Off-pump versus on-pump coronary artery bypass grafting: Insights from the Arterial Revascularization Trial

Umberto Benedetto, MD, PhD,^a Douglas G. Altman, DSc,^b Stephen Gerry, MSc,^b Alastair Gray, PhD,^c Belinda Lees, BSc, PhD,^d Marcus Flather, MD,^e and David P. Taggart, MD, PhD,^d on behalf of the Arterial Revascularization Trial investigators

ABSTRACT

Background: The long-term effects of off-pump coronary artery bypass continue to be controversial because some studies have reported increased adverse event rates with off-pump coronary artery bypass when compared with on-pump coronary artery bypass. The Arterial Revascularization Trial compared survival after bilateral versus single internal thoracic artery grafting. The choice of off-pump coronary artery bypass versus on-pump coronary artery bypass was based on the surgeon's discretion. We performed a post hoc analysis of the Arterial Revascularization Trial to compare 5-year outcomes with 2 strategies.

Methods: Among 3102 patients enrolled in the Arterial Revascularization Trial, we selected 1260 patients who underwent off-pump coronary artery bypass versus 1700 patients who underwent on-pump coronary artery bypass with cardioplegic arrest for the present comparison. Primary outcomes were 5-year mortality and incidence of major cardiac and cerebrovascular events, including cardiovascular death, myocardial infarction, cerebrovascular accident, and revascularization after index procedure. Propensity score matching selected 1260 pairs for final comparison. Stratified Cox models were used for treatment effect estimate.

Results: Hospital mortality was comparable between off-pump coronary artery bypass and on-pump coronary artery bypass groups (12 [1.0%] vs 15 [1.2%]; $P = .7$). Conversion rate to on-pump during off-pump coronary artery bypass was 29 of 1260 (2.3%). When compared with off-pump coronary artery bypass not converted, off-pump coronary artery bypass converted to on-pump presented a remarkably higher hospital mortality (10.3% vs 0.7%; $P < .001$). At 5 years, the mortality rate was 110 (8.9%) versus 102 (8.3%) in the off-pump coronary artery bypass and on-pump coronary artery bypass groups, respectively, with no significant difference (hazard ratio, 1.14; 95% confidence interval, 0.86-1.52; $P = .35$). Incidence of major cardiac and cerebrovascular events was 175 (14.3) versus 169 (13.8) in the off-pump coronary artery bypass and on-pump coronary artery bypass groups, respectively, with no significant difference (hazard ratio, 1.05; 95% confidence interval, 0.84-1.31; $P = .65$).

Conclusions: The present post hoc Arterial Revascularization Trial analysis supports the hypothesis that both off-pump coronary artery bypass and on-pump coronary artery bypass are equally effective and safe. (J Thorac Cardiovasc Surg 2018;155:1545-53)

Five-year cumulative incidence for mortality in the matched OPCAB and ONCAB groups.

Central Message

OPCAB and ONCAB grafting are comparable in terms of the 5-year rate of death and MACCE.

Perspective

Some studies have reported increased adverse event rates with OPCAB when compared with ONCAB. The present post hoc analysis of the ART trial found no significant difference between off-pump and on-pump coronary surgery in the rate of death and MACCE.

See Editorial Commentary page 1554.

From the ^aBristol Heart Institute, University of Bristol, School of Clinical Sciences, United Kingdom; ^bCentre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology, and Musculoskeletal Sciences, ^cDepartment of Public Health, Health Economics Research Centre, University of Oxford, Oxford, United Kingdom; ^dNuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom; and ^eResearch and Development Unit, Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom.

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Address for reprints: Umberto Benedetto, MD, PhD, Bristol Heart Institute, University of Bristol, Senate House, Tyndall Ave, Bristol BS8 1TH, United Kingdom (E-mail: Umberto.benedetto@hotmail.com).

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Abbreviations and Acronyms

ART	= Arterial Revascularization Trial
CI	= confidence interval
CORONARY	= CABG Off or On Pump Revascularization Study
CVA	= cerebrovascular accident
MACCE	= major cardiac and cerebrovascular events
MI	= myocardial infarction
ONCAB	= on-pump coronary artery bypass
OPCAB	= off-pump coronary artery bypass
ROOBY	= Randomized On/Off Bypass

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Despite the potential advantages of avoiding cardiopulmonary bypass, the postulated benefits of off-pump coronary artery bypass (OPCAB) in terms of perioperative mortality and morbidity including stroke were not realized in the majority of studies comparing the 2 strategies.¹ Furthermore, the long-term effects of OPCAB continue to be controversial. The increased technical complexity of OPCAB can result in less complete revascularization and reduced graft patency rates, with some studies reporting increased adverse event rates with OPCAB when compared with on-pump coronary artery bypass (ONCAB).²⁻⁵

Two large randomized controlled trials comparing OPCAB with ONCAB have recently reported conflicting findings. The CABG Off or On Pump Revascularization Study (CORONARY)⁶ has recently shown comparable 5-year results between the 2 techniques. However, CORONARY enrolled only higher-risk patients, and this aspect may limit the generalizability of the study findings. On the other hand, the Department of Veterans Affairs Randomized On/Off Bypass (ROOBY) Trial⁷ has reported increased 5-year mortality with OPCAB. However, the ROOBY trial was criticized for the fact that the conversion rate to cardiopulmonary bypass was unacceptably high at 12%, and this brought some skepticism on the level of “off-pump” experience of the surgeons involved in the study.

Consequently, the question whether OPCAB increases the risk of adverse events over the longer term when

compared with ONCAB continues. The Arterial Revascularization Trial (ART) is designed to compare 10-year survival after bilateral internal thoracic artery versus single left internal thoracic artery grafting, and an interim report at 5 years has not shown any clear difference between the 2 groups.⁸ In the ART, the choice of OPCAB versus ONCAB was based on the surgeon’s discretion. We sought to achieve further insights into the comparison between the 2 strategies by performing a post hoc analysis of the ART.

MATERIALS AND METHODS

The present study is a post hoc retrospective analysis of 5-year outcomes of the ART trial. This research adheres to the principles set forth in the Declaration of Helsinki (<http://www.wma.net/en/30publications/10policies/b3/index.html>). In the ART, the choice of OPCAB versus ONCAB was based on the surgeon’s discretion. OPCAB versus ONCAB strategy adopted was available for all patients enrolled. Among patients enrolled in the ART (n = 3102) from 2004 to 2007, we excluded those who did not undergo surgery (n = 23). In 2 cases, there was no information regarding the use of cardiopulmonary bypass. We also excluded patients who received on-pump beating heart surgery (n = 19) and 95 patients who received crossclamp fibrillation. The present analysis compared 1260 patients who underwent OPCAB versus 1700 patients who underwent ONCAB with cardioplegic arrest. OPCAB cases requiring intraoperative conversion to on-pump were included in the OPCAB group in the primary analysis (Figure 1). A total of 156 surgeons were involved. For 134 patients (60 OPCAB, 74 ONCAB), no information on participating surgeon was available. The total number of procedures performed by each surgeon and the choice between OPCAB versus ONCAB presented a large variation with a large proportion of surgeons performing only a few procedures (Table E1). No information was available on individual surgeon practice pattern and OPCAB experience before they took part in the trial (ie, the number of OPCAB vs ONCAB procedures performed per year).

Trial Design

The ART has been approved by the institutional review board of all participating centers, and informed consent was obtained from each participant. The protocol for the ART has been published.⁹ Briefly, the ART is a 2-arm, randomized multicenter trial conducted in 28 hospitals in 7 countries, with patients being randomized equally to single internal thoracic artery or bilateral internal thoracic artery grafts. Eligible patients were those with multivessel coronary artery disease undergoing coronary artery bypass grafting, including patients requiring urgent treatment. Only patients requiring emergency treatment (refractory myocardial ischemia/cardiogenic shock) and patients requiring single grafts or redo surgery were excluded.

Follow-up

Questionnaires were sent to study participants by mail at 12 months and then every year after surgery. No clinic visits were planned apart from the routine clinical 6-week postoperative visit. Participants were sent stamped addressed envelopes to improve the return rates of postal questionnaires. Study coordinators contacted participants by telephone to alert them to the questionnaire’s arrival and to ask them about medications, adverse events, and health services resource use. Mean follow-up time for the present analysis was 4.9 ± 1.0 years. Follow-up at 5 years was completed for 2833 of 2960 patients (96%).

Study Outcomes

The 2 strategies were compared in terms of hospital outcomes, 5-year mortality, and incidence of major cardiac and cerebrovascular events

FIGURE 1. Study flow chart for patient inclusion/exclusion. *OPCAB*, Off-pump coronary artery bypass; *ONCAB*, on-pump coronary artery bypass.

(MACCE), which included cardiovascular death, nonfatal myocardial infarction (MI), nonfatal cerebrovascular accident (CVA), and repeat revascularization. Treatment effect on individual MACCE components was also investigated. Adverse events were adjudicated blind to surgical procedure by a member of the Clinical Event Review Committee.

Outcomes Definitions

Death was classified into cardiovascular and noncardiovascular, when possible, using autopsy reports and death certificates. Congestive heart failure, arrhythmia or MI, pulmonary embolus, and dissection were considered cardiovascular causes of death.

MI was diagnosed when 2 of the following 3 criteria were present: (1) unequivocal electrocardiogram changes; (2) elevation of cardiac enzyme(s) above twice the upper limit of normal or diagnostic troponin increases; and (3) chest pain typical for acute MI that lasted more than 20 minutes. CVA was defined as new neurologic deficit evidenced by clinical signs of paresis, plegia, or new cognitive dysfunction including any mental status alteration lasting more than 24 hours or evidence on computed tomography or magnetic resonance imaging scan of recent brain infarct (<6 months). Repeat revascularization was defined as coronary bypass surgery or percutaneous coronary intervention performed after trial procedure. Acute kidney injury was defined as a 0.3 mg/dL (≥ 26.5 mmol/L) creatinine increase from baseline within 48 hours of surgery.

Statistical Analysis

Multiple imputation ($m = 3$) was used to address missing data. Rubin's method¹⁰ was used to combine results from each of the imputed data sets (Amelia R package). Because of the lack of randomization with regard to receiving OPCAB, a propensity score was generated for each patient from a multivariable logistic regression model based on 23 pretreatment covariates as independent variables with OPCAB versus ONCAB as a binary dependent variable.¹⁰ Pairs of patients were derived using greedy 1:1 matching with a caliper of width of 0.2 standard deviation of the logit of the propensity score (nonrandom R package). The quality of the match was assessed by comparing selected pretreatment variables in propensity score-matched patients using the standardized mean difference, with an absolute standardized difference of greater than 10% taken to represent meaningful covariate imbalance.¹¹ McNemar's test and paired *t* test were used to assess

the statistical significance of the risk difference for hospital outcomes.¹² Cox regression models stratified on the matched pairs¹² were used to estimate the treatment effect on 5-year outcomes. This approach accounts for the within-pair homogeneity by allowing the baseline hazard function to vary across matched sets. Risk competing framework was used to estimate the treatment effect on MACCE individual components. The Schoenfeld residuals test was used to test the independence between residuals and time, and thus to test the proportional hazards assumption in Cox models (survival R package).

Because of the large number of participating surgeons and the marked variability of total number of procedures and OPCAB procedures performed individually, performing surgeons could not be included in the propensity score model. To account for the potential influence of individual surgeon's OPCAB experience, we classified each patient according to quartiles of total number of OPCAB procedures performed in the trial by the relative surgeon (0 [on-pump only], 1-5 [small OPCAB volume], 6-60 [moderate OPCAB volume], >60 [high OPCAB volume]), and outcomes in the matched sample were reported accordingly for descriptive purpose. Finally, baseline characteristics and outcomes between OPCAB cases converted to on pump versus not converted were also reported. All statistical analysis was performed using R Statistical Software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients' Characteristics and Operative Data

The OPCAB group was more likely to have higher creatinine and to receive a bilateral internal thoracic artery graft, and was less likely to have treated hypertension, to have a history of smoking, and to receive saphenous vein grafts. The total number of grafts per patient was comparable in the OPCAB and ONCAB groups (3.20 ± 0.97 vs 3.19 ± 0.76 ; $P = .7$). However, in the OPCAB group, the right coronary artery was less likely to be revascularized (62.1% vs 73.4%; $P < .001$), whereas diagonal branches were more likely to be grafted in the OPCAB group (35.7% vs 29.2%; $P < .001$). The 2 groups did not differ

in the rate of left anterior descending artery grafting (98.1% vs 98.7%; $P = .24$) and circumflex artery grafting (91.8% vs 92.6%; $P = .45$).

Propensity score matching selected 1260 matched pairs for final comparison (C statistic = 0.71) (Figure E1). No residual imbalance was observed between matched groups (all standardized mean difference <10%) (Table 1 and Figure E2). After matching, the number of grafts in the OPCAB and ONCAB groups was comparable (3.20 ± 0.97 vs 3.17 ± 0.87 ; $P = .35$).

Hospital Outcomes

Hospital outcome comparisons before and after matching are shown in Table 2. In-hospital mortality was low and comparable between OPCAB and ONCAB groups (1.0% vs 1.2% $P = .70$). OPCAB was associated with a lower creatine kinase MB peak at 24 hours postoperatively and a relatively lower incidence of MI. However, the rate of intra-aortic balloon pump requirement was comparable between the 2 groups. OPCAB was associated with a lower rate of red blood cell transfusion and

TABLE 1. Baseline characteristics of patients undergoing off-pump coronary artery bypass versus on-pump coronary artery bypass

	OPCAB	ONCAB unmatched	SMD before PSM	ONCAB matched	SMD after PSM
n	1260	1700		1260	
Age (y) mean (SD)	64 (9)	64 (9)	1	64 (9)	1
Female n (%)	180 (14.3)	240 (14.1)	0	180 (14.3)	0
BMI mean (SD)	28.10 (4.10)	28.28 (3.87)	5	28.13 (3.87)	1
SBP (mm Hg) mean (SD)	133 (19)	131 (17)	9	132.30 (18)	2
DBP (mm Hg) mean (SD)	75 (11)	75 (11)	5	75.24 (11.32)	-1
Creatinine (mmol/L) mean (SD)	100 (23)	94 (21)	26	97.75 (21.58)	9
Treated hypertension, n (%)	943 (75)	1360 (80.0)	-12	950 (75.4)	-1
Treated hyperlipemia, n (%)	1176 (93.3)	1601 (94.2)	-4	1178 (93.5)	-1
Diabetes, n (%)			-6		1
No	980 (77.8)	1286 (75.6)		983 (78.0)	
Insulin dependent	70 (5.6)	93 (5.5)		67 (5.3)	
Noninsulin dependent	210 (16.7)	321 (18.9)		210 (16.7)	
Smoking, n (%)			-14		-9
Current	180 (14.3)	242 (14.2)		149 (11.8)	
Ex-smoker	664 (52.7)	999 (58.8)		723 (57.4)	
Never	416 (33.0)	459 (27.0)		388 (30.8)	
COPD, n (%)	29 (2.3)	43 (2.5)	-2	28 (2.2)	1
Asthma, n (%)	63 (5.0)	65 (3.8)	6	59 (4.7)	2
PVD, n (%)	90 (7.1)	120 (7.1)	0	81 (6.4)	3
TIA, n (%)	40 (3.2)	60 (3.5)	-2	40 (3.2)	0
CVA, n (%)	40 (3.2)	46 (2.7)	3	38 (3.0)	1
MI, n (%)	510 (40.5)	726 (42.7)	-5	513 (40.7)	-1
PCI, n (%)	208 (16.5)	270 (15.9)	2	214 (17.0)	-1
Preoperative AF, n (%)	19 (1.5)	24 (1.4)	1	16 (1.3)	2
Preoperative LVEF (%)			5		2
$\geq 50\%$ (good)	950 (75.4)	1289 (75.8)		939 (74.5)	
31%-49% (moderate)	268 (21.3)	389 (22.9)		303 (24.0)	
$\leq 30\%$ (poor)	42 (3.3)	22 (1.3)		18 (1.4)	
LMD, n (%)	282 (22.4)	356 (20.9)	4	277 (22.0)	1
RA, n (%)	240 (19.0)	381 (22.4)	-8	252 (20.0)	-2
SVG, n (%)	936 (74.3)	1344 (79.1)	-11	956 (75.9)	-4
BITA, n (%)	598 (47.5)	691 (40.6)	14	575 (45.6)	4

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; SMD, standardized mean difference; PSM, propensity score matching; SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; TIA, transient ischemic attack; CVA, cerebrovascular accident; MI, myocardial infarction; PCI, percutaneous coronary intervention; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LMD, left main disease; RA, radial artery; SVG, saphenous vein graft; BITA, bilateral internal thoracic artery.

TABLE 2. Hospital outcomes of patients undergoing off-pump coronary artery bypass versus on-pump coronary artery bypass in the Arterial Revascularization Trial

	OPCAB	ONCAB unmatched	<i>P</i> value before PSM*	ONCAB matched	<i>P</i> value after PSM†
n	1260	1700		1260	
Death, n (%)	12 (1.0)	18 (1.1)	.92	15 (1.2)	.70
CVA, n (%)	20 (1.6)	19 (1.1)	.34	13 (1.0)	.29
Perioperative MI, n (%)	10 (0.8)	40 (2.4)	.002	32 (2.5)	.001
CK-MB 24 h (U/L) mean (SD)	34 (179)	80 (125)	.007	83 (139)	.02
IABP insertion, n (%)	58 (4.6)	59 (3.5)	.14	46 (3.7)	.27
Repeat revascularization, n (%)	8 (0.6)	7 (0.4)	.56	7 (0.6)	1
POAF, n (%)	279 (22.1)	451 (26.5)	.007	333 (26.4)	.01
Renal replacement therapy, n (%)	72 (5.7)	79 (4.6)	.22	64 (5.1)	.54
AKI, n (%)	225 (17.9)	290 (17.1)	.61	221 (17.5)	.88
Sternal wound complication, n (%)	35 (2.8)	67 (3.9)	.11	52 (4.1)	.08
Reexploration for bleeding, n (%)	40 (3.2)	62 (3.6)	.55	51 (4.0)	.29
RBC transfusion, n (%)	165 (13.1)	280 (16.5)	.01	207 (16.4)	.02

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; PSM, propensity score matching; CVA, cerebrovascular accident; MI, myocardial infarction; CK-MB, creatine kinase-MB; SD, standard deviation; IABP, intra-aortic balloon pump; POAF, postoperative atrial fibrillation; AKI, acute kidney injury; RBC, red blood cell.

*Chi-square test or *t* test. †McNemar test or paired *t* test.

a trend toward a lower incidence of sternal wound complication. OPCAB did not reduce the incidence of postoperative CVA, acute kidney injury, and renal replacement therapy.

Five-Year Outcomes

Five-year outcome comparisons before and after matching are shown in Table 3. Five-year mortality (hazard ratio, 1.14; 95% confidence interval [CI], 0.86-1.52; *P* = .35) (Figure 2) and MACCE risk (hazard ratio, 1.05; 95% CI, 0.84-1.31; *P* = .65) were comparable between the 2 groups. In terms of individual MACCE components, OPCAB was associated with a marginally nonsignificant 1.1% absolute risk reduction in MI. Cardiovascular death, CVA, and repeat revascularization rates were comparable between the 2 groups (Figure 3).

Impact of Intraoperative Conversion to On-Pump on Outcomes

Intraoperative conversion to on-pump occurred in 29 of 1260 OPCAB (2.3%) procedures. Notably, the distribution of risk factors between the OPCAB converted to on-pump group and OPCAB not converted group was similar (Table E2). When compared with OPCAB not converted, OPCAB converted to on-pump presented a remarkably higher hospital mortality (10.3% vs 0.7%; *P* < .001) and increased rate of hospital complications despite similar distribution of baseline risk factors. The trend toward poorer outcomes among OPCAB cases converted to on-pump persisted at 5 years (Table E3 and Figure E3).

Surgeon Off-Pump Coronary Artery Bypass Volume and Outcomes

A total of 95 surgeons performed on-pump only (951 patients); 33 surgeons performed 1 to 5 OPCAB procedures (531 patients; 62 OPCAB; 469 ONCAB); 25 surgeons performed 6 to 60 OPCAB procedures (in total 779 patients; 530 OPCAB; 249 ONCAB); and 3 surgeons performed more than 60 OPCAB procedures (in total 699 patients; 668 OPCAB; 31 ONCAB).

Baseline characteristics and outcomes in the matched OPCAB and ONCAB groups stratified per surgeon OPCAB volume are reported in Tables E4 and E5 and Figure E4. OPCAB cases performed by “sporadic” OPCAB surgeons (1-5 OPCAB procedures) presented a high rate of conversion (12.9%), a lower number of grafts performed (2.60 ± 0.88), and a higher rate of operative mortality (4.8%) compared with other OPCAB subgroups despite that distribution of risk factors was similar.

When OPCAB performed by 3 high-volume OPCAB surgeons (>60) was compared with ONCAB by 95 “on-pump only” surgeons performing on-pump only, we found similar 5-year overall mortality and MACCE rates.

Among 28 ONCAB cases performed by 3 high-volume OPCAB surgeons (>60), we observed a high hospital mortality rate (7.1%). However, this subgroup presented a higher prevalence of important risk factors, including left ventricular ejection fraction less than 30% and increased creatinine compared with other ONCAB subgroups, suggesting that these 3 surgeons selectively used on-pump for high-risk cases.

TABLE 3. Five-year outcomes of patients undergoing on-pump coronary artery bypass versus off-pump coronary artery bypass in the Arterial Revascularization Trial (expressed in number of events and cumulative incidence)

	OPCAB	ONCAB unmatched	ONCAB matched	HR (95% CI) after PSM*	P value after PSM*
n	1260	1700	1260		
Mortality, n (%)	110 (8.9)	134 (8.0)	102 (8.3)	1.14 (0.86-1.52)	.35
MACCE, n (%)	175 (14.3)	217 (13.1)	169 (13.8)	1.05 (0.84-1.31)	.65
CV death, n (%)	51 (4.1)	47 (2.8)	39 (3.1)	1.39 (0.90-2.13)	.13
MI, n (%)	37 (3.0)	61 (3.6)	51 (4.1)	0.66 (0.43-1.02)	.06
CVA, n (%)	41 (3.3)	42 (2.5)	32 (2.6)	1.32 (0.83-2.11)	.24
Revascularization, n (%)	90 (7.5)	108 (6.4)	84 (6.8)	1.09 (0.80-1.49)	.58

OPCAB, Off-pump coronary artery bypass; ONCAB, on-pump coronary artery bypass; HR, hazard ratio; CI, confidence interval; PSM, propensity score matching; MACCE, major cardiac and cerebrovascular event; CV, cardiovascular; MI, myocardial infarction; CVA, cerebrovascular accident. *Cox model stratified for matched pairs.

DISCUSSION

The main finding of the present post hoc analysis of the ART showed that when compared with ONCAB, OPCAB was associated with a comparable number of grafts performed, a reduced operative morbidity, and comparable 5-year mortality and incidence of MACCE. Conversion rate to on-pump was relatively low (2.3%) but was associated with a remarkable increase in hospital mortality and morbidity and poorer 5-year outcomes.

In the ART, more than 50% of OPCAB procedures (668/1260) were performed by 3 of 156 participating surgeons, whereas 95 surgeons performed on-pump only. OPCAB performed by 3 high-volume OPCAB surgeons was associated with hospital and 5-year mortality comparable to those observed after ONCAB performed by 95 “on-pump only” surgeons.

We found that OPCAB performed by “sporadic” OPCAB surgeons (1-5 OPCAB procedures) was associated

with a marked increase in conversion rate (12.9%), a lower number of grafts performed, and increased hospital mortality (4.8%).

There is continued debate as to whether OPCAB may affect long-term outcomes because of a lower number of grafts performed and subsequent effect of incomplete revascularization. Takagi and colleagues² pooled 5 randomized controlled trials and 17 adjusted observational studies that had reported long-term (≥ 5 -year) all-cause mortality. In observational studies (102,820 patients) but not in randomized trials (1486 patients), OPCAB was associated with increased late mortality.

Criticisms for observational studies comparing OPCAB and ONCAB include a possible bias toward including higher-risk patients in the OPCAB group.¹³ Furthermore, incomplete revascularization in retrospective studies may be a surrogate marker for higher burden of comorbidities and per se might not be particularly relevant to patients' outcomes.¹⁴

FIGURE 2. Five-year cumulative incidence for mortality and MACCE in the matched OPCAB and ONCAB groups. ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass.

FIGURE 3. Five-year cardiovascular death, MI, CVA, and revascularization cumulative incidence in the OPCAB and ONCAB groups. CV, Cardiovascular; ONCAB, on-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; MI, myocardial infarction; CVA, cerebrovascular accident.

The CORONARY trial⁶ is a large trial ($n = 4502$ patients) designed to compare the 2 strategies. The final 5-year results showed similar outcomes with OPCAB and ONCAB. The difference between OPCAB and ONCAB in terms of number of grafts (3.0 vs 3.2) and incidence of incomplete revascularization (11.8% vs 10.0%) were only marginal. In the CORONARY, each procedure was performed by a surgeon who had expertise in the specific type of surgery (completion of >100 cases of the specific technique, off-pump or on-pump). A limitation of the CORONARY is that only patients at higher risk were enrolled, and this aspect might limit the generalizability of the study findings.

In contrast, in the ROOBY trial,⁷ which enrolled 2203 patients, OPCAB has been recently reported to be associated with increased 5-year mortality (15.2% in the OPCAB group vs 11.9% in the ONCAB group, relative risk, 1.28; 95% CI, 1.03-1.58; $P = .02$) and MACCE rates (31.0%

in the OPCAB group vs 27.1% in the ONCAB group; relative risk, 1.14; 95% CI, 1.00-1.30; $P = .046$). This trial also demonstrated that the patency rate in the off-pump arm was lower than in the on-pump arm at 12-month angiography.¹⁵ Such findings can be partially explained on the basis that the 53 participating surgeons enrolled on average only 8 patients per year during the study period and had unacceptably high conversion rates to on-pump surgery (12%) and incomplete revascularization (18%). Moreover, in 60% of the cases, a resident was the primary surgeon, again raising concerns about the relative inexperience translating into poor graft patency.

The present post hoc analysis supports the equipoise between OPCAB and ONCAB in terms of safety and efficacy. We found a trend toward a lower incidence of MI in the OPCAB group, mainly related to the early phase. It is well recognized that OPCAB is associated with a lower release

VIDEO 1. Off-pump coronary artery bypass grafting. Video available at: [http://www.jtcvsonline.org/article/S0022-5223\(17\)32725-3/fulltext](http://www.jtcvsonline.org/article/S0022-5223(17)32725-3/fulltext).

of myocardial enzymes,¹⁶ but the clinical relevance of this observation remains unclear. Moreover, the definition of perioperative MI after myocardial revascularization remains controversial, as well as its clinical implication.¹⁷

In the ART, more than 50% of OPCAB procedures were performed by 3 high-volume OPCAB surgeons only, and this can partially explain the present findings. When OPCAB was performed by “sporadic” off-pump surgeons, this was associated with a lower number of grafts, higher conversion rate, and higher hospital mortality. This observation supports the central role of surgeon expertise in determining short- and long-term results after off-pump surgery.

The unique technical challenges of OPCAB promote the perception that adoption of this myocardial revascularization strategy may lead to poorer outcomes during each surgeon’s “learning curve.”¹⁸ However, the learning curve in off-pump CABG can be safely negotiated with appropriate patient selection, individualized grafting strategy, peer-to-peer training of the entire team, and graded clinical experience. Centers with established off-pump training programs have consistently shown that OPCAB can be safely and successfully taught to trainees without jeopardizing outcomes.¹⁹

In the current era, an increasing number of patients with a high-risk profile are being referred for surgical myocardial revascularization, and off-pump surgery represents an attractive strategy to reduce operative morbidity especially in this subgroup, as recently supported by a large meta-analysis of randomized controlled trials.²⁰ Therefore, OPCAB should remain in the armamentarium of cardiac surgeons (Video 1). However, these superior outcomes in high-risk patients can be achieved only if off-pump surgery is offered to high- and low-risk patients alike, and this further emphasizes the need for recognition

of off-pump surgery as a subspecialty with structured training program.

Study Limitations

The present analysis has intrinsic limitations. The main limitation is the retrospective analysis. The propensity technique can adjust only for measurable and included variables, and we cannot exclude a selection bias based on a nonmeasurable “eye-balling,” including the quality of the targets. We had no information on specific surgeon off-pump expertise, and we used the total number of off-pump procedures performed in the ART as a surrogate of off-pump expertise. However, the validity of this approach was further limited by the large variability of the number of procedures performed per surgeon with a large proportion of surgeons performing less than 5 procedures (67 of 156 surgeons). Moreover, we had no information on reasons for preferring off-pump over on-pump and vice versa across surgeon subgroups. Therefore, subgroup analysis based on surgeon OPCAB volume should be considered only as descriptive and hypothesis generating. Despite that the present analysis did not show a significant difference in terms of mortality between the 2 strategies, there is a marginal trend toward an excess of cardiovascular deaths in the OPCAB group (4.1% vs 3.1%), and it can be argued that the present analysis is underpowered to demonstrate a significant difference between the 2 groups. However, this difference is irrelevant when all-cause mortality is considered (8.9% vs 8.3%). All-cause death is the most robust and unbiased index in cardiovascular research because no adjudication is required, thus avoiding inaccurate or biased documentation and inconsistency in end point definition.

CONCLUSIONS

The present post hoc ART analysis found no significant difference at 5 years between OPCAB and ONCAB in the rate of death, nonfatal stroke, nonfatal MI, or subsequent revascularization procedures. Our results indicate that both procedures are equally effective and safe, at least in the medium term.

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Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: off-pump coronary artery bypass grafting, survival, propensity score matching

FIGURE E1. Propensity score density before and after matching.

FIGURE E2. Changes in standardized mean difference for baseline characteristics between OPCAB and ONCAB before (red) and after matching (blue). *ONCAB*, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *PCI*, percutaneous coronary intervention; *MI*, myocardial infarction; *LVEF*, left ventricular ejection fraction; *BITA*, bilateral internal thoracic artery; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *BMI*, body mass index; *LMD*, left main disease; *CVA*, cerebrovascular accident; *AF*, atrial fibrillation; *PVD*, peripheral vascular disease; *TIA*, transient ischemic attack; *COPD*, chronic obstructive pulmonary disease; *RA*, radial artery; *SVG*, saphenous vein graft.

FIGURE E3. Five-year cumulative incidence for mortality and MACCE in the OPCAB group according to the incidence of conversion to on-pump. *OP-CAB*, Off-pump coronary artery bypass; *MACCE*, major cardiac and cerebrovascular event.

FIGURE E4. Five-year cumulative incidence for mortality and MACCE in the OPCAB and ONCAB groups according to surgeon trial OPCAB volume (0 = performing on-pump only; 1-5 = low OPCAB volume; 6-60 = moderate volume; >60 = high volume). *OPCAB*, Off-pump coronary artery bypass; *MACCE*, major cardiac and cerebrovascular event.

TABLE E1. Off-pump coronary artery bypass, on-pump coronary artery bypass, and total number of cases performed according to individual surgeon

Surgeon no.	ONCAB	OPCAB	Total
Not available	74	60	134
1	4	0	4
2	0	1	1
3	0	2	2
4	0	2	2
5	1	5	6
6	1	0	1
7	26	0	26
8	18	0	18
9	1	10	11
10	0	1	1
11	1	0	1
12	16	0	16
13	1	0	1
14	1	1	2
15	1	0	1
16	4	0	4
17	2	0	2
18	4	0	4
19	2	0	2
20	37	0	37
21	0	9	9
22	8	2	10
23	25	15	40
24	28	1	29
25	2	1	3
26	1	0	1
27	10	0	10
28	1	0	1
29	0	38	38
30	21	0	21
31	28	0	28
32	20	0	20
33	51	0	51
34	9	0	9
35	13	0	13
36	0	15	15
37	9	0	9
38	17	0	17
39	14	7	21
40	10	0	10
41	63	17	80
42	1	0	1

(Continued)

TABLE E1. Continued

Surgeon no.	ONCAB	OPCAB	Total
43	5	0	5
44	1	47	48
45	18	1	19
46	2	0	2
47	3	0	3
48	5	16	21
49	2	0	2
50	26	0	26
51	0	6	6
52	4	0	4
53	1	0	1
54	0	6	6
55	20	1	21
56	22	0	22
57	4	43	47
58	29	0	29
59	37	0	37
60	5	0	5
61	0	10	10
62	0	6	6
63	53	4	57
64	1	0	1
65	15	0	15
66	1	0	1
67	5	0	5
68	6	9	15
69	3	0	3
70	0	1	1
71	6	0	6
72	11	0	11
73	1	0	1
74	17	1	18
75	25	0	25
76	0	3	3
77	32	0	32
78	1	0	1
79	2	47	49
80	1	0	1
81	26	0	26
82	6	0	6
83	1	1	2
84	0	1	1
85	0	48	48
86	1	77	78
87	34	0	34

(Continued)

TABLE E1. Continued

Surgeon no.	ONCAB	OPCAB	Total
88	37	0	37
89	9	2	11
90	1	0	1
91	8	0	8
92	3	0	3
93	71	2	73
94	7	2	9
95	1	0	1
96	13	0	13
97	2	0	2
98	1	34	35
99	0	2	2
100	1	0	1
101	40	0	40
102	1	0	1
103	21	0	21
104	27	8	35
105	2	2	4
106	31	2	33
107	4	0	4
108	6	12	18
109	2	0	2
110	11	20	31
111	47	0	47
112	0	3	3
113	3	0	3
114	1	0	1
115	1	10	11
116	1	0	1
117	65	1	66
118	1	0	1
119	2	0	2
120	18	5	23
121	1	0	1
122	26	5	31
123	1	0	1
124	1	8	9
125	6	0	6
126	1	0	1
127	1	1	2
128	6	0	6
129	36	0	36
130	5	1	6
131	2	18	20

(Continued)

TABLE E1. Continued

Surgeon no.	ONCAB	OPCAB	Total
132	1	0	1
133	7	0	7
134	4	0	4
135	1	0	1
136	0	1	1
137	0	412	412
138	1	0	1
139	1	0	1
140	29	0	29
141	0	2	2
142	2	0	2
143	5	11	16
144	1	0	1
145	1	0	1
146	17	0	17
147	9	1	10
148	1	0	1
149	19	0	19
150	5	0	5
151	1	0	1
152	1	0	1
153	76	1	77
154	30	179	209
155	6	0	6
156	1	0	1

ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass.

TABLE E2. Baseline characteristics in patients undergoing off-pump coronary artery bypass converted versus not converted to on-pump

	OPCAB not converted	OPCAB converted to on-pump	P value*
n	1231	29	
Age (y) mean (SD)	63.59 (9.06)	64.40 (9.77)	.634
Female, n (%)	179 (14.5)	1 (3.4)	.16
BMI mean (SD)	28.10 (4.11)	28.15 (3.99)	.95
SBP (mm Hg) mean (SD)	132.75 (19.11)	130.66 (17.94)	.56
DBP (mm Hg) mean (SD)	75.40 (11.07)	72.48 (11.85)	.16
Creatinine (mmol/L) mean (SD)	99.68 (22.19)	107.76 (41.54)	.06
Treated hypertension, n (%)	919 (74.7)	24 (82.8)	.44
Treated hyperlipemia, n (%)	1147 (93.2)	29 (100.0)	.28
Diabetes, n (%)			.78
No	959 (77.9)	21 (72.4)	
Insulin dependent	68 (5.5)	2 (6.9)	
Noninsulin dependent	204 (16.6)	6 (20.7)	
Smoking, n (%)			.02
Current	173 (14.1)	7 (24.1)	
Ex-smoker	645 (52.4)	19 (65.5)	
Never	413 (33.5)	3 (10.3)	
COPD, n (%)	29 (2.4)	0 (0.0)	.83
Asthma, n (%)	58 (4.7)	5 (17.2)	.009
PVD, n (%)	87 (7.1)	3 (10.3)	.76
TIA, n (%)	40 (3.2)	0 (0.0)	.65
CVA, n (%)	40 (3.2)	0 (0.0)	.65
MI, n (%)	493 (40.0)	17 (58.6)	.07
PCI, n (%)	199 (16.2)	9 (31.0)	.06
Preoperative AF, n (%)	18 (1.5)	1 (3.4)	.92
Preoperative LVEF (%)			.37
≥50% (good)	927 (75.3)	23 (79.3)	
31%-49% (moderate)	264 (21.4)	4 (13.8)	
≤30% (poor)	40 (3.2)	2 (6.9)	
LMD, n (%)	276 (22.4)	6 (20.7)	1
RA, n (%)	231 (18.8)	9 (31.0)	.15
SVG, n (%)	916 (74.4)	20 (69.0)	.65
BITA, n (%)	582 (47.3)	16 (55.2)	.51

OPCAB, Off-pump coronary artery bypass; SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; TIA, transient ischemic attack; CVA, cerebrovascular accident; MI, myocardial infarction; PCI, percutaneous coronary intervention; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LMD, left main disease; RA, radial artery; SVG, saphenous vein graft; BITA, bilateral internal thoracic artery. *Chi-square test or *t* test.

TABLE E3. Baseline characteristics of off-pump coronary artery bypass and matched on-pump coronary artery bypass patients stratified for surgeon trial off-pump coronary artery bypass volume

	Matched ONCAB				OPCAB			
Surgeon trial OPCAB volume quartiles	0	1-5	6-60	>60	0	1-5	6-60	>60
No. of surgeons	95	33	25	3	95	33	25	3
No. of patients	688	340	204	28	–	62	530	668
Age (y) mean (SD)	64 (9)	62 (9)	6 (9)	66 (9)	–	64 (8)	62 (8)	65 (9)
Female, n (%)	93 (13.5)	55 (16.2)	28 (13.7)	4 (14.3)	–	7 (11.3)	55 (10.4)	118 (17.7)
BMI mean (SD)	28 (4)	28 (4)	28 (4)	29 (4)	–	27 (4)	28 (4)	28 (4)
SBP (mm Hg) mean (SD)	133 (17)	132 (17)	133 (21)	134 (15)	–	132 (17)	131 (19)	134 (20)
DBP (mm Hg) mean (SD)	75.50 (11.51)	74.91 (10.99)	75.22 (11.02)	72.72 (13.01)	–	75.11 (8.85)	76.51 (10.96)	74.42 (11.30)
Creatinine (mmol/L) mean (SD)	98 (23)	95 (20)	101 (19)	111 (17)	–	94 (31)	96 (22)	104 (22)
Treated hypertension, n (%)	508 (73.8)	272 (80.0)	146 (71.6)	24 (85.7)	–	53 (85.5)	389 (73.4)	501 (75.0)
Treated hyperlipemia, n (%)	629 (91.4)	323 (95.0)	201 (98.5)	25 (89.3)	–	59 (95.2)	516 (97.4)	601 (90.0)
Diabetes n (%)					–			
No	540 (78.5)	257 (75.6)	163 (79.9)	23 (82.1)	–	49 (79.0)	415 (78.3)	516 (77.2)
Insulin dependent	28 (4.1)	24 (7.1)	13 (6.4)	2 (7.1)	–	2 (3.2)	25 (4.7)	43 (6.4)
Noninsulin dependent	120 (17.4)	59 (17.4)	28 (13.7)	3 (10.7)	–	11 (17.7)	90 (17.0)	109 (16.3)
Smoking, n (%)					–			
Current	78 (11.3)	50 (14.7)	18 (8.8)	3 (10.7)	–	8 (12.9)	85 (16.0)	87 (13.0)
Ex-smoker	384 (55.8)	196 (57.6)	131 (64.2)	12 (42.9)	–	37 (59.7)	264 (49.8)	363 (54.3)
Never	226 (32.8)	94 (27.6)	55 (27.0)	13 (46.4)	–	17 (27.4)	181 (34.2)	218 (32.6)
COPD, n (%)	14 (2.0)	6 (1.8)	8 (3.9)	0 (0.0)	–	1 (1.6)	11 (2.1)	17 (2.5)
Asthma, n (%)	35 (5.1)	11 (3.2)	11 (5.4)	2 (7.1)	–	2 (3.2)	24 (4.5)	37 (5.5)
PVD, n (%)	45 (6.5)	20 (5.9)	14 (6.9)	2 (7.1)	–	2 (3.2)	29 (5.5)	59 (8.8)
TIA, n (%)	18 (2.6)	10 (2.9)	11 (5.4)	1 (3.6)	–	1 (1.6)	19 (3.6)	20 (3.0)
CVA, n (%)	28 (4.1)	7 (2.1)	3 (1.5)	0 (0.0)	–	1 (1.6)	11 (2.1)	28 (4.2)
MI, n (%)	272 (39.5)	148 (43.5)	81 (39.7)	12 (42.9)	–	28 (45.2)	226 (42.6)	256 (38.3)
PCI, n (%)	102 (14.8)	63 (18.5)	46 (22.5)	3 (10.7)	–	17 (27.4)	135 (25.5)	56 (8.4)
Preoperative AF, n (%)	8 (1.2)	3 (0.9)	5 (2.5)	0 (0.0)	–	0 (0.0)	7 (1.3)	12 (1.8)
Preoperative LVEF (%)					–			
≥50% (good)	516 (75.0)	253 (74.4)	153 (75.0)	17 (60.7)	–	52 (83.9)	405 (76.4)	493 (73.8)
31%-49% (moderate)	162 (23.5)	85 (25.0)	48 (23.5)	8 (28.6)	–	10 (16.1)	112 (21.1)	146 (21.9)
≤30% (poor)	10 (1.5)	2 (0.6)	3 (1.5)	3 (10.7)	–	0 (0.0)	13 (2.5)	29 (4.3)
LMD, n (%)	149 (21.7)	85 (25.0)	34 (16.7)	9 (32.1)	–	6 (9.7)	101 (19.1)	175 (26.2)
RA, n (%)	137 (19.9)	84 (24.7)	27 (13.2)	4 (14.3)	–	9 (14.5)	90 (17.0)	141 (21.1)
SVG, n (%)	524 (76.2)	232 (68.2)	175 (85.8)	25 (89.3)	–	38 (61.3)	400 (75.5)	498 (74.6)
BITA, n (%)	308 (44.8)	171 (50.3)	85 (41.7)	11 (39.3)	–	23 (37.1)	252 (47.5)	323 (48.4)

ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; TIA, transient ischemic attack; CVA, cerebrovascular accident; MI, myocardial infarction; PCI, percutaneous coronary intervention; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LMD, left main disease; RA, radial artery; SVG, saphenous vein graft; BITA, bilateral internal thoracic artery.

TABLE E4. Outcomes in patients undergoing off-pump coronary artery bypass converted versus not converted to on-pump

	OPCAB converted to on-pump	OPCAB not converted	P value
N	29	1231	
In-hospital outcomes*			
Death, n (%)	3 (10.3)	9 (0.7)	<.001
CVA, n (%)	1 (3.4)	19 (1.5)	.95
MI, n (%)	0 (0.0)	10 (0.8)	1
CK-MB at 24 h (U/L) mean (SD)	182 (102)	31 (179)	.15
IABP insertion, n (%)	10 (34.5)	48 (3.9)	<.001
Repeat revascularization, n (%)	1 (3.4)	7 (0.6)	.46
POAF, n (%)	15 (51.7)	264 (21.4)	<.001
Renal replacement therapy, n (%)	4 (13.8)	68 (5.5)	.14
AKI, n (%)	16 (55.2)	209 (17.0)	<.001
Sternal wound complication, n (%)	1 (3.4)	34 (2.8)	1
Reexploration for bleeding, n (%)	3 (10.3)	37 (3.0)	.09
RBC transfusion, n (%)	17 (58.6)	148 (12.0)	<.001
5-y outcomes†			
Mortality, n (%)	4 (13.8)	106 (8.8)	.3
MACCE, n (%)	8 (27.9)	167 (14.0)	.02
CV death, n (%)	3 (10)	48 (4.0)	.08
MI, n (%)	2 (6.9)	35 (2.9)	.18
CVA, n (%)	1 (3.4)	40 (3.3)	.92
Repeat revascularization	4 (13.8)	86 (7.1)	.12

OPCAB, Off-pump coronary artery bypass; CVA, cerebrovascular accident; MI, myocardial infarction; CK-MB, creatine kinase-MB; SD, standard deviation; IABP, intra-aortic balloon pump; POAF, postoperative atrial fibrillation; AKI, Acute kidney injury; RBC, red blood cell; MACCE, major cardiac and cerebrovascular event; CV, Cardiovascular.

*Chi-square test or *t* test. †Cox regression model.

TABLE E5. Outcomes among off-pump coronary artery bypass and matched on-pump coronary artery bypass patients stratified for surgeon trial off-pump coronary artery bypass volume

	Matched ONCAB				OPCAB			
Surgeon trial OPCAB volume quartiles	0	1-5	6-60	>60	0	1-5	6-60	>60
No. of surgeons	95	33	25	3	95	33	25	3
No. of patients	688	340	204	28	—	62	530	668
Hospital death, n (%)	8 (1.2)	4 (1.2)	1 (0.5)	2 (7.1)	—	3 (4.8)	3 (0.6)	6 (0.9)
Conversion rate, n (%)	—	—	—	—	—	8 (12.9)	14 (2.6)	7 (1.0)
No. of grafts mean (SD)	3.14 (0.77)	3.12 (0.78)	3.31 (0.72)	3.43 (0.57)	—	2.60 (0.88)	3.20 (0.85)	3.26 (0.87)
5-y mortality, n (%)	65 (9.6)	22 (6.7)	10 (4.9)	5 (17.9)	—	5 (8.2)	40 (7.8)	65 (9.9)
5-y MACCE, n (%)	94 (14.0)	44 (13.4)	24 (11.9)	7 (25.7)	—	9 (14.9)	52 (10.2)	114 (17.5)
5-y CV death, n (%)	23 (3.4)	8 (2.4)	4 (2.0)	28 (14.3)	—	3 (4.8)	15 (2.9)	33 (5.0)
5-y MI, n (%)	23 (3.4)	19 (5.6)	8 (3.9)	1 (3.6)	—	3 (4.8)	9 (1.7)	25 (3.8)
5-y CVA, n (%)	16 (2.4)	8 (2.4)	6 (3.0)	2 (7.1)	—	2 (3.3)	16 (3.1)	23 (3.5)
5-y revascularization, n (%)	52 (7.7)	16 (4.9)	14 (6.9)	28 (7.1)	—	3 (5.0)	23 (4.5)	64 (9.7)

ONCAB, On-pump coronary artery bypass; OPCAB, off-pump coronary artery bypass; SD, standard deviation; MACCE, major cardiac and cerebrovascular event; CV, cardiovascular; MI, myocardial infarction; CVA, cerebrovascular accident.