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On-Pump versus Off-Pump Coronary-Artery Bypass Surgery

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ABSTRACT

BACKGROUND

Coronary-artery bypass grafting (CABG) has traditionally been performed with the use of cardiopulmonary bypass (on-pump CABG). CABG without cardiopulmonary bypass (off-pump CABG) might reduce the number of complications related to the heart–lung machine.

METHODS

We randomly assigned 2203 patients scheduled for urgent or elective CABG to either on-pump or off-pump procedures. The primary short-term end point was a composite of death or complications (reoperation, new mechanical support, cardiac arrest, coma, stroke, or renal failure) before discharge or within 30 days after surgery. The primary long-term end point was a composite of death from any cause, a repeat revascularization procedure, or a nonfatal myocardial infarction within 1 year after surgery. Secondary end points included the completeness of revascularization, graft patency at 1 year, neuropsychological outcomes, and the use of major resources.

RESULTS

There was no significant difference between off-pump and on-pump CABG in the rate of the 30-day composite outcome (7.0% and 5.6%, respectively; P=0.19). The rate of the 1-year composite outcome was higher for off-pump than for on-pump CABG (9.9% vs. 7.4%, P=0.04). The proportion of patients with fewer grafts completed than originally planned was higher with off-pump CABG than with on-pump CABG (17.8% vs. 11.1%, P<0.001). Follow-up angiograms in 1371 patients who underwent 4093 grafts revealed that the overall rate of graft patency was lower in the off-pump group than in the on-pump group (82.6% vs. 87.8%, P<0.01). There were no treatment-based differences in neuropsychological outcomes or short-term use of major resources.

CONCLUSIONS

At 1 year of follow-up, patients in the off-pump group had worse composite outcomes and poorer graft patency than did patients in the on-pump group. No significant differences between the techniques were found in neuropsychological outcomes or use of major resources. (ClinicalTrials.gov number, NCT00032630.)

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During the past 30 years, coronary-artery bypass grafting (CABG) primarily was performed with the use of cardiopulmonary bypass ("on pump") with cardioplegic arrest. Historically, on-pump CABG was shown to improve ischemic symptoms and, in selected patients, prolong survival.[1-3] In the mid-1990s, interest emerged in performing CABG without the use of cardiopulmonary bypass (off pump), in order to reduce postoperative complications associated with the use of cardiopulmonary bypass,[4-7] including generalized systemic inflammatory response,[8,9] cerebral dysfunction,[10-12] myocardial depression, and hemodynamic instability.[13,14]

At the time this trial was being planned, initial enthusiasm for off-pump CABG became tempered by concern about the completeness of revascularization, the rate of perioperative myocardial infarction, and long-term graft patency.[15-17] Therefore, to further assess the relative efficacy of on-pump and off-pump CABG, the Department of Veterans Affairs (VA) Cooperative Studies Program funded the Randomized On/Off Bypass (ROOBY) trial (Cooperative Studies Program number 517) as a prospective study designed to evaluate the primary outcomes of major morbidity and mortality at both 30 days and 1 year and the secondary outcomes of completeness of revascularization, 1-year graft patency, neuropsychological test scores, and other outcomes. We hypothesized that there would be no difference between the on-pump and off-pump procedures for the two primary outcomes.

METHODS

STUDY DESIGN

The ROOBY trial was a controlled, single-blind, randomized trial conducted from February 2002 through May 2008 at 18 VA medical centers (see the Supplementary Appendix, available with the full text of this article at NEJM.org). The trial was designed by the principal investigators (with oversight by a planning committee), sponsored by the VA Cooperative Studies Program, approved by the institutional review board of each participating VA medical center, and assessed routinely by an independent data and safety monitoring board. All participants provided written informed consent.

Before patients underwent randomization, participating surgeons were required to document that they had performed at least 20 off-pump CABG surgeries, including some in which complete revascularization was performed for all vascular territories of the heart. The prestudy off-pump experience of the surgeons averaged 120 cases (median, 50). Sixteen sites had training programs in which cardiothoracic trainees (postgraduate year 6 to 10) were designated before randomization as the primary surgeon or first assistant surgeon. Postoperatively, enrolled patients were followed every 2 months for up to 1 year.

Baseline and follow-up angiograms and neuropsychological tests were assessed and scored by angiographic and neuropsychological core-laboratory staff who were unaware of the treatment assignment. Data collection, analysis, and reporting were performed by the VA Cooperative Studies Program Coordinating Center at Perry Point, Maryland.

SELECTION OF PATIENTS AND RANDOMIZATION

Patients who were scheduled for urgent or elective CABG-only procedures were screened for enrollment. Exclusion criteria were any clinically significant valve disease (i.e., moderate, moderate-to-severe, or severe valve disease), a status requiring immediate surgery, small target vessels (<1.1 mm in internal diameter) or diffuse coronary disease, clinical reservations of the surgical team regarding patients with risk-factor profiles that predisposed them to an extremely high risk of an adverse event, or the inability or unwillingness of the patient to provide consent. While in the preoperative holding area, patients underwent randomization with the use of an automated central telephone system in a blocked randomization scheme. Assignments of the patients were balanced for each attending surgeon.

TREATMENT

A standard median sternotomy was performed in all patients. Protocol details have been published previously.[18] During the trial, various stabilization devices were used during off-pump surgery to provide a motionless surgical field. The use of one of these devices was required. Conversion from the assigned procedure to the other procedure was performed when clinically necessary.

STUDY END POINTS

The primary short-term end point was a composite of death or major complications (reoperation,

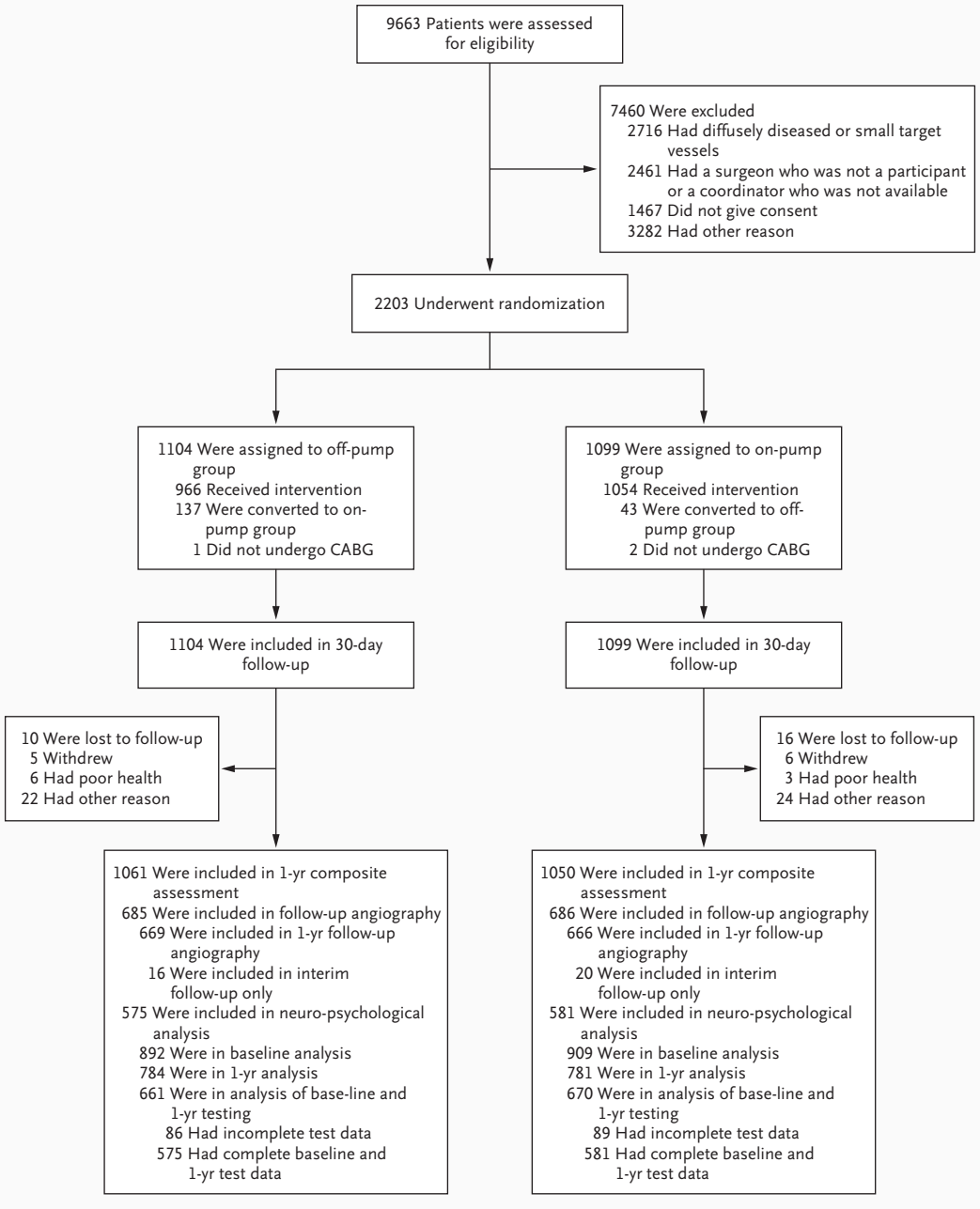

Figure 1. Enrollment, Randomization, and Follow-up of Patients.

For some of the 7460 patients who were excluded, there was more than one reason for exclusion. CABG denotes coronary-artery bypass grafting.

new mechanical support, cardiac arrest, coma, stroke, or renal failure requiring dialysis) occurring within 30 days after surgery or before discharge, whichever was later. The primary long-term composite end point was death from any cause within 1 year, nonfatal myocardial infarction between 30 days and 1 year, or repeat revascularization between 30 days and 1 year. Composite end points were selected for feasibility and fiscal reasons. Secondary end points included the

completeness of revascularization (determined by the number of grafts performed as compared with the number planned), graft patency at 1 year, and scores on a battery of neuropsychological tests (derived from previously published tests), which were performed preoperatively and 1 year postoperatively.

STATISTICAL ANALYSIS

The required sample size of 2200 patients was based on the use of a two-tailed continuity-corrected chi-square test, a P value of 0.05 to indicate statistical significance for primary end points, a power of 0.80, a 10% rate of loss to follow-up, and the ability to detect a reduction of 40% in the rate of the primary 1-year composite end point in the off-pump group as compared with the expected 8% rate in the on-pump group. This sample size also allowed the detection of a 30% reduction in the primary short-term composite end point from the expected 14% rate in the on-pump group. The two primary end points were analyzed with the use of continuity-corrected chi-square tests. Mantel–Haenszel chi-square tests were used to adjust for study-center effects. Baseline characteristics and secondary outcomes were compared with the use of chi-square techniques and t-tests as appropriate. Log-rank tests with

Table 1. Baseline and Operative Characteristics of Patients Undergoing Off-Pump or On-Pump CABG.*

Variable	Off-Pump Group (N=1104)	On-Pump Group (N=1099)	P Value
Demographic characteristics			
Age — yr	63.0±8.5	62.5±8.5	0.13
Male sex — no. (%)	1097 (99.4)	1092 (99.5)	1.00
Race or ethnic group — no. (%)†			0.21
Black	77 (7.0)	93 (8.5)	
Hispanic	71 (6.4)	52 (4.7)	
White	931 (84.3)	926 (84.3)	
Medical characteristics			
Urgent status — no. (%)	179 (16.2)	156 (14.2)	0.19
Previous CABG surgery — no. (%)	9 (0.8)	4 (0.4)	0.27
Chronic obstructive pulmonary disease — no. (%)	220 (19.9)	238 (21.7)	0.32
Creatinine level >1.5 mg/dl (133 μmol/liter) — no. (%)	94 (8.5)	79 (7.2)	0.27
Stroke — no. (%)	82 (7.4)	88 (8.0)	0.63
Peripheral vascular disease — no. (%)	179 (16.2)	163 (14.8)	0.38
Diabetes — no. (%)	470 (42.6)	491 (44.7)	0.32
Hypertension — no. (%)	948 (85.9)	952 (86.6)	0.62
Left ventricular ejection fraction — no./total no. (%)			0.88
<35%	61/1065 (5.7)	61/1062 (5.7)	
35–44%	122/1065 (11.5)	132/1062 (12.4)	
45–54%	249/1065 (23.4)	253/1062 (23.8)	
>54%	633/1065 (59.4)	616/1062 (58.0)	
Current smoker — no./total no. (%)	360/1100 (32.7)	384/1097 (35.0)	0.26
History of atrial fibrillation — no. (%)	52 (4.7)	41 (3.7)	0.29
Coronary disease — no./total no. (%)			0.32
1-Vessel	65/1097 (5.9)	65/1091 (6.0)	
2-Vessel	317/1097 (28.9)	284/1091 (26.0)	
3-Vessel	715/1097 (65.2)	742/1091 (68.0)	
Estimated risk of death before discharge or within 30 days after the procedure — %	1.9±1.8	1.8±1.8	0.25

Table 1. (Continued.)

Variable	Off-Pump Group (N=1104)	On-Pump Group (N=1099)	P Value
Operative details			
Resident was "primary" surgeon — no. of patients/total no. (%)	611/1102 (55.4)	702/1097 (64.0)	<0.001
Patients receiving red cells — no./total no. (%)	571/1099 (52.0)	616/1097 (56.2)	0.05
Conversion to other treatment — no. (%)	137 (12.4)	40 (3.6)	<0.001
No. of grafts planned per patient	3.0±0.9	3.0±0.9	0.98
No. of grafts performed per patient	2.9±0.9	3.0±1.0	0.002
No. of grafts planned vs. no. performed per patient — no. of patients/total no. (%)			<0.001
No. planned equaled no. performed	804/1100 (73.1)	829/1096 (75.6)	
No. planned was less than no. performed	100/1100 (9.1)	145/1096 (13.2)	
No. planned was greater than no. performed	196/1100 (17.8)	122/1096 (11.1)	
Use of resources‡			
Hours in the operating room§	4.5±1.4	4.4±1.3	0.05
Postoperative length of stay in the surgical intensive care unit — days	3.7±3.8	3.8±4.0	0.69
Postoperative length of stay in the hospital — days	8.2±8.8	7.8±6.1	0.22
Total hours on ventilator	17.1±36.5	15.8±40.3	0.43

* Plus–minus values are means ±SD. Percentages may not sum to 100 because of rounding. CABG denotes coronary-artery bypass grafting.
† Race or ethnic group was reported by the research nurse on the basis of the medical records or information from the patient or family.
‡ Data are for 1085 patients in the off-pump group and 1084 patients in the on-pump group.
§ Hours were calculated from the initial incision of the skin to closure of the skin incision.

Kaplan–Meier curves were used to report time to death. For secondary outcome measures, a P value of 0.01 was considered to indicate statistical significance. Confidence intervals were reported for all outcome measures.

RESULTS

ENROLLMENT AND RANDOMIZATION

From February 2002 through May 2007, a total of 9663 patients who were scheduled for urgent or elective CABG were screened for enrollment (Fig. 1). Of these, 7460 patients (77.2%) were excluded, most commonly because of diffusely diseased or small coronary arteries (2716 patients), a surgeon who was not participating in the study or a coordinator who was unavailable to enroll the patient (2461), and the unwillingness or inability of the patient to provide consent (1467). More excluded patients than enrolled patients had chronic obstructive pulmonary disease (22.8% vs. 20.8%), renal insufficiency (12.2% vs. 7.9%), peripheral vascular disease (19.0% vs. 15.5%), hypertension (88.5% vs. 86.2%), and previous CABG (4.0% vs. 0.6%). Enrolled patients had a lower predicted risk of death before discharge or within 30 days after the procedure than those who were excluded (1.9% vs. 2.5%, P<0.001). About 15% of enrolled patients were categorized as having urgent status but not requiring immediate surgery.

Overall, 2203 patients were randomly assigned to either on-pump surgery (1099 patients) or off-pump surgery (1104 patients). Baseline demographic and clinical characteristics were similar in the two groups and consistent with those of the overall VA CABG population (Table 1). Most patients were white men who were current or former smokers and had at least one coexisting condition. More than 40% of the patients had diabetes mellitus. A majority of patients had three-vessel coronary artery disease and normal left ventricular function. There was no significant difference between patients in the off-pump group and those in the on-pump group in the predicted risk of

Table 2. Short-Term and Long-Term Primary End Points According to Treatment Group.*

Primary End Point	Off-Pump Group (N=1104)	On-Pump Group (N=1099)	Absolute Percentage-Point Difference (95% CI)	Relative Risk (95% CI)	P Value†
	no. (%)				
Short-term					
30-Day composite‡	77 (7.0)	61 (5.6)	1.4 (–0.6 to 3.5)	1.26 (0.91 to 1.74)	0.19
Death within 30 days after surgery or before discharge	18 (1.6)	13 (1.2)	0.4 (–0.5 to 1.4)	1.38 (0.68 to 2.80)	0.47
Complications within 30 days after surgery or before discharge					
Cardiac arrest	20 (1.8)	12 (1.1)	0.7 (–0.3 to 1.7)	1.66 (0.82 to 3.38)	0.21
Renal failure requiring dialysis	9 (0.8)	10 (0.9)	–0.1 (–0.9 to 0.7)	0.90 (0.37 to 2.20)	0.82
Stroke	14 (1.3)	8 (0.7)	0.5 (–0.3 to 1.4)	1.75 (0.74 to 4.14)	0.28
Coma	4 (0.4)	3 (0.3)	0.1 (–0.4 to 0.6)	1.33 (0.30 to 5.93)	1.00
Repeat cardiac surgery	8 (0.7)	8 (0.7)	–0.0 (–0.7 to 0.7)	1.00 (0.38 to 2.65)	1.00
Reoperation for bleeding	30 (2.7)	23 (2.1)	0.6 (–0.7 to 1.9)	1.30 (0.76 to 2.22)	0.40
New mechanical support	17 (1.5)	9 (0.8)	0.7 (–0.2 to 1.6)	1.88 (0.84 to 4.21)	0.17
Mediastinitis	11 (1.0)	14 (1.3)	–0.3 (–1.1 to 0.6)	0.78 (0.36 to 1.72)	0.55
Tracheostomy	5 (0.5)	7 (0.6)	–0.2 (–0.8 to 0.4)	0.71 (0.23 to 2.24)	0.58
Long-term					
1-Yr composite§	105 (9.9)	78 (7.4)	2.5 (0.1 to 4.9)	1.33 (1.01 to 1.76)	0.04
1-Yr composite with death from cardiac causes rather than from any cause	93 (8.8)	62 (5.9)	2.9 (0.6 to 5.1)	1.48 (1.09 to 2.02)	0.01
1-Yr composite with all end points from time of CABG	155 (14.6)	104 (9.9)	4.7 (1.9 to 7.5)	1.47 (1.17 to 1.86)	0.001
Nonfatal myocardial infarction between 30 days and 1 yr after surgery	21 (2.0)	23 (2.2)	–0.2 (–1.4 to 1.0)	0.90 (0.50 to 1.62)	0.76
Revascularization between 30 days and 1 yr after surgery	49 (4.6)	36 (3.4)	1.2 (–0.5 to 2.9)	1.35 (0.88 to 2.05)	0.18
Death from any cause within 1 yr	43 (4.1)	30 (2.9)	1.2 (–0.4 to 2.8)	1.41 (0.90 to 2.24)	0.15
Death from cardiac causes within 1 yr	29 (2.7)	14 (1.3)	1.4 (0.2 to 2.6)	2.05 (1.09 to 3.86)	0.03

* CABG denotes coronary-artery bypass grafting, and CI confidence interval. There were 1061 patients in the off-pump group and 1050 in the on-pump group for analyses of all long-term end points except death.
† P values are based on statistical-test comparisons with missing data excluded.
‡ The primary short-term composite end point was death, reoperation, new mechanical support, cardiac arrest, coma, stroke, or renal failure requiring dialysis before discharge or within 30 days after surgery.
§ The primary long-term composite end point was death from any cause within 1 year after surgery, nonfatal myocardial infarction between 30 days and 1 year, and any revascularization procedure between 30 days and 1 year.

death before discharge or within 30 days after the procedure (1.9% and 1.8%, respectively; P=0.25).

Other than the use of myocardial preservation and aortic cross-clamping in the on-pump group, the study protocol required that surgical techniques and intraoperative monitoring be consistent; the use of Swan–Ganz catheters occurred 93% of the time in each group, and the use of optional transesophageal echocardiography occurred 68% of the time in each group. However, patients in the on-pump group were more likely than those in the off-pump group to have had the cardiothoracic resident as the primary surgeon (64.0% vs. 55.4%, P<0.01). Conversion to the off-pump procedure occurred in 40 patients in the on-pump group (3.6%), and conversion to the on-pump procedure occurred in 137 patients in the off-pump group (12.4%).

PRIMARY COMPOSITE END POINTS

There was no significant difference between the off-pump group and the on-pump group in the rate of the primary short-term (30-day) composite end point (7.0% and 5.6%, respectively; P=0.19). The rate of death from any cause before discharge or within 30 days after the procedure was 1.6% in the off-pump group and 1.2% in the on-pump group (P=0.47). Major complications were also low in number and similar in the two treatment groups (Table 2).

The primary long-term (1-year) composite end point was determined in 2111 of the patients (95.8%). The VA death registry provided the 1-year survival status for all patients. The rate of the long-term composite outcome was higher in the off-pump group than in the on-pump group (9.9% vs. 7.4%, P=0.04). No significant differences were found for any of the individual components of the 1-year composite end point. There was a trend toward more deaths from cardiac causes in the off-pump group than in the on-pump group (2.7% vs. 1.3%, P=0.03) (Table 2).

To ensure that the long-term composite findings were robust, sensitivity analyses were performed. We replaced death from any cause with death from cardiac causes, and we replaced myocardial infarction or repeat revascularization between 30 days and 1 year after CABG with cumulative 1-year events from the time of surgery for nonfatal myocardial infarction and revascularization procedures. These sensitivity analyses showed even stronger advantages for on-pump procedures (Table 2). Despite better 1-year composite outcomes in the on-pump group, Kaplan–Meier analysis for death from any cause, reported as of May 2008, showed no significant difference in survival between off-pump and on-pump treatments (P=0.25) (Fig. 2).

Since the primary analysis was based on the intention-to-treat principle, a supplementary analysis excluded all patients for whom the assigned procedure was converted to the other procedure. For patients who underwent the assigned procedure, without conversion to the other procedure (928 patients in the off-pump group and 1013 in the on-pump group), the directionality of the 1-year primary end point remained consistent between the off-pump and on-pump groups but did not reach statistical significance (9.4% and 7.1%, respectively; P=0.08).

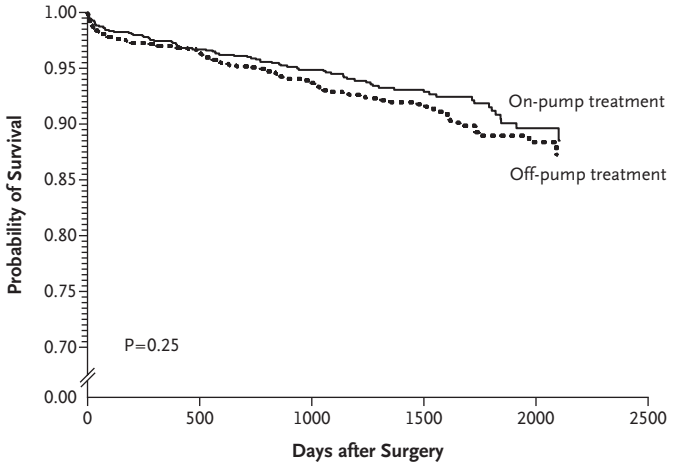

Figure 2. Kaplan–Meier Estimates of Survival after Surgery.

MAJOR SECONDARY END POINTS

Completeness of Revascularization

Before randomization, the participating surgeons recorded the planned target arteries for the coronary-artery bypass. Most CABG procedures were planned as two-vessel (23%), three-vessel (45%), or four-vessel (24%) procedures. The number of bypasses planned was the same in the two groups (mean [±SD] number of bypasses per patient, 3.0±0.9). There was a significant difference between the off-pump group and the on-pump group in the average number of bypasses performed per patient (2.9±0.9 and 3.0±1.0, respectively; P=0.002). The proportion of patients with fewer grafts than originally planned was higher in the off-pump group than in the on-pump group (17.8% vs. 11.1%, P<0.01) (Table 1).

Graft Patency

Of the 2127 patients who underwent CABG and were alive at 12 months, 1371 (64.5%) had follow-up angiograms; 1335 had angiograms at the 12-month end-of-study visit, and 36 patients had only an interim angiogram. Of the 759 surviving patients with no follow-up angiograms, 573 (75.5%) declined angiography, 52 had an elevated creatinine level, 55 moved or did not want to travel, 32 had unidentified reasons, and 47 were lost to follow-up. There were no significant differences between the study groups in the reasons for missing follow-up catheterization. Also, there were no significant differences between the treat-

Table 3. Core-Laboratory Results of Angiographic Tests.*

Variable	Off-Pump Group	On-Pump Group	Absolute Percentage-Point Difference, Off-Pump vs. On-Pump (95% CI)	Relative Risk of Occlusion, Off-Pump vs. On-Pump (95% CI)	P Value
At least one occluded graft — no. of patients/total no. (%)	250/685 (36.5)	197/686 (28.7)	7.8 (2.8 to 12.7)	1.27 (1.09 to 1.48)	0.002
Graft patency — no. of grafts/total no. (%)					
Overall	1650/1998 (82.6)	1839/2095 (87.8)	–5.2 (–7.4 to –3.0)	0.94 (0.92 to 0.97)	<0.001
Saphenous vein	967/1262 (76.6)	1122/1339 (83.8)	–7.2 (–10.2 to –4.1)	0.91 (0.88 to 0.95)	<0.001
Left internal thoracic to left anterior descending artery	589/618 (95.3)	611/635 (96.2)	–0.9 (–3.1 to 1.3)	0.99 (0.97 to 1.01)	0.48
Left internal thoracic to left anterior descending artery, FitzGibbon grade A†	550/618 (89.0)	592/635 (93.2)	–4.2 (–7.4 to –1.1)	0.95 (0.92 to 0.99)	0.01

* CI denotes confidence interval.
† A FitzGibbon grade of A indicates an excellent graft.

ment groups in baseline clinical and demographic characteristics for patients who underwent follow-up angiography.

Grafts were evaluated for patency (open vs. closed) and assigned a FitzGibbon grade of A (excellent graft), B (impaired graft, with ≥50% stenosis and a reduction in the caliber of the graft to <50% of the grafted artery), or O (100% occluded graft).[19] Overall, 4093 grafts were analyzed: 1253 left internal thoracic-artery pedicle grafts to the left anterior descending artery, 2601 saphenous-vein grafts, 112 radial-artery grafts, 60 left internal thoracic-artery grafts to other arteries, 64 right internal thoracic-artery or free left internal thoracic-artery grafts, and 3 other grafts (Table 3).

The rate of graft patency was significantly lower in the off-pump group than in the on-pump group (82.6% vs. 87.8%, P<0.01). The lower rate of patency of saphenous-vein grafts in the off-pump group than in the on-pump group (76.6% vs. 83.8%, P<0.01) accounted for most of this difference. The patency rate for left internal thoracic-artery pedicle grafts to the left anterior descending artery was similar in the off-pump group and the on-pump group (95.3% and 96.2%, respectively; P=0.48). However, when left internal thoracic-artery grafts to the left anterior descending artery were classified according to the FitzGibbon grade, there were fewer grade A grafts in the off-pump group than in the on-pump group (89.0% vs. 93.2%, P=0.01).

Finally, more patients in the off-pump group than in the on-pump group had at least one occluded graft (36.5% vs. 28.7%, P<0.01). For patients with no occluded grafts, the rate of the primary 1-year composite outcome was higher in the off-pump group than in the on-pump group (6.4% vs. 3.3%, P=0.03), perhaps because there was less complete revascularization in the off-pump group.

Neuropsychological Outcomes

The battery of neuropsychological tests was designed to evaluate dysfunction in attention, memory, and visuospatial skills. Test data from the study sites were rescored at a core laboratory to ensure excellent reliability.[20] Of the 2203 patients who underwent randomization, 892 of 1104 patients in the off-pump group (80.8%) and 909 of 1099 patients in the on-pump group (82.7%) completed baseline (i.e., preoperative) neuropsychological testing. Baseline tests were missing for 402 patients; the primary reasons included scheduling problems (267 patients), lack of physical ability to be tested (62), and patients who declined testing (54).

Of the 1801 patients who completed baseline testing, 1331 (73.9%) also underwent testing 12 months after surgery. Analysis of z scores was based on matched assessments of each patient's baseline and follow-up tests. Of the 1331 patients whose baseline and 1-year tests were matched, 175 were excluded because at least 1 of the 10 test measures was missing. Patients missed 1-year evaluations because, among other reasons, study participation was terminated early (198 patients), the patient was not available for testing (110), or

Table 4. Core-Laboratory Results of Neuropsychological Tests.*

Neuropsychological Test	Change in z Score in Off-Pump Group (N=575)	Change in z Score in On-Pump Group (N=581)	Absolute Difference in z Score Change, Off-Pump vs. On-Pump (95% CI)	P Value†
WMS-III Logical Memory Immediate Recall	0.25±0.73	0.19±0.69	0.06 (–0.02 to 0.14)	0.13
WMS-III Logical Memory Delayed Recall	0.38±0.72	0.31±0.70	0.07 (–0.01 to 0.16)	0.08
WMS-III Logical Memory Recognition	0.22±0.97	0.17±0.86	–0.05 (–0.05 to 0.16)	0.34
WMS-III Faces Immediate Recall	0.30±0.91	0.31±0.99	–0.01 (–0.12 to 0.10)	0.89
WMS-III Faces Delayed Recall	0.29±0.94	0.34±0.98	–0.05 (–0.16 to 0.06)	0.38
WAIS-III Digit Span Total	0.05±0.68	0.10±0.63	–0.05 (–0.12 to 0.03)	0.21
WAIS-III Digit Symbol Total	0.07±0.53	0.07±0.54	0.00 (–0.07 to 0.06)	0.90
Trail Making Test — Part A	–0.01±0.60	–0.04±0.93	0.03 (–0.06 to 0.12)	0.55
Trail Making Test — Part B	–0.05±0.56	–0.04±0.65	–0.01 (–0.08 to 0.06)	0.87
Clock-drawing test	0.26±0.99	0.09±0.90	0.18 (0.07 to 0.29)	0.001
Composite z score change	0.19±0.31	0.17±0.34	0.02 (–0.01 to 0.06)	0.21

* Plus–minus values are means ±SD. CI denotes confidence interval, WAIS III Wechsler Adult Intelligence Scale, 3rd edition, and WMS III Wechsler Memory Scale, 3rd edition. The z scores were calculated from the mean and standard deviation of all baseline neuropsychological test scores.

† P values were determined by an analysis of covariance with adjustment for baseline z scores. Positive changes in scores indicate improvement from baseline, except for scores on the Trail Making Tests, for which negative changes in scores indicate an improvement.

the patient declined (78). There was no significant difference between treatment groups in follow-up rates or reasons for missed tests.

Neuropsychological data for the 1156 patients with complete and matched test measures at baseline and at 1 year of follow-up (54.3% of the 2127 survivors) were analyzed (Table 4). This number of records represents a sample size that allows detection of a difference as small as 0.20 SD, with a power of 80 and a P value of 0.01 indicating statistical significance, which was equivalent to a difference of 0.07 for the global z score (the sum of all the z scores for each patient÷10). As compared with patients with nonmatched baseline and 1-year records, the 1156 patients were younger (P<0.01), were more likely to be white (P=0.04), and had a lower estimated risk of 30-day operative death (P<0.001). There were no significant differences between the treatment groups in age, education, medical characteristics, or the Beck Depression Inventory score; there were significant but not clinically relevant differences in three baseline cognitive scores. There was no significant difference between the two treatment groups in the global z score from baseline to follow-up. Only the clock-drawing test showed a statistically significant (but probably not a clinically significant) improvement in the off-pump group. Most notably, the long-term postoperative changes in individual test scores were similar to or improved from baseline for both treatment groups.

Resource Use

Patients in the off-pump group required red-cell transfusions less frequently and had slightly longer operating-room times than did patients in the on-pump group. No significant differences were shown for postoperative length of stay in the surgical intensive care unit, postoperative length of stay in the hospital, or postoperative length of time on a ventilator (Table 1). Furthermore, no differences were found for the rate of rehospitalization within 30 days after surgery or the use of fresh-frozen plasma, platelets, or cryoprecipitate.

DISCUSSION

The ROOBY trial was a large, randomized, controlled study of off-pump versus on-pump CABG. The majority of previous trials have included smaller patient cohorts (e.g., <250 patients per treatment group), a smaller number of participating centers (e.g., <3 facilities), or both.[21] In our trial, 2203 patients underwent randomization, and 53 attending surgeons at 18 participating centers were involved.

Generally, off-pump CABG has been shown to

be a safe and effective technique.[21-23] Like the Octopus (ClinicalTrials.gov number, NCT00189215) and PRAGUE-4 multicenter trials,[24,25] our trial showed no significant difference in the early composite outcome of death or complications. Several studies indicate that surgeons in a single center or a single surgeon may perform off-pump CABG with excellent results.[26-29] In our trial, however, 1-year composite outcomes, completeness of revascularization, and graft patency were significantly worse with off-pump than with on-pump CABG. Given concern that outcomes may have been influenced by the surgeon's experience, a sensitivity analysis based on classifying participating surgeons as either high-volume or low-volume operators (>50 or ≤50 prestudy cases of off-pump CABG, respectively) showed no significant difference in the primary 30-day and 1-year composite outcomes, supporting the idea that these results may be generalized to surgeons with variable off-pump experience.

The majority of patients in our trial had multivessel disease. Complete revascularization was the goal, and in both groups the average number of grafts planned was 3.0 per patient. There tended to be less complete revascularization with off-pump CABG (mean, 2.9 grafts completed per patient) than with on-pump CABG (mean, 3.0 per patient). Furthermore, patients in the off-pump group were more likely than those in the on-pump group to have fewer grafts completed than had been planned.

As in smaller randomized trials involving surgeons who were experienced in off-pump CABG, the rate of patency of left internal thoracic-artery grafts to the left anterior descending artery in our trial was excellent (about 95% in each group). This finding was similar to findings by Widimsky et al.,[25] who reported an arterial-graft patency rate of 91% for both techniques, and Puskas et al.,[26] who reported arterial-graft patency rates of 94.1% for off-pump CABG and 98.1% for on-pump CABG. The 1-year patency rate for saphenous-vein grafts was 80% in our trial, which is similar to previously reported rates. As in smaller studies, the rate of saphenous-vein-graft patency was significantly better in the on-pump group than in the off-pump group (83.8% vs. 76.6%, $P<0.001$).[25,26,29]

The early literature indicated that off-pump approaches had the potential to improve neuropsychological outcomes. Despite loss to follow-up at 1 year, our trial had sufficient power to show differences between treatments in terms of neuropsychological outcomes. However, we found no significant differences between the groups. This is an important finding, because the results of a number of studies have suggested that cardiopulmonary bypass causes permanent neurologic dysfunction or decreases cognition and motor abilities.[4,10-12,29,30] Our trial did not show a cognitive decline within 1 year after surgery in either group. Studies involving cardiac or surgical controls, or both, have shown that on-pump CABG procedures may not be the main element associated with cognitive decline.[31-33] Future studies with neuropsychological control groups are warranted to evaluate the frequency of cognitive impairment or improvement over time.

Our study population consisted almost exclusively of men. Otherwise, the findings of the trial can be extrapolated to low-to-moderate-risk patients undergoing CABG only and having multiple noncardiac coexisting conditions and multivessel disease. A potential bias was that the role of the primary surgeon was not balanced between treatment groups. Residents were somewhat more likely than attending physicians to perform on-pump rather than off-pump procedures. However, an analysis of the primary 30-day and 1-year composite outcomes showed no significant differences between treatment groups, regardless of whether the resident or the attending physician was the primary surgeon.

In conclusion, our trial did not show any overall advantage to the use of the off-pump as compared with the on-pump cardiac surgical approach for coronary bypass. Instead, there was a consistent trend toward better outcomes in patients undergoing the conventional on-pump CABG technique, including better 1-year composite outcomes and 1-year patency rates. Moreover, no significant differences between the off-pump and the on-pump techniques were identified in neuropsychological outcomes or the use of major resources.

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