Risk-Adjusted Short- and Long-Term Outcomes for On-Pump Versus Off-Pump Coronary Artery Bypass Surgery

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Background—Surgeons have adopted off-pump coronary artery bypass grafting (OPCAB) in an effort to reduce the morbidity of surgical revascularization. However, long-term outcome of OPCAB compared with conventional coronary artery bypass grafting (CABG) remains poorly defined.

Methods and Results—Using logistic regression analysis and proportional hazards modeling, short-term and long-term outcomes (perioperative mortality and complications, risk-adjusted survival, and survival/freedom from revascularization) were investigated for patients who underwent OPCAB (641 patients) and CABG-cardiopulmonary bypass (5026 patients) from 1998 to 2003 at our institution. For these variables, follow-up was 98% complete. OPCAB patients were less likely to receive transfusion (odds ratio for OPCAB, 0.80; \( P = 0.037 \)), and there were trends toward improvement in other short-term outcomes compared with CABG-cardiopulmonary bypass. Long-term outcomes analysis demonstrated no difference in survival, but OPCAB patients were more likely to require repeat revascularization (OPCAB hazard ratio, 1.29; \( P = 0.020 \)).

Conclusions—OPCAB patients were less likely to receive transfusion during their hospitalization for surgery but had higher risk for revascularization in follow-up. These results highlight the need for a large randomized, controlled trial to compare these 2 techniques. (Circulation. 2005;112[Suppl I]:I-366–I-370.)

Key Words: CABG surgery • off-pump surgery • OPCAB • long-term

John Gibbon introduced cardiopulmonary bypass (CPB) to clinical practice in 1953 when he repaired a young woman’s atrial septal defect. His contribution has allowed surgeons to approach and repair cardiac disease that would have otherwise progressed unchecked. In particular, CPB has facilitated surgery on the coronary arteries and, as a result, millions of patients with coronary artery disease have led healthier, longer lives. In a motionless, bloodless field, surgeons can construct an optimal anastomosis between the bypass conduit and the native coronary artery. When the internal mammary artery is used in coronary artery bypass grafting (CABG) with CPB (CABG-CPB), patency rates exceed 80% at 10 years. However, CPB has become recognized as a potentially avoidable hazard.

The development of cardiac stabilizers in the late 1990s allowed widespread application of alternative techniques of coronary revascularization that do not require CPB. Satisfactory coronary revascularization without the attendant morbidity of CPB holds obvious appeal, and off-pump CABG (OPCAB) has become popular. Many studies have reported reduced operative morbidity with OPCAB relative to CABG-CPB. Some randomized controlled trials (RCTs) have been conducted, but these studies have been small and produced equivocal results. The quality and durability of OPCAB revascularization remain poorly defined. To address this issue, we have evaluated the short-term and long-term outcomes of patients who underwent CABG at our institution from 1998 to 2003.

**Methods**

The Institutional Review Board at Duke University Medical Center approved the project. Outcome data were collected prospectively. Patients who underwent an isolated CABG procedure through a median sternotomy incision from January 1998 to September 2003 were identified and included in the analysis. For the variables analyzed, preoperative data were 99% complete. According to Duke Heart Center Database protocol, patients were contacted by telephone at 6 months and 1 year after surgery and yearly thereafter. If any percutaneous or operative intervention was reported to have
occurred at an outside institution, hospital records were obtained and reviewed with patient consent. The median length of follow-up was 2.6 years, and follow-up was 98% complete. To compare preoperative characteristics and unadjusted short-term outcomes between OPCAB and CABG-CPB, \( \chi^2 \) Fisher’s exact, or Wilcoxon rank-sum tests were used for statistical analysis, as appropriate. To account for bias in the selection of patients to undergo OPCAB, a propensity score analysis was undertaken. Logistic regression analysis was used to generate a score for each patient that predicted the chance of undergoing OPCAB versus CABG-CPB. A list of the preoperative characteristics included in the logistic regression can be found in Table 1. The full results of the logistic regression used to determine the propensity scores can be found in the accompanying online-only data supplement. Definitions for important variables have been published previously. The variable “target quality” was a 3-level qualitative evaluation of the worst target vessel as judged by the attending surgeon at the time of operation.

For short-term outcome analysis, logistic regression was used to identify variables that were associated with the complication of interest. Because of the low frequency of some short-term complications, only those factors deemed most likely to be associated with the outcome of interest were selected for inclusion in the multivariable model, whereas other preoperative characteristics were omitted. For perioperative mortality (in-house death), comorbidities, including diabetes, peripheral vascular disease, cerebrovascular disease, history of stroke, renal failure, and chronic obstructive pulmonary disease were grouped into a binary variable labeled “comorbidity.” This binary variable, along with ejection fraction, New York Heart Association (NYHA) class, gender, emergency status, preoperative intraaortic balloon pump, age, propensity score, and on-pump or off-pump status, was included in the logistic regression to determine the risk factors for perioperative mortality. For the logistic regression designed to determine risk factors for mediastinitis (defined using Centers for Disease Control and Prevention criteria), body mass index, NYHA class, operative time, propensity score, and on-pump or off-pump status were included as independent variables. These variables were chosen, because they have been implicated as important risk factors in previous studies. For the outcome of postoperative stroke (any central neurologic deficit persisting for >72 hours), the presence of cerebrovascular disease, peripheral vascular disease, age, propensity score, and on-pump or off-pump status were included as independent variables. These variables were selected, because they have been implicated as the most important risk factors for postoperative stroke from a previous study. Logistic regressions to determine risk factors for the need for transfusion and length of stay >1 week were also performed. In these 2 regression models, all of the preoperative characteristics in Table 1, along with the propensity score and on-pump or off-pump status, were included as independent variables.

For long-term results, the outcome of death and the composite outcome of death or revascularization [percutaneous intervention (PCI) or repeat CABG] were analyzed using Cox proportional hazards models. For each Cox model, all of the preoperative characteristics seen in Table 1 were used as independent variables along with OPCAB or CABG-CPB status and the propensity score for each patient. The Cox models were then used to construct risk-adjusted Kaplan-Meier curves.

To analyze the effect of a learning curve, an additional analysis was limited to only those surgeons who had performed >10 OPCAB surgeries. The first 10 cases of OPCAB for each surgeon were then eliminated from the analysis. This group of OPCAB cases performed by experienced surgeons (n=578) was then compared with CABG-CPB cases with respect to long-term outcomes. For both short-term and long-term outcomes, subgroup analysis was performed to determine whether comorbidities or advanced age interacted with OPCAB status.

Some previous studies suggest that when surgeons use the OPCAB technique, they may more commonly accept incomplete revascularization. To determine whether incomplete revascularization was a common cause of reinterventions, we analyzed those patients from the original cohort identified as undergoing PCI at our institution after surgery. Chart review was performed to determine whether the reintervention occurred in a territory (right coronary artery, left circumflex artery, or left anterior descending artery) that had been grafted at surgery, and these proportions were compared (OPCAB versus CABG-CPB). Repeat CABG was not included in this analysis, because it was difficult to define the diseased vessel(s) that prompted repeat operation from the data available. All of the statistical analyses were performed using SAS version 8.2 (SAS Inc.).

### Results

Between January 1998 and September 2003, 5667 patients underwent isolated CABG through a median sternotomy incision at our institution. Of this total, 641 were performed without CPB. A total of 14 surgeons are included in the analysis. Ten different surgeons performed OPCABs, but 3 surgeons accounted for the majority of OPCAB cases. It can be seen from Table 1 that the OPCAB and CABG-CPB groups were dissimilar. In general, patients who underwent OPCAB had fewer comorbidities, better left-ventricular function, and better targets for grafting. Not surprisingly, patients who underwent OPCAB experienced fewer adverse events after surgery as depicted in Table 2; OPCAB patients experienced shorter hospital stays, fewer transfusions, less mediastinitis, and less perioperative mortality. Table 2 also demonstrates that the number of grafts placed per diseased vessel was slightly but significantly higher in the CABG-CPB group (CABG-CPB 1.16 versus OPCAB 1.12; \( P<0.001 \)). We used propensity score analysis to control for selection bias. Results from the logistic regression used to predict the likelihood of undergoing OPCAB can be seen in the Appendix; the c-statistic for this regression was 0.74. Table 3 depicts the results of logistic regressions used to test for a protective

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CABG-CPB (n=5026)</th>
<th>OPCAB (n=641)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.5±11.7</td>
<td>63.7±10.7</td>
<td>0.562</td>
</tr>
<tr>
<td>Gender (male), %</td>
<td>70.5</td>
<td>64.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%, %</td>
<td>22.1</td>
<td>17.7</td>
<td>0.011</td>
</tr>
<tr>
<td>Left main disease, %</td>
<td>21.4</td>
<td>12.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>History of stroke, %</td>
<td>9.7</td>
<td>7.6</td>
<td>0.090</td>
</tr>
<tr>
<td>Cerebrovascular disease, %</td>
<td>11.7</td>
<td>11.7</td>
<td>0.999</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>54.2</td>
<td>59.1</td>
<td>0.019</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>68.9</td>
<td>70.0</td>
<td>0.541</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>34.7</td>
<td>30.0</td>
<td>0.018</td>
</tr>
<tr>
<td>COPD, %</td>
<td>10.3</td>
<td>12.2</td>
<td>0.244</td>
</tr>
<tr>
<td>Tobacco abuse, %</td>
<td>47.0</td>
<td>51.5</td>
<td>0.035</td>
</tr>
<tr>
<td>Renal failure, %</td>
<td>4.7</td>
<td>4.2</td>
<td>0.837</td>
</tr>
<tr>
<td>Peripheral vascular disease, %</td>
<td>15.4</td>
<td>14.0</td>
<td>0.215</td>
</tr>
<tr>
<td>NYHA class &gt;1, %</td>
<td>12.7</td>
<td>10.3</td>
<td>0.083</td>
</tr>
<tr>
<td>Redo surgery, %</td>
<td>4.8</td>
<td>0.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Emergency status, %</td>
<td>3.1</td>
<td>2.5</td>
<td>0.384</td>
</tr>
<tr>
<td>Preoperative IABP, %</td>
<td>4.8</td>
<td>2.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Target quality poor, %</td>
<td>18.8</td>
<td>10.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2.77±0.5</td>
<td>2.26±0.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

IABP indicates intraaortic balloon pump.
The estimated odds ratio and associated 95% CI of OPCAB versus CABG-CPB are displayed along with the associated c-statistics of the regression models. Similar to other observational studies, OPCAB was found to be independently associated with a reduced need for transfusion (odds ratio for OPCAB 0.80; \( P = \text{0.037} \)). For other short-term outcomes, such as postoperative stroke, mediastinitis, length of stay, and perioperative survival, treatment with OPCAB did not significantly predict improved outcomes.

Table 4 describes the results of Cox proportional hazard models for the 2 long-term outcomes analyzed. Figures 1 and 2 depict the risk-adjusted death and death/revascularization curves respectively. There was no significant difference in survival, but CABG-CPB patients were more likely to be free from death or revascularization (hazard ratio for OPCAB, 1.29; \( P = \text{0.020} \)). When the OPCAB group was limited to only experienced surgeons, the results were similar (data displayed in Appendix).

In parallel to multivariable adjustment, we applied the propensity score in a matched-pairs analysis, and results were found to be consistent with findings as detailed above. The full results of this analysis, as well as the details regarding the matching strategy, can be found in the accompanying appendix.

To determine whether the cause of reinterventions was different for OPCAB as compared with CABG-CPB, we compared the proportion of percutaneous reinterventions that occurred in previously grafted territories between the OPCAB and CABG-CPB groups if the PCI occurred at our institution (n=407). The nature of the vessel requiring reintervention was similar between the 2 groups: for OPCAB, 83% of interventions occurred in previously grafted territories, whereas for CABG-CPB, 85% of interventions occurred in previously grafted territories. The subgroup analysis showed no significant interactions between preoperative comorbidities or advanced age and OPCAB surgery (data not shown).
CABG-CPB represents the most complete and durable method of revascularization for advanced coronary artery disease. The accompanying mortality (1% to 3%) and morbidity have spurred efforts to find alternative methods that would maintain the durability of revascularization but reduce CABG-associated morbidity. The development of advanced cardiac stabilizers enabled surgeons to more easily bypass occluded coronary arteries without the use of CPB. Despite many encouraging reports on the improved early outcomes achieved with OPCAB, questions concerning the durability of revascularization have remained.

Published studies from large databases show an advantage of OPCAB over conventional CABG-CPB in terms of early morbidity and/or mortality. Several small RCTs suggest less benefit for OPCAB; perioperative mortality, perioperative stroke, and event-free survival up to 1 year were not significantly different. Furthermore, a recently completed RCT reported that patency rates for grafts in OPCAB were worse at 3 months, although another single-surgeon RCT with 30-day and 1-year follow-up has shown graft patency rates to be equivalent. Unfortunately, none of the RCTs completed to date have been adequately powered to detect smaller but important differences in outcomes between the 2 techniques, and follow-up times have been relatively brief (≤1 year).

Despite the paucity of RCT data, the literature surrounding OPCAB surgery argues that early outcomes with OPCAB are improved. Long-term outcomes, however, are less well described, and questions remain as to the durability of the coronary revascularization achieved with OPCAB. Our study is one of the first to compare long-term outcomes between the 2 techniques. Although our study is an observational rather than a randomized comparison, the data are derived from a large number of patients, and follow-up is excellent.

In this report, it appears that healthier patients with less-extensive cardiovascular disease were preferentially treated with OPCAB. This reflects surgeons’ preference to apply a new technique to patients with fewer comorbidities and less-difficult anatomy, although, as our experience with OPCAB grew, more patients with multivessel disease were treated with OPCAB (data not shown). Patients treated with OPCAB were more likely to do well after surgery, because they were healthier before surgery. We attempted to account for this selection bias through risk-adjustment analysis.

As in other published studies, there was less need for transfusion in our OPCAB patients. Notably, there were important trends toward reduced operative mortality, length of stay, and mediastinitis. It is possible that our study was underpowered to detect significant early outcome differences in patients treated with OPCAB because of the overall low frequency of adverse events.

Survival with freedom from revascularization differed significantly between the 2 groups. At any point in time after surgery, patients treated with OPCAB were less likely to avoid the combined end point of second revascularization procedure or death. There are many possible reasons for the increased likelihood of revascularization in the OPCAB cohort: OPCAB surgery is more technically demanding than CABG-CPB, and this may have contributed to the higher rate of reinterventions observed in the OPCAB cohort; other technology more commonly used in OPCAB, such as proximal connector devices, may have adversely affected graft patency; OPCAB surgery may have negatively altered the location of distal anastomoses. In addition, each additional graft in OPCAB carries a higher marginal cost in terms of difficulty and stress on a patient (possibly requiring inotropic support with heart displacement), and grafts that would have been constructed in conventional CABG-CPB might be less-frequently performed using the OPCAB technique. Our analysis, however, demonstrated that the proportion of percutaneous reinterventions that involved ungrafted territories did not differ between groups. Also, anticoagulant or other systemic effects of CPB during the perioperative period may protect against graft failure. One possible intervention that deserves consideration is the use of antiplatelet drugs in the perioperative period after OPCAB, because it is possible that the platelet dysfunction that accompanies CPB protects against graft failure.

Although healthier patients were preferentially treated with OPCAB at our institution, it may be that OPCAB would be more beneficial to those patients with higher perioperative risk and a shorter life expectancy. Subgroup analysis was applied to our cohort of patients, but no important associations were found between particular preoperative characteristics and OPCAB in terms of long-term or short-term outcomes. The cohort of patients is simply not large enough to draw any firm conclusions about subgroups that may benefit from OPCAB.

In this study, there is an early advantage with OPCAB at the cost of reduced durability of revascularization. This finding partially corroborates a recently published study documenting long-term outcomes in New York state, although in that study there were lower rates of survival in OPCAB patients, an observation not supported by analysis of our cohort of patients.

Significant changes in OPCAB surgery have occurred during the period of observation in our study. The developments of proximal anastomotic devices, suction-stabilizers, and apical cup suction devices have made off-pump revascu-
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larization easier to achieve. It could be argued that a comparison between OPCAB and CABG-CPB that includes surgeries performed before the development of one or more advances is not valid. It is important to note, though, that advances have been made in CABG-CPB as well; coated circuits, systemic agents to modify the inflammatory response to CPB, and use of a single cross-clamp technique guided by epiaortic scanning have altered practice at our institution in recent years. Both OPCAB and CABG-CPB are evolving treatments, but contemporaneous comparisons provide valuable information and should be taken into consideration when making treatment decisions in the future.

This study has several weaknesses. As a single-institution study, the conclusions may not be applicable in general because of differences in practice patterns at other centers. Because this is an observational study rather than a RCT, it is possible that unobserved biases might not have been eliminated despite our rigorous statistical analysis. Most importantly, conversion from OPCAB to CABG-CPB was not noted in our database for all of the study period, and all of the converted patients were counted as having undergone CABG-CPB. Thus, this study is not based on an “intention-to-treat” analysis.

Despite these shortcomings, this study raises important questions as to the durability of the revascularization achieved with OPCAB. More generally, it emphasizes the need to evaluate new techniques with both early and late outcome analysis. Notably, commercial pressures may lead to overemphasis of early outcomes. The durability of surgical revascularization has traditionally been the greatest advantage of CABB-CPB relative to medical treatment or PCI. The OPCAB technique may forfeit some of this relative advantage, and the results from our analysis should caution those who wish to apply the OPCAB technique universally. Our study highlights the need for a large-scale, multi-institutional RCT.

References
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