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# Effects of off-pump and on-pump coronary-artery bypass grafting at 1 year

Lamy, André ; Devereaux, P J ; Prabhakaran, Dorairaj ; Taggart, David P ; Hu, Shengshou ; Paolasso, Ernesto ; Straka, Zbynek ; Piegas, Leopoldo S ; Akar, Ahmet Ruchan ; Jain, Anil R ; Noiseux, Nicolas ; Padmanabhan, Chandrasekar ; Bahamondes, Juan-Carlos ; Novick, Richard J ; Vaijyanath, Prashant ; Reddy, Sukesh Kumar ; Tao, Liang ; Olavegogeascoechea, Pablo A ; Airan, Balram ; Sulling, Toomas-Andres ; Whitlock, Richard P ; Ou, Yongning ; Pogue, Janice ; Chrolavicius, Susan ; Yusuf, Salim

Abstract: BACKGROUND: Previously, we reported that there was no significant difference at 30 days in the rate of a primary composite outcome of death, myocardial infarction, stroke, or new renal failure requiring dialysis between patients who underwent coronary-artery bypass grafting (CABG) performed with a beating-heart technique (off-pump) and those who underwent CABG performed with cardiopulmonary bypass (on-pump). We now report results on quality of life and cognitive function and on clinical outcomes at 1 year. METHODS: We enrolled 4752 patients with coronary artery disease who were scheduled to undergo CABG and randomly assigned them to undergo the procedure off-pump or on-pump. Patients were enrolled at 79 centers in 19 countries. We assessed quality of life and cognitive function at discharge, at 30 days, and at 1 year and clinical outcomes at 1 year. RESULTS: At 1 year, there was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (12.1% and 13.3%, respectively; hazard ratio with off-pump CABG, 0.91; 95% confidence interval [CI], 0.77 to 1.07; P=0.24). The rate of the primary outcome was also similar in the two groups in the period between 31 days and 1 year (hazard ratio, 0.79; 95% CI, 0.55 to 1.13; P=0.19). The rate of repeat coronary revascularization at 1 year was 1.4% in the off-pump group and 0.8% in the on-pump group (hazard ratio, 1.66; 95% CI, 0.95 to 2.89; P=0.07). There were no significant differences between the two groups at 1 year in measures of quality of life or neurocognitive function. CONCLUSIONS: At 1 year after CABG, there was no significant difference between off-pump and on-pump CABG with respect to the primary composite outcome, the rate of repeat coronary revascularization, quality of life, or neurocognitive function. (Funded by the Canadian Institutes of Health Research; CORONARY ClinicalTrials.gov number, NCT00463294.).

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# Effects of Off-Pump and On-Pump Coronary-Artery Bypass Grafting at 1 Year

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## ABSTRACT

### BACKGROUND

Previously, we reported that there was no significant difference at 30 days in the rate of a primary composite outcome of death, myocardial infarction, stroke, or new renal failure requiring dialysis between patients who underwent coronary-artery bypass grafting (CABG) performed with a beating-heart technique (off-pump) and those who underwent CABG performed with cardiopulmonary bypass (on-pump). We now report results on quality of life and cognitive function and on clinical outcomes at 1 year.

### METHODS

We enrolled 4752 patients with coronary artery disease who were scheduled to undergo CABG and randomly assigned them to undergo the procedure off-pump or on-pump. Patients were enrolled at 79 centers in 19 countries. We assessed quality of life and cognitive function at discharge, at 30 days, and at 1 year and clinical outcomes at 1 year.

### RESULTS

At 1 year, there was no significant difference in the rate of the primary composite outcome between off-pump and on-pump CABG (12.1% and 13.3%, respectively; hazard ratio with off-pump CABG, 0.91; 95% confidence interval [CI], 0.77 to 1.07; P=0.24). The rate of the primary outcome was also similar in the two groups in the period between 31 days and 1 year (hazard ratio, 0.79; 95% CI, 0.55 to 1.13; P=0.19). The rate of repeat coronary revascularization at 1 year was 1.4% in the off-pump group and 0.8% in the on-pump group (hazard ratio, 1.66; 95% CI, 0.95 to 2.89; P=0.07). There were no significant differences between the two groups at 1 year in measures of quality of life or neurocognitive function.

### CONCLUSIONS

At 1 year after CABG, there was no significant difference between off-pump and on-pump CABG with respect to the primary composite outcome, the rate of repeat coronary revascularization, quality of life, or neurocognitive function. (Funded by the Canadian Institutes of Health Research; CORONARY ClinicalTrials.gov number, NCT00463294.)

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† Investigators in the CABG Off or On Pump Revascularization Study (CORONARY) are listed in the Supplementary Appendix, available at NEJM.org.

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Coronary-artery bypass grafting (CABG) reduces mortality among patients with extensive coronary artery disease.[1] CABG is usually performed with the use of cardiopulmonary bypass (on-pump CABG). With this approach, perioperative mortality is about 2%, and myocardial infarction, stroke, or renal failure requiring dialysis develop in an additional 5 to 7% of patients. The technique of performing CABG on a beating heart (off-pump CABG) was developed to reduce perioperative complications, some of which may be related to the use of cardiopulmonary bypass and to the cross-clamping of the aorta associated with the on-pump CABG procedure, and to improve long-term outcomes.

A number of trials have compared off-pump CABG with on-pump CABG.[2-6] Among the largest trials are the Randomized On/Off Bypass (ROOBY)[7,8] trial, which enrolled 2203 patients from the Veterans Affairs medical system, and the Danish On-Pump versus Off-Pump Randomization Study (DOORS), which enrolled 900 patients.[9,10] Neither of these trials had sufficient power to accurately assess moderate but clinically important differences between the groups with respect to death, myocardial infarction, stroke, or renal failure. As shown in a number of smaller trials,[11-14] the skills of the participating surgeons can influence the outcome of a specific surgical procedure, and the level of surgical expertise required by the protocol, particularly for the off-pump procedure, varied among these trials.

To evaluate the effects of off-pump CABG as compared with on-pump CABG, we conducted a large, international trial — the CABG Off or On Pump Revascularization Study (CORONARY) — in which 4752 patients were enrolled. To overcome some of the limitations of prior trials, we conducted the trial at a wider range of hospital types than those in the previous trials and included only experienced surgeons. Previously we reported the 30-day outcomes of the trial.[15] The rate of the primary outcome (a composite of death, myocardial infarction, stroke, or new renal failure requiring dialysis) was similar in the two groups at 30 days. The rate of repeat revascularization (percutaneous coronary intervention [PCI] or CABG) early after CABG (<30 days after randomization) was higher in the off-pump group. The rates of bleeding, acute kidney injury, and respiratory complications were lower with off-pump CABG than with on-pump CABG.

Similar to the results of CORONARY, the results of the ROOBY trial showed no significant difference in the 30-day primary outcome; in the ROOBY trial, however, the rate of the primary composite outcome at 1 year (death from any cause, repeat revascularization, or nonfatal myocardial infarction) was higher with off-pump CABG than with on-pump CABG. Because the 1-year results in the ROOBY trial have raised concern about the value of off-pump surgery, we report the 1-year results in CORONARY.

## Methods

### Trial Design

CORONARY was a randomized, controlled trial, with blinded adjudication of outcomes, that compared off-pump CABG with on-pump CABG among patients undergoing isolated CABG. The primary hypothesis was that the rate of major clinical events would be lower with off-pump CABG than with on-pump CABG in the short term (30 days) and that the benefits would be maintained in the long term (5 years). The study protocol has been published previously[16] and is also available with the full text of this article at NEJM.org. The 30-day results have also been published previously.[15]

The trial was designed by the authors and approved by national regulatory authorities and by the ethics committee at each participating center. The data were gathered and analyzed by the Population Health Research Institute (McMaster University, Hamilton, Ontario, Canada). All the authors vouch for the accuracy and completeness of the data and analyses and for the fidelity of this report to the trial protocol.

### 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, peripheral arterial disease, cerebrovascular disease or carotid stenosis of 70% or more of the luminal diameter, or renal insufficiency. Patients 60 to 69 years of age were eligible if they had at least one of the following risk factors: diabetes requiring treatment with an oral hypoglycemic agent or insulin, the need for urgent revascularization after an acute coronary syndrome, a left ventricular ejec-



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tion fraction of 35% or less, or a recent history of smoking (<1 year before randomization); patients 55 to 59 years of age were eligible if they had at least two of those risk factors. All patients were required to provide written informed consent.

### QUALIFICATION OF SURGEONS

To ensure that surgeons were skilled in the technique assigned, we used the approach of an expertise-based, randomized, controlled trial.[17] Each procedure was performed by a surgeon with expertise in the specific type of surgery that the patient was assigned to undergo. A surgeon was considered to have expertise if he or she had more than 2 years of experience after residency training and had completed more than 100 cases of the specific technique (either on-pump or off-pump CABG). 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 surgery during the trial. Trainees were not allowed to be the primary surgeon.

### TRIAL OUTCOMES

The trial included two coprimary outcomes. The first was a composite rate of death, nonfatal stroke, nonfatal myocardial infarction, or nonfatal new renal failure requiring dialysis at 30 days after randomization. This outcome was also assessed at 1 year. The second coprimary outcome consisted of the first coprimary outcome plus the rate of repeat coronary revascularization at a mean of 5 years. All deaths in the first 30 days were considered to be cardiovascular-related deaths. All reported events of the components of the primary outcome and of recurrent angina were reviewed by an adjudication committee whose members were unaware of the group assignments. The outcome events as adjudicated by that committee were included in the statistical analyses.

We used the European Quality of Life–5 Dimensions questionnaire (EQ-5D)[18,19] and the EQ-5D visual-analogue scale to assess the quality of life. The EQ-5D score ranges from 0 to 1, with higher scores indicating a better quality of life. The EQ-5D visual-analogue scale ranges from 0 to 100, with higher scores indicating a better quality of life.

To assess neurocognitive function, we followed the guidelines on vascular cognitive impairment harmonization standards from the joint National Institute of Neurological Disorders and Stroke–Canadian Stroke Network (NINDS-CSN).[20] We used three neurocognitive tests: the Montreal Cognitive Assessment,[21] the Digit Symbol Substitution Test,[22,23] and the Trail Making Test Part B.[24-26] Scores on the Montreal Cognitive Assessment range from 0 to 30, with higher scores indicating better cognitive function. The lowest score on the Digit Symbol Substitution Test is 0 and there is no upper limit; higher scores indicate better cognitive function. The Trail Making Test Part B is a timed test in which a lower score (in seconds) indicates better function.

The quality-of-life and neurocognitive assessments were originally intended to be mandatory for all participants but were made optional early in the course of the trial to improve recruitment. The decision about a patient's participation in these assessments was made on an individual basis; centers could select for these assessments patients who might be more likely to return to the hospital during the follow-up period to complete the tests. The decision to participate was made before randomization, to avoid biases. All the quality-of-life and neurocognitive tests were administered before CABG was performed (before randomization), at the time of discharge, at 30 days, and at 1 year.

### STATISTICAL ANALYSIS

All analyses were conducted according to the intention-to-treat principle. After testing the assumption of proportional hazards, we conducted a time-to-event analysis, using Cox regression to report the 1-year outcomes. 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 with the use of a log-rank test. The treatment effect is expressed as the hazard ratio (with 95% confidence intervals), which was derived from the Cox proportional-hazards model for the first coprimary outcome at 1 year. The comparison between the two operative techniques was assessed in subgroups defined according to the presence or absence of diabetes, the presence or absence of cerebrovascular disease, left ventricular function, the number of diseased vessels, sex, age, body-mass index, region, and European System for Cardiac Operative Risk Evaluation (EuroSCORE) grade, and tests for interaction were performed with the use of a Cox proportional-hazards model.



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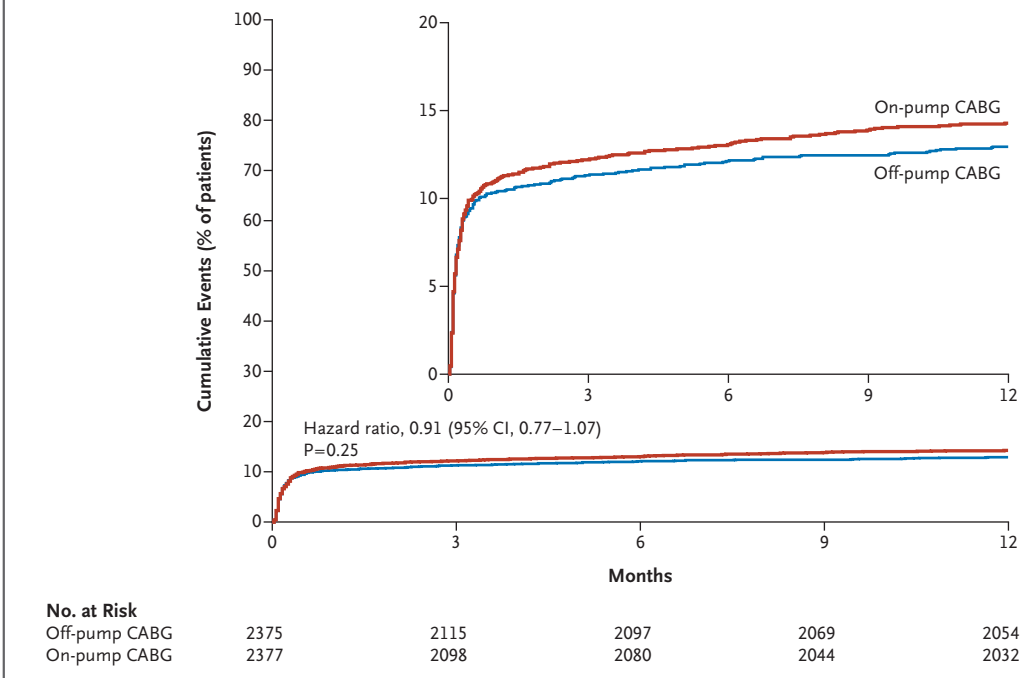



**Figure 1. Kaplan–Meier Curves for the Primary Composite Outcome at 1 Year.**

The primary outcome was the composite of death, nonfatal myocardial infarction, nonfatal stroke, or nonfatal new renal failure requiring dialysis. The inset shows the same data on an enlarged y axis.

We also conducted landmark analyses assessing these outcomes between 31 days and 1 year; in these analyses, data from patients who had a primary outcome in the first 30 days or who were not followed up after 30 days were not included.

To analyze the quality-of-life and neurocognitive data at each follow-up point (i.e., hospital discharge, 30 days, and 1 year), we calculated the changes in assessment scores from baseline to the follow-up point for each patient, limiting the analysis to patients for whom data were available both at baseline and at the follow-up point being analyzed. The mean value for the change in score was then calculated within each group,[27] and these means were compared between the two groups.

## RESULTS

### PATIENTS

From November 2006 through October 2011, a total of 4752 patients were enrolled at 79 hospitals in 19 countries and were randomly assigned to undergo either off-pump CABG (2375 patients) or on-pump CABG (2377 patients). The baseline characteristics of the overall trial population have been reported previously and are also provided in Table S1 in the Supplementary Appendix, available at NEJM.org. One-year follow-up data on the clinical outcomes were available for 98.7% of the patients.

### PRIMARY AND OTHER CLINICAL OUTCOMES

At 1 year, a primary outcome event had occurred in 288 participants (12.1%) in the off-pump group and 316 participants (13.3%) in the on-pump group (hazard ratio with the off-pump procedure, 0.91; 95% confidence interval [CI], 0.77 to 1.07; P=0.24) (Fig. 1 and Table 1). The rates of individual components of this composite outcome did not differ significantly between the groups. No significant interactions were seen between the procedure and any of the subgroup variables (Fig. 2). There were no significant differences between the off-pump group and the on-pump group in the rates of recurrent angina (1.0% and 0.9%, respectively) or in the need for repeat revascularization by means of PCI or CABG (1.4% [33 patients] and 0.8% [20 patients], respectively; haz-



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**Table 1. Outcomes at 1 Year.***

| Outcome | Off-Pump CABG (N=2375) | On-Pump CABG (N=2377) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| Primary outcome — no. (%)† | 288 (12.1) | 316 (13.3) | 0.91 (0.77–1.07) | 0.24 |
| Components of primary outcome — no. (%) | | | | |
| Death | 122 (5.1) | 119 (5.0) | 1.03 (0.80–1.32) | |
| Myocardial infarction | 161 (6.8) | 178 (7.5) | 0.90 (0.73–1.12) | |
| Stroke | 36 (1.5) | 40 (1.7) | 0.90 (0.57–1.41) | |
| New renal failure requiring dialysis | 30 (1.3) | 31 (1.3) | 0.97 (0.59–1.60) | |
| Other prespecified outcomes — no. (%) | | | | |
| Cardiovascular-related death‡ | 99 (4.2) | 96 (4.0) | 1.03 (0.78–1.37) | 0.83 |
| Angina | 23 (1.0) | 22 (0.9) | 1.05 (0.58–1.88) | 0.87 |
| Other outcomes | | | | |
| Repeat revascularization — no. (%)§ | 33 (1.4) | 20 (0.8) | 1.66 (0.95–2.89) | 0.07 |
| PCI | 27 (1.1) | 19 (0.8) | 1.43 (0.79–2.57) | 0.23 |
| CABG | 7 (0.3) | 1 (<0.1) | 7.00 (0.86–57.0) | 0.07 |
| Primary outcome in per protocol population — no./total no. (%) | 252/2191 (11.5) | 295/2227 (13.2) | 0.86 (0.73–1.02) | 0.08 |

* CABG denotes coronary-artery bypass grafting, and PCI percutaneous coronary intervention.
† The primary outcome was a composite of death, nonfatal stroke, nonfatal myocardial infarction, or new renal failure requiring dialysis.
‡ All deaths in the first 30 days were considered to be cardiovascular-related deaths.
§ One patient underwent both CABG and PCI.

ard ratio, 1.66; 95% CI, 0.95 to 2.89; P=0.07). The rate of the primary outcome among patients who underwent the assigned procedure (i.e., without crossing over to the other procedure) was similar to the rate in the intention-to-treat population (11.5% in the off-pump group and 13.2% in the on-pump group; hazard ratio, 0.86; 95% CI, 0.73 to 1.02; P=0.08).

The landmark analysis for the period between 31 days and 1 year showed a similar risk of the primary outcome in the two groups: 55 of the 2142 patients in the off-pump group included in this analysis (2.6%) and 69 of the 2130 patients in the on-pump group included in this analysis (3.2%) had a primary outcome event (hazard ratio, 0.79; 95% CI, 0.55 to 1.13; P=0.19) (Table 2). These landmark analyses also showed that the rates of recurrent angina and repeat revascularization by means of PCI or CABG were similar in the on-pump and off-pump groups for the period between 31 days and 1 year (recurrent angina: 0.8% and 0.7%, respectively; hazard ratio, 1.13; 95% CI, 0.56 to 2.26; P=0.74; and repeat revascularization: 0.7% and 0.6%, respectively; hazard ratio, 1.22; 95% CI, 0.59 to 2.54; P=0.59).

### QUALITY-OF-LIFE AND NEUROCOGNITIVE OUTCOMES

A total of 2850 patients initially agreed to provide data for the substudies of quality of life and neurocognitive function (Table S1 in the Supplementary Appendix). However, some of these patients did not provide data for one or more of the substudy tests at the various follow-up points (Table 3, and Table S2 in the Supplementary Appendix). The rates of the primary outcome were lower among patients who agreed to participate in the substudies than among those who did not, but there was no interaction between substudy participation and group assignment with respect to the primary outcome (Table S3 in the Supplementary Appendix). There was a small decline in quality of life, as measured by the EQ-5D, in both groups at the time of discharge (Table 3), but this was followed by a sharp increase in perceived quality of life by patients in both groups at 30 days and at 1 year after surgery. There was no significant difference between the two groups in quality-of-life scores at any time point. There was less reduction from baseline in neurocognitive function, as assessed with the use of the Digit



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| Subgroup | No. of Patients | Hazard Ratio (95% CI) | P Value | P Value for Interaction |
|---|---|---|---|---|
| Age | | | | 0.46 |
| <70 yr | 2815 | 0.97 (0.77–1.22) | 0.77 | |
| ≥70 yr | 1935 | 0.86 (0.69–1.07) | 0.17 | |
| Sex | | | | 0.46 |
| Male | 3843 | 0.93 (0.78–1.12) | 0.47 | |
| Female | 908 | 0.81 (0.59–1.12) | 0.21 | |
| Cerebrovascular disease | | | | 0.41 |
| Yes | 456 | 1.10 (0.69–1.75) | 0.69 | |
| No | 4296 | 0.89 (0.75–1.06) | 0.18 | |
| Peripheral arterial disease | | | | 0.54 |
| Yes | 385 | 0.79 (0.48–1.28) | 0.33 | |
| No | 4366 | 0.93 (0.78–1.10) | 0.37 | |
| Diabetes | | | | 0.13 |
| Yes | 2228 | 0.80 (0.63–1.01) | 0.06 | |
| No | 2523 | 1.02 (0.82–1.28) | 0.84 | |
| Renal failure (with dialysis) | | | | 0.51 |
| Yes | 66 | 0.63 (0.23–1.74) | 0.37 | |
| No | 4594 | 0.90 (0.76–1.06) | 0.20 | |
| Congestive heart failure | | | | 0.20 |
| Yes | 296 | 0.66 (0.40–1.11) | 0.12 | |
| No | 4455 | 0.95 (0.80–1.12) | 0.52 | |
| EuroSCORE | | | | 0.27 |
| 0 to 2 | 1339 | 1.18 (0.82–1.69) | 0.37 | |
| 3 to 5 | 2516 | 0.85 (0.68–1.06) | 0.16 | |
| >5 | 828 | 0.83 (0.60–1.15) | 0.27 | |
| Region | | | | 0.22 |
| South America | 843 | 0.76 (0.55–1.05) | 0.10 | |
| North America, Australia, Europe | 1821 | 0.83 (0.65–1.06) | 0.14 | |
| India | 1307 | 1.18 (0.84–1.67) | 0.34 | |
| China | 781 | 1.10 (0.67–1.81) | 0.71 | |
| Body-mass index | | | | 0.70 |
| 16.0–24.9 | 1737 | 1.00 (0.76–1.31) | 0.98 | |
| 25.0–27.9 | 1393 | 0.83 (0.61–1.14) | 0.26 | |
| 28.0–44.9 | 1561 | 0.94 (0.72–1.21) | 0.62 | |
| Left ventricular ejection fraction | | | | 0.72 |
| ≥50%, grade 1 | 3294 | 0.95 (0.78–1.17) | 0.64 | |
| 35–49%, grade 2 | 1103 | 0.76 (0.56–1.05) | 0.10 | |
| 20–34%, grade 3 | 244 | 0.84 (0.48–1.47) | 0.53 | |
| <20%, grade 4 | 11 | — | — | |
| Diseased vessels | | | | 0.17 |
| Left main | 1001 | 0.86 (0.62–1.20) | 0.37 | |
| Triple | 2711 | 1.00 (0.81–1.23) | 0.99 | |
| Double | 817 | 0.81 (0.52–1.25) | 0.33 | |
| Single | 119 | 0.19 (0.04–0.90) | 0.04 | |
| Operator experience with off-pump CABG | | | | 0.78 |
| <350 cases, lowest third | 1492 | 0.91 (0.66–1.24) | 0.54 | |
| 350–900 cases, middle third | 1577 | 0.83 (0.63–1.09) | 0.18 | |
| >900 cases, highest third | 1611 | 0.95 (0.73–1.22) | 0.67 | |

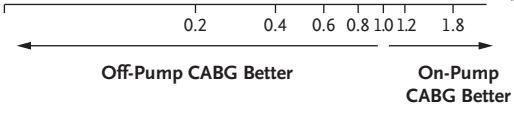



**Figure 2. Hazard Ratios for the Primary Outcome in Prespecified Subgroups.**

Grades of 0 to 2 on the European System for Cardiac Operative Risk Evaluation (EuroSCORE) for CABG indicate low risk; 3 to 5, moderate risk; and more than 5, high risk. The body-mass index is the weight in kilograms divided by the square of the height in meters.



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**Table 2. Outcomes between 31 Days and 1 Year.***

| Outcome | Off-Pump CABG (N=2142) | On-Pump CABG (N=2130) | Hazard Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *number (percent)* | | | |
| Primary outcome | 55 (2.6) | 69 (3.2) | 0.79 (0.55–1.13) | 0.19 |
| Components of primary outcome | | | | |
| Death | 44 (2.1) | 50 (2.3) | 0.87 (0.58–1.31) | |
| Myocardial infarction | 4 (0.2) | 8 (0.4) | 0.5 (0.15–1.65) | |
| Stroke | 10 (0.5) | 12 (0.6) | 0.83 (0.36–1.92) | |
| New renal failure requiring dialysis | 2 (0.1) | 4 (0.2) | 0.5 (0.09–2.71) | |
| Other prespecified outcomes | | | | |
| Cardiovascular-related death | 33 (1.5) | 31 (1.5) | 1.06 (0.65–1.73) | 0.82 |
| Angina | 17 (0.8) | 15 (0.7) | 1.13 (0.56–2.26) | 0.74 |
| Repeat revascularization | 16 (0.7) | 13 (0.6) | 1.22 (0.59–2.54) | 0.59 |
| PCI | 15 (0.7) | 13 (0.6) | 1.15 (0.55–2.41) | 0.72 |
| CABG | 1 (<0.1) | 0 | | 0.99 |

* The landmark analyses of data between 31 days and 1 year excluded data from patients who had a primary outcome in the first 30 days or who were not followed up after 30 days.

Symbol Substitution Test, in the off-pump group than in the on-pump group at discharge (P=0.04), but there was no significant between-group difference at 30 days or at 1 year. We found no differences between the two groups in the change in scores on the Montreal Cognitive Assessment or the Trail Making Test Part B. Sensitivity analyses comparing centers that had rates of participation in these assessments in the highest quartile with centers that had participation rates in the lower three quartiles also showed similar results (Table S4 in the Supplementary Appendix).

## DISCUSSION

In this trial, we compared off-pump CABG with on-pump CABG in 4752 patients from 19 countries on five continents. We found no significant between-group difference at 1 year in the rate of the first coprimary outcome of death, nonfatal stroke, nonfatal myocardial infarction, or nonfatal new renal failure requiring dialysis; in the rate of each component of the coprimary outcome; or in the rate of repeat revascularization. Although there was a small difference in cognitive function in favor of off-pump CABG at discharge, this benefit did not persist at 1 year.

Our results differ from those of the ROOBY trial.[7,8] That trial showed a significantly higher rate of the composite outcome at 1 year with off-pump CABG than with on-pump CABG (9.9% vs. 7.4%; relative risk, 1.33; 95% CI, 1.01 to 1.76; P=0.04), whereas there was no significant difference in CORONARY. There are important differences between the two trials. CORONARY included more than twice as many participants as were included in the ROOBY trial. In addition, the participants in our trial were enrolled at a diverse array of clinical settings, whereas the ROOBY trial recruited patients exclusively from the Veterans Affairs system. We specified a higher level of surgical expertise at the beginning of the trial than was required in the ROOBY trial; each operation was performed by a surgeon who had more than 2 years of experience and had completed more than 100 cases of the specific technique (either on-pump or off-pump CABG) to be performed. In CORONARY, trainees were not allowed to be the primary surgeon. The rate of crossover from off-pump to on-pump CABG was lower in CORONARY than in the ROOBY trial (7.9% vs. 12.4%), and the rate of repeat revascularization between 31 days and 1 year was also lower in CORONARY (0.7% in the off-pump group and 0.6% in the on-pump group vs. 4.6% and 3.4%, respectively, in the ROOBY trial), suggest-



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**Table 3. Quality of Life and Results of Neurocognitive Testing.***

| Measure | Off-Pump CABG | | On-Pump CABG | | P Value |
|---|---|---|---|---|---|
| | No. of Patients | Score | No. of Patients | Score | |
| **EQ-5D†** | | | | | |
| Baseline | 1424 | 0.77±0.22 | 1421 | 0.77±0.22 | 0.97 |
| Change from baseline | | | | | |
| To discharge | 1265 | −0.03±0.28 | 1251 | −0.03±0.26 | 0.75 |
| To 30 days | 1154 | 0.07±0.26 | 1161 | 0.08±0.25 | 0.25 |
| To 1 year | 1024 | 0.13±0.24 | 1035 | 0.14±0.24 | 0.25 |
| **EQ-5D visual-analogue scale‡** | | | | | |
| Baseline | 1423 | 65.8±17.6 | 1422 | 66.6±17.8 | 0.24 |
| Change from baseline | | | | | |
| To discharge | 1264 | 1.8±18.2 | 1250 | 1.0±17.8 | 0.26 |
| To 30 days | 1154 | 8.5±17.6 | 1159 | 8.0±17.6 | 0.44 |
| To 1 year | 1023 | 11.3±18.1 | 1035 | 11.4±17.6 | 0.88 |
| **Montreal Cognitive Assessment§** | | | | | |
| Baseline | 1053 | 23.2±4.4 | 1028 | 23.2±4.3 | 0.90 |
| Change from baseline | | | | | |
| To discharge | 896 | 0.2±2.9 | 881 | 0.1±2.9 | 0.22 |
| To 30 days | 797 | 1.0±3.1 | 784 | 0.8±3.1 | 0.26 |
| To 1 year | 645 | 0.4±4.0 | 628 | 0.3±4.0 | 0.51 |
| **Digit Symbol Substitution Test¶** | | | | | |
| Baseline | 989 | 33.0±17.8 | 986 | 31.9±18.0 | 0.15 |
| Change from baseline | | | | | |
| To discharge | 812 | −1.6±11.4 | 797 | −2.7±10.0 | 0.04 |
| To 30 days | 694 | 1.8±11.4 | 685 | 1.3±10.8 | 0.40 |
| To 1 year | 522 | 1.8±13.2 | 528 | 1.3±12.3 | 0.56 |
| **Trail Making Test Part B‖** | | | | | |
| Baseline | 721 | 158.0±88.1 | 711 | 163.7±89.5 | 0.22 |
| Change from baseline | | | | | |
| To discharge | 523 | 5.2±55.4 | 498 | 7.0±52.6 | 0.59 |
| To 30 days | 470 | −10.9±58.1 | 487 | −4.7±71.2 | 0.14 |
| To 1 year | 353 | −6.8±64.0 | 340 | −3.2±70.2 | 0.49 |

* Plus–minus values are means ±SD. The number of patients at baseline indicates the number of patients who completed the baseline test. The number of patients at a subsequent time indicates the number of patients who completed the test at baseline and at that specific time.

† The European Quality of Life–5 Dimensions (EQ-5D) questionnaire assesses five dimensions of quality of life. The total score ranges from 0 to 1, with higher scores indicating better quality-of-life status.

‡ The EQ-5D visual-analogue scale assesses the respondent's self-rated health on a vertical, visual analogue scale. The total score ranges from 0 to 100, with higher scores indicating better health status.

§ The Montreal Cognitive Assessment assesses executive function and detects subtle memory impairment. The total score ranges from 0 to 30, with higher scores indicating better cognitive function.

¶ The Digit Symbol Substitution Test was designed to assess differences among cognitively intact persons in a wide array of cognitive domains such as visual-motor speed and coordination, capacity for learning, capacity for sustained effort, attention, concentration, ability to imitate newly learned visual material, and short-term memory. The lowest score is 0, and there is no upper limit; higher scores indicate better cognitive function.

‖ The Trail Making Test Part B is a test of scanning, visual-motor tracking, divided attention, and cognitive flexibility. The test is timed, and therefore a lower score (in seconds) indicates a better function.



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ing a higher level of surgical expertise in our trial. In both CORONARY and the ROOBY trial, the rates of the primary outcomes at 1 year among patients who underwent the assigned procedure (i.e., without crossing over to the other procedure) were consistent with those in the intention-to-treat analysis. In CORONARY, the rate of the primary end point was lower in the off-pump group than in the on-pump group (11.5% and 13.2%, respectively; P=0.08), whereas in the ROOBY trial, the rate was lower in the on-pump group (9.4% in the off-pump group vs. 7.1% in the on-pump group; P=0.08).

It is possible that the relative success of the two procedures is influenced by the risk level of the patients, since new techniques tend to show benefits in patients at higher surgical risk, who have more to gain with newer, less invasive techniques.[28,29] The participants in our trial were at a higher surgical risk than were patients in the ROOBY trial, as evidenced by the selection criteria, the baseline characteristics, and the 30-day mortality. In the ROOBY trial, the 30-day mortality was 1.6% in the off-pump group and 1.2% in the on-pump group. In contrast, the 30-day mortality in CORONARY was 2.5% in each group. The patients in CORONARY were older than were the patients in the ROOBY trial (mean age, 67.5 years vs. 62.7 years), and more patients in CORONARY required emergency surgery (38.8% vs. 15.2%). Our trial also included a group of patients with more complex coronary anatomy. As compared with the ROOBY trial, CORONARY included more women (19.2% vs. 0.5%), more patients with left main coronary artery disease (21.5% vs. 0), and more patients with three-vessel disease (after exclusion of patients with left main coronary artery disease) (74.2% vs. 66.6%). In addition, 44% of the patients in CORONARY were of South Asian or East Asian ethnic groups, populations that are known to have smaller coronary arteries.[30-32] Therefore the apparent differences in results between the ROOBY trial and CORONARY may be due to differences in the baseline risk of the patients as well as the differences in the experience levels of the surgeons.

Our trial has some limitations. The quality-of-life and neurocognitive tests were optional, and some centers had low participation rates for these tests. We found that the patients who completed these tests were generally somewhat healthier than were patients who did not participate (Table S1 in the Supplementary Appendix). In addition, among patients who agreed to participate, many, despite our best efforts, refused to complete the more demanding neurocognitive tests. These tests could also not be completed if the follow-up was conducted only by telephone. Patients who chose not to participate initially or who refused to participate later during the follow-up period may differ in some ways from those who did participate. Although the possibility of a bias in favor of a particular technique cannot be excluded, various sensitivity analyses suggested that the results were robust and indicated little difference, if any, in quality of life or neurocognitive function between the patients in the two groups.

In conclusion, we conducted a large, randomized trial to compare the outcomes of on-pump CABG with off-pump CABG. At 1 year, we found no significant differences between the two groups in the rate of death, nonfatal stroke, nonfatal myocardial infarction, or nonfatal new renal failure requiring dialysis or in the rate of subsequent revascularization procedures. We also found no significant differences in quality of life or in neurocognitive function.

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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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