of the cases, respectively. Gobaly, ITA were patent in 96% (90% grade A and 6% grade B), vein graft in 75% (67% grade A and 8% grade B) and radial artery in 71% (all grade A). The worst patency rates were observed on the circumflex and posterior descending artery territories with occlusion rates of 23% and 35%, respectively, on long-term follow-up.

Discussion

Comparing outcomes after OPCAB and on-pump CABG in randomized trials is methodologically extremely challenging because of the infrequent occurrence of adverse outcomes. Randomized trials in the literature to date have limited statistical power to detect these differences as it would require a very high number of patients to achieve clinical and statistical significance.5,15,16 Moreover, even when randomized, these trials comprise selection biases, because they do not always represent the overall patient population encountered in everyday practice. In one randomized study comparing on-pump versus off-pump CABG, Legare et al enrolled 300 patients out of 933 eligible for randomization.15 Furthermore, 14% of their OPCAB patients crossed over because of necessary conversion to CPB during surgery. Therefore, although the present study is a retrospective look at nonrandomized but prospectively followed-up patients, it provides long-term data on a series of patients among whom the use of OPCAB was quasi-systematically applied with a very limited conversion rate to CPB (0.4%), a high rate of complete revascularization, and a follow-up completion.

Completeness of revascularization after OPCAB was a serious concern during the initial experience with beating heart surgery and, according to some reports, was not as
TABLE 6. Clinical Predictors of Cardiac Death or Rehospitalization for Cardiac Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Cox Regression Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
</tr>
<tr>
<td>Ischemic mitral regurgitation</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.006</td>
</tr>
<tr>
<td>Diffuse disease</td>
<td>0.004</td>
</tr>
</tbody>
</table>

optimal as with conventional on-pump surgery. However, with the advent of newer stabilizers and low-profile apical suction devices, this problem has been all but solved. Defining completeness of revascularization is often a matter of debate, and the definition used in this report is the CASS report’s definition, ie, at least 1 bypass graft per territory. In the present series, complete coronary revascularization was accomplished in 95% of cases (average 3.2 grafts/patient).

Technical feasibility and mid-term safety of OPCAB surgery have been demonstrated through numerous reports in the literature. Long-term clinical results and angiographic follow-up of OPCAB patients are, however, scarce. Systematic coronary angiography of all revascularized patients is hardly justifiable in the current era. Even in clinical trial protocol full patient compliance is difficult to obtain. In PRAGUE-4 trial, almost one-third of patients refused the control angiography because they “felt completely well.” That study reported angiographic results at 1 year after OPCAB with 91% patency of left internal mammary artery grafts at 1 year and 49% patency of the saphenous vein grafts at 1 year. The only long-term angiographic study in OPCAB patients in the literature by Vural et al reports angiographic results on 265 patients (≈10% of their overall cohort) at an average 4.2 years after surgery. They report 93% left internal mammary artery patency and 65% saphenous vein graft patency. However, these patients underwent operation before the era of modern OPCAB surgery (from 1993 to 1996) and most patients had single- or double-vessel disease (96%), therefore representing a carefully selected patient population.

Therefore, the present study is the first to our knowledge to look at an all-comer, nonselected patient population operated on during and after the more recent era of beating heart surgery. As for all studies, the patients undergoing coronary angiography are those requiring it for any medical reason (recurrent angina, MI, or heart failure). Almost 10% of the cohort required coronary artery imaging. Patency was defined according to the target vessel bypassed to illustrate the variability between various targets. Bypass grafts on the LAD were patent in 94% of the cases and 96% of all ITA grafts were patent. Although the patency of these IMA grafts is lower than desired at this time period after surgery, it is important to note that these results represent the “symptomatic patients” and then the “worst scenario.” Comparing off-pump to on-pump patients, Gundry et al reported 92% patency of left internal mammary artery in conventional surgery compared with 49% in OPCAB. However, OPCAB cases were performed without stabilization, which was responsible for low patency rate. Interestingly, over a period of 7 years, 7% of the CPB patients underwent PTCA for recurrent symptoms, whereas only 2.4% (24 patients, annual rate of 1.25%) of our cohort needed a new revascularization over an 8-year period. Among our patients requiring new PTCA or surgery <50% needed it for a previously bypassed native artery. Furthermore, the occurrence of cardiac adverse events has remained low throughout the 8-year study, with an annual rate of 2%.

This study comprises several limitations. It is a descriptive study and therefore does not allow for comparison of OPCAB patients to their on-pump counterparts. Second, angiographic data are not available for all patients. Therefore, angiographic results reported are directly subject to selection bias with patients experiencing a less favorable outcome undergoing coronary imaging.

Conclusion
OPCAB grafting is a well-established alternative to conventional on-pump CABG using cardiopulmonary bypass in terms of short and mid-term outcomes. The present study demonstrates the safety and efficacy of OPCAB surgery in nonselected patients on long-term outcomes. Event-free survival was favorable and need for new revascularization low throughout the follow-up. Therefore, with increasing follow-up periods, OPCAB surgery remains a viable and widely applicable surgical option for patients with coronary insufficiency.

Disclosures
Dr Cartier is a Senior Medical Adviser for CoroNéo Inc.

References


Long-Term Results After Systematic Off-Pump Coronary Artery Bypass Graft Surgery in 1000 Consecutive Patients
Ismail El-Hamamsy, Raymond Cartier, Philippe Demers, Denis Bouchard and Michel Pellerin

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