ORIGINAL ARTICLE

Off-Pump or On-Pump Coronary-Artery Bypass Grafting at 30 Days

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ABSTRACT

BACKGROUND

The relative benefits and risks of performing coronary-artery bypass grafting (CABG) with a beating-heart technique (off-pump CABG), as compared with cardiopulmonary bypass (on-pump CABG), are not clearly established.

METHODS

At 79 centers in 19 countries, we randomly assigned 4752 patients in whom CABG was planned to undergo the procedure off-pump or on-pump. The first coprimary outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis at 30 days after randomization.

RESULTS

There was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (9.8% vs. 10.3%; hazard ratio for the off-pump group, 0.95; 95% confidence interval [CI], 0.79 to 1.14; P=0.59) or in any of its individual components. The use of off-pump CABG, as compared with on-pump CABG, significantly reduced the rates of blood-product transfusion (50.7% vs. 63.3%; relative risk, 0.80; 95% CI, 0.75 to 0.85; P<0.001), reoperation for perioperative bleeding (1.4% vs. 2.4%; relative risk, 0.61; 95% CI, 0.40 to 0.93; P=0.02), acute kidney injury (28.0% vs. 32.1%; relative risk, 0.87; 95% CI, 0.80 to 0.96; P=0.01), and respiratory complications (5.9% vs. 7.5%; relative risk, 0.79; 95% CI, 0.63 to 0.98; P=0.03) but increased the rate of early repeat revascularizations (0.7% vs. 0.2%; hazard ratio, 4.01; 95% CI, 1.34 to 12.0; P=0.01).

CONCLUSIONS

There was no significant difference between off-pump and on-pump CABG with respect to the 30-day rate of death, myocardial infarction, stroke, or renal failure requiring dialysis. The use of off-pump CABG resulted in reduced rates of transfusion, reoperation for perioperative bleeding, respiratory complications, and acute kidney injury but also resulted in an increased risk of early revascularization. (Funded by the Canadian Institutes of Health Research; CORONARY ClinicalTrials.gov number, NCT00463294.)

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Coronary-artery bypass grafting (CABG) reduces mortality in patients with extensive coronary artery disease.[1] CABG has generally been performed with the use of cardiopulmonary bypass (on-pump). With this approach, perioperative mortality is about 2%, with an additional 5 to 7% of patients having complications such as myocardial infarction, stroke, and renal failure requiring dialysis. The technique of operating on a beating heart (off-pump) for CABG was developed to decrease perioperative complications, some of which may be related to the use of cardiopulmonary bypass and to cross-clamping of the aorta associated with the on-pump CABG procedure.

Several previous trials have compared off-pump CABG with on-pump CABG.[2-6] The largest of these studies was the Randomized On/Off Bypass (ROOBY) trial (ClinicalTrials.gov number, NCT00032630), which enrolled 2203 patients from the Veterans Affairs medical system.[7,8] However, none of the previous trials had sufficient power to accurately assess moderate but clinically important differences in rates of death, myocardial infarction, stroke, and renal failure. Furthermore, the skills of the participating surgeons can influence the outcome of a specific surgical procedure,[9-12] and in the previous trials, the required level of surgical expertise, particularly for the off-pump procedure, varied. By conducting a larger trial in a wider range of hospital settings, with specific requirements for surgical experience, we sought to overcome some of the limitations of the previous studies.

Methods

Trial Design

The CABG Off or On Pump Revascularization Study (CORONARY) was a randomized, controlled trial with blinded adjudicated outcome assessments, comparing off-pump CABG with on-pump CABG in patients undergoing isolated CABG surgery. The primary hypothesis was that off-pump CABG, as compared with on-pump CABG, would reduce the rate of major clinical events in the short term (30 days) and that the benefits would be maintained in the long term (5 years). Protocol details have been published previously.[13] All patients provided written informed consent.

The trial was designed by the authors and approved by national regulatory authorities and the ethics committee at each participating center. All funding was provided by the Canadian Institutes of Health Research. No manufacturers of off-pump or on-pump CABG supplies or devices had any role in the study. The data were gathered and analyzed by the Population Health Research Institute at McMaster University and Hamilton Health Sciences. The authors vouch for the accuracy and completeness of the data and all analyses, and for the fidelity of this report to the trial protocol, which is available with the full text of this article at NEJM.org.

Patients

Patients who were scheduled to undergo CABG were eligible to participate in the trial if they required isolated CABG with median sternotomy and had one or more of the following risk factors: an age of 70 years or more; the presence of peripheral arterial disease, cerebrovascular disease, or carotid stenosis of 70% or more; or renal insufficiency. Patients 60 to 69 years of age were also eligible if they had at least one of the following risk factors: the presence of diabetes (requiring an oral hypoglycemic agent, insulin, or both), urgent revascularization (after an acute coronary syndrome), a left ventricular ejection fraction of 35% or less, or a recent history of smoking (<1 year before randomization). After the recruitment of 1700 patients, the protocol was amended to allow enrollment of patients 55 to 59 years of age with at least two of the risk factors listed for patients 60 to 69 years of age.

Patients were excluded for the following reasons: planned valve surgery, any contraindication to off-pump CABG or on-pump CABG, a decision by a surgeon that one of the two techniques was not feasible for that patient, a life expectancy of less than 2 years, emergency or repeat CABG surgery, and previous enrollment in CORONARY. The inclusion and exclusion criteria are described in more detail in the Supplementary Appendix, available at NEJM.org.

Qualification of Surgeons

To ensure that surgeons were skilled in the assigned technique (either on-pump or off-pump CABG), we used the approach of an expertise-based, randomized, controlled trial.[14] Each operation was performed by a surgeon with expertise

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in the specific type of surgery that the patient was assigned to receive. Expertise was defined as having more than 2 years of experience and having completed more than 100 procedures involving the specific technique. Surgeons who met these criteria for each type of operation separately were considered to have expertise in both techniques and were allowed to perform both types of CABG during the trial. Trainees were not allowed to be the primary surgeon for any procedure.

TRIAL PROCEDURES

Patients were assigned to undergo either off-pump or on-pump CABG with the use of a 24-hour automated voice-activated telephone randomization service. All patients and investigators were aware of study-group assignments.

Surgeons were requested to submit their operative plans (including anatomy and targets) before surgery. CABG was performed by means of a standard median sternotomy in all patients. Surgeons used the stabilizers and pump devices that they typically used in their regular practice. Crossovers from the assigned procedure were recorded as well as the reasons and the timing of such crossovers.

Patients were followed by the site investigators during hospitalization. At 30 days, patients were seen either in the clinic or (if they were still hospitalized or rehospitalized) in the hospital to obtain short-term follow-up data. Subsequent follow-up, which is ongoing, is planned to include clinic visits at 1 year and 5 years and telephone follow-up at 6 months, 2 years, 3 years, and 4 years.

TRIAL OUTCOMES

The first coprimary outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis at 30 days after randomization. The second coprimary outcome was the first coprimary outcome plus repeat coronary revascularization at a mean of 5 years. Secondary outcomes included rates of blood transfusion, recurrent angina, and death from cardiovascular causes. A tertiary outcome was designated as the first coprimary outcome at the time of discharge after CABG surgery. All deaths in the first 30 days were deemed to be due to cardiovascular causes. Definitions of end-point events and monitoring techniques that were used to ensure event capture are described in the Supplementary Appendix. All reported components of the primary outcome and recurrent angina were reviewed by an adjudication committee whose members were unaware of study-group assignments.

STATISTICAL ANALYSIS

We calculated that a sample size of 4700 patients would provide a power of 80% to detect a 28% relative risk reduction in the rate of the first coprimary outcome at 30 days and a power of 90% to detect a 20% relative risk reduction in the rate of the second coprimary outcome at 5 years. An independent data and safety monitoring board reviewed the interim analyses of efficacy data. Three formal interim analyses for safety and efficacy were planned and undertaken when 25%, 50%, and 75% of the 30-day follow-up data were available.

All analyses were conducted on an intention-to-treat basis. A time-to-event analysis by means of Cox regression was used to report the 30-day outcomes after testing of the assumption of proportional hazards. The time to the first occurrence of any one of the components of the primary outcome was described with the use of Kaplan–Meier survival curves, and the comparisons between the two study groups were performed by means of a log-rank test. The treatment effect is expressed in hazard ratios and 95% confidence intervals, derived from the Cox proportional-hazards model for the first coprimary outcome at 30 days. The comparison between the two surgical techniques was assessed in subgroups according to age, sex, body-mass index, the presence or absence of diabetes or cerebrovascular disease, left ventricular function, the number of diseased vessels, geographic region, and the grade on the European System for Cardiac Operative Risk Evaluation (EuroSCORE); all subgroup analyses were performed with the use of tests for interaction in a Cox proportional-hazards model. The lengths of stay in the intensive care unit and hospital were compared with the use of the Wilcoxon test.

RESULTS

PATIENTS

From November 2006 through October 2011, a total of 4752 patients (including 122 who were recruited during an initial vanguard phase) were enrolled from 79 hospitals in 19 countries. Of these patients, 2375 were assigned to undergo off-pump CABG and 2377 to undergo on-pump CABG (Fig. 1). Baseline characteristics of the patients

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Off-Pump CABG (N=2375)	On-Pump CABG (N=2377)
Age — yr	67.6±6.7	67.5±6.9
Male sex — no. (%)	1901 (80.0)	1942 (81.7)
Body-mass index†	26.7±4.3	26.7±4.4
Clinical history — no. (%)		
Previous myocardial infarction	802 (33.8)	836 (35.2)
Previous percutaneous coronary intervention	238 (10.0)	225 (9.5)
Previous stroke	159 (6.7)	185 (7.8)
Peripheral arterial disease	189 (8.0)	196 (8.2)
Never smoked	1094 (46.1)	1093 (46.0)
Diabetes	1104 (46.5)	1129 (47.5)
Renal failure requiring dialysis	40 (1.7)	25 (1.1)
Congestive heart failure	140 (5.9)	156 (6.6)
Hypertension	1810 (76.2)	1794 (75.5)
Chronic atrial fibrillation‡	60 (2.6)	68 (2.9)
Left ventricular ejection fraction — no./total no. (%)		
Grade 1 (≥50%)	1643/2329 (70.5)	1651/2328 (70.9)
Grade 2 (35 to 49%)	560/2329 (24.0)	543/2328 (23.3)
Grade 3 (20 to 34%)	118/2329 (5.1)	126/2328 (5.4)
Grade 4 (<20%)	6/2329 (0.3)	5/2328 (0.2)
EuroSCORE grade — no. (%)§		
0 to 2	679 (28.6)	660 (27.8)
3 to 5	1229 (51.7)	1287 (54.1)
>5	429 (18.1)	399 (16.8)
Urgent surgery — no. (%)	937 (39.5)	905 (38.1)
Use of antiplatelet agent before surgery — no. (%)	1818 (76.5)	1802 (75.8)
Diseased vessels — no./total no. (%)¶		
Left main	514/2329 (22.1)	487/2328 (20.9)
Triple	1306/2329 (56.1)	1405/2328 (60.4)
Double	436/2329 (18.7)	381/2328 (16.4)
Single	70/2329 (3.0)	49/2328 (2.1)

* Plus–minus values are means ±SD. There were no significant differences between groups, except for the number of diseased vessels (P<0.01).
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Chronic atrial fibrillation was measured in 2329 patients in the off-pump group and 2328 in the on-pump group.
§ Grades on the European System for Cardiac Operative Risk Evaluation (EuroSCORE) for CABG are 0 to 2, low risk; 3 to 5, moderate risk; and more than 5, high risk.
¶ Since the interval between randomization and surgery was short, surgeons may have reported the coronary anatomy after surgery rather than before, as per protocol. In 8.6% of patients, these data were entered into the database before randomization, and in this subgroup there was no significant difference in the numbers of diseased vessels in the off-pump group as compared with the on-pump group (left main, 2.0% vs. 1.9%; triple, 4.5% vs. 4.7%; double, 2.0% vs. 1.8%; and single, 0.2% vs. 0.1%).

are shown in Table 1; 81% were men, and the mean age was 68 years. One third of the patients had had a previous myocardial infarction.

PERIOPERATIVE EVENTS

A total of 34 patients (0.7%) did not undergo surgery, including 6 patients who died (Fig. 1). With respect to crossovers between groups, 184 of 2332 patients (7.9%) who were assigned to the off-pump group actually underwent on-pump surgery, and 150 of 2333 patients (6.4%) who were assigned to the on-pump group underwent off-pump surgery (P=0.06). The timing of and reasons for the crossovers are reported in the Supplementary Appendix.

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Fewer grafts were performed in the off-pump group than in the on-pump group (3.0 vs. 3.2, P<0.001), and the rate of incomplete revascularization (as assessed by the surgeon at the time of surgery) was higher, though the P value for the difference was only marginally significant (11.8% vs. 10.0%, P=0.05) (Table 1 in the Supplementary Appendix). Off-pump surgery was associated with shorter operations (4.0 hours vs. 4.2 hours, P<0.001) and shorter duration of ventilator support (9.6 hours vs. 11.2 hours, P<0.001).

The rate of transfusion of blood products was significantly reduced in the off-pump group (50.7% vs. 63.3%; relative risk, 0.80; 95% confidence interval [CI], 0.75 to 0.85; P<0.001) (Table 1 in the Supplementary Appendix), despite a reduced use of antifibrinolytic agents (26.1% vs. 37.0%; relative risk, 0.71; 95% CI, 0.64 to 0.77; P<0.001). Perioperative repeat operations for bleeding occurred in 34 patients (1.4%) in the off-pump group, as compared with 56 (2.4%) in the on-pump group (relative risk, 0.61; 95% CI, 0.40 to 0.93; P=0.02).

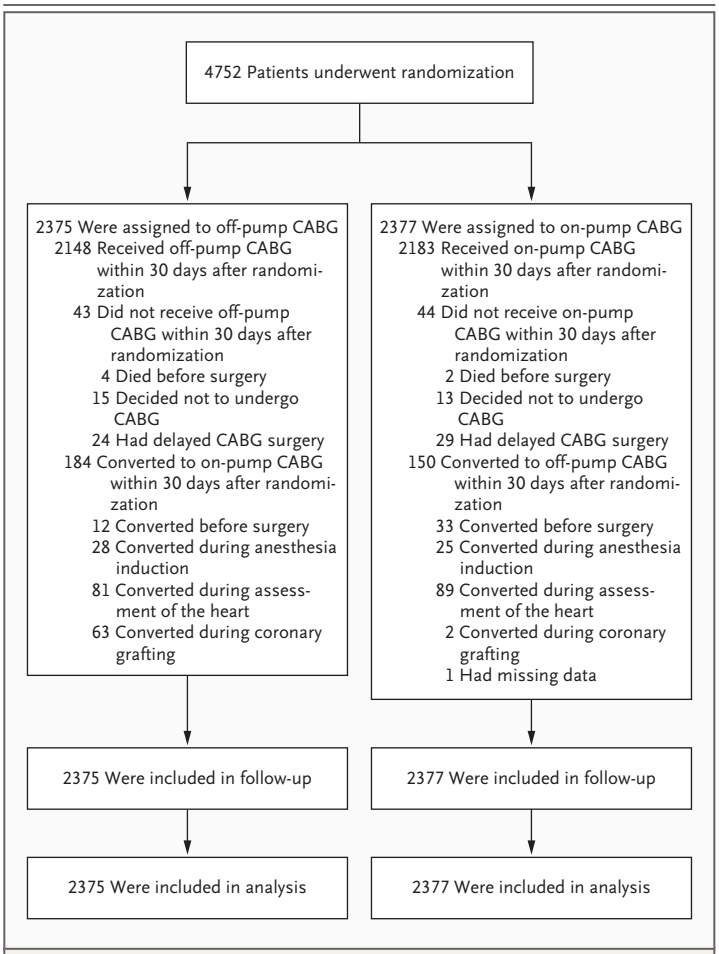

Figure 1. Enrollment and Outcomes.

PRIMARY AND OTHER PRESPECIFIED OUTCOMES

The primary outcome at 30 days occurred in 233 patients (9.8%) in the off-pump group and 245 (10.3%) in the on-pump group (hazard ratio, 0.95; 95% CI, 0.79 to 1.14; P=0.59) (Table 2 and Fig. 2). The individual components of this composite outcome did not differ significantly between the two study groups. No significant interactions between the relative effects of the two procedures and any of the different subgroups were seen (Fig. 3). Rates of recurrent angina and the first coprimary outcome at discharge from the index hospitalization were similar in the two groups (Table 2).

OTHER OUTCOMES

Repeat revascularization (percutaneous coronary intervention [PCI] or CABG) early after CABG (<30 days after randomization) occurred in 16 patients (0.7%) in the off-pump group and 4 (0.2%) in the on-pump group (hazard ratio, 4.01; 95% CI, 1.34 to 12.0; P=0.01) (Table 2). The numbers of reoperations for any cause (including early revascularization and bleeding) were similar in the two study groups.

Rates of respiratory complications (failure or infection) were significantly reduced in the off-pump group. There was a significant reduction in the off-pump group in the rate of acute kidney injury, which was defined according to the Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (RIFLE)[15] criteria and stage 1 criteria of the Acute Kidney Injury Network (AKIN)[16] (Table 2, and Section 6 in the Supplementary Appendix).

DISCUSSION

In this study, we compared off-pump CABG with on-pump CABG in 4752 patients from 19 countries. We found no significant difference in the rate of the first coprimary composite outcome of death, nonfatal stroke, nonfatal myocardial infarction, or nonfatal new renal failure requiring dialysis at 30 days, nor did we find significant differences in any of the components of that outcome. We found reductions in numerous secondary outcomes in patients undergoing off-pump CABG, including rates of transfusion of blood products, acute kidney injury, respiratory complications, and reoperation for perioperative bleeding; ventilation and operating room time; and the duration of ad-

Table 2. Outcomes at 30 Days.

Outcome	Off-Pump CABG (N=2375)	On-Pump CABG (N=2377)	Hazard Ratio (95% CI)	P Value
Primary outcome — no. (%)*	233 (9.8)	245 (10.3)	0.95 (0.79–1.14)	0.59
Death	60 (2.5)	59 (2.5)	1.02 (0.71–1.46)	
Myocardial infarction	158 (6.7)	170 (7.2)	0.93 (0.75–1.15)	
Stroke	24 (1.0)	27 (1.1)	0.89 (0.51–1.54)	
New renal failure requiring dialysis	28 (1.2)	27 (1.1)	1.04 (0.61–1.76)	
Other prespecified outcome — no. (%)				
Death from cardiovascular causes†	60 (2.5)	59 (2.5)	1.02 (0.71–1.46)	0.93
Angina	3 (0.1)	2 (0.1)	1.50 (0.25–8.99)	0.66
Primary outcome at discharge‡	228 (9.6)	246 (10.3)	0.94 (0.78–1.13)	0.50
Other outcome — no./total no. (%)				
Repeat revascularization	16/2330 (0.7)	4/2328 (0.2)	4.01 (1.34–12.0)	0.01
Percutaneous coronary intervention	11/2330 (0.5)	3/2328 (0.1)	3.67 (1.02–13.2)	0.05
Repeat CABG	6/2330 (0.3)	1/2328 (<0.1)	6.00 (0.72–49.8)	0.10
Other surgeries	38/2330 (1.6)	34/2328 (1.5)	1.12 (0.71–1.77)§	0.63
Any reoperation				
Including CABG¶	77/2330 (3.3)	91/2328 (3.9)	0.85 (0.63–1.14)§	0.27
Including repeat revascularization	87/2330 (3.7)	93/2328 (4.0)	0.94 (0.70–1.25)§	0.65
Respiratory failure or infection	138/2330 (5.9)	175/2338 (7.5)	0.79 (0.63–0.98)§	0.03
Rehospitalization (from discharge to 30 days)	123/2375 (5.2)	120/2377 (5.0)	1.03 (0.80–1.31)§	0.84
AKIN stage 1 or more‖	631/2251 (28.0)	728/2270 (32.1)	0.87 (0.80–0.96)§	0.01
RIFLE risk‖	382/2251 (17.0)	443/2270 (19.5)	0.87 (0.76–0.98)§	0.02
RIFLE injury, AKIN stage 2	138/2251 (6.1)	168/2270 (7.4)	0.83 (0.66–1.03)§	0.09
RIFLE failure, AKIN stage 3	45/2251 (2.0)	59/2270 (2.6)	0.77 (0.52–1.13)§	0.18
Atrial fibrillation	435/2375 (18.3)	426/2377 (17.9)	1.02 (0.90–1.15)§	0.72

* The first coprimary outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis at 30 days. Patients could have more than one component of the composite.
† All deaths during the first 30 days were considered to be due to cardiovascular causes.
‡ The primary outcome at discharge was the same as the first coprimary outcome but was evaluated at the time of hospital discharge rather than at 30 days after randomization.
§ Relative risk was calculated instead of hazard ratio.
¶ One patient underwent both CABG and percutaneous coronary intervention.
‖ Stages in the Acute Kidney Injury Network (AKIN) criteria and scores on the Risk, Injury, Failure, Loss, and End-Stage Kidney Disease (RIFLE) criteria are provided in Section 6 in the Supplementary Appendix.

mission to an intensive care unit. However, among patients undergoing off-pump surgery, we also found that fewer grafts were performed per procedure and that there was an increased rate of early revascularization procedures during the index hospitalization. These findings may influence the long-term outcome in the two groups of patients; the off-pump group would benefit in the short term from fewer deleterious effects of blood transfusions,[17] respiratory complications, and renal dysfunction,[18] which may be counterbalanced by the risk of lower rates of long-term graft patency.

Our findings are similar to the short-term (30-day) results from the ROOBY trial.[7,8] However, in that trial, there was a trend against off-pump CABG with respect to the rate of the composite outcome, which increased during long-term follow-up and became a significant harm at 1 year (for details, see the Supplementary Appendix). There are a number of important differences between the two trials. Our study enrolled more than

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twice as many patients from a much more diverse array of clinical settings. We specified a higher level of surgical expertise. In addition, the patients in our trial were at higher surgical risk, as shown by the 30-day mortality. In the ROOBY trial, rates of death were 1.6% in the off-pump group and 1.2% in the on-pump group. In our study, the rate of death at 30 days was 2.5% in each group. It is possible that the trend toward harm for the off-pump group at 30 days in the ROOBY trial, which was not seen in our study, suggests that the longer-term results of our trial will differ from those of the ROOBY trial. However, we caution that our 30-day data do not allow a firm prediction regarding the long-term results.

The results of our study are aligned with findings in various meta-analyses.[19-21] However, the lack of a beneficial effect on stroke in our trial was surprising. Such a benefit was anticipated because aortic cannulation and cross-clamping, as they are performed with on-pump CABG, create a significant embolic risk in patients with a calcified ascending aorta. The lack of benefit may have occurred because surgeons opted to use off-pump surgery in patients who were assigned to undergo on-pump surgery if they had calcification of the aorta (102 patients). In addition, the lack of benefit may have been due to limited statistical power, since only 1% of patients in each study group had a stroke.

Although the short-term results of our trial are encouraging, it is important to recognize that we stipulated a high level of expertise for participating surgeons. It seems likely that successful performance of off-pump CABG may be more dependent on initial technical risks than on-pump CABG is because of the inherent difficulties in performing delicate anastomoses on a beating heart and the potential degree of completeness and quality of the revascularization. Therefore, surgeons, particularly trainees or inexperienced surgeons who are early in the learning curve, may choose to tailor their surgical approach according to the expected technical difficulties and potential benefits for each patient. It is possible that the relative success of the two procedures is influenced by measures of patient surgical risk, such as the EuroSCORE[22,23] or the Society of Thoracic Surgeons (STS) score,[24] although we found no evidence of heterogeneity according to prespecified EuroSCORE strata.

Our trial has a number of limitations. Study centers did not collect a screening log. Therefore, we cannot report the total number of patients who were screened and deemed to be eligible or the reasons for exclusions. We have observed that slightly fewer grafts were performed in the off-pump group. Since the delay between recruitment, randomization, and surgery was short (median, 2 days), surgeons may have reported the coronary anatomy (the expected number and location of grafts) in the case report forms after surgery rather than before surgery, as we had instructed. The technical ability to bypass more or fewer vessels with each approach may have influenced the reporting of the numbers of diseased vessels. This could explain the significant between-group difference in the proportion of patients with specific numbers of diseased vessels at baseline. In patients for whom data on the numbers of diseased vessels were entered into the database before the date of surgery, the extent of disease and the number of vessels to be bypassed were identical in the two surgical groups. Therefore, the analyses of the number of diseased vessels and completeness of revascularization need to be cautiously interpreted.

We have reported the primary outcome at 30 days. Neurocognitive outcomes and economic data may have an important effect on and substantially influence the ultimate interpretation of the primary findings. In addition, the long-term results

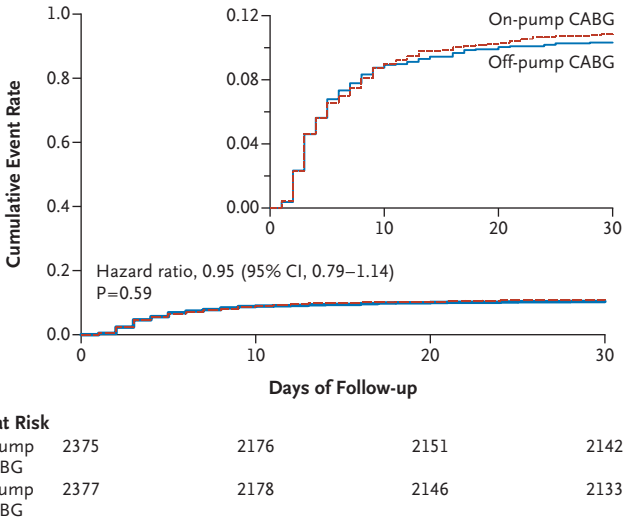

Figure 2. Kaplan–Meier Curves for the Primary Composite Outcome at 30 Days.

The primary composite outcome was death, myocardial infarction, stroke, or new renal failure requiring dialysis.

Subgroup	No. of Patients	Hazard Ratio (95% CI)	P Value	P Value for Interaction
Age				0.46
<70 yr	2815	1.02 (0.79–1.32)	0.88	
≥70 yr	1935	0.89 (0.69–1.14)	0.37	
Sex				0.99
Male	3843	0.95 (0.77–1.16)	0.60	
Female	908	0.94 (0.65–1.36)	0.75	
Cerebrovascular disease				0.58
Yes	456	1.10 (0.66–1.83)	0.72	
No	4296	0.94 (0.77–1.14)	0.51	
Peripheral arterial disease				0.21
Yes	385	0.66 (0.36–1.21)	0.18	
No	4366	0.99 (0.82–1.19)	0.88	
Diabetes				0.08
Yes	2233	0.80 (0.61–1.04)	0.10	
No	2518	1.10 (0.86–1.41)	0.44	
Renal failure requiring dialysis				0.16
Yes	65	0.38 (0.11–1.36)	0.14	
No	4595	0.95 (0.79–1.15)	0.61	
Congestive heart failure				0.11
Yes	296	0.61 (0.34–1.09)	0.10	
No	4455	1.00 (0.83–1.21)	0.97	
EuroSCORE				0.13
0 to 2	1339	1.35 (0.92–1.99)	0.12	
3 to 5	2516	0.87 (0.68–1.11)	0.26	
>5	828	0.85 (0.58–1.25)	0.41	
Region				0.06
South America	843	0.68 (0.46–0.99)	0.05	
North America, Australia, and Europe	1821	0.89 (0.67–1.17)	0.39	
India	1307	1.41 (0.95–2.08)	0.09	
China	781	1.12 (0.66–1.90)	0.69	
Body-mass index				0.37
16 to 24.9	1737	1.10 (0.81–1.50)	0.54	
25 to 27.9	1393	0.79 (0.55–1.13)	0.19	
28 to 44.9	1561	0.99 (0.74–1.32)	0.94	
Left ventricular ejection fraction				0.46
Grade 1 (≥50%)	3294	1.02 (0.82–1.28)	0.83	
Grade 2 (35–49%)	1103	0.71 (0.49–1.04)	0.08	
Grade 3 (20–34%)	244	0.91 (0.47–1.74)	0.77	
Grade 4 (<20%)	11	—	—	
Diseased vessels				0.16
Left main	1001	0.80 (0.55–1.16)	0.24	
Triple	2711	1.08 (0.85–1.36)	0.53	
Double	817	0.90 (0.55–1.46)	0.66	
Single	119	0.13 (0.02–1.15)	0.07	
Off-pump experience of surgeon				0.45
Lower third (<350 cases)	1492	0.85 (0.58–1.24)	0.40	
Middle third (350–900 cases)	1577	0.84 (0.62–1.13)	0.25	
Upper third (>900 cases)	1611	1.07 (0.80–1.42)	0.65	

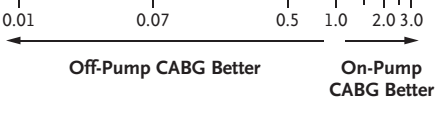

Figure 3. Subgroup Analyses.

The body-mass index is the weight in kilograms divided by the square of the height in meters. EuroSCORE denotes European System for Cardiac Operative Risk Evaluation.

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of the primary outcomes and neurocognitive outcomes will have a determinant influence on the interpretation of this trial.

In conclusion, we conducted a large, randomized trial to compare the outcomes of off-pump CABG with those of on-pump CABG. At 30 days, we found no significant difference between the two groups in the rate of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis. Some secondary end points, including rates of bleeding, acute kidney injury, and respiratory complications, favored off-pump CABG. However, fewer grafts were performed and more revascularization procedures were necessary in the off-pump CABG group.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

APPENDIX

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