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Predictors and impact of postoperative atrial fibrillation on patients' outcomes: A report from the Randomized On Versus Off Bypass trial

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Objective: The study objective was to determine the predictors of postoperative atrial fibrillation (POAF) in patients randomized to conventional coronary artery bypass graft (on-pump coronary artery bypass [ONCAB]) versus beating heart coronary surgery (off-pump coronary artery bypass [OPCAB]).

Methods: The subgroup of 2103 patients (of 2203 enrollees) in the Randomized On Versus Off Bypass trial with no POAF was studied (1056 patients in the ONCAB group and 1047 patients in the OPCAB group). Univariate and multivariate analyses were used to identify the predictors of POAF and the impact of POAF on outcomes.

Results: Use of ONCAB versus OPCAB was not associated with increased rates of POAF. Older age ($P < .0001$), white race ($P < .001$), and hypertension ($P < .002$) were predictors of POAF on multivariate analysis. In general, POAF led to a higher rates of reintubation (ONCAB: 6.3% vs 0.8% no POAF, $P < .001$; OPCAB: 7.4% vs 1.8% no POAF, $P < .0001$) and prolonged ventilatory support (ONCAB: 7.1% vs 2.3% no POAF, $P = .001$; OPCAB: 9.2% vs 3.4% no POAF, $P = .0003$). The rate of any early adverse outcome was higher in patients with POAF (all patients: 10% POAF vs 4.7% no POAF, $P < .0001$; ONCAB: 9% POAF vs 4.3% no POAF, $P = .008$; OPCAB: 11% POAF vs 5.1% no POAF, $P = .001$). The 1-year all cause mortality was higher with POAF for both groups (ONCAB: 5.4% POAF vs 2% no POAF, $P = .009$; OPCAB: 5.1% POAF vs 2.6% no POAF, $P = .07$). POAF was independently associated with early composite end point (odds ratio [OR], 2.23; confidence interval [CI], 1.55–3.22; $P < .0001$), need for new mechanical support (OR, 3.25; CI, 1.39–7.61; $P = .007$), prolonged ventilatory support (OR, 2.93; CI, 1.89–4.55; $P < .0001$), renal failure (OR, 5.42; CI, 1.94–15.15; $P = .001$), and mortality at 12 months (OR, 1.94; CI, 1.14–3.28; $P = .01$).

Conclusions: In the Randomized On Versus Off Bypass trial, the strategy of revascularization did not affect the rate of POAF. Age, race, and hypertension were predictors of POAF. POAF was independently associated with a higher short-term morbidity and higher 1-year mortality rates. (J Thorac Cardiovasc Surg 2012;143:93-102)

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Postoperative atrial fibrillation (POAF) remains the most common arrhythmic complication after coronary artery bypass grafting (CABG). Although for the most part self-limiting, POAF can adversely affect patients' outcomes in terms of morbidity, mortality, intensive care unit and hospital stay, and long-term outcome.[1-4] In a prior publication, we had outlined the predictors of POAF and the relationship of POAF to postoperative events in a large observational Veterans Affairs (VA) cooperative study.[1] At the time of that study, beating heart CABG (off-pump coronary artery bypass [OPCAB]) was not yet practiced by surgeons in the United States. Although there are multiple reports on the predictors of POAF in patients undergoing conventional CABG with the use of cardiopulmonary bypass (on-pump coronary artery bypass [ONCAB]),[1-4] data are lacking in a large multi-institution group of patients undergoing OPCAB. Available data are from single center studies with a small patient sample size.[5,6] The aim of this study was to identify the predictors of POAF for patients undergoing CABG procedures and to elucidate the impact of POAF on patients' outcome comparing OPCAB with ONCAB strategies.

RANDOMIZED ON VERSUS OFF BYPASS TRIAL

The Randomized On Versus Off Bypass (ROOBY) trial was a prospective, randomized, single blinded, multicenter,

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Abbreviations and Acronyms

AF = atrial fibrillation
CABG = coronary artery bypass grafting
CI = confidence interval
FFP = fresh-frozen plasma
ONCAB = on-pump coronary artery bypass
OPCAB = off-pump coronary artery bypass
OR = odds ratio
POAF = postoperative atrial fibrillation
RBC = red blood cell
ROOBY = Randomized On Versus Off Bypass
VA = Veterans Affairs

ACD

VA cooperative study conducted at 18 VA medical centers between February 2002 and May of 2008, enrolling 2203 patients. Data were prospectively collected by a dedicated research nurse at each participating institution. The ROOBY trial's primary short-term end point was a composite of death or complications (reoperation, new mechanical support, cardiac arrest, stroke, and renal failure) before hospital discharge or within 30 days. For 1-year follow-up, the primary ROOBY trial's longer term end point was a composite of all-cause death and repeat revascularization or nonfatal myocardial infarction occurring between 30 days and discharge up to 1-year follow-up. The details of the main ROOBY trial have been published.[7] Participating institutions are outlined in Appendix 1. The current study extracted ROOBY trial patient data to examine the predictors of POAF in the off-pump versus on-pump patient cohorts and the effect of atrial fibrillation (AF) on outcomes in patients overall and in both groups.

The ROOBY trial protocol, including the present subanalysis, was approved by each participating VA Medical Center's Institutional Review Board and Research and Development Office. Informed consent was obtained for each patient, and a Health Insurance Portability and Accountability Act waiver of authorization was provided.

MATERIALS AND METHODS

AF was defined as any abnormal atrially originated irregular rhythm lasting more than 30 minutes. Because this ROOBY trial subanalysis was focused to identify the predictors related to patients with new AF as a new postoperative complication, all patients with preoperative AF were excluded. Thus, a total of 2103 ROOBY trial patient records (95.5% of ROOBY trial enrollees, n = 2203) were extracted for this ROOBY trial subanalysis. As part of the original ROOBY trial, preoperative demographics, intraoperative practice parameters, and postoperative outcome data were collected. On the basis of each local center's standard of care, both off-pump and on-pump groups received comparable postoperative care, such as monitoring in the intensive care unit or telemetry ward until discharge from the hospital.

All ROOBY trial patients were closely followed by the research nurse every 2 months by phone until 1 year post-CABG when they were requested to return for follow-up coronary angiogram and neuropsychologic testing. Of the 2103 patients included in this subanalysis, 1636 (77.79%) returned for 1-year follow-up with a similar percentage between groups.

Statistical Methods

More than 100 variables (deemed clinically relevant to a patient's predisposition for POAF including preoperative clinical and laboratory parameters (Appendix 2) and off-pump versus on-pump strategy were compared using univariate analyses for patients with and without POAF complications. As appropriate to the ONCAB versus OPCAB treatment received, the intraoperative surgical variables and postoperative care variables data were assessed for a possible univariate association with POAF.

The 2 groups (with and without POAF) being used in this subanalysis means that only larger differences will be significant and that there is reduced power. Because this is a subanalysis with 2 comparison groups and multiple outcome measures, a P value of .01 is considered significant.

For univariate analyses, chi-square or Fisher exact tests were used to compare the patient subgroups for the discrete variables, and t tests or analysis of variance techniques were used for continuous variables. Log-rank tests with Kaplan–Meier curves were used to report time until death. Multivariable logistic regression analyses were used to identify predictors of POAF and to determine the significance of POAF on the 30-day and 1-year composite measures, holding other baseline patient characteristics constant. In separate analyses and in addition to on-pump versus off-pump treatment effect, variables with significant association with POAF on univariate analysis at $P = .05$ were entered into multivariate logistic regression model. Propensity matching techniques were used to corroborate the results of the multiple logistic regression findings.

RESULTS

Demographics and medical characteristics were similar in both groups at randomization. The incidence of POAF in the entire series was 26.2% (551 patients) ranging from 12.14% to 35.29% among the 18 participating centers. Patients in the POAF group were older than patients in the no POAF group (mean age, 65.3 ± 8.5 years vs 61.6 ± 8.2 years; $P < .0001$). POAF developed in 268 of 1056 patients (25.4%) in the ONCAB group and in 283 of 1047 patients (27%) in the OPCAB cohort ($P = .40$). Thus, there was no difference in POAF rates based on ONCAB versus OPCAB strategy of revascularization.

There was no difference between ONCAB and OPCAB groups regarding the postoperative day that AF occurred or the conversion back to a sinus rhythm (2.8 ± 2.3 days vs 2.7 ± 2.5 days, respectively, for POAF occurrence, $P = .84$, and 4.1 ± 2.9 days vs 4.0 ± 3.0 days for conversion, $P = .57$). Likewise, the use of prophylactic antiarrhythmic medications did not affect the incidence of POAF in either group. A total of 508 patients (92.2%) with POAF received medications for treatment of AF. Moreover, 95.3% of patients (range, 82.6%–100%) converted back to a sinus rhythm. Electrical cardioversion was required in 10.2% of patients (range, 0.0%–22.6%).

Across both revascularization strategies, there were several differences in the rates of complications observed between POAF and no POAF groups. Prolonged ventilatory support for more than 48 hours was required in 45 of 551

TABLE 1. Preoperative demographics of patients with and without postoperative atrial fibrillation

	All patients			ONCAB			OPCAB		
	POAF (551)	No POAF (1552)	*P* value	POAF (268)	No POAF (788)	*P* value	POAF (283)	No POAF (764)	*P* value
Age (y)	65.3 ± 8.5	61.6 ± 8.2	<.0001	65.4 ± 8.5	61.3 ± 8.3	<.0001	65.1 ± 8.5	62 ± 8.2	<.0001
HTN	494 (90%)	1218 (85%)	.005	242 (90%)	671 (85%)	.04	252 (89%)	647 (85%)	.07
COPD	130 (24%)	297 (19%)	.03	70 (26%)	153 (19%)	.02	60 (21%)	144 (19%)	.43
Diabetes	254 (46%)	664 (43%)	.19	128 (48%)	342 (43%)	.23	126 (44.5%)	322 (42%)	.53
Serum creatinine > 1.5	59 (11%)	106 (7%)	.006	27 (10%)	48 (6%)	.04	32 (11%)	58 (8%)	.06
PVD	105 (19%)	218 (14%)	.006	47 (17.5%)	109 (14%)	.16	58 (20.5%)	109 (14%)	.02
EF < 45%	80 (14.5%)	263 (17%)	.20	44 (16%)	135 (17%)	.85	36 (13%)	128 (17%)	.13
Current smoker	154 (28%)	561 (36%)	.001	78 (29%)	294 (37%)	.02	76 (27%)	267 (35%)	.04

ONCAB, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *POAF*, postoperative atrial fibrillation; *EF,* ejection fraction; *COPD,* chronic obstructive pulmonary disease; *HTN,* hypertension; *PVD,* peripheral vascular disease.

patients (8.2%) with POAF compared with 44 of 1551 patients (2.8%) with no POAF ($P < .0001$) . For the entire series, age, hypertension, renal dysfunction with a serum creatinine greater than 1.5, and peripheral vascular disease were all associated with POAF on univariate analysis (Table 1). Table 1 also shows comparison of ONCAB and OPCAB groups.

By using nonparametric test (Wilcoxon test) for the comparison of POAF versus no POAF for units of red blood cells (RBCs) and fresh-frozen plasma (FFP) transfused and volume of salvaged blood reinfused, the parameters associated with POAF in the entire series included more use of packed RBCs, FFP, and higher volume of salvaged blood reinfused: RBC 1.2 ± 2 units POAF, 0.9 ± 1.7 units no POAF, $P = .0009$; FFP 0.6 ± 1.5 units POAF, 0.4 ± 1.3 units no POAF, $P = .001$; salvaged blood 582 ± 513 mL POAF, 504 ± 464 mL no POAF, $P = .001$. For the OPCAB group, the corresponding values were RBC 1.3 ± 2.1 units POAF, 0.9 ± 1.6 units no POAF, $P = .001$; FFP 0.7 ± 1.7 units POAF, 0.4 ± 1.1 units no POAF, $P = .003$; salvaged blood 607 ± 529 mL POAF, 513 ± 481 mL no POAF, $P = .001$. For the OPCAB group, a higher volume of salvaged blood reinfusion was associated with a higher rate of conversion ($P < .0001$), take-down and redo of distal anastomoses ($P = .0003$), and excessive bleeding ($P = .006$). In contrast, no association was found between transfusion and POAF in the ONCAB group ($P > .02$). Cardiopulmonary bypass time, aortic crossclamp time, use of cardioplegia and mode of delivery, composition of cardioplegia solution, and topical ice slush or cold saline irrigation were not associated with a higher incidence of POAF in the ONCAB group.

In the postoperative period in both the ONCAB and OPCAB groups, there was a higher rate of prolonged ventilatory support, reintubation, and any early adverse outcome with POAF (Table 2). There were 20 strokes in this series of 2103 patients for an incidence of 1.0%. Of these, 9 patients (1.6%) in the POAF group had a stroke versus 11 patients (0.7%) in the no POAF group ($P = .07$). Patients with POAF had a longer hospital stay (13.2 vs 10.3 days, $P < .0001$).

The 1-year all cause mortality rate for POAF was 5.2% vs 2.3% in the no POAF group ($P <$. 001). In the ONCAB group, the 1-year mortality was 5.4% for the POAF group versus 2% for the no POAF group ($P = .009$). This difference was not statistically significant for the OPCAB group, in which the mortality was 5.1% in the POAF group vs 2.6% in no POAF group ($P = .07$). Kaplan–Meier survival curves at 1 year for the entire series and each subgroup of ONACB and OPCAB are depicted in Figure 1.

For all patients, logistic regression analysis revealed older age ($P <.0001$), white race ($P <.0006$), and hypertension ($P < .002$) as predictors of POAF. Revascularization

TABLE 2. Thirty-day postoperative outcomes

	ONCAB			OPCAB		
Variables	POAF (%) 268	No POAF (%) 788	*P* value	POAF (%) 283	No POAF (%) 764	*P* value
Operative mortality	6 (2)	6 (0.8)	.09	6 (2)	6 (0.80)	.10
Reoperation for bleeding	6 (2)	17 (2)	1.00	16 (6)	14 (2)	.003
New mechanical support	4 (1.5)	4 (0.5)	.12	8 (3)	7 (0.09)	.04
Any reoperation	9 (3)	21 (3)	.53	16 (6)	18 (2)	.01
Reintubation	17 (6)	14 (2)	.001	21 (7.4)	14 (2)	<.0001
Prolonged ventilatory support	19 (7)	18 (2)	.001	26 (9)	26 (3)	<.0003
Renal failure	5 (2)	3 (0.4)	.03	6 (2)	3 (0.40)	.01
Any early outcome	24 (9)	34 (4)	.008	31 (11)	39 (5)	.001

ONCAB, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *POAF*, postoperative atrial fibrillation.

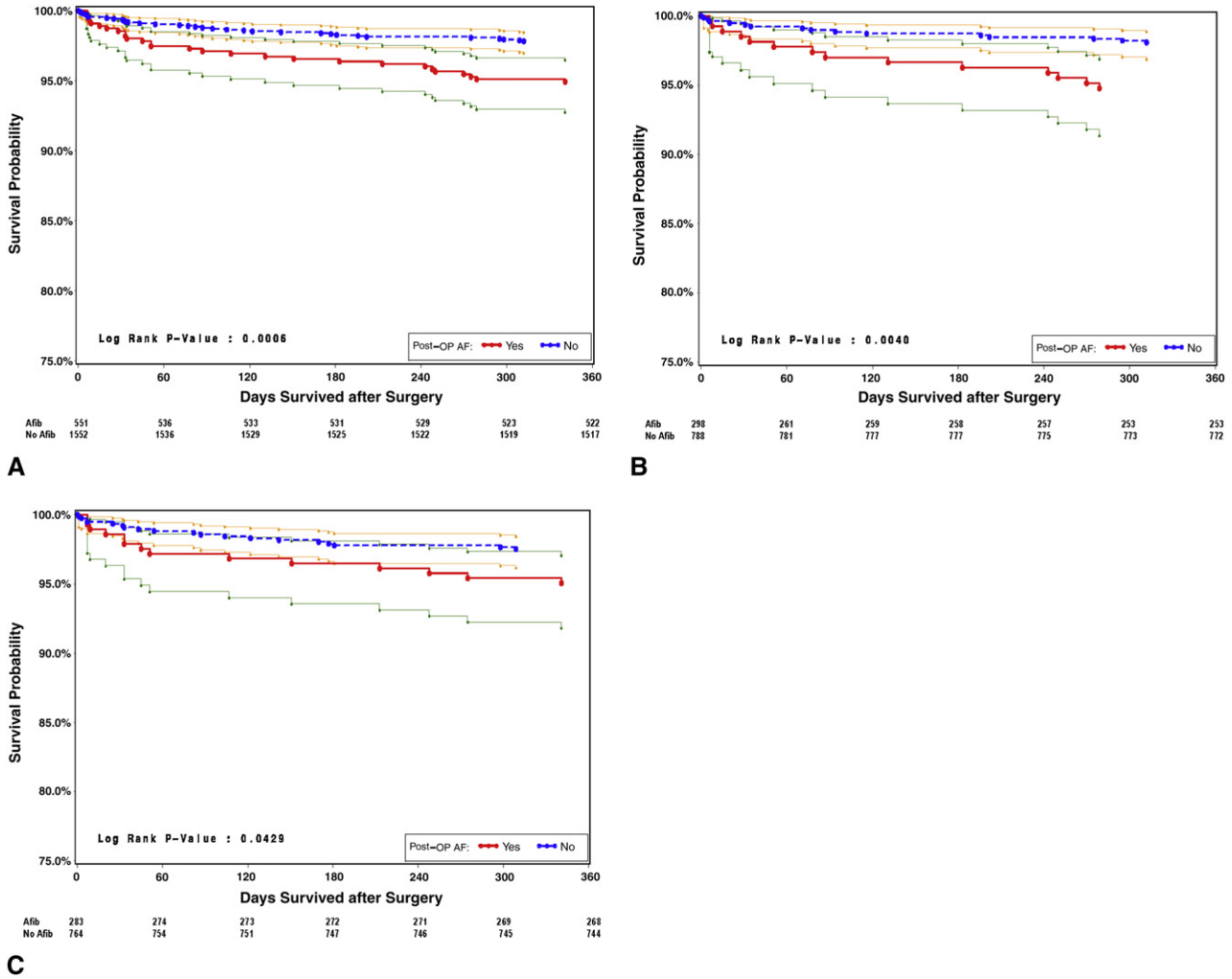

FIGURE 1. One-year survival of patients with and without POAF (*green* represents 95% CI for POAF; *yellow* represents 95% CI for no POAF). A, All patients. B, ONCAB group. C, OPCAB group. *Afib,* Atrial fibrillation.

strategy was not a predictor of POAF. Older age ($P < .001$) was the only predictor in the OPCAB group (Table 3). In addition to the off-pump versus on-pump treatment effect and on the basis of univariate screening, all variables identified with an association with the presence/absence of AF at $P < .05$ were deemed eligible for entry into a multivariable logistic model. The logistic regression model's predictive power, as measured by the c-index, was estimated at 0.664. Older age, white race, and hypertension were the only predictors of POAF on this propensity model approach.

In separate regression analyses of early and late outcomes using the treatment group and POAF as independent variables in addition to age, race, and hypertension, POAF was independently associated with early composite end point (odds ratio [OR], 2.23; confidence interval [CI], 1.55–3.22; $P < .0001$), need for new mechanical support (OR, 3.25; CI, 1.39–7.61; $P = .007$), prolonged ventilatory

TABLE 3. Predictors of postoperative atrial fibrillation

	All patients			ONCAB			OPCAB		
Variable	**OR**	**99% CI**	***P* value**	**OR**	**99% CI**	***P* value**	**OR**	**99% CI**	***P* value**
Age	1.044	1.03–1.058	<.0001	1.	1.03–1.07	<.0001	1.	1.01–1.053	<.0009
White race	1.831	1.30–2.58	<.001	2.2	1.31–3.78	.003	1.5	0.94–2.39	.08
Hypertension	1.760	1.23–2.50	<.002	1.9	1.14–3.22	.01	1.6	1.–2.66	.05

ONCAB, On-pump coronary artery bypass; *OPCAB*, off-pump coronary artery bypass; *OR*, odds ratio; *CI*, confidence interval.

support (OR, 2.93; CI, 1.89–4.55; $P < .0001$), renal failure (OR, 5.42; CI, 1.94–15.15; $P = .001$), and mortality at 12 months (OR, 1.94; CI, 1.14–3.28; $P = .01$). Treatment group was not a factor.

DISCUSSION

AF continues to be a common problem after coronary artery bypass surgery. A lower incidence of POAF has been quoted as one of the advantages of beating heart surgery by the advocates of OPCAB technique.[5,8] The literature contains conflicting reports regarding POAF in patients undergoing OPCAB versus ONCAB.[9,10] The present report is the largest randomized comparison of patients undergoing ONCAB and OPCAB in whom the data for the POAF and its management were prospectively collected from the early stages in the study. In addition, patients' characteristics were similar at randomization. The treatment group did not have an impact on the incidence of POAF. In a recent report of long-term follow-up of patients in the MASS III trial, the incidence of POAF in those undergoing OPCAB was 35% versus 4% for those undergoing ONCAB.[11] The low incidence of POAF in the ONCAB group in the MASS III trial was attributed to the routine administration of corticosteroids to patients undergoing ONCAB, although the methods of postoperative monitoring were not detailed in this study.

In almost all reported series, older age has been a risk factor for the development of POAF.[1,2,4,6] Development of fibrosis in the atria and structural changes in the heart associated with aging may be some of the contributing factors for a higher incidence of POAF in older patients.[12,13] In the current series and for both groups, older age was a predictor of POAF.

White race was associated with a significantly higher incidence of POAF. The association of race and POAF has not been well reported in the literature. Most studies are from population survey or epidemiologic studies. In the Large Health Survey of Veteran Enrollees in 664,754 male responders, the age-adjusted prevalence of AF was 5.7% in whites versus 3.4% in blacks and 3% in Hispanics.[14] Another study using pooled data from 3 cohort studies with adjustment for potential confounders found 3.8-fold greater odds for whites having AF than African Americans.[15] White race was associated with a higher rate of POAF in a recent large retrospective study.[4]

The use of cardiopulmonary bypass, right atrial cannulation, and the systemic inflammatory response have all been cited as reasons for a purportedly higher incidence of POAF in patients undergoing ONCAB.[5,16] Our report is the first large-scale, prospectively randomized study to show that patients undergoing coronary revascularization with the OPCAB technique did not have a lower incidence of POAF than patients undergoing ONCAB. In support of this finding is the fact that cardiopulmonary bypass was not found to be associated with POAF on univariate or multivariable analysis. Moreover, the method of myocardial protection in ONCAB group had no impact on the incidence of POAF. This implies that the mechanism of POAF is not related to the cannulation of the atrium per se or the cardiopulmonary bypass. In fact, the ONCAB group received more grafts and had a longer operative time, yet the AF rate was slightly lower than in the OPCAB group. Possible left atrial stretching with heart dislocation during coronary revascularization has been suggested as one theoretic mechanism for a higher rate of POAF in patients undergoing OPCAB.[11]

The association of postoperative blood transfusion and POAF has been reported in the literature.[17] Reinfusion of a higher volume of salvaged blood for patients undergoing OPCAB was associated with a higher rate of POAF. This may be related to technical difficulties in the operating room and excessive bleeding encountered. POAF has been associated with a higher incidence of stroke in cardiac surgical patients.[4,18,19] Overall, the stroke rate was low in this series (20 patients, 1%). Although not statistically significant, the stroke rate in patients with POAF appeared to be trending higher compared with patients with no AF (1.6% vs 0.7%, $P = .07$). However, no definitive statements related to these treatment arm comparisons could be made because of low numbers of perioperative stroke in both treatment groups.

Patients with POAF had a longer hospital stay. This is consistent with other reports in the literature.[2,4] POAF was associated with a higher rate of in-hospital mortality (5.8% vs 2.2%, $P = .003$). The mortality rate at 1 year was higher in those with POAF in both the ONCAB and the OPCAB groups, although the P value for the OPCAB group did not reach statistical significance. An increased rate for 6-month mortality with POAF was first reported by our coauthor team in an earlier publication.[1] Subsequent reports have confirmed that POAF is a predictor of late mortality in patients undergoing CABG.[20] The reasons behind this increased mortality are not well understood, but older age may be one factor (Table 1).

In conclusion, in this large prospective randomized ROOBY trial's substudy, an OPCAB versus ONCAB technique had no impact on the incidence of POAF. Older age, white race, and hypertension were predictors of POAF. Regardless of the revascularization strategy, POAF was associated with a higher early adverse outcome and a lower 1-year survival. Given the limited successes to-date with existing treatment approaches, it is imperative to develop and evaluate new strategies to prevent the occurrence of postoperative AF that may lead to improved short-term outcome and long-term survival in patients undergoing CABG.

Limitations

As with any VA-based study, the almost all male population enrolled was typical of the veterans who received

CABG procedures during the study time frame. Therefore, no conclusions can be drawn for female patients. However, this study reflects the typical cardiac surgical practice for most VA-based surgeons across different VA medical centers, given the diversity of POAF-related practice patterns reported. Because such no statements can be made regarding the wide range of POAF seen among the participating centers, these findings are in contradistinction to other published smaller series reported by a single surgeon or a single institution, where the single-center's data may not be broadly generalizable to a community practice setting.

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Discussion

Dr David McGiffin *(Birmingham, Ala)*. The investigators in the ROOBY trial and the authors of this substudy are to be congratulated for taking on this important project, the results of which will be of benefit to all of us.

At first glance, this study would seem to be straightforward. However, in reality, it does have a number of methodological and analytic conundrums, and I would like you to respond to a couple of concerns that I have, and we will deal with them one at a time.

My first concern is about the relationship between postoperative AF and the early postoperative outcome events that you examined, including reintubation and renal failure. The use of the phrase ''impact of postoperative atrial fibrillation on outcomes,'' which appears in the abstract, and the word ''impact,'' which appears in your title, implies cause and effect. However, as far as I can see from the presentation, it is possible that the outcome event may have occurred before the episode of postoperative AF, and furthermore, postoperative AF is frequently part of the clinical presentation of a number of outcome events, including respiratory failure. Are you implying cause and effect, and if so, could you reconcile the inference of cause and effect with the realities of the study?

Dr Almassi. In regard to the cause and effect, it is really difficult, like the chicken and egg question, which one came first, but in terms of the incidence of AF, we have the occurrences, as I showed here, when it occurred. But in terms of the AF, I don't have the data to show when, for example, renal failure developed. However, the reintubation and mechanical support, prolonged mechanical support beyond 48 hours, would indicate that AF probably happened earlier, but I don't have the data to show that that is in fact the case. Because the patients were similar in baseline characteristics at randomization, it would seem that postoperative AF may be the cause rather than the effect, although, as I said, with the data as they are, I cannot state with certainty that is the case.

Dr McGiffin. So my summary of that would be that before claiming cause and effect or impact, this would require considerably more analysis?

Dr Almassi. We can certainly see association. I agree with you.

Dr McGiffin. Another concern is the suggestion from your presentation that the occurrence of postoperative AF is a determinant of survival 12 months after operation, which is implied from your Kaplan–Meier curves of survival, stratified by the presence or absence of postoperative AF. I think one could fairly ask the question, what does 30 minutes of postoperative AF have to do with increased probability of dying over the next 12 months? An alternative explanation is that postoperative AF is really a marker for an as yet unidentified cause of death. I think that before concluding that the occurrence of postoperative AF directly and adversely affects survival 12 months after surgery, a thorough investigation of the late causes of death and their relationship to postoperative AF would need to be undertaken. If you are hypothesizing a cause-and-effect relationship between postoperative AF and late

mortality, do you have the information about late causes of death that would lead you to this inference?

Dr Almassi. We do not have the causes of late death. However, we did a number of multivariate analyses in terms of the different effects, such as the cardiopulmonary bypass circuit and the interaction between the technique of surgery versus other factors, and in all of these, AF stood out as the significant factor rather than other causes. However, because we do not have the exact cause of death in the patients who died, I could not give an answer in terms of why they died.

However, the available information in the literature, which is mainly from retrospective analysis and some data from Italy on autopsy of patients who died postoperatively in AF, indicates that most of the deaths in those retrospective studies were cardiac.

Dr McGiffin. So perhaps it would be fair to say that we need to temper the inference that there is a cause-and-effect relationship between early postoperative AF and late mortality at this stage?

Dr Almassi. Yes.

Dr McGiffin. Finally, I think you have put to rest the idea that postoperative AF is caused by purely atrial cannulation for cardiopulmonary bypass and the consequences of myocardial protection in the ONCAB group. One possible mechanism of postoperative AF that is common to both the ONCAB and OPCAB techniques is pericardial inflammation. Now, this would seem to have support from animal models in which AF can be readily induced by pericardial inflammation and the known efficacy of corticosteroids in preventing postoperative AF.

In light of your findings, what are your thoughts on the mechanism of postoperative AF and are there perioperative measures that you would recommend to reduce the incidence of postoperative AF?

Dr Almassi. We do not know the exact mechanism of postoperative AF. There are no available studies that have shown that. Therefore, any strategies that have been used—and there is plenty of information in the literature on various strategies, atrial pacing, as we yesterday heard about biatrial pacing, different medications that are used, method of use of medication, length of preoperative use, and intra- and postoperative use—everything has been tried, and none have proven successful in preventing postoperative AF. In our analysis we have looked at the perioperative use of antiarrhythmic medications, and that did not seem to have an impact on the postoperative AF incidence. As you mentioned, cardiopulmonary bypass and the method of myocardial preservation in the ONCAB group did not have any effect on the rate of AF. So I am not sure that I have any strategy to prevent postoperative AF at this time.

Dr Niv Ad *(Falls Church, Va)*. I have 2 issues that I believe would require clarifications. The definition of AF as an event of 30 minutes or longer is unique. Can you tell us how did you decide to define it in such a way? It is hard to believe that a short event would have an impact and 30 minutes can't be compared with 1 hour and longer.

The second comment I have is related to your conclusions with regard to the future treatment of POAF. It seams to me that the data should be analyzed further because some of centers had only an approximately 10% rate of postoperative AF, whereas the others had more than 30%. This leads to a potential bias in which not all centers treated their patients the same and the management of perioperative antiarrhythmic drugs across all centers was different?

Dr Almassi. No, it was not. Every center for the 2 groups in the study used their standard of care at each center. That doesn't mean that all centers used the same protocol, no.

In terms of the incidence of AF, as I showed among centers here, it was from 12.14% to 35%. Some of the reported incidences depend on the method of monitoring patients and the extent of monitoring. If a patient is only monitored in the intensive care unit and then on the stepdown or telemetry unit, there is no monitoring, just relied on physical examination and an occasional electrocardiogram, clearly the incidence of postoperative AF is going to be underestimated. To enter into the study in terms of following patients with AF, we used a minimum of 30 minutes being in AF. That doesn't mean that patients converted to sinus rhythm immediately. We didn't want to include any patients who developed AF for 1 or 2 minutes to be included in this study. Therefore, we used that definition, more than 30 minutes.

Dr Ad. Okay, thank you, but I believe that you should include those 2 points in your study limitations.

Dr Almassi. Okay.

Dr Richard Shemin *(Los Angeles, Calif)*. I want to echo the concerns that Dr Ad brought up, the variation in preoperative prophylaxis and the variation in the study from 10% to 30%. Again, I am concerned about the definition. We are measuring a postoperative outcome of AF, and I am still not sure what 30 minutes of AF means. If someone goes into AF in the intensive care unit or on the floor and they get amiodarone and they convert within 10 minutes, does that mean they did not have AF?

Dr Almassi. For the study, that doesn't mean they didn't have AF. Yes, they did. But to include them in this study for the sake of follow-up, we picked 30 minutes. You can pick a minute or any episode of AF. For this study, for the numbers that we have, which is large enough, those patients who had AF were similar at baseline and after randomization, but the outcome was not as good as the patients with no postoperative AF. That is the message that our data show.

Dr Frank Baciewicz *(Detroit, Mich)*. The Society of Thoracic Surgery in Michigan looks at all the differences between hospitals, and one of the things they look at is AF, which has been looked at carefully. We have not been able to glean out any differences in why one hospital has a 10% and one has a 30% rate of AF. Have you been able to glean that out? I know you mentioned that the monitoring certainly makes a difference, and our data were looked at carefully and we can't seem to find anything. Could you find any difference between the hospitals to explain this variation?

Dr Almassi. I don't have those data, no. But when we looked at each individual hospital, there was no difference in AF between the patients who underwent OPCAB versus the on-pump group. That we know. But in terms of the practice for each individual hospital, I don't have those data, no.

APPENDIX 1. ROOBY participating centers

ROOBY trial participating medical centers	Principle investigator	Study coordinator
VA Medical Center, Albuquerque, NM	Stuart Pett, MD	Jeannie Coltz, RN
VA Medical Center, Asheville, ND	John Lucke, MD	Mariette Coyle, RN
VA Medical Center, Cleveland, Ohio	Diana Whittlesey, MD	Barbara Bauer, RN
VA Medical Center, Dallas, Tex	Michael Jessen, MD	Wanda Frey, RN
VA Medical Center, Denver, Colo	Joseph Cleveland, MD	Shauna Brennan, RN
VA Medical Center, Durham, NC	Shu Lin, MD	Jean Kistler, RN
VA Medical Center, Gainesville, Fla	Edward Staples, MD	Jan Hutchinson, RN
VA Medical Center, Los Angeles, Calif	Abbas Ardehali, MD	Eileen Ziff, RN
VA Medical Center, Manhattan, NY	Eugene Grossi, MD	Estelita Antoeola, RN
VA Medical Center, Miami, Fla	Kushagra Katariya MD	Michele Landi, RN
VA Medical Center, Milwaukee, Wis	G. Hossein Almassi, MD	Sharon Pecsi, RN
VA Medical Center, Palo Alto, Calif	Thomas Burden, MD	Gerald Georgette, RN
VA Medical Center, Pittsburg, Pa	Marco Zenati, MD	Jennifer Gabany, RN
VA Medical Center, Portland, Ore	Passala Ravichandran, MD	Karina Dana, RN
VA Medical Center, San Antonio, Tex	Edward Sako, MD	Regina Whitener, RN
VA Medical Center, Tampa, Fla	Dimitri Novitzky, MD	Jennifer Shippy, RN
VA Medical Center, Washington, DC	Pendleton Alexander, MD	Mary Bloom, RN

APPENDIX 2. Variables used for analyses

Variable	Measurement
Baseline/preoperative variables	
1. Age	y
2. Race	
3. No. of previous cardiac surgeries requiring CPB	No.
4. No. of previous cardiac surgeries not requiring CPB	No.
5. No. of previous cardiac surgical procedures	No.
6. Ejection fraction	
7. Elective surgery	Yes – No
8. Valve disease	Yes – No
9. Mitral valve regurgitation	Yes – No
10. Mitral valve stenosis	Yes – No
11. Aortic valve regurgitation	Yes – No
12. Aortic valve stenosis	Yes – No
13. Left ventricular aneurysm	Yes – No
14. COPD	Yes – No
15. Serum creatinine > 1.5 mg/dL	Yes – No
16. Direct bilirubin > 0.5 mg/dL	Yes – No
17. CVA	Yes – No
18. Peripheral vascular disease	Yes – No
19. Diabetes	Yes – No
20. Hypertension	Yes – No
21. Hyperlipidemia	Yes – No
22. Other major comorbidity	Yes – No
23. CPK–MB	% of total; ng/mL; or IUL
24. Total CPK	U/L
25. Troponin I	ng/mL
26. C–reactive protein	mg/dL
27. Smoking history	Never, former, current
28. Previous revascularization by CABG	Yes – No
29. Beta–blocker use	Yes – No
30. ACE inhibitor use	Yes – No
31. Lipid-lowering medication use	Yes – No
32. Received prophylactic antiarrhythmics	Yes – No
33. Timing of prophylactic antiarrhythmics	Day of surgery, 1 d preoperatively, >1 d preoperatively
34. Current smoker	Yes – No
Intraoperative assessments	
35. Lowest hematocrit during surgery	%
36. Units of packed RBC used	No. units
37. Units of FFP transfused	No. units
38. Unites of platelets transfused	No. units
39. Volume of salvaged blood transfused	No. units
40. Units of cryoprecipitate	No. units
41. Cell saver used	Yes – No
42. Pump sucker used	Yes – No
43. Amicar used intraoperatively	Yes – No
44. DDAVP used intraoperatively	Yes – No
45. Aprotinin used intraoperatively	Yes – No
46. Other antifibrinolytic agent used intraoperatively	Yes – No
47. Lowest systemic temperature	Degrees C
48. Heparin-bonded circuit used	Yes – No
49. Coated system used	Yes – No
50. Coating tip to tip when coating used	Yes – No
51. Lowest core temperature	Degrees C
52. Any intraoperative complications	Yes – No
53. New mechanical support requiring IABP	Yes – No
54. New mechanical support requiring ventricular assist device	Yes – No
55. Excessive bleeding require > 4 units packed RBCs	Yes – No
56. Take–down and redo distal anastomoses	Yes – No
57. Cardiac arrest or ventricular fibrillation after arrival in operating room	Yes – No
58. Chest left open after surgery	Yes – No
59. Conversion to other treatment arm	Yes – No
60. Any other major complications	Yes – No
61. No myocardial preservation technique for patients on CPB	Yes – No
62. Cold antegrade cardioplegia for patients on CPB	Yes – No
63. Warm antegrade cardioplegia for patients on CPB	Yes – No
64. Cold retrograde cardioplegia for patients on CPB	Yes – No
65. Warm retrograde cardioplegia for patients on CPB	Yes – No
66. Fibrillatory arrest for patients on CPB	Yes – No
67. Topical cold saline for patients on CPB	Yes – No
68. Topical ice slush for patients on CPB	Yes – No
69. Heart jacket for patients on CPB	Yes – No
70. Myocardial temperature monitoring for patients on CPB	Yes – No
71. Myocardial pH monitoring for patients on CPB	Yes – No
72. Composition of cardioplegia for patients on CPB	None, blood, crystalloid, both
73. Total bypasses performed	No.
74. CPB time	min
75. Aortic crossclamp time	min
Postoperative assessments	
76. CPK–MB	% of total; ng/mL; or IUL
77. CPK total	U/L
78. Troponin I	ng/mL
79. No inotropic agent used for > 24 h	Yes – No
80. Dopamine used for > 24 h	Yes – No
81. Dobutamine used for > 24 h	Yes – No
82. Epinephrine used for > 24 h	Yes – No
83. Norepinephrine used for > 24 h	Yes – No
84. Amrinone used for > 24 h	Yes – No

(Continued)

APPENDIX 2. Continued

Variable	Measurement
85. Other inotropic agent used for > 24 h	Yes – No
86. IABP time	h
87. Ventricular assist device time	h
88. Units of RBC transfused during first 48 h	No. units
89. Units of FFP transfused during first 48 h	No. units
90. Units of platelets transfused during first 48 h	No. units
91. Units of cryoprecipitate during first 48 h	No. units
92. C-reactive protein	mg/dL
93. History of AF before surgery	Yes – No
94. Postoperative CVA/stroke	Yes – No
95. Days CVA/stroke developed postoperatively	d
96. Patient reintubated	Yes – No
97. Redo CABG	Yes – No
98. Prophylactic antiarrhythmics given	Yes – No
99. Amiodarone given	Yes – No
100. Beta–blocker given	Yes – No
101. Both amiodarone and beta–blocker given	Yes – No
102. Other antiarrhythmic given	Yes – No
103. POAF	Yes – No
104. Day POAF developed	
105. Prolonged ventilator support	Yes – No
106. Tracheostomy	Yes – No
107. Any early outcome	Yes – No
108. Any late outcome	Yes – No
109. Death 12 mo	Yes – No
110. Myocardial infarction, 12 mo	Yes – No
111. Revascularization, 12 mo	Yes – No

CPB, Cardiopulmonary bypass; *COPD,* chronic obstructive pulmonary disease; *CVA,* cerebrovascular accident; *CPK-MB,* creatine phosphokinase-MB; *ACE,* angiotensin-converting enzyme; *DDAVP,* desmopressin; *IABP,* intraaortic balloon pump.