Reduced Mortality and Strokes With Off-Pump Coronary Artery Bypass Grafting Surgery in Octogenarians

Roland G. Demaria, MD; Michel Carrier, MD; Simon Fortier, MD; Raymond Martineau, MD; Annick Fortier, MSc; Raymond Cartier, MD; Michel Pellerin, MD; Yves Hébert, MD; Denis Bouchard, MD; Pierre Pagé, MD; Louis P. Perrault, MD, PhD

Background—Off-pump coronary artery bypass surgery (OPCAB) has been revived and has gained popularity, although the exact subsets of patients who might benefit most from this technique are unknown. The aim of this retrospective study was to compare the results of coronary artery bypass grafting surgery (CABG) in octogenarians using cardiopulmonary bypass (CPB) or OPCAB techniques.

Methods and Results—Over a 5-year period (1995–1999), 125 patients older than 80 years of age were operated for isolated myocardial revascularization (63 using CPB and 62 with OPCAB). There was no statistically significant difference in preoperative comorbidities between groups or in mean left ventricular ejection fraction (54.5±15.3% in the CPB group and 50.9±13.5% in the OPCAB group, respectively). The mean number of distal anastomosis per patient was 2.9 in CPB group and 2.6 in OPCAB group (P=ns). The majority of patients in both groups had unstable angina and were operated on an urgent basis. The operative mortality was 15.9% in the CPB group and 4.8% in the OPCAB group (P=0.04). There were 4 postoperative strokes (6.3%) in the CPB group and none (0%) in the OPCAB group (P=0.04). The percentage of patients transfused was 92.1% in the CPB group and 72.6% in the OPCAB group (P<0.01). Postoperative myocardial infarction occurred in 11.3% in the CPB group and 14.5% in the OPCAB group (P=NS). For all the parameters entered in the multivariate analysis with logistic regression model, the type of surgery (CPB or OPCAB) was an independent predictor of operative mortality and stroke (P=0.0375). The odds ratio (OR) indicates that operative mortality and stroke occur 4 times (OR=4.171) more often in CPB patients than in OPCAB patients. Follow-up showed no significant difference between the 2 groups in terms of cardiac events and mortality.

Conclusions—This retrospective study suggests a benefit of OPCAB in terms of operative mortality and stroke for octogenarian patients when compared with CPB in our institution. (Circulation. 2002;106[suppl I]:I-5-I-10.)

Key Words: cardiopulmonary bypass ■ coronary disease ■ elderly ■ morbidity ■ mortality ■ surgery

Coronary artery bypass graft surgery (CABG) is efficient in alleviating symptoms of angina, improving quality of life and longevity of patients with coronary artery disease in the general population.1-3 Previous studies have revealed that CABG surgery in patients above the age of 80 is associated with a higher operative mortality than in younger patients,4,5 although published results have shown a steady improvement6,7 because of advances in surgical techniques, cardioprotective agents, and anesthetic and perioperative care.8 However, octogenarians remain a high-risk population for cardiac surgery,9 hence the interest of evaluating a potentially less morbid approach in this group.

Off-pump coronary artery bypass surgery (OPCAB) has been proposed in recent years as a less invasive technique of myocardial revascularization. It avoids the systemic inflammatory effects of cardiopulmonary bypass (CPB), such as activation of the complement system and neutrophils, induction of adhesion molecules, release of cytokines, and endothelial activation, which are a source of major complications.10 Furthermore, the feasibility of this technique, more challenging and skill demanding, at least initially, for the surgeon, has recently been facilitated by use of new stabilizers.11

The increasing number of elderly patients with coronary artery disease requiring revascularization prompted a retrospective review of our results in a group of 125 consecutive octogenarian patients who underwent isolated CABG. The aforementioned studies have demonstrated acceptable surgical mortality and good long-term results in octogenarian patients who underwent elective CABG. The aim of this
study was to compare retrospectively the postoperative results of octogenarians who underwent CABG with CPB or with OPCAB to define the optimal surgical technique in these high-risk patients.

Methods

Study Design
Between January 1995 and December 1999, the records of all patients operated at the Montreal Heart Institute were entered in a database. Over this 5-year period, data were acquired in 5221 patients undergoing isolated CABG. Among this cohort, 125 patients (2.4%) were 80 years or older. Of these patients, 63 were operated using CPB (CPB group) and 62 patients were operated with OPCAB techniques (OPCAB group). The choice between the 2 techniques depended on the surgeon’s choice and technical preferences. Seven surgeons with a mixed practice of OPCAB and CPB operated this cohort of patients.

Left ventricular ejection fraction (LVEF) was obtained from the cardiac catheterization or echocardiography. Unstable angina was defined as an acute coronary syndrome treated with intravenous heparin and/or intravenous nitroglycerin. Recent myocardial infarction (MI) was defined as those occurring within 6 weeks of the operation. Peripheral atherosclerosis disease included patients with a history of claudication and/or peripheral vascular surgery. Preoperative renal disease was defined as a serum creatinine >133 μmol/L.

Operative mortality was defined as death occurring within 30 days of the operation. Postoperative renal failure was defined as an increase of creatinine of >100 μmol/L above the preoperative value and a postoperative MI was defined as a maximal creatine kinase-MB fraction (CK-MB) level >100 UI/L.

Surgical Technique and Postoperative Management

All patients in the CPB group underwent CPB with a single venous and ascending aortic cannula using a membrane oxygenator (Monolymph; Sorin Biomedica Inc, Richmond Hill, CAN) equipped with an arterial filter and under moderate hypothermia (32 to 34°C). The CPB circuit was primed with a crystalloid solution and with or without a colloid solution (albumin or hetastarch 200/0.5). Myocardial protection was left at the discretion of the attending surgeon with the majority using intermittent antegrade sanguineous tepid cardioplegia. The heparin dosage was 300 U/kg in the CPB group and 100 U/kg in the OPCAB group, respectively (for an ACT>400 seconds). For the OPCAB group, vessel occlusion was achieved by external encircling with silicone rubber bands (Retract-O-tape; Quest Medical Inc, Allen, TX). Coronary artery immobilization was achieved with a variety of mechanical stabilizers (Cor-Vase System [patent obtained], CoroNéo Inc, Montreal, Canada; Cohn Stabilizer, Genzyme, Cambridge, MA, USA; CTS Stabilizer, CTS Guidant, Markham, CAN) or a home made stabilizer in the early period. Postoperatively, all patients received AAS 325 mg daily and no patients received GpIIbIIIa inhibitors. Patients in the OPCAB group received 100 mL/h of continuous hemofiltration 3 (4.8%) 0 (0%) 0.08

Use of venous grafts 61 (96.8%) 54 (87.1%) 0.045

Intraoperative blood loss (mL) 474±242 442±259 0.48

Fluid balance (in-out; mL) 1671±1006 473±830 <0.01

Continuous hemofiltration 3 (4.8%) 0 (0%) 0.08

TABLE 1. Preoperative Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>CPB</th>
<th>OPCAB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable angina</td>
<td>59 (93.7%)</td>
<td>56 (90.3%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Recent MI</td>
<td>14 (22.2%)</td>
<td>13 (21.0%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Reoperation</td>
<td>1 (1.6%)</td>
<td>2 (3.2%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Preoperative IABP</td>
<td>9 (14.3%)</td>
<td>4 (6.5%)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

CPB indicates cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass grafting; SD, standard deviation; NYHA, New-York Heart Association; TIA, transient ischemic attack; MI, myocardial infarction; IABP, intraaortic balloon pump.

Patient Profiles

Preoperative parameters were assessed for their effect on hospital survival and complications by using univariate analysis (Table 1). There was no statistically significant difference between the 2 groups for all preoperative characteristics (Table 1). The 2 groups were not statistically different in terms of age, gender ratio, cardiovascular risk factors, and comorbidities. Similarly, the preoperative LVEF, the incidence of previous MI, previous cardiac operations, significant stenosis of the left main coronary artery, and the use of preoperative intra-aortic balloon pump (IABP) were not different in either group.

Intraoperative patient characteristics are listed in Table 2. The mean number of distal anastomosis was not statistically different in the 2 groups (Table 2).

TABLE 2. Intraoperative Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>CPB</th>
<th>OPCAB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean no. of distal anastomosis</td>
<td>2.9±0.7</td>
<td>2.6±0.8</td>
<td>0.053</td>
</tr>
<tr>
<td>Use of LIMA</td>
<td>55 (87.3%)</td>
<td>55 (88.7%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Use of RIMA</td>
<td>1 (1.6%)</td>
<td>6 (9.7%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Use of venous grafts</td>
<td>61 (96.8%)</td>
<td>54 (87.1%)</td>
<td>0.045</td>
</tr>
<tr>
<td>Intraoperative blood loss (mL)</td>
<td>474±242</td>
<td>442±259</td>
<td>0.48</td>
</tr>
<tr>
<td>Fluid balance (in-out; mL)</td>
<td>1671±1006</td>
<td>473±830</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Continuous hemofiltration</td>
<td>3 (4.8%)</td>
<td>0 (0%)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

CPB indicates cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass grafting; LIMA, left internal mammary artery; RIMA, right internal mammary artery.

Results

Follow-Up

The follow-up for survival analysis was obtained in January and February 2002 from direct telephone calls with the surviving patients or with families and referring cardiologists. Questions were addressed in regard to their actual functional status, level of angina, cardiac related hospitalization with eventually percutaneous transluminal angioplasty or reoperation for CABG, and, if applicable, cause and date of death.

Statistical Analysis

Univariate analysis was performed on preoperative and intraoperative patient characteristics listed in Tables 1 and 2, respectively, and on CK-MB elevation in Figure 1. The Pearson χ² test was used to compare categorical variables and the unpaired t test was used to compare the continuous variables with the two-tailed probability values.
CK-MB Elevation After CABG in Octogenarians

![Graph showing CK-MB elevation after coronary artery bypass grafting (CABG) in octogenarians.](image)

Figure 1. CK-MB elevation after coronary artery bypass grafting surgery in octogenarians on admittance to the intensive care unit after the surgery (day 0), at postoperative day (POD) 1 and POD 2. There was a statistically significant difference between the 2 groups in favor of the OPCAB group after the surgery (day 0), but not at POD 1 or POD 2. CPB, cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass grafting.

Operative Mortality and Morbidity
Data on operative mortality and morbidity are listed in Table 3. The operative mortality rate was 15.9% in the CPB group and 4.8% in the OPCAB group (P=0.04) (Table 3). There was proportionately more cardiac-related mortalities from MI and low cardiac output in the CPB group than in the OPCAB group, although this difference was not statistically significant. The causes of death in the CPB group (10 patients) were MI in 5 cases, low cardiac output without MI in 3 patients, and multisystemic organ failure in 2 patients. The 3 deaths in the OPCAB group were due to MI, low cardiac output without MI, and respiratory failure. There was a 6.4% stroke rate in the CPB group and none in the OPCAB group (P=0.04). The incidence of atrial fibrillation occurring within the first 2 postoperative days was similar for the 2 groups. There was no statistically significant difference between the 2 groups for postoperative renal failure and for MI. The average postoperative release of CK-MB was significantly lower in the OPCAB group on the day of surgery (P=0.0001) but not in the following days (Figure 1). Hypothermia on admittance to the intensive care unit (ICU) was significantly more frequent in the OPCAB group. The duration of stay in ICU and the hospital length of stay were not significantly different for the 2 groups. Patients operated under CPB required significantly more red cells units, platelets, and fresh frozen plasma units transfusion than patients in the OPCAB group.

Prediction of Mortality and Stroke
Of all the preoperative parameters entered in the logistic regression model to take into account the effect of potential confounding factors, only atherosclerotic peripheral vascular disease showed a trend toward prediction of mortality and/or stroke (P=0.073). However, the type of surgery (CPB or OPCAB) was an independent predictor of mortality and/or stroke (P=0.0375) (Table 4). The odds ratio (OR) indicates that mortality and/or stroke occurred 4 times (OR=4.17) as often among CPB patients, than in OPCAB patients. The overall model was statistically significant ($\chi^2=8.3521$ with 2 df, P = 0.0154) and the Hosmer-Lemeshow goodness-of-fit test indicated adequacy of the model ($\chi^2=0.9979$ with 2 df, P=0.6072).

Follow-Up Status
The follow-up was 97.6% complete (3 patients missing: 2 in the OPCAB group and 1 in the CPB group). The remote

<table>
<thead>
<tr>
<th>TABLE 3. Operative Mortality, Morbidity, and Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Operative mortality</td>
</tr>
<tr>
<td>Cardiac or hemodynamic</td>
</tr>
<tr>
<td>Septic or MOF</td>
</tr>
<tr>
<td>Respiratory failure</td>
</tr>
<tr>
<td>Major complications</td>
</tr>
<tr>
<td>MI (CK-MB $\geq$100 $\mu$g/L)</td>
</tr>
<tr>
<td>Prolonged intubation $&gt;$ 24 hours</td>
</tr>
<tr>
<td>Bleeding/tamponade</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Neurological deficit/stroke</td>
</tr>
<tr>
<td>Minor complications</td>
</tr>
<tr>
<td>AF</td>
</tr>
<tr>
<td>Renal failure</td>
</tr>
<tr>
<td>CWH</td>
</tr>
<tr>
<td>Hepatic failure</td>
</tr>
<tr>
<td>Hypothermia ($T^\circ &lt;34$ at ICU)</td>
</tr>
<tr>
<td>Hemodynamic support</td>
</tr>
<tr>
<td>Vasopressive drugs $&gt;$ 24 hours</td>
</tr>
<tr>
<td>IABP</td>
</tr>
<tr>
<td>Transfusions</td>
</tr>
<tr>
<td>% of patients requiring transfusion</td>
</tr>
<tr>
<td>Total (mean units $\pm$ SD)</td>
</tr>
<tr>
<td>Length of ICU stay (days)</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
</tr>
</tbody>
</table>

CPB indicates cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass grafting; MI, myocardial infarction; CK-MB, creatine kinase-MB fraction; AF, atrial fibrillation; CWH, continuous venovenous hemofiltration; ICU, intensive care unit; IABP, intraaortic balloon pump; SD, standard deviation; d, days.

Follow-Up Status
The follow-up was 97.6% complete (3 patients missing: 2 in the OPCAB group and 1 in the CPB group). The remote

<table>
<thead>
<tr>
<th>TABLE 4. Logistic Regression on Operative Mortality and/or Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters</td>
</tr>
<tr>
<td>Atherosclerotic peripheral vascular disease (presence of)</td>
</tr>
<tr>
<td>Type of surgery (CPB vs OPCAB)</td>
</tr>
</tbody>
</table>

CPB indicates cardiopulmonary bypass; OPCAB, off-pump coronary artery bypass grafting; OR, odds ratio.
outcomes of patients is summarized in Table 5. Among the 5 patients who died of cardiac causes in the OPCAB group, 4 died of progressive cardiac failure a mean of 2.9 years (2.5 to 3.5) after surgery, and 3 had poor preoperative left ventricular function. However, there was no significant difference between the 2 groups for all the postoperative variables studied (Table 5) and no significant difference between the 2 survival curves of the 2 groups (Figure 2).

Discussion

The major findings of this study are that OPCAB is associated with significantly less operative mortality and strokes in octogenarians than conventional CABG under CPB. Use of CPB in octogenarians is a significant predictor of operative mortality and stroke. Mid-term follow-up showed no significant difference between the 2 groups in terms of mortality and nonlethal cardiac events.

Surgical intervention improves survival and provides a functional benefit over the continuation of medical therapy in some subgroups of patients such as octogenarians. An increasing number of octogenarians with symptomatic coronary artery disease will require CABG in the coming years, and this has provided an impetus for recent studies of CABG in the elderly. Several centers have reported satisfactory surgical mortalities and favorable long-term survival in octogenarians who underwent CABG. The next area of investigation to consider is whether the OPCAB surgical technique provides an advantage in terms of mortality and morbidity compared with patients operated with conventional CPB. A comparative study on septuagenarians has shown that OPCAB is safe in the geriatric population and significantly reduces postoperative morbidity and cost. Overall operative mortality is significantly higher in the CPB group mainly due to cardiac causes specifically MI. Postoperative MI was defined as a maximal creatine kinase-MB fraction (CK-MB) level >100 U/L during the postoperative period and was usually associated with EKG or segmental hypokinesia at the echocardiography. Although the absolute number of MI was slightly higher in the OPCAB group ($P=NS$), only 1 patient died from MI and the operative mortality was lower in OPCAB group. The greater number of MIs in the OPCAB could be related to the lower number of grafts in the OPCAB, although not statistically significant ($P=0.053$), which could reflect a less complete revascularization in OPCAB patients compared with the CPB group. This observation may raise the issue of the need for complete revascularization, even in the elderly patient, however, incomplete revascularization with OPCAB may yield better operative results than complete revascularization under CPB in patients older than 75 years of age. The higher significant level of CK-MB observed on admittance to the ICU (Day 0 only) in the CPB group, which has been reported in a larger study from our institution, does not reflect occurrence of MI as defined earlier but may indicate a greater amount of myocardial damage due to the aortic cross clamping and global ischemia during cardioplegic arrest. However, the clinical consequences of mild cardiac enzyme elevations are unknown in octogenarians especially since the senescent human myocardium has a reduced capacity to recover contractile function after in vitro hypoxia or simulated ischemia compared with the myocardium of younger adults.

There was a 6.4% stroke rate in CPB and none in OPCAB group ($P=0.04$), whereas the preoperative number of previous transient ischemic attacks, carotid stenosis, or postoperative atrial fibrillation were not different between the 2 groups, as already described. This result confirms those of a previous study in octogenarians in which the incidence of stroke was 0% in the OPCAB cohort compared with 9.3% in the CPB cohort. This difference in stroke rate was not observed in our institution and others when CPB and OPCAB were compared irrespective of the age of the patients. The “no touch” technique...
for the ascending aorta in OPCAB with the use of both IMA and Y grafting may be specifically indicated to avoid strokes in patients with severe aortic atheroma, guided by systematic intraoperative assessment of atheromatous plaques by transesophageal or epiaortic echocardiography. Indeed, total avoidance of “side-biting” clamps in OPCAB could reduce the incidence of neurological complications in case of severely atheromatous aortas found more frequently in elderly patients. The more frequent use of RIMA in the OPCAB group to avoid any manipulation of atheromatous and calcified ascending aortas may explain the lower stroke rate in the OPCAB group.

Although there was no statistically significant difference in perioperative blood loss between the 2 groups, the need of transfusion was higher in the CPB group, as previously reported. Furthermore, among patients receiving transfusions, there were fewer different blood products administered in the OPCAB group compared with the CPB group.

Hypothermia may have major drawbacks in elderly patients operated for CABG, as it alters the metabolism, favors bleeding and the occurrence of postoperative arrhythmia. The percentage of hypothermic patients transferred to ICU was significantly higher in the OPCAB group than in the CPB group which were rewarmed with the CPB machine. However, although at the beginning of the OPCAB experience more than 30% of patients were hypothermic at the end of surgery, now hypothermia occurs in less than 2% of patients on admittance into ICU due to the systematic use of warming blankets and prevention of heat loss.

Limitations

This study has 2 main limitations. First, it is a retrospective study in a relatively small number of patients with comparison between 2 nonrandomized groups. However, the data were extracted from the same period of time and from the same database and the preoperative characteristics were similar between 2 groups of equal size operated by the same surgeons in a single institution. Secondly, this study takes into account the initial experience of OPCAB surgery in our institution including the learning curve, which may skew negatively the results in the OPCAB group compared with the CPB group. Because of these facts, the introduction of a selection bias in choosing OPCAB versus CABG on CPB in octogenarians cannot be excluded. Although sicker patients may have been operated on CPB and the number of patients with preoperative IABP support was higher in the CPB group, but did not reach statistical significance, there were no significant differences in the preoperative morbidity conditions between the 2 groups. The more frequent use of pedicled RIMA grafts in the OPCAB group to minimize aortic manipulation could also influence the lower occurrence of neurological complications.

Notwithstanding these limitations, the results of patients operated for isolated CABG in our institution during the same period were significantly better with OPCAB than with CPB in terms of operative mortality and strokes in a homogeneous population of octogenarians. Although the mean length of follow-up was longer in the CPB group (because more were operated in the early period), mid-term outcomes in terms of mortality and cardiac events were not significantly different. These patients in the early part of the ninth decade of life may enjoy many years of high-quality life. The present study demonstrated improved survival and functional benefits with OPCAB compared with conventional CPB surgery. OPCAB may be the technique of choice in elderly patients and other high risk groups. A prospective randomized study is mandatory and presently underway in our center in this population to confirm these results.

Acknowledgments

We would like to acknowledge Jean Lambert, PhD, for his expert statistical assistance, Department of Biostatistics, Université de Montréal, and Annie Laprade and Diane Campeau for the preparation of the manuscript.

References


Reduced Mortality and Strokes With Off-Pump Coronary Artery Bypass Grafting Surgery in Octogenarians

Roland G. Demaria, Michel Carrier, Simon Fortier, Raymond Martineau, Annick Fortier, Raymond Cartier, Michel Pellerin, Yves Hébert, Denis Bouchard, Pierre Pagé and Louis P. Perrault

_Circulation._ 2002;106:I-5-I-10
doi: 10.1161/01.cir.0000032891.55215.6e

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/106/12_suppl_1/I-5

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/