Off-Pump Coronary Artery Bypass Grafting Reduces Mortality and Stroke in Patients With Atheromatous Aortas: A Case Control Study

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Background—Patients with severe atheromatous aortic disease (AAD) who undergo coronary artery bypass (CABG) have an increased risk of death and stroke. We hypothesized that in these high risk patients, off-pump coronary artery bypass (OPCAB) technique is associated with lower morbidity and mortality.

Methods and Results—Between June 1993 and January 2002, 5737 patients undergoing CABG had routine intra-operative TEE with 913 (15.9%) found to have severe AAD in the aortic arch or ascending aorta. Of these, 211 patients who underwent OPCAB were matched with 211 on-pump CABG patients by age, ejection fraction, history of stroke, cerebrovascular disease, diabetes, renal disease, nonelective operation, and previous cardiac surgery. Hospital mortality was 11.4% (24/211) for on-pump CABG and 3.8% (8/211) for OPCAB (P = 0.003). Multivariate analysis revealed that increased mortality was associated with on-pump CABG (P = 0.001), acute MI (P = 0.03), number of grafts (P = 0.01), age (P = 0.01), history of stroke or cerebrovascular disease (P = 0.04), CHF (P = 0.02), and peripheral vascular disease (P = 0.03). Multivariate analysis showed that OPCAB technique was associated with decreased stroke (P = 0.05). Freedom from any complication was 78.7% for on-pump CABG and 91.9% for OPCAB (P < 0.001). At 36 month follow-up multivariate analysis revealed that increased mortality was associated with age (P = 0.001), previous MI (P = 0.03), and renal disease (P = 0.04), whereas increased survival was associated with increased number of grafts (P = 0.001) and OPCAB (P = 0.01).

Conclusions—OPCAB surgery in patients with severe AAD is associated with lower risk of death, stroke and complications and improved mid-term survival. Routine intra-operative TEE allows identification of these patients and directs choice of appropriate surgical technique.

Key Words: bypass ■ arteriosclerosis ■ revascularization ■ cardiopulmonary bypass ■ stroke

Severe atherosclerosis of the ascending aorta or aortic arch is associated with increased risk of peri-operative stroke for patients undergoing coronary artery bypass graft (CABG) surgery. Moreover, the severity of the aortic atheroma as graded by transesophageal echocardiography (TEE) is directly related to the perioperative risk of neurologic complications after CABG. Operative mortality as high as 14.6% has been reported in patients with severe aortic atheroma undergoing CABG.

In cases of severe aortic atheromatous lesions several techniques have been used in an attempt to reduce the risk of mortality and neurologic complications following traditional cardio-pulmonary bypass CABG (CPB-CABG). A "no-touch" technique that avoids any manipulation of the ascending aorta has been proposed, and use of a Foley catheter instead of an external cross clamp to minimize trauma to the ascending aorta and the associated risks of embolization has been described. However, the application of these approaches and other surgical techniques in this subset of high risk patients has yielded unpredictable and disappointing results.

During the past decade, off-pump coronary artery bypass (OPCAB) has come into common use worldwide. Compared with CPB-CABG, OPCAB has been associated with lower rates of postoperative atrial fibrillation, a shorter length of stay, and a decreased need for intra-aortic balloon pumps postoperatively. Most studies that analyzed high-risk patients undergoing OPCAB have demonstrated only a trend

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toward reduction in mortality when compared with CPB-CABG. One recent retrospective report, however, showed a significant reduction in mortality among unmatched octogenarians undergoing OPCAB. Only a few recent case-matched comparative studies have shown significant reduction in major neurologic deficits in patients undergoing OPCAB compared with CPB-CABG. To date no study has focused on patients with atheromatous disease of the aorta in its analysis of the surgical results of OPCAB.

Routine intra-operative TEE has been used in our institution for all cardiac operations for over a decade. Each patient had routine intra-operative TEE evaluation of the aorta. The degree of atherosclerotic disease was graded according to the system developed by Katz and co-investigators: grade 1 = absence of significant disease, grade 2 = extensive intimal thickening, grade 3 = sessile atheroma < 4 mm thick, grade 4 = protruding atheroma > 4 mm, and grade 5 = mobile atheroma. Significant atheromatous disease (grade 4 or 5) of the ascending aorta and/or arch of the aorta was found in 913 of these patients (15.9%). If there was concern that disease in the distal ascending aorta was not fully evaluated by TEE, or that more precise localization of ascending aortic disease was necessary for technique modification, handheld epiaortic scanning was performed. Of note, the proximal extent of the severe atheromatous disease was limited to the transverse arch in 85% of the patients. Of these 913 patients, 678 (74.3%) underwent traditional CABG using cardiopulmonary bypass, whereas 235 (25.7%) underwent OPCAB surgery according to the availability of OPCAB technology and surgeon’s preference. A case matched cohort drawn from these 235 patients was created according to age (<45 years, 46 to 60 years, 61 to 75 years, >75 years), ejection fraction (greater than or less than 30%), history of stroke or cerebrovascular disease, urgency of operation, diabetes, previous cardiac surgery, renal disease and acute MI. Of these 235 OPCAB patients, 211 were fully matched with an equal number of on-pump CABG patients and were suitable for analysis in this report. The mean age ± SD for both groups was 74 ± 9 years with a range of 45 to 94 years.

In the OPCAB cases the heart was stabilized using coronary artery stabilization devices. CABG with CPB was performed via median sternotomy using a membrane oxygenator equipped with an arterial filter under moderate hypothermia (30 to 34°C). All data were prospectively collected by trained nurse clinicians and entered into an institutional database. The database conforms to the definitions used by the New York State Cardiac Surgery Reporting Form, an audited data collection instrument used to record and analyze all cardiac surgery performed in New York State. Using this nomenclature, stroke was defined as a permanent new focal neurologic deficit occurring anytime during the postoperative hospitalization or a new lesion found on computed tomography (CT) or magnetic resonance imaging (MRI). Table 1 lists patient clinical characteristics and risk factors by procedure group. Follow-up survival was ascertained from the Social Security Death Index.

Following the accumulation of data, statistical models were formed and analyzed using SPSS statistical software (version 11.0; SPSS Inc, Chicago, IL). The Chi-square test was used for categorical univariate tests, and stepwise logistic regression was used for multivariate analysis. Survival analysis was performed using life table methodology and differences were tested with a Wilcoxon statistic; P < 0.05 was considered significant. Results are expressed as the mean ± SD unless otherwise indicated.

**Methods**

Between June 1993 and January 2002, 5737 consecutive patients underwent isolated CABG at our institution. Each of these patients had routine intra-operative TEE evaluation of the aorta. The degree of atherosclerotic disease was graded according to the system developed by Katz and co-investigators: grade 1 = absence of significant disease, grade 2 = extensive intimal thickening, grade 3 = sessile atheroma < 4 mm thick, grade 4 = protruding atheroma > 4 mm, and grade 5 = mobile atheroma. Significant atheromatous disease (grade 4 or 5) of the ascending aorta and/or arch of the aorta was found in 913 of these patients (15.9%). If there was concern that disease in the distal ascending aorta was not fully evaluated by TEE, or that more precise localization of ascending aortic disease was necessary for technique modification, handheld epiaortic scanning was performed. Of note, the proximal extent of the severe atheromatous disease was limited to the transverse arch in 85% of the patients. Of these 913 patients, 678 (74.3%) underwent traditional CABG using cardiopulmonary bypass, whereas 235 (25.7%) underwent OPCAB surgery according to the availability of OPCAB technology and surgeon’s preference. A case matched cohort drawn from these 235 patients was created according to age (<45 years, 46 to 60 years, 61 to 75 years, >75 years), ejection fraction (greater than or less than 30%), history of stroke or cerebrovascular disease, urgency of operation, diabetes, previous cardiac surgery, renal disease and acute MI. Of these 235 OPCAB patients, 211 were fully matched with an equal number of on-pump CABG patients and were suitable for analysis in this report. The mean age ± SD for both groups was 74 ± 9 years with a range of 45 to 94 years.

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**Results**

The overall hospital mortality was 11.4% (24/211) in the high risk conventional CABG group versus 3.8% (8/211) in the risk matched OPCAB group (P = 0.003). The mean number of bypass grafts was 2.84 ± 0.82 in the conventional CABG group.
group and 2.16±0.83 in the OPCAB group (P<0.001). Table 2 contrasts intra-operative and postoperative complications between the conventional CABG and OPCAB patient groups. Significantly lower incidences of reoperation for bleeding, prolonged ventilation, stroke, and any complication was noted in the OPCAB group. Univariate risk factor analysis (Table 3) for all patients in both groups demonstrated that age ≥70, renal disease, CHF, history of stroke or cerebrovascular disease, peripheral vascular disease, and ejection fraction <30% were associated with increased mortality. Multivariate analysis (Table 4) revealed that increased mortality was independently associated with previous MI (P=0.001), decreased number of grafts (P=0.01), acute MI (P=0.03), age (P=0.01), CHF (P=0.02), PVD (P=0.03), and history of stroke or cerebrovascular disease (P=0.04). Additionally, multivariate testing revealed that neither surgeon identity nor operative year were significant risk factors for mortality.

Stoke occurred in 4.7% of the conventional CABG patients and in 2.5% of the OPCAB patients (P=0.08). Multivariate risk factor analysis for perioperative stroke, however, revealed that CPB-CABG technique was an independent risk factor for stroke (OR=3.3, P=0.05). History of stroke or cerebrovascular disease was of borderline significance as an independent risk factor for stroke (OR=2.6, P=0.08). Likewise, freedom from all complications and hospital death was significantly improved in the OPCAB technique group (OR=3.2, P<0.001), but adversely affected by CHF (OR=2.5, P<0.03) and peripheral vascular disease (OR=2.3, P<0.004).

Multivariate analysis of number of grafts performed revealed that OPCAB (P=0.001), previous MI (P=0.05), and decreased ejection fraction (P=0.03) were independently associated with fewer bypass grafts being performed. Follow-up analysis (96.6% complete) showed (Figure 1) a 36 month survival rate of 75.1% for the OPCAB group and 75.6% for the CPB-CABG group. Cox multivariate regression analysis demonstrated that increased risk of late death was associated with age (P=0.001), previous MI (OR=1.63; 95% CI=1.06 to 2.5, P=0.03), and renal disease (OR=1.77; 95% CI=1.04 to 3.02, P=0.04), whereas increased survival was associated with increasing number of grafts (P=0.001) and the OPCAB technique (OR=1.82, 95% CI=1.14 to 2.89, P=0.01).

Discussion

The present study shows that off-pump operations in patients with severe atheromatous aortic disease were

### TABLE 2. Comparison of Intraoperative and Postoperative Data Between CPB-CABG and OPCAB Groups (chi-square test with Fisher's correction)

<table>
<thead>
<tr>
<th>Variable</th>
<th>CPB-CABG (n=211)</th>
<th>OPCAB (n=211)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bypass time (min)±SD</td>
<td>107.6</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Cross clamp time (min)±SD</td>
<td>57.6</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>24 (11.4%)*</td>
<td>8 (3.8%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>2.84±0.82</td>
<td>2.16±0.83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Re-operation for postoperative bleeding (%)</td>
<td>10 (4.7%)</td>
<td>1 (0.5%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Deep wound infection (%)</td>
<td>3 (1.4%)</td>
<td>1 (0.5%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Sepsis (%)</td>
<td>6 (2.8%)</td>
<td>2 (0.9%)</td>
<td>0.28</td>
</tr>
<tr>
<td>New renal failure (%)</td>
<td>8 (3.8%)</td>
<td>7 (3.3%)</td>
<td>0.79</td>
</tr>
<tr>
<td>Mechanical ventilation&gt;24 hour (%)</td>
<td>20 (9.5%)</td>
<td>9 (4.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>GI bleeding (%)</td>
<td>3 (1.4%)</td>
<td>3 (1.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>10 (4.7%)</td>
<td>5 (2.4%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Mean length of stay±SE (median)</td>
<td>15.8±1.15 (10)</td>
<td>9.7±0.9 (7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Complication free (%)</td>
<td>166 (78.7%)</td>
<td>194 (91.9%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Mortality for CPB patients was not different between the first and second halves of the study period (P=0.30).

CABG, coronary artery bypass graft; OPCAB, off pump coronary artery bypass; Stroke, a new focal neurologic deficit, lasting greater than 24 hours occurring anytime during the postoperative hospitalization or a new lesion found on CT or MRI.

### TABLE 3. Risk Factor Analysis for Hospital Mortality for All Patients (chi-square test)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Hospital Mortality With</th>
<th>Hospital Mortality Without</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal disease</td>
<td>6/44 (13.6%)</td>
<td>26/378 (6.9%)</td>
<td>0.10</td>
</tr>
<tr>
<td>History of stroke or cerebrovascular disease</td>
<td>15/124 (12.1%)</td>
<td>17/298 (5.7%)</td>
<td>0.02</td>
</tr>
<tr>
<td>PVD</td>
<td>20/137 (14.6%)</td>
<td>12/285 (4.2%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EF ≥30%</td>
<td>9/52 (17.3%)</td>
<td>23/370 (6.2%)</td>
<td>0.005</td>
</tr>
<tr>
<td>CHF</td>
<td>14/87 (16.1%)</td>
<td>18/335 (5.4%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous MI</td>
<td>25/267 (9.4%)</td>
<td>7/155 (4.5%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Urgent/emergency operation</td>
<td>29/360 (8.1%)</td>
<td>3/62 (4.8%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Age ≥70</td>
<td>30/300 (10.0%)</td>
<td>2/122 (1.6%)</td>
<td>0.002</td>
</tr>
<tr>
<td>COPD</td>
<td>5/74 (6.8%)</td>
<td>27/348 (7.8%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>0/8 (0%)</td>
<td>32/414 (7.7%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Male gender</td>
<td>16/277 (5.8%)</td>
<td>16/45 (11.0%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>8/118 (6.8%)</td>
<td>24/304 (7.9%)</td>
<td>0.70</td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>2/34 (5.9%)</td>
<td>30/388 (7.7%)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; IABP, intra aortic balloon pump; MI, myocardial infarction; OPCAB, off pump coronary artery bypass; PVD, peripheral vascular disease.

### TABLE 4. Multivariate Analysis of Hospital Mortality

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Exp B</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB-CABG</td>
<td>6.36</td>
<td>2.33–17.36</td>
<td>0.001</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>0.48</td>
<td>—</td>
<td>0.01</td>
</tr>
<tr>
<td>Age</td>
<td>1.07</td>
<td>—</td>
<td>0.01</td>
</tr>
<tr>
<td>CHF</td>
<td>2.70</td>
<td>1.16–6.25</td>
<td>0.02</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>17.3</td>
<td>1.23–250</td>
<td>0.03</td>
</tr>
<tr>
<td>PVD</td>
<td>2.55</td>
<td>1.10–5.92</td>
<td>0.03</td>
</tr>
<tr>
<td>History of stroke or cerebrovascular disease</td>
<td>2.46</td>
<td>1.04–5.81</td>
<td>0.04</td>
</tr>
</tbody>
</table>

EF, ejection fraction; MI, myocardial infarction; OPCAB, off pump coronary artery bypass.
associated with a lower risk of hospital death, stroke, all complications, and late death when compared with risk adjusted patients undergoing CPB-CABG. Previous studies have shown OPCAB to be safe and effective with early outcomes and graft patency rates at least as good as those seen with traditional CPB-CABG. Most studies of OPCAB that have focused on high risk groups (elderly, previous neurologic event, re-operation or impaired LV function) did not demonstrate a significant difference in peri-operative mortality between OPCAB and conventional CABG. One study, which was not case matched and studied only a limited number of patients (n = 62), focused on octogenarian patients and reported a survival benefit with OPCAB. Significant reductions for OPCAB in post-operative morbidity, intensive care unit length of stay, and mortality in the elderly was reported by a group from Harefield, England.

Atheromatous disease of the aorta has been identified as an independent risk factor for stroke and mortality associated with CPB-CABG. An operative mortality up to 14.6% has been reported in patients with severe aortic atheroma undergoing CABG. Additionally, most of the patients in the current study were referred on an urgent or emergent basis, and the majority of the patients had a previous MI. These factors have been well described as risk factors for mortality among patients undergoing coronary revascularization. Therefore, the mortality rate in the CPB-CABG group reported here should be interpreted in light of the exceedingly high risk in this subset of patients. The increase in hospital survival associated with OPCAB emphasizes the benefit of this technique in this group of patients. We additionally note that in the current study, the majority of this severe atheromatous disease was limited proximally to the transverse arch. This underscores the importance of evaluation of the transverse aorta. It has been shown in a prospective study of 2108 patients undergoing CABG that aortic calcification is the leading risk factor for stroke with an odds ratio of 3.0.

A large multi-center analysis of patients registered in the New York State Cardiac Surgery Reporting System Database showed similar results with a 4.4 fold risk of stroke in association with a diseased aorta. Another study found a 6.3% stroke rate in patients with moderate or severe aortic atheromatous disease undergoing CABG. However, a significantly lower incidence of permanent focal neurologic events was observed with OPCAB compared with CPB-CABG. Other studies that did not focus on high risk groups (elderly, previous neurologic event, re-operation or impaired LV function) did not demonstrate a reduction in stroke rate with OPCAB.

A recent propensity case-match study of post CABG morbidity did not demonstrate fewer focal neurologic deficits with OPCAB. However, the propensity model did not include history of stroke, cerebrovascular disease, peripheral vascular disease, or the presence of aortic atheroma. The OPCAB group itself was at higher overall neurologic risk, with greater baseline incidences of carotid, peripheral vascular, and renal disease. The fact that equivalent focal neurologic outcomes were demonstrated in the above study indicates the importance of our case match construction including variables that would allow clearer identification of etiologic factors for neurologic events.

It is not clear whether the avoidance of CPB has an independent advantage in reducing neurologic events, whether it is more important just to avoid aortic manipulation and proximal anastomoses, or whether elimination of CPB combined with complete avoidance of aortic manipulation may further reduce the incidence of perioperative stroke. The current study shows that avoidance of CPB is independently associated with a lower stroke rate.
when there is significant atheromatous disease in the ascending aorta or arch. The separate effect of a ‘no-touch’ technique for the diseased ascending aorta could not be ascertained from our dataset.

Routine use of intra-operative TEE was used to identify those patients at high risk for neurologic complications. This modality has been shown to be a safe and accurate means of evaluating the extent of atherosclerotic disease of the aortic arch. Additionally, it provides a more reliable assessment of disease than the surgeon’s intraoperative manual palpation of the aorta. Intra-operative TEE also provides a more thorough assessment of the entire aorta when compared with the use of a hand held probe. However, the hand held probe is superior to TEE for selection of sites for placement of proximal anastomoses and cannulation, but is limited in its degree of accuracy when examining the transverse aortic arch.

The differential number of distal bypass grafts in the patient groups requires comment. Although approximately 0.5 fewer grafts per patient were performed in the OPCAB group, there was still an independently decreased hospital mortality and increased long term survival with the OPCAB technique. Independently, the number of grafts performed was incrementally associated with ejection fraction and decrementally associated with previous MI. Therefore, to some extent, the number of grafts performed serves as a surrogate variable for ventricular function, explaining its impact on both short and mid-term survival.

Limitations

Although patient data have been gathered prospectively, important limitations of this study are the nonrandomized approach by different surgeons of the application of the OPCAB technique over the time interval of this study. However, we used the case-match analysis to minimize bias between OPCAB and the CPB-CABG groups. The size of our dataset precluded inclusion of ‘number of grafts’ as a variable in the case-matching algorithm. Advances in case matching cohort techniques may allow future construction of matched cohorts where the number of grafts can be more rigorously controlled. This series also encompasses improvements in the technology for the OPCAB technique that became widely available only in the later part of the study period. Additionally, our dataset did not allow identification of patients in whom a ‘no touch’ aortic technique was used.

Conclusions

Intra-operative TEE evaluation is indicated in all patients undergoing coronary revascularization. This strategy allows identification of patients with severe aortic atheromatous disease who are at high risk for neurologic events after coronary artery bypass grafting. It also directs the surgeon to the appropriate operative approach. Use of OPCAB in these high-risk patients can minimize hospital mortality, neurologic complications, and overall morbidity and improve long-term survival.

References


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