

Comparing On-Pump and Off-Pump Coronary Artery Bypass Grafting

Numerous Studies but Few Conclusions

A Scientific Statement From the American Heart Association Council on Cardiovascular Surgery and Anesthesia in Collaboration With the Interdisciplinary Working Group on Quality of Care and Outcomes Research

Frank W. Sellke, MD, Co-Chair; J. Michael DiMaio, MD, Co-Chair; Louis R. Caplan, MD; T. Bruce Ferguson, MD; Timothy J. Gardner, MD; Loren F. Hiratzka, MD; Eric M. Isselbacher, MD; Bruce W. Lytle, MD; Michael J. Mack, MD; John M. Murkin, MD; Robert C. Robbins, MD

Abstract—One of the most hotly debated and polarizing issues in cardiac surgery has been whether coronary artery bypass grafting (CABG) without the use of cardiopulmonary bypass or cardioplegia (off-pump CABG, or OPCAB) is superior to that performed with the heart-lung machine and the heart's being chemically arrested (standard CABG). Various clinical trials are reviewed comparing the 2 surgical strategies, including several large retrospective analyses, meta-analyses, and the randomized trials that address different aspects of standard CABG and OPCAB. Although definitive conclusions about the relative merits of standard CABG and OPCAB are difficult to reach from these varied randomized and nonrandomized studies, several generalizations may be possible. Patients may achieve an excellent outcome with either type of procedure, and individuals' outcomes likely depend more on factors other than whether they underwent standard CABG or OPCAB. Nevertheless, there appear to be trends in most studies. These trends include less blood loss and need for transfusion after OPCAB, less myocardial enzyme release after OPCAB up to 24 hours, less early neurocognitive dysfunction after OPCAB, and less renal insufficiency after OPCAB. Fewer grafts tend to be performed with OPCAB than with standard CABG. Length of hospital stay, mortality rate, and long-term neurological function and cardiac outcome appear to be similar in the 2 groups. To definitively answer the remaining questions of whether either strategy is superior and in which patients, a large-scale prospective randomized trial is required. (*Circulation*. 2005;111:2858-2864.)

Key Words: AHA Scientific Statements ■ grafting ■ trials ■ morbidity ■ mortality

One of the most hotly debated and polarizing issues in cardiac surgery has been whether coronary artery bypass grafting (CABG) without the use of cardiopulmonary bypass (CPB) or cardioplegia (off-pump CABG, or OPCAB) is superior to that performed with the heart-lung machine and the heart's being chemically arrested (standard CABG). Initial descriptive studies reported excellent to outstanding outcomes with OPCAB, with the suggestion in many studies of less use of resources, less blood loss, less morbidity, and a shortened length of hospital stay; however, these early studies tended to be nonrandomized clinical reports rather than

rigorously controlled clinical studies. Since these early reports, several randomized trials have been completed. Nevertheless, it remains uncertain whether OPCAB is associated with a distinct advantage or whether the outcome with OPCAB is similar or identical to that achieved by CABG with CPB, which has been the "gold standard." Various clinical trials are reviewed comparing the 2 surgical strategies, including several large retrospective analyses, meta-analyses, and the randomized trials that address different aspects of standard CABG and OPCAB. Finally, we examine the various subtopics involving specific discussion criteria for

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on March 22, 2005. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0322. To purchase additional reprints: up to 999 copies, call 800-611-6083 (US only) or fax 413-665-2671; 1000 or more copies, call 410-528-4121, fax 410-528-4264, or e-mail kgray@lww.com. To make photocopies for personal or educational use, call the Copyright Clearance Center, 978-750-8400.

Expert peer review of AHA Scientific Statements is conducted at the AHA National Center. For more on AHA statements and guidelines development, visit <http://www.americanheart.org/presenter.jhtml?identifier=3023366>.

© 2005 American Heart Association, Inc.

Circulation is available at <http://www.circulationaha.org>

DOI: 10.1161/CIRCULATIONAHA.105.165030

these studies. Because of space constraints, this article cannot be an exhaustive review of studies that have compared the 2 strategies on clinical or physiological grounds. It is the purpose of this consensus article to briefly review selected clinical data comparing OPCAB with standard CABG and to summarize the relative merits of and indications for the 2 strategies for myocardial revascularization.

Retrospective Studies

Because techniques of OPCAB have markedly improved during the past several years and many surgeons have reached a plateau on the "learning curve," older studies may not be as useful for comparison. A retrospective study by Racz et al¹ analyzed >68 000 patients treated in New York state between 1997 and 2000. Of these patients, >9000 revascularizations were performed off pump. Of those patients undergoing OPCAB, there were higher proportions of older patients; women; and patients with low ejection fraction, previous CABG, stroke, peripheral vascular disease, left ventricular hypertrophy, congestive heart failure, calcified aortic disease, and renal failure. In the standard CABG group, a high number of patients had acute myocardial infarction (MI), shock, cardiopulmonary resuscitation, and left main disease, as well as more diseased arteries than in the OPCAB group. Thus, a comparison is difficult to make; however, risk-adjusted mortality was not different between the groups. In this study, no significant difference was found in the incidence of death, perioperative MI, wound infection, renal failure requiring dialysis, or respiratory failure. There were, however, significantly higher rates of stroke (2.0% versus 1.6%, $P=0.003$) and bleeding requiring reoperation (2.2% versus 1.6%, $P<0.001$) in the standard CABG group. A significantly higher risk of gastrointestinal complications (1.2% versus 0.9%, $P=0.003$) was observed in the OPCAB group. Hospital length of stay was longer in the standard CABG group by 1 day. At 3-year follow-up, patients in the standard CABG group had a higher survival rate (89.6% versus 88.8%, $P=0.022$) and need for repeat revascularization (percutaneous coronary intervention or CABG, 84.7% versus 82.1%, $P<0.0001$). In data from the last 2 years of the study (ie, excluding the first year), the survival benefit disappeared but the freedom from death and revascularization remained. The authors concluded that patients undergoing standard CABG with CPB have better rates of long-term survival and freedom from repeat revascularization.

In another retrospective nonrandomized study, Mack et al² reviewed 17 401 patients (7283 OPCAB) who underwent surgery between 1999 and 2001. The percentage of patients with congestive heart failure, chronic obstructive pulmonary disease, renal failure, stroke, peripheral vascular disease, and previous CABG was higher in the OPCAB group. The unadjusted mortality rate was 1.9% in the OPCAB group, versus 3.5% in the standard CABG group ($P<0.001$). Propensity matching was done in all patients with multivessel disease to minimize selection bias and to provide for similar predicted risks for multiple variables. In the propensity-matched groups, the mortality rate was 2.2% in the OPCAB group, versus 3.7% in the CPB group ($P<0.001$). The rate of complications was significantly

lower in the OPCAB group, including overall number of complications, use of blood products, wound infection, reoperation for bleeding, atrial fibrillation, permanent stroke, gastrointestinal and respiratory complications, renal failure, MI, and multiorgan failure. Only transient stroke, reoperation for graft occlusion, and pulmonary embolus were not significantly different between the groups. These authors concluded that OPCAB is associated with less morbidity and mortality and that patients at high risk tend to yield the most benefit (ie, women, older adults, and patients undergoing reoperation).

The Cleveland Clinic reviewed a retrospective series of 812 propensity-matched patients (out of a total of 3712 patients undergoing isolated CABG during a 4-year period), with 406 patients in both the standard CABG and OPCAB groups.³ Patients in both groups were well-matched with regard to multiple preoperative variables, except that peripheral vascular disease and previous stroke were more common in the OPCAB group and NYHA classification was higher in the standard CABG group. Standard CABG patients received a greater number of bypass grafts (3.5 ± 1.1 versus 2.8 ± 1.0 , $P<0.001$) and had less incomplete revascularization (18% versus 31%, $P<0.001$) than did OPCAB patients as judged by the operating surgeon. Death, stroke, and MI were similar in both groups. OPCAB patients had less frequent renal failure requiring dialysis (1.5% versus 0%, $P=0.03$), red blood cell use (53% versus 42%, $P=0.002$), and sternal wound infections (2.0% versus 0.2%, $P=0.04$). The median follow-up period was 3.8 years for the standard CABG patients and 2.6 years for OPCAB patients. Rates of survival and freedom from MI and coronary reintervention were not significantly different, either alone or in combination, between groups. These authors concluded that mid-term outcomes with OPCAB and standard on-pump CABG were equivalent.

Meta-Analyses

This section briefly examines the results of the 2 strategies described in meta-analysis studies published between 1997 and 2003, in which large groups of patients from several institutions were reviewed. Reston et al⁴ reviewed 53 studies, of which 10 were randomized control trials, 5 were prospective controlled trials, and 38 were retrospective controlled studies. The total review involved 46 621 patients. These authors found significantly less MI, stroke, reoperation for bleeding, renal failure, atrial fibrillation, and wound infection in the OPCAB group in the short term. In terms of mid-term outcome, the recurrence of angina was no different (odds ratio [OR]=1.28, $P=0.309$, confidence interval [CI]=0.79 to 2.05), but the risk of repeat intervention by percutaneous or open strategy (OR=3.63, $P=0.0001$, CI=1.91 to 6.78) or death was lower in the standard CABG group (OR=0.49, $P=0.008$, CI=0.29 to 0.82).

Parolari et al⁵ reviewed 9 randomized trials reported in the literature from 1990 to 2002. Six of these studies were included in Reston and associates' article. The analysis involved 558 patients who had undergone standard CABG and 532 patients who had undergone OPCAB. The only studies reviewed were those in which the average number

of grafts was >2 . The conclusions were that the composite end points of death, stroke, and MI within 30 days favored the OPCAB group but were not significantly different between the 2 groups (OR=0.48, $P=0.08$, CI=0.21 to 1.09).

Prospective Randomized Trials

The best of the large clinical trials remain those that are prospective, randomized, blinded studies. In this setting, however, such studies would be difficult to design because the surgeon performing the operation, anesthesiologist, nurses, and other personnel clearly know which patient received what type of operation, and thus there may be bias in the treatment of the patients during and after surgery.

A multicenter prospective randomized study was performed by Gerola and colleagues⁶ in Brazil and involved 160 selected low-risk patients with 1- or 2-vessel coronary artery disease. The exclusion criteria included left ventricular dysfunction (ejection fraction $<35\%$), renal failure, left circumflex territory lesions, urgent or emergent procedures, hemodynamic instability, concomitant significant carotid disease, age >70 years, and other comorbidities such as hepatitis, AIDS, and morbid obesity. No significant difference was seen in time to extubation, pulmonary complications (anything causing hypoxia), MI, postoperative blood loss, need for blood transfusions, wound infections, neurological dysfunction, or atrial fibrillation. Length of stay in the intensive care unit (ICU) was similar. Postoperative length of stay was not significantly different (8.0 ± 3.1 days in the standard CABG group versus 7.6 ± 3.4 days in the OPCAB group [$P=0.75$]). On the other hand, creatine kinase-MB levels were significantly higher in the standard CABG group at 0 ($P=0.0001$), 8 ($P=0.0014$), and 16 ($P=0.0071$) hours postoperatively, as compared with the respective levels in patients in the OPCAB group. Enzyme release was not different at 24 hours. The number of patients requiring vasoactive drugs in the postoperative period was higher in the standard CABG group (23.8% versus 8.8% patients, $P=0.004$). Mortality rate was not significantly different between groups (3.7% versus 1.2%, $P=0.62$). The authors concluded that in these groups of patients neither procedure was superior to the other.

A single institutional trial was undertaken by Straka and colleagues⁷ in the Czech Republic. This study involved 400 consecutive, unselected patients randomized to standard CABG or OPCAB. The only exclusion criterion was the need for an emergency operation. There were no significant differences between groups in postoperative mortality, MI, stroke, atrial fibrillation, wound infections, or renal failure requiring dialysis. The number of distal anastomoses for patients was higher in the standard CABG group (2.7 versus 2.3, $P<0.001$). The total blood loss was higher in the standard CABG group (680 versus 560 mL, $P<0.001$), but the number of transfused patients and reoperations for bleeding was not significantly different. Creatine kinase-MB levels were higher at 6, 18, and 36 hours after surgery in the standard CABG group, as compared with the respective levels in the OPCAB group

($P<0.001$). The time to extubation, length of ICU stay, and total hospital length of stay were not significantly different between groups. The authors concluded that the OPCAB strategy can be applied widely to unselected patients and is as safe and effective as conventional standard CABG.

The results of a single institutional trial were reported from Emory University by Puskas and colleagues.⁸ Two hundred patients were randomized to standard CABG or OPCAB. Candidate targets for revascularization were determined before randomization. The only exclusion criteria were the presence of cardiogenic shock or preoperative intra-aortic balloon pump. There were no significant differences between groups in terms of mortality, reoperation for bleeding, MI, arrhythmias, stroke, new renal failure and/or dialysis, wound infections, or operative time. The number of grafts for patients was 3.4 ± 1.0 in the OPCAB group versus 3.4 ± 1.1 in the standard CABG group ($P=NS$). Thus, in this study, the completeness of revascularization was not different between groups. Fewer patients required red cell transfusions postoperatively (26% versus 44%, $P=0.007$) in the OPCAB group than in the standard CABG group. Hematocrit on postoperative day 3 (29.3 ± 4.16 versus 28.2 ± 3.23 , $P=0.05$) and at discharge (30.6 ± 3.74 versus 29.5 ± 3.30 , $P<0.05$) was marginally higher in the OPCAB group than in the standard CABG group. Creatine kinase-MB and troponin I levels were significantly higher at 8, 16, and 24 hours postoperatively in the standard CABG group ($P<0.001$). The ICU length of stay was not significantly different (23.9 ± 14.5 versus 26.8 ± 24.9 hours, $P=0.82$). The postoperative hospital length of stay was 1 day shorter in the OPCAB group (5.1 ± 6.5 versus 6.1 ± 8.1 days, $P=0.005$). The authors' conclusions were that the OPCAB strategy provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay.

Recently, Puskas and colleagues reported additional results from the above study in a separate article.⁹ They reported graft patency, clinical and quality-of-life outcomes, and cost among patients while in the hospital and at 1-year follow-up in the OPCAB and CABG groups. They found that graft patency was similar for the OPCAB versus the standard CABG group at 30 days (absolute difference, 1.3%; -0.66% to 3.31% ; $P=0.19$) and at 1 year (absolute difference, -2.2% ; -6.1% to 1.7% ; $P=0.27$). There were no differences in the rates of death, stroke, MI, angina, or reintervention up to 1 year. The true generalizability of this study may be questionable because the pattern of referrals to this surgeon may favor patients who are suitable for OPCAB.

Another recent trial by Khan et al¹⁰ was carried out at the Royal Brompton Hospital in London and involved 103 patients who required at least 3 grafts (as determined by preoperative angiography) and were randomized to standard CABG or OPCAB. Exclusion criteria included recent stroke or MI (6 months/3 months), age <30 or >80 years, carotid stenosis $>70\%$, and a left ventricular ejection fraction $<20\%$. The groups were similar with regard to preoperative variables, except that the number of planned grafts was higher in the standard CABG group than in the

of grafts was >2 . The conclusions were that the composite end points of death, stroke, and MI within 30 days favored the OPCAB group but were not significantly different between the 2 groups (OR=0.48, $P=0.08$, CI=0.21 to 1.09).

Prospective Randomized Trials

The best of the large clinical trials remain those that are prospective, randomized, blinded studies. In this setting, however, such studies would be difficult to design because the surgeon performing the operation, anesthesiologist, nurses, and other personnel clearly know which patient received what type of operation, and thus there may be bias in the treatment of the patients during and after surgery.

A multicenter prospective randomized study was performed by Gerola and colleagues⁶ in Brazil and involved 160 selected low-risk patients with 1- or 2-vessel coronary artery disease. The exclusion criteria included left ventricular dysfunction (ejection fraction $<35\%$), renal failure, left circumflex territory lesions, urgent or emergent procedures, hemodynamic instability, concomitant significant carotid disease, age >70 years, and other comorbidities such as hepatitis, AIDS, and morbid obesity. No significant difference was seen in time to extubation, pulmonary complications (anything causing hypoxia), MI, postoperative blood loss, need for blood transfusions, wound infections, neurological dysfunction, or atrial fibrillation. Length of stay in the intensive care unit (ICU) was similar. Postoperative length of stay was not significantly different (8.0 ± 3.1 days in the standard CABG group versus 7.6 ± 3.4 days in the OPCAB group [$P=0.75$]). On the other hand, creatine kinase-MB levels were significantly higher in the standard CABG group at 0 ($P=0.0001$), 8 ($P=0.0014$), and 16 ($P=0.0071$) hours postoperatively, as compared with the respective levels in patients in the OPCAB group. Enzyme release was not different at 24 hours. The number of patients requiring vasoactive drugs in the postoperative period was higher in the standard CABG group (23.8% versus 8.8% patients, $P=0.004$). Mortality rate was not significantly different between groups (3.7% versus 1.2%, $P=0.62$). The authors concluded that in these groups of patients neither procedure was superior to the other.

A single institutional trial was undertaken by Straka and colleagues⁷ in the Czech Republic. This study involved 400 consecutive, unselected patients randomized to standard CABG or OPCAB. The only exclusion criterion was the need for an emergency operation. There were no significant differences between groups in postoperative mortality, MI, stroke, atrial fibrillation, wound infections, or renal failure requiring dialysis. The number of distal anastomoses for patients was higher in the standard CABG group (2.7 versus 2.3, $P<0.001$). The total blood loss was higher in the standard CABG group (680 versus 560 mL, $P<0.001$), but the number of transfused patients and reoperations for bleeding was not significantly different. Creatine kinase-MB levels were higher at 6, 18, and 36 hours after surgery in the standard CABG group, as compared with the respective levels in the OPCAB group

($P<0.001$). The time to extubation, length of ICU stay, and total hospital length of stay were not significantly different between groups. The authors concluded that the OPCAB strategy can be applied widely to unselected patients and is as safe and effective as conventional standard CABG.

The results of a single institutional trial were reported from Emory University by Puskas and colleagues.⁸ Two hundred patients were randomized to standard CABG or OPCAB. Candidate targets for revascularization were determined before randomization. The only exclusion criteria were the presence of cardiogenic shock or preoperative intra-aortic balloon pump. There were no significant differences between groups in terms of mortality, reoperation for bleeding, MI, arrhythmias, stroke, new renal failure and/or dialysis, wound infections, or operative time. The number of grafts for patients was 3.4 ± 1.0 in the OPCAB group versus 3.4 ± 1.1 in the standard CABG group ($P=NS$). Thus, in this study, the completeness of revascularization was not different between groups. Fewer patients required red cell transfusions postoperatively (26% versus 44%, $P=0.007$) in the OPCAB group than in the standard CABG group. Hematocrit on postoperative day 3 (29.3 ± 4.16 versus 28.2 ± 3.23 , $P=0.05$) and at discharge (30.6 ± 3.74 versus 29.5 ± 3.30 , $P<0.05$) was marginally higher in the OPCAB group than in the standard CABG group. Creatine kinase-MB and troponin I levels were significantly higher at 8, 16, and 24 hours postoperatively in the standard CABG group ($P<0.001$). The ICU length of stay was not significantly different (23.9 ± 14.5 versus 26.8 ± 24.9 hours, $P=0.82$). The postoperative hospital length of stay was 1 day shorter in the OPCAB group (5.1 ± 6.5 versus 6.1 ± 8.1 days, $P=0.005$). The authors' conclusions were that the OPCAB strategy provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay.

Recently, Puskas and colleagues reported additional results from the above study in a separate article.⁹ They reported graft patency, clinical and quality-of-life outcomes, and cost among patients while in the hospital and at 1-year follow-up in the OPCAB and CABG groups. They found that graft patency was similar for the OPCAB versus the standard CABG group at 30 days (absolute difference, 1.3%; -0.66% to 3.31% ; $P=0.19$) and at 1 year (absolute difference, -2.2% ; -6.1% to 1.7% ; $P=0.27$). There were no differences in the rates of death, stroke, MI, angina, or reintervention up to 1 year. The true generalizability of this study may be questionable because the pattern of referrals to this surgeon may favor patients who are suitable for OPCAB.

Another recent trial by Khan et al¹⁰ was carried out at the Royal Brompton Hospital in London and involved 103 patients who required at least 3 grafts (as determined by preoperative angiography) and were randomized to standard CABG or OPCAB. Exclusion criteria included recent stroke or MI (6 months/3 months), age <30 or >80 years, carotid stenosis $>70\%$, and a left ventricular ejection fraction $<20\%$. The groups were similar with regard to preoperative variables, except that the number of planned grafts was higher in the standard CABG group than in the

OPCAB group. The authors emphasized that the patients were randomized after their angiograms had been reviewed and the need for >3 grafts per patient determined. The groups were similar with regard to completeness of revascularization, territories grafted, and subjective native vessel quality. There were no deaths in either group. The time to extubation and lengths of ICU stay and hospital stay were not significantly different. There were 2 reoperations for bleeding in the standard CABG group versus 0 in the OPCAB group ($P=0.13$). Whereas blood loss was not significantly different (898 ± 434 mL in the standard CABG group versus 1031 ± 552 mL in the OPCAB group; $P=NS$), more patients required transfusion of both packed red blood cells (32 versus 20 patients) and clotting factors (14 versus 2 patients) in the standard CABG group than in the OPCAB group. Troponin levels were higher in the standard CABG group at 6 ($P<0.001$) and 12 hours ($P<0.001$) but were not different at 24 hours. Of the 103 patients, 82 were reevaluated and underwent angiography at 3 months. There were no deaths, strokes, or MIs, and Canadian Cardiovascular Society/NYHA classes were similar at 3 months. The striking finding in this study was that graft patency was 98% in the standard CABG group and 88% in the OPCAB group ($P=0.002$). Graft patency of the left anterior descending graft was 100% in the standard CABG group and 92% in the OPCAB group ($P=0.07$). Circumflex graft patency was 95% in the CPB group and 87% in the OPCAB group ($P=0.25$). Right coronary artery graft patency was 100% in the standard CABG group and 84% in the OPCAB group ($P=0.01$). The left internal thoracic artery graft patency was 100% in the standard CABG group and 92% in the OPCAB group ($P=0.05$). The patency of the radial arteries operated on in this study was 100% in the standard CABG group and 76% in the OPCAB group ($P=0.01$). Saphenous vein graft patency was 95% in the standard CABG group and 91% in the OPCAB group ($P=0.42$). The authors concluded that OPCAB may not be widely applicable but may have a role in selected patients with good targets or serious comorbidities. The reduced graft patency at 3 months in the OPCAB group has been questioned by other investigators, and this study has been criticized because of the perceived inexperience of the surgeons and other issues.

Finally, Nathoe et al¹¹ performed a multicenter study involving 281 patients, 142 of whom underwent OPCAB. Patients in this study had predominantly 1- or 2-vessel coronary artery disease. Patients were excluded from this study if they required emergency surgery, had a recent MI, or had poor left ventricular function. The mean number of grafts was similar in both groups, with 2.6 in the standard CABG group and 2.4 in the OPCAB group. No significant difference was observed between groups in the primary composite end points of freedom from death, MI, stroke, and revascularization. No significant difference was observed between groups with regard to the secondary end points of freedom from angina and myocardial ischemia (as demonstrated by exercise stress test). Seventy patients (63.6%) underwent angiography at 1 year (42 on pump and 28 off pump). Unfortunately, 36.4% of patients declined to

undergo angiography because of a lack of symptoms. In contrast to the prior study, no significant difference in graft patency was seen between the groups. Overall patency rates were 93% and 91%, respectively, in the CABG and OPCAB groups (absolute difference, 2.0%; CI = -6.5 to 10.4). Nathoe et al concluded that there was no significant difference in cardiac outcome between on-pump CABG and OPCAB.

The following sections discuss prospective randomized trials of patients at high risk of neurological morbidity, patients with poor left ventricular function, patients who are at high risk by virtue of multiple comorbidities, older adult patients, patients with an atheromatous aorta, and patients who have had a recent acute MI.

Patients With Neurological Morbidity

Multiple studies with transcranial Doppler have suggested higher rates of cerebral embolization in CPB patients than in OPCAB patients. Most studies that examine neurocognitive function show slightly more decline among standard CABG patients relative to OPCAB patients in the short term (<2 to 3 months) but fail to show significant differences at 1 year.¹² Quality-of-life assessments have not been shown to be significantly different at 1 year.¹³⁻¹⁵

Patients With Left Ventricular Dysfunction

Three recent studies have reviewed, in a retrospective nonrandomized fashion, the outcomes of patients with left ventricular ejection fractions <35% undergoing surgical revascularization. The OPCAB patients tended to have higher NYHA class scores, fewer recent MIs, and more type 1 diabetes mellitus but otherwise were well matched for other variables. In 2 of the 3 studies, standard CABG patients had significantly more grafts, with the third study showing a trend toward more grafts. There were no significant differences in MI, renal failure, reoperation for bleeding, wound infections, or stroke. Thirty-day mortality rates tended to be higher in the standard CABG patients than in the OPCAB group (14.1% versus 6.6%, $P=0.05$).¹⁶ In one study, mid-term survival was slightly higher at 1 (92% versus 85%), 2 (90% versus 82%), and 3 (87% versus 73%) years, respectively, in the standard CABG group than in the OPCAB group, but the differences were not statistically significant.¹⁶⁻¹⁸

Patients With Multiple Comorbidities

Four recent studies reviewed, in a retrospective nonrandomized fashion, patients who were considered high risk because of the presence of multiple preoperative comorbid factors. These risk factors included recent MI, left main disease, left ventricular dysfunction, renal failure, previous stroke, unstable angina, heart failure, shock, chronic obstructive pulmonary disease, age >70 years, and urgent or emergent surgery.¹⁹⁻²²

The mean age at the time of operation was significantly higher in the OPCAB group in one study²¹ and tended to be higher in another.²² More patients in the standard CABG group had unstable angina, severe heart failure symptoms, and 3-vessel disease. The OPCAB patients tended to have higher numbers of risk factors. There were no significant

differences for the majority of preoperative risk factors. In 2 studies, the number of grafts placed was greater in the standard CABG group than in the OPCAB group, but the numbers were similar in the other studies. Mortality was significantly higher in the standard CABG group in one study and not different in the other 3 studies. ICU and hospital length of stay were lower in the OPCAB group. In these reports, postoperative blood loss, need for transfusion, arrhythmias, and ventilation time were higher in the standard CABG group than in the OPCAB group. Perioperative MI was lower in the OPCAB group in one study but was not significantly different in the other 3 studies. Neurological, renal, and infectious complications were similar in all studies. Only one study looked at mid-term outcomes (mean follow-up, 16 ± 9 months) and found that cardiac death ($P=0.001$), recurrent ischemia ($P<0.0001$), and graft dysfunction ($P=0.05$) all were significantly higher in the OPCAB group.²²

Older Adult Patients

Two retrospective and nonrandomized studies reviewed the specific subgroup of older adult patients. In one study, patients >75 years old were examined, and in the other study, patients were >80 years old. Preoperative characteristics were similar in both studies. The number of grafts placed was higher in the standard CABG groups in both studies.^{23,24} The incidence of stroke, prolonged respiratory failure, bleeding, transfusions, and ICU and hospital length of stay all were higher in the standard CABG groups than in the OPCAB group. Reoperation for bleeding, MI, renal failure, wound infections, and operative mortality were not significantly different. One study had mid-term follow-up data, and no significant difference between groups for overall survival and event-free survival was observed.

Patients With Atheromatous Aorta

Two retrospective and nonrandomized studies addressed the question of whether coronary revascularizations in patients with a severely atheromatous aorta should be performed off pump.^{25,26} Both studies used propensity matching to identify an equal number of patients in the OPCAB and standard CABG groups with similar preoperative characteristics and intraoperative transesophageal echocardiography findings of severe ascending aortic atheromatous disease. Mortality and stroke were higher in the standard CABG groups in both studies. The first study by Sharony et al²⁵ reported an in-hospital mortality rate of 11.4% for standard CABG, versus 3.8% for OPCAB ($P=0.003$), and a stroke rate of 4.7% for standard CABG, versus 2.4% for the OPCAB group ($P=0.08$). In their second study 1 year later, they reported an in-hospital mortality rate of 11.4% for the standard group and 6.5% for OPCAB ($P=0.058$) and a stroke rate of 5.7% versus 1.6% ($P=0.03$).²⁶ Freedom from any complication was higher in the OPCAB group in both studies. Three-year follow-up was done in both studies, with one study showing increased survival in the OPCAB group and the other showing no significant difference.^{25,26} It is thought that the decreased rate of complications in the OPCAB group is the result of the decreased clamping of the difficult aorta for that technique.

Findings Favoring On-Pump CABG or OPCAB

Findings favoring OPCAB

- Probably less bleeding
- Probably less renal dysfunction
- Probably less short-term neurocognitive dysfunction, especially if aorta is calcified
- Possibly shorter overall length of hospital stay

Findings favoring on-pump CABG

- Less technically demanding
- Shorter "learning curve"
- Possibly better long-term graft patency
- Easier to graft posterior (circumflex) bypass targets
- Probably more bypass grafts constructed

Patients With Acute MI

A retrospective study from Israel reviewed 225 patients undergoing CABG soon after acute MI (106 CABGs were performed off pump),²⁷ and all patients had similar preoperative characteristics. All operations were performed on patients within 1 week of experiencing an acute MI. The OPCAB group had significantly more patients with 1 or 2 grafts, and standard CABG patients had significantly more patients with ≥ 3 grafts. The standard CABG patients had more bilateral internal thoracic artery grafts (58% versus 1.9%, $P<0.001$) and more circumflex grafts (90% versus 11.5%, $P<0.001$). The mortality rate was higher in the standard CABG group (12% versus 3.8%, $P=0.027$), but the majority of deaths occurred in patients undergoing standard CABG within 48 hours of MI. The mortality rate of patients operated on >48 hours after MI was not significantly different (5.8% versus 3.4%, $P=0.44$). Late mortality was lower and freedom from angina and reintervention was higher in the standard CABG group, with a follow-up of 2 to 9 years.²⁷

Summary

Although definitive conclusions about the relative merits of standard CABG and OPCAB are difficult to reach from these varied randomized and nonrandomized studies, several generalizations may be warranted (Table). Patients may achieve an excellent outcome with either type of procedure, and individuals' outcomes likely depend more on factors other than whether they underwent standard CABG or OPCAB. Mortality rates vary between $<1\%$ to $>6\%$ in most databases, and thus the skill of the surgeon, quality of the institution, and systems approach play a much greater role in determining the outcome after surgical coronary revascularization.

There appear to be trends in most studies, however. These trends include less blood loss and need for transfusion after OPCAB, less myocardial enzyme release after OPCAB up to 24 hours, less early neurocognitive dysfunction after OPCAB, and less renal insufficiency after OPCAB. Of note, patients who require urgent or emergent conversion from off-pump to on-pump revascularization have a much greater risk of mortality, postoperative cardiac arrest, and multisystem organ failure than do patients initially undergoing on-pump CABG.^{28,29} In addition, fewer grafts tend to be performed with OPCAB than

with standard CABG in many studies, and no study in the literature reports more grafts being placed with OPCAB. Length of hospital stay, mortality, and long-term neurological function and cardiac outcome appear to be similar in the 2 groups. A recent report from a prospective study suggested that graft patency may be significantly lower with OPCAB than with standard CABG,¹⁰ but this needs to be verified or dismissed by additional prospective randomized studies. The greatest utility for OPCAB is probably the severely calcified or diseased aorta in which manipulation or clamping of the aorta can be associated with dire neurological consequences. To definitively answer whether either strategy is superior and in which patients, a large-scale prospective randomized trial will be required in which the surgeons and other physicians caring for the patient do not have prior knowledge of the operation the patient is to undergo. Also, optimally, the surgeon should not know the revascularization strategy until just before entering the operating room, and subsequent caregivers in the ICU should remain blinded after surgery. Finally, the

surgeons should be equally skilled with either type of procedure. Surgeons who perform either OPCAB or standard CABG almost exclusively should not be part of such a study. Criticism has been aimed at Khan et al with regard to the relative inexperience of the surgeons in their study in performing off-pump surgery.¹⁰ On the other side, there is the question of a randomized study performed by a single surgeon whose referral pattern may reflect those cases more easily amenable to OPCAB. Such a trial will be difficult to design and execute. The need for such a large prospective trial was suggested at a recent NIH working group composed of cardiac surgeons and other clinicians. The Department of Veterans Affairs currently is enrolling patients into a large prospective trial. Ultimately, whether a patient benefits more from standard on-pump CABG or OPCAB may depend more on the familiarity, comfort, and skill of the individual surgeon with either procedure than on an intrinsic benefit. Both the OPCAB and standard CABG procedures usually result in excellent outcomes, and neither should be judged to be inferior to the other.

Disclosures

Writing Group Disclosures

Writing Group Member	Employment	Research Grants/Other Research Support	Speakers Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
Frank W. Sellke	Beth Israel Deaconess Medical Center	None	Bayer	None	None	None
J. Michael DiMaio	University of Texas Southwestern Medical Center	None	None	None	None	None
Louis R. Caplan	Beth Israel Deaconess Medical Center	None	None	None	GlaxoSmithKline, Novovision, Neurologica, Wyeth Laboratories	None
T. Bruce Ferguson	Louisiana State University Health Sciences Center	None	None	None	None	None
Timothy J. Gardner	University of Pennsylvania	None	None	None	None	None
Loren F. Hiratzka	Cardiac, Vascular & Thoracic Surgeons, Inc; TriHealth	None	None	None	None	None
Eric M. Isselbacher	Massachusetts General Hospital	None	Merck, Pfizer	None	None	None
Bruce W. Lytle	The Cleveland Clinic Foundation	None	None	None	None	None
Michael J. Mack	COR Specialty Associates of North Texas (CSANT)	None	None	None	None	None
John M. Murkin	University of Western Ontario	None	Bayer, Somanetics	None	None	None
Robert C. Robbins	Stanford University	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit.

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
William E. Cohn	Texas Heart Institute	None	Cardiovation	Teleflex Medical	None	Teleflex Medical	None
Robert A. Guyton	Emory University	None	None	None	None	Medtronic, Quest Medical	None
Robert H. Jones	Duke (University) Clinical Research Institute	None	None	None	None	None	None
Gus J. Vlahakes	Massachusetts General Hospital	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Reviewer Disclosure Questionnaire, which all reviewers are required to complete and submit.

References

- Racz MJ, Hannan EL, Isom OW, Subramanian VA, Jones RH, Gold JP, Ryan TJ, Hartman A, Culliford AT, Bennett E, Lancey RA, Rose EA. A comparison of short- and long-term outcomes after off-pump and on-pump coronary artery bypass graft surgery with sternotomy. *J Am Coll Cardiol*. 2004;43:557–564.
- Mack MJ, Pfister A, Bachand D, Emery R, Magee MJ, Connolly M, Subramanian VA. Comparison of coronary bypass surgery with and without cardiopulmonary bypass in patients with multivessel disease. *J Thorac Cardiovasc Surg*. 2004;127:167–173.
- Sabik JF, Blackstone EH, Lytle BW, Houghtaling PL, Gillinov AM, Cosgrove DM. Equivalent midterm outcomes after off-pump and on-pump coronary surgery. *J Thorac Cardiovasc Surg*. 2004;127:142–148.
- Reston JT, Tregear SJ, Turkelson CM. Meta-analysis of short-term and mid-term outcomes following off-pump coronary artery bypass grafting. *Ann Thorac Surg*. 2003;76:1510–1515.
- Parolari A, Alamanni F, Cannata A, Naliato M, Bonati L, Rubini P, Veglia F, Tremoli E, Biglioli P. Off-pump versus on-pump coronary artery bypass: meta-analysis of currently available randomized trials. *Ann Thorac Surg*. 2003;76:37–40.
- Gerola LR, Buffolo E, Jasbik W, Botelho B, Bosco J, Brasil LA, Branco JN. Off-pump versus on-pump myocardial revascularization in low-risk patients with one or two vessel disease: perioperative results in a multicenter randomized controlled trial. *Ann Thorac Surg*. 2004;77:569–573.
- Straka Z, Widimsky P, Jirasek K, Stros P, Potava J, Vanek T, Brucke P, Kolesar M, Spacek R. Off-pump versus on-pump coronary surgery: final results from a prospective randomized study PRAGUE-4. *Ann Thorac Surg*. 2004;77:789–793.
- Puskas JD, Williams WH, Duke PG, Staples JR, Glas KE, Marshall JJ, Leimbach M, Huber P, Garas S, Sammons BH, McCall SA, Petersen RJ, Bailey DE, Chu H, Mahoney EM, Weintraub WS, Guyton RA. Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: a prospective randomized comparison of two hundred unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. *J Thorac Cardiovasc Surg*. 2003;125:797–808.
- Puskas JD, Williams WH, Mahoney EM, Huber PR, Block PC, Duke PG, Staples JR, Glas KE, Marshall JJ, Leimbach ME, McCall SA, Petersen RJ, Bailey DE, Weintraub WS, Guyton RA. Off-pump vs conventional coronary artery bypass grafting: early and 1-year graft patency, cost, and quality-of-life outcomes: a randomized trial. *JAMA*. 2004;291:1841–1849.
- Khan NE, De Souza A, Mister R, Flather M, Clague J, Davies S, Collins P, Wang D, Sigwart U, Pepper J. A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. *N Engl J Med*. 2004;350:21–28.
- Nathoe HM, van Dijk D, Jansen EW, Suyker WJ, Diephuis JC, van Boven WJ, de la Riviere AB, Borst C, Kalkman CJ, Grobbee DE, Buskens E, de Jaegere PP, Octopus Study Group. A comparison of on-pump and off-pump coronary bypass surgery in low-risk patients. *N Engl J Med*. 2003;348:394–402.
- Van Dijk D, Jansen EW, Hijman R, Nierich AP, Diephuis JC, Moons KG, Lahpor JR, Borst C, Keizer AM, Nathoe HM, Grobbee DE, De Jaegere PP, Kalkman CJ, Octopus Study Group. Cognitive outcome after off-pump and on-pump coronary artery bypass graft surgery: a randomized trial. *JAMA*. 2002;287:1405–1412.
- Lund C, Hol PK, Lundblad R, Fosse E, Sundet K, Tennoe B, Brucher R, Russell D. Comparison of cerebral embolization during off-pump and on-pump coronary artery bypass surgery. *Ann Thorac Surg*. 2003;76:765–770.
- Keizer AM, Hijman R, van Dijk D, Kalkman CJ, Kahn RS. Cognitive self-assessment one year after on-pump and off-pump coronary artery bypass grafting. *Ann Thorac Surg*. 2003;75:835–839.
- Lee JD, Lee SJ, Tsushima WT, Yamauchi H, Lau WT, Popper J, Stein A, Johnson D, Lee D, Petrovitch H, Dang CR. Benefits of off-pump bypass on neurologic and clinical morbidity: a prospective randomized trial. *Ann Thorac Surg*. 2003;76:18–26.
- Al-Ruzzeh S, Athanasiou T, George S, Glenville BE, DeSouza AC, Pepper JR, Amrani M. Is the use of cardiopulmonary bypass for multivessel coronary artery bypass surgery an independent predictor of operative mortality in patients with ischemic left ventricular dysfunction? *Ann Thorac Surg*. 2003;76:444–452.
- Shennib H, Endo M, Benhamed O, Morin JF. Surgical revascularization in patients with poor left ventricular function: on- or off-pump? *Ann Thorac Surg*. 2002;74:S1344–S1347.
- Ascone R, Narayan P, Rogers CA, Lim KH, Capoun R, Angelini GD. Early and midterm clinical outcome in patients with severe left ventricular dysfunction undergoing coronary artery surgery. *Ann Thorac Surg*. 2003;76:793–799.
- Bittner HB, Savitt MA. Off-pump coronary artery bypass grafting decreases morbidity and mortality in a selected group of high-risk patients. *Ann Thorac Surg*. 2002;74:115–118.
- Chamberlain MH, Ascone R, Reeves BC, Angelini GD. Evaluation of the effectiveness of off-pump coronary artery bypass grafting in high-risk patients: an observational study. *Ann Thorac Surg*. 2002;73:1866–1873.
- Meharwal ZS, Mishra YK, Kohli V, Bapna R, Singh S, Trehan N. Off-pump multivessel coronary artery surgery in high-risk patients. *Ann Thorac Surg*. 2002;74:S1353–S1357.
- Gaudino M, Gliaca F, Alessandrini F, Nasso G, Pragliola C, Luciani N, Morelli M, Possati G. High risk coronary artery bypass patient: incidence, surgical strategies, and results. *Ann Thorac Surg*. 2004;77:574–580.
- Hoff SJ, Ball SK, Coltharp WH, Glassford DM Jr, Lea JW IV, Petracek MR. Coronary artery bypass in patients 80 years and over: is off-pump the operation of choice? *Ann Thorac Surg*. 2002;74:S1340–S1343.
- Hirose H, Amano A, Takahashi A. Off-pump coronary artery bypass grafting for elderly patients. *Ann Thorac Surg*. 2001;72:2013–2019.
- Sharony R, Bizakis CS, Kanchuger M, Galloway AC, Saunders PC, Applebaum R, Schwartz CF, Ribakove GH, Culliford AT, Baumann FG, Kronzon I, Colvin SB, Grossi EA. Off-pump coronary artery bypass grafting reduces mortality and stroke in patients with atherosclerotic aortas: a case control study. *Circulation*. 2003;108(suppl II):II-15–II-20.
- Sharony R, Grossi EA, Saunders PC, Galloway AC, Applebaum R, Ribakove GH, Culliford AT, Kanchuger M, Kronzon I, Colvin SB. Propensity case-matched analysis of off-pump coronary artery bypass grafting in patients with atherosclerotic aortic disease. *J Thorac Cardiovasc Surg*. 2004;127:406–413.
- Locker C, Mohr R, Paz Y, Kramer A, Lev-Ran O, Pevni D, Shapira I. Myocardial revascularization for acute myocardial infarction: benefits and drawbacks of avoiding cardiopulmonary bypass. *Ann Thorac Surg*. 2003;76:771–777.
- Edgerton JR, Dewey TM, Magee MJ, Herbert MA, Prince SL, Jones KK, Mack MJ. Conversion in off-pump coronary artery bypass grafting: an analysis of predictors and outcomes. *Ann Thorac Surg*. 2003;76:1138–1143.
- Jin R, Hiratzka LF, Grunkemeier GL, Krause A, Page US. Aborted off-pump coronary artery bypass patients have much worse outcomes than on-pump or successful off-pump patients. *Circulation*. In press.