Coronary Artery Bypass Performed Without the Use of Cardiopulmonary Bypass Is Associated With Reduced Cerebral Microemboli and Improved Clinical Results*

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Study objectives: Strokes and neurocognitive dysfunction have been correlated with cerebral microemboli produced during cardiopulmonary bypass (CPB). The purpose of this study was to determine whether, and to what extent, off-pump coronary artery bypass (OPCAB) reduces the occurrence of cerebral microemboli compared with traditional coronary artery bypass grafting (CABG) with CPB and to compare clinical results.

Design and patients: A retrospective review of 137 patients undergoing elective CABG was performed, 70 of whom underwent traditional CABG and 67 of whom underwent OPCAB. Using transcranial Doppler ultrasonography, 40 patients (20 CABG, 20 OPCAB) were continuously monitored intraoperatively for the occurrence and pattern of cerebral microemboli.

Setting: Private, university-affiliated tertiary care hospitals.

Results: There was no statistical difference in the age, sex, or underlying comorbidities between those patients undergoing CABG and OPCAB. CABG patients did have a slightly lower preoperative ejection fraction (50.9% vs 55.5%, p = 0.03). Despite these similar preoperative characteristics, the OPCAB group experienced significant reductions in cerebral microemboli (27 vs 1,766, p = 0.003), transfusion requirements (29.9% vs 47.1%, p = 0.04), intubation time (3.3 vs 9.5 h, p < 0.001), ICU length of stay (1.5 vs 2.8 days, p = 0.02), and overall hospitalization (4.9 vs 6.6 days, p = 0.01) without an increase in mortality. Fewer strokes and deaths were observed in the OPCAB group, but these trends failed to reach statistical significance.

Conclusions: In similar patient populations, OPCAB was associated with significantly fewer cerebral microemboli and improved clinical results without an increase in mortality. We believe that these early results support OPCAB as a viable and potentially safer alternative to traditional CABG.

Key words: cerebral microemboli; coronary artery bypass graft; off-pump; transcranial Doppler ultrasonography

Abbreviations: CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; MCA = middle cerebral artery; OPCAB = off-pump coronary artery bypass; TCD = transcranial Doppler ultrasonography

Neurologic dysfunction is recognized as an associated complication of cardiac surgery with cardiopulmonary bypass (CPB). Major neurologic events, such as disabling strokes, are some of the most feared complications, with a reported incidence of 0.8 to 5.2%. Additional neurologic complications, such as seizures and transient ischemic attacks, have also been reported with comparable frequency. Neurocognitive dysfunction is often more subtle, manifesting as cognitive deficits or encephalopathy of variable duration. When all of these potential neurologic complications are considered, the overall incidence of neurologic morbidity after cardiac surgery has been reported in as many as 80% of patients.

Microembolic phenomenon also has been recog-
nized as an unwanted complication of CPB\textsuperscript{13} and has been implicated as a possible source of the neurologic complications associated with CPB.\textsuperscript{14,15} Although the cannulation and manipulations required during CPB account for some of the measured cerebral microemboli, the CPB circuit itself has been shown to introduce a significant number of microemboli.\textsuperscript{16} Renewed interest in off-pump coronary artery bypass (OPCAB), attributable in part to improvements in local cardiac wall stabilization techniques, has provided an alternative to traditional coronary revascularization without the potentially deleterious effects of CPB.\textsuperscript{17} The purpose of this study was to compare the results of OPCAB vs traditional coronary artery bypass grafting (CABG) with CPB, and to determine whether, and to what extent, OPCAB reduces the cerebral microembolic burden.

**MATERIALS AND METHODS**

**Patient Population**

A retrospective review of consecutive patients undergoing elective CABG between January 1998 and May 1999 was performed. Both OPCAB and CABG procedures were performed in consecutive patients during the same time period. Only patients undergoing their first cardiac revascularization were included. Patients with significant renal dysfunction (creatinine $>$ 2.0) or poor underlying cardiac function (ejection fraction $<$ 20\%) were excluded. To compare patient populations undergoing a similar number of bypass grafts, traditional CABG patients having four or more grafts were excluded. As data collection was retrospective, outcome variables were obtained from the medical record. Subtle neurologic deficits not detected or documented by the surgeon but was influenced by a variety of factors, including number and size of target vessels, cardiac performance, and associated comorbidities.

**Anesthesia Management**

Anesthesia was provided in a consistent manner for both CABG and OPCAB patients. All heart surgery patients were considered eligible for immediate extubation and received the same basic anesthetic management using short-acting, easily reversible agents for induction and volatile agents for maintenance. Most patients did not receive sedative premedication. Minimal narcotic ($<$ 100 $\mu g$ sufentanil) and sedative ($<$ 2 mg midazolam) dosages were used. A short-acting neuromuscular blocking agent (mivacurium) was used for induction. Maintenance anesthesia was provided with isoflurane or propofol ($<$ 500 $\mu g$). All patients in hemodynamically stable condition (both OPCAB and CABG) were eligible for a “fast track” protocol to facilitate earlier extubation. Postoperative pain management did not differ between groups. In the early postoperative period, pain was controlled with IV fentanyl as needed. This was rapidly converted to oral oxycodone and acetaminophen once a diet was started.

**Statistical Analysis**

Statistical analysis was performed with the Statistical Package for the Social Sciences software (SPSS/PC+; Chicago, IL). All continuous variables are expressed as mean $\pm$ SD. Categorical variables are expressed as percent of those exhibiting the trait out of all patients for whom data were available. All $p$ values are two-tailed, with $p$ values $\leq 0.05$ considered to indicate statistical significance. The statistical analysis was based on two independent groups of patients (CABG, $n = 70$; OPCAB, $n = 67$). Baseline characteristics, outcome measures, and complications between the two groups were compared using the Pearson coefficient of correlation ($\chi^2$) test. Similar comparisons were performed on the subgroup of each population that underwent TCD monitoring (CABG, $n = 20$; OPCAB, $n = 20$). Within these subgroups, the quantity and distribution of microemboli were compared. A multivariate linear regression model was used.
to identify factors associated with increasing numbers of microemboli while controlling for dissimilarities between populations.

Results

Demographics

One-hundred thirty-seven patients met the inclusion criteria, 70 undergoing traditional CABG with CPB and 67 undergoing OPCAB. OPCAB patients had a slightly higher ejection fraction than the traditional CABG group (55.5% vs 50.9%, p = 0.03). There was no statistical difference in the remaining preoperative characteristics or comorbidities between the two groups (Table 1). Despite the exclusion of CABG patients having four or more vessels bypassed, a small but statistically significant discrepancy in numbers of vessels bypassed remained (2.5 vs 3.0, p = 0.004). There was no significant difference identified, however, in the distribution (left, right, or circumflex) of vessels bypassed.

Surgical Results

Although preoperative characteristics were comparable, significant differences in perioperative complications and outcome measures were identified. Statistically significant reductions in the need for transfusion, time to extubation, ICU length of stay, and overall hospital length of stay were seen in the OPCAB group (Table 2). There were no perioperative deaths or cerebrovascular accidents in the OPCAB group, whereas two deaths and two strokes were observed in the traditional CABG group. These interesting trends, however, failed to achieve statistical significance. There were three patients in whom OPCAB was attempted who could not tolerate the procedure and required intraoperative conversion to traditional CABG with CPB (conversion rate, 4.3%).

Table 1—Preoperative Demographics*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OPCAB (n = 67)</th>
<th>CABG (n = 70)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>73</td>
<td>77</td>
<td>NS</td>
</tr>
<tr>
<td>Age, yr</td>
<td>64.8 ± 10.3</td>
<td>66.0 ± 10.7</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>55.5</td>
<td>50.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>50.1</td>
<td>41.4</td>
<td>NS</td>
</tr>
<tr>
<td>Previous CVA, %</td>
<td>20.9</td>
<td>10.1</td>
<td>NS</td>
</tr>
<tr>
<td>COPD, %</td>
<td>17.9</td>
<td>11.4</td>
<td>NS</td>
</tr>
<tr>
<td>↑ Cholesterol, %</td>
<td>56.7</td>
<td>63.8</td>
<td>NS</td>
</tr>
<tr>
<td>HTN, %</td>
<td>76.1</td>
<td>70.0</td>
<td>NS</td>
</tr>
<tr>
<td>Previous MI, %</td>
<td>22.4</td>
<td>34.3</td>
<td>NS</td>
</tr>
<tr>
<td>Tobacco use, %</td>
<td>56.7</td>
<td>62.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

*CVA = cerebrovascular accident; ↑ Cholesterol = hypercholesterolemia; HTN = hypertension; MI = myocardial infarction; NS = not significant.

These patients, hemodynamic instability resulted from either lifting or stabilizing the heart, necessitating conversion. These patients were included in the CABG group for data analysis as they underwent CPB and all of the procedural events associated with this. There were no myocardial infarctions or other significant complications in these three patients, and they were discharged home safely with total hospitalization ranging from 5 to 9 days.

Transcranial Doppler Results

Bilateral MCA monitoring was successful in 16 of 20 OPCAB patients (80%) and in 14 of 20 CABG patients (70%). Those not monitored bilaterally were monitored unilaterally. Inability to obtain a reliable bilateral MCA signal was the reason for unilateral monitoring. There was no significant discrepancy in emboli counts between sonographers. The number of cerebral microemboli was significantly higher in patients undergoing traditional CABG compared with OPCAB (1,766 ± 2,455 vs 27 ± 35, p = 0.003). Multivariate analysis identified the type of operation (OPCAB vs CABG) as having the most significant association with the number of microemboli detected (p = 0.002). The only comorbidity with a significant association with the number of microemboli detected was the history of a previous myocardial infarction (p = 0.04).

In those patients able to be monitored bilaterally, emboli detection in the left and right MCAs was compared. Emboli tended to be more numerous on the right in OPCAB patients and more numerous on the left in CABG patients. This difference, however, did not reach statistical significance. Table 3 summarizes the embolic data.

The temporal distribution of microembolic events was also examined. Emboli counts by operative maneuver are represented in Figure 1. The operative events that accounted for the greatest number of emboli during OPCAB (Fig 1, top) were manipulat-

Table 2—Comparison of Operative Results and Complications*

<table>
<thead>
<tr>
<th>Variable</th>
<th>OPCAB (n = 67)</th>
<th>CABG (n = 70)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of grafts</td>
<td>2.5 ± 0.9</td>
<td>3.0 ± 0.8</td>
<td>0.004</td>
</tr>
<tr>
<td>Required transfusion, %</td>
<td>29.9</td>
<td>47.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Intubation</td>
<td>3.3 ± 7.4</td>
<td>9.5 ± 8.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU stay, d</td>
<td>1.5 ± 1.0</td>
<td>2.5 ± 4.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Total length of stay, d</td>
<td>4.9 ± 2.2</td>
<td>6.6 ± 4.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>32.8</td>
<td>34.3</td>
<td>NS</td>
</tr>
<tr>
<td>CVA, %</td>
<td>0</td>
<td>2.9</td>
<td>NS</td>
</tr>
<tr>
<td>Death, %</td>
<td>0</td>
<td>2.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

*See footnote of Table 1 for abbreviations.
ing or lifting the heart (30%) and placing and removing the partial aortic clamp (16%). Other emboli occurred at seemingly random times during the procedure. During CABG, however, the vast majority of cerebral microemboli (84%) occurred during CPB alone, without an associated surgical maneuver (Fig 1, bottom). The initiation of CPB accounted for the second highest number (7.5%) of emboli.

**Discussion**

We believe that these early results support OPCAB as a safe and effective alternative to traditional coronary revascularization. Eliminating CPB greatly reduces the systemic inflammatory response associated with cardiac surgery, and tangible benefits may be realized. Decreased interstitial pulmonary edema, surfactant degradation, and hypothermia may, in part, account for the decreased need for postoperative mechanical ventilation after OPCAB. The damaging effects of CPB on platelets and clotting factors, and the higher doses of heparin required, contribute to the increased need for blood and blood product transfusions with traditional CABG. Finally, ICU and overall hospital length of stay were both significantly decreased in those undergoing OPCAB, supportive of the cumulative benefits and decreased physiologic demands of this procedure relative to traditional CABG.

Adverse effects of CPB can also occur in the CNS. The occurrence of neurologic complications after cardiac surgery cannot be attributed to a single causative element in most cases. As with most disease processes, the cause is multifactorial. Preexisting cerebrovascular disease and postoperative arrhythmias have been shown to increase the risk of stroke. The observed 65-fold increase in measured cerebral microemboli with traditional CABG with CPB is a point of significant concern, as this iatrogenic insult may contribute to the risk of adverse neurologic events.

Comparative studies examining the occurrence of microemboli in patients undergoing CABG or valve replacement have been performed. More emboli are generated during valve replacement surgery, particularly when the heart regains effective ejection. This increased embolic burden has been correlated with a higher degree of neuropsychological deficit in patients undergoing valve replacement. In the series by Brækken et al, embolic counts were significantly higher in patients undergoing valve replacement compared to those undergoing CABG.

**Table 3—Comparison of Microemboli OPCAB vs CABG**

<table>
<thead>
<tr>
<th>Microemboli</th>
<th>OPCAB (n = 20)</th>
<th>CABG (n = 20)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean No. of emboli/patient</td>
<td>27 ± 35</td>
<td>1,766 ± 2,455</td>
<td>0.003</td>
</tr>
<tr>
<td>Median No. of emboli/patient</td>
<td>12</td>
<td>1,041</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0 to 133</td>
<td>131 to 10,703</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distribution of microemboli (mean)</th>
<th>Left MCA</th>
<th>Right MCA</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPCAB</td>
<td>12 ± 13 (42%)</td>
<td>17 ± 26 (58%)</td>
<td>NS</td>
</tr>
<tr>
<td>CABG</td>
<td>1,237 ± 1,608 (56%)</td>
<td>975 ± 1,238 (44%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Figure 1.** Occurrence of microemboli (average number per patient event) in OPCAB (top) and CABG (bottom). Induc = induction; Lift = lift heart; D = distal anastomosis; P = proximal anastomosis; Manip = manipulation; Ao Clamp = aortic partial occlusion clamp (top); Ao Cann = aortic cannulation; On CPB = initiation of CPB; PA Vent = pulmonary artery vent; X Clamp On/Off = cross-clamp aorta; Partial On/Off = aortic partial occlusion clamp (bottom); Defib = defibrillation; Decan = remove cannulas.
higher in those patients with neurologic deficits than in those without deficits (2,083 vs 645, \( p = 0.04 \)). Our study is limited in that it involved retrospective data collection, which did not include neuropsychological testing.

In this series comparing the occurrence of microemboli in patients undergoing coronary revascularization with and without CPB, we have demonstrated a significant reduction in the cerebral embolic burden with the elimination of the extracorporeal bypass circuit. Although manipulation does account for some of the emboli during CABG, the vast majority (84%) occurred while the patient was receiving CPB with no specific surgical manipulation identified. In contrast, the relatively sparse emboli count recorded during OPCAB was more often related to surgical manipulation, especially lifting the heart for distal anastomoses and placing and releasing the partial occlusion aortic clamp.

In general, we found our emboli counts during CABG with CPB to be higher than values previously reported in the literature. One element contributing to higher counts in our series is the tendency toward unilateral MCA monitoring in prior studies. Others have hypothesized that emboli preferentially follow the right brachiocephalic trunk, thus the large number of studies in which only the right MCA is monitored. We found no significant difference in the occurrence of microemboli in the right or left MCA in patients who were monitored bilaterally, in either OPCAB or CABG. Studies measuring only the right MCA therefore may quantify only half of the total embolic load. Other factors that may contribute to variability in emboli counts between studies are the size of the arterial line filter used and the predetermined minimum intensity threshold (which ranges from 3 to 40 dB in some series). A 40-μm arterial line filter was used for all CABG patients in our study. All emboli were recorded and included (no minimum intensity threshold was used).

Although the size of the arterial filter in the CPB circuit may affect the number of emboli reaching the brain, the other factors mentioned do not influence the occurrence of microemboli, only the relative number detected. In fact, histologic evidence suggests that we are detecting only a very small fraction of the emboli reaching the brain. Based on the histologic appearance of small capillary and arteriolar dilations in one autopsy study, the estimated embolic insult to the brain in a patient having undergone open heart surgery was 15,300,000 microemboli. The relative insensitivity of TCD in detecting these pathologically identifiable lesions suggests that microemboli smaller than the detectable resolution of the TCD monitor may be significant. We have shown that OPCAB reduces detectable emboli counts by two orders of magnitude on average. Whether this magnitude of reduction also applies to emboli not detected by TCD is unknown. Other nonembolic phenomena, such as changes in MCA flow velocity, have been associated with neurologic dysfunction as well.

Although our uniform inclusion criteria did create statistically comparable groups for analysis, truly homogenous populations for comparison cannot be achieved in a retrospective study. Another significant limitation of this study is the surgical selection bias inherent in all but prospective, randomized trials. To establish whether OPCAB offers an advantage in reducing the neurologic complications associated with cardiac surgery, further investigation is needed. A larger study population and a prospective evaluation of neurologic sequelae (strokes and neurocognitive dysfunction) might validate this hypothesis.

The results of our study are interesting. We have demonstrated a significant reduction in the number of microemboli detected by TCD, as well as a trend toward a reduction in the stroke rate in patients undergoing OPCAB compared with CABG. The true clinical significance of this dramatic reduction in cerebral microemboli, however, remains to be determined.

**References**

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