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# New-Onset Atrial Fibrillation After PCI or CABG for Left Main Disease

## The EXCEL Trial

Ioanna Kosmidou, MD, PhD,[a,b] Shmuel Chen, MD,[a] A. Pieter Kappetein, MD, PhD,[c] Patrick W. Serruys, MD, PhD,[d] Bernard J. Gersh, MB, ChB, DPhil,[e] John D. Puskas, MD,[f] David E. Kandzari, MD,[g] David P. Taggart, MD,[h] Marie-Claude Morice, MD,[i] Paweł E. Buszman, MD, PhD,[j,k] Andrzej Bochenek, MD,[j,k] Erick Schampaert, MD,[l] Pierre Pagé, MD,[l] Joseph F. Sabik III, MD,[m] Thomas McAndrew, PhD,[a] Björn Redfors, MD, PhD,[a] Ori Ben-Yehuda, MD,[a,n] Gregg W. Stone, MD[a,n]

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**CME/MOC Objective for This Article:** Upon completion of this activity, the learner should be able to: 1) describe the incidence and predictors of new-onset atrial fibrillation following PCI and CABG; 2) define the impact of post-operative new-onset atrial fibrillation on the long-term risk of death and stroke following revascularization for left main disease; and 3) consider the impact that strategies to prevent, monitor for and treat new-onset atrial fibrillation may have on improving the prognosis of patients undergoing surgical revascularization for left main disease.

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From the [a]Clinical Trials Center, Cardiovascular Research Foundation, New York, New York; [b]Arrhythmia Center, Department of Cardiology, St. Francis Hospital, Roslyn, New York; [c]Thoraxcenter, Erasmus Medical Center, Rotterdam, the Netherlands; [d]Imperial College of Science, Technology and Medicine, London, United Kingdom; [e]Department of Cardiovascular Medicine, Mayo Clinic College of Medicine, Rochester, Minnesota; [f]Icahn School of Medicine at Mount Sinai, New York, New York; [g]Piedmont Heart Institute, Atlanta, Georgia; [h]Department Cardiac Surgery, John Radcliffe Hospital, Oxford, United Kingdom; [i]Ramsay Générale de Santé, Institut Cardiovasculaire Paris Sud, Paris, France; [j]Medical University of Silesia, Katowice, Poland; [k]American Heart of Poland, Ustron, Poland; [l]Hôpital du Sacré-Coeur de Montréal, Montréal, Canada; [m]Department of Surgery, UH Cleveland Medical Center, Cleveland, Ohio; and the [n]NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, New York. The EXCEL trial was funded by Abbott Vascular. Dr. Kappetein is an employee of Medtronic. Dr. Serruys is a consultant for Abbott Laboratories, AstraZeneca Pharmaceuticals, Biotronik, Cardialysis B.V., GLG Research, Medtronic, Sino Medical Sciences Technology, Inc., Société Europa Digital & Publishing, Svelte Medical Systems, Inc., Volcano Europe B.V.B.A., and Q3Medical Devices, Ltd. Dr. Gersh is a consultant for Boston Scientific and Medtronic. Dr. Kandzari has received grant support from Abbott Vascular, Boston Scientific, Medtronic, Biotronik, and Medinol; and is a consultant for Boston Scientific, Medtronic, Micell Technologies, and Biotronik. Dr. Schampaert is a consultant for Abbott Vascular, Boston Scientific, Medtronic, and Philips Medical. Dr. Sabik III is a consultant for Medtronic, Edwards Lifesciences, and Sorin. Dr. Stone's employer, Columbia University, receives

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# New-Onset Atrial Fibrillation After PCI or CABG for Left Main Disease

## The EXCEL Trial

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**ABSTRACT**

**BACKGROUND** There is limited information on the incidence and prognostic impact of new-onset atrial fibrillation (NOAF) following percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for left main coronary artery disease (LMCAD).

**OBJECTIVES** This study sought to determine the incidence of NOAF following PCI and CABG for LMCAD and its effect on 3-year cardiovascular outcomes.

**METHODS** In the EXCEL (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial, 1,905 patients with LMCAD and low or intermediate SYNTAX scores were randomized to PCI with everolimus-eluting stents versus CABG. Outcomes were analyzed according to the development of NOAF during the initial hospitalization following revascularization.

**RESULTS** Among 1,812 patients without atrial fibrillation on presentation, NOAF developed at a mean of 2.7 ± 2.5 days after revascularization in 162 patients (8.9%), including 161 of 893 (18.0%) CABG-treated patients and 1 of 919 (0.1%) PCI-treated patients ($p < 0.0001$). Older age, greater body mass index, and reduced left ventricular ejection fraction were independent predictors of NOAF in patients undergoing CABG. Patients with versus without NOAF had a significantly longer duration of hospitalization, were more likely to be discharged on anticoagulant therapy, and had an increased 30-day rate of Thrombolysis In Myocardial Infarction major or minor bleeding (14.2% vs. 5.5%; $p < 0.0001$). By multivariable analysis, NOAF after CABG was an independent predictor of 3-year stroke (6.6% vs. 2.4%; adjusted hazard ratio [HR]: 4.19; 95% confidence interval [CI]: 1.74 to 10.11; $p = 0.001$), death (11.4% vs. 4.3%; adjusted HR: 3.02; 95% CI: 1.60 to 5.70; $p = 0.0006$), and the primary composite endpoint of death, MI, or stroke (22.6% vs. 12.8%; adjusted HR: 2.13; 95% CI: 1.39 to 3.25; $p = 0.0004$).

**CONCLUSIONS** In patients with LMCAD undergoing revascularization in the EXCEL trial, NOAF was common after CABG but extremely rare after PCI. The development of NOAF was strongly associated with subsequent death and stroke in CABG-treated patients. Further studies are warranted to determine whether prophylactic strategies to prevent or treat atrial fibrillation may improve prognosis in patients with LMCAD who are undergoing CABG. (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization [EXCEL]; NCT01205776)
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Recent randomized trials have suggested that percutaneous coronary intervention (PCI) with contemporary drug-eluting stents is an acceptable alternative to coronary artery bypass graft surgery (CABG) for selected patients with left main coronary artery disease (LMCAD) (1,2). As such, identification of pre-procedural and post-procedural factors that affect outcomes after both revascularization modalities may affect the choice between PCI and CABG. New-onset atrial fibrillation (NOAF) is a common post-operative complication of CABG, and in earlier studies (mostly in patients with multivessel disease), NOAF was associated with prolonged hospitalization, increased rates of adverse events, and greater health care costs (3,4). A recent analysis from the MAIN-COMPARE registry (Revascularization for Unprotected Left MAIN Coronary Artery Stenosis: COMparison of Percutaneous Coronary Angioplasty versus Surgical REvascularization From Multi-Center Registry) in Asia reported that pre-operative atrial fibrillation (AF) was a predictor of long-term morbidity and mortality after CABG in patients with LMCAD (5); however, the incidence and prognostic impact of NOAF following contemporary PCI and CABG in patients with LMCAD in sinus rhythm are largely unknown. In the present study, we sought to determine the incidence, predictors, and outcomes of NOAF in patients with LMCAD who underwent percutaneous or surgical revascularization in the randomized EXCEL trial (Evaluation of XIENCE Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization).

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## METHODS

**STUDY DESIGN AND ENDPOINTS.** The design of the EXCEL trial has been reported previously (1,6). In brief, EXCEL was an international, multicenter, randomized trial that compared everolimus-eluting stents with CABG in patients with LMCAD and low or intermediate SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) scores (≤32) in whom equipoise for revascularization with both techniques was present after heart team review. Randomization was performed with the use of an interactive voice-based or Internet-based system in block sizes of 16, 24, or 32, with stratification according to diabetes (present vs. absent), SYNTAX score (≤22 vs. ≥23), and study center. The goal of PCI was complete revascularization of all ischemic territories with fluoropolymer-based cobalt-chromium everolimus-eluting stents (Xience, Abbott Vascular, Santa Clara, California). CABG was performed with or without cardiopulmonary bypass according to the discretion of the operator, with the goal of complete anatomic revascularization of all vessels ≥1.5 mm in diameter with ≥50% diameter stenosis; the use of multiple arterial grafts was strongly recommended. Beta-blockers (or amiodarone for patients with contraindications to beta-blocker use) were recommended for pre-operative prophylaxis of post-operative AF in the surgical arm of the trial. All CABG-treated patients were to receive beta-blockers post-procedure unless contraindicated. Amiodarone use for 5 days post-CABG was also allowed in all patients for rhythm control according to the local standard of care. Use of other medications in the PCI and CABG arms of the trial has been described previously (1,6).

The primary endpoint was a composite of death from any cause, stroke, or myocardial infarction (MI) at 3 years. Major powered secondary endpoints included the primary composite endpoint at 30 days and the composite of death, stroke, MI, or ischemia-driven revascularization at 3 years. Additional secondary endpoints included the components of the primary and secondary endpoints at 30 days and 3 years, stent thrombosis and symptomatic graft stenosis or occlusion at 30 days and 3 years, and periprocedural major adverse events occurring within 30 days, all as previously defined (1,6). NOAF was defined as the occurrence of any episode of AF or flutter (collectively termed AF for this analysis) following the index procedure through the time of discharge that lasted at least 30 s and was captured on a standard 12-lead electrocardiogram or cardiac telemetry, or that required medical treatment.

The investigation was approved by the Institutional Review Board or Ethics Committee at each participating center, and all patients signed written informed consent forms. Major endpoints were adjudicated by an independent clinical events committee (Cardiovascular Research Foundation, New York, New York). Angiographic analyses were performed at an angiographic core laboratory (Cardiovascular Research Foundation). Follow-up is currently complete for all patients through 3 years. Median follow-up for clinical outcomes was 3 years.

**STATISTICAL METHODS.** For the purpose of this study, arrhythmic events during the hospitalization following the index CABG or PCI procedure were analyzed. All analyses were performed in the

### ABBREVIATIONS AND ACRONYMS

**AF** = atrial fibrillation or flutter
**BMI** = body mass index
**CABG** = coronary artery bypass grafting
**CI** = confidence interval
**HR** = hazard ratio
**LMCAD** = left main coronary artery disease
**LVEF** = left ventricular ejection fraction
**MI** = myocardial infarction
**NOAF** = new-onset atrial fibrillation or flutter
**PCI** = percutaneous coronary intervention

**TABLE 1 Baseline Characteristics According to the Development of In-Hospital New-Onset Atrial Fibrillation**

| | NOAF (n = 162) | No NOAF (n = 1,650) | p Value |
|---|---|---|---|
| Age, yrs | 69.0 ± 8.1 | 65.4 ± 9.6 | <0.0001 |
| Female | 33/162 (20.4) | 383/1,650 (23.2) | 0.41 |
| Hyperlipidemia | 122/162 (75.3) | 1,143/1,647 (69.4) | 0.12 |
| Hypertension | 119/162 (73.5) | 1,211/1,650 (73.4) | 0.99 |
| Prior stroke or transient ischemic attack | 9/162 (5.6) | 102/1,649 (6.2) | 0.75 |
| Congestive heart failure | 6/162 (3.7) | 107/1,645 (6.5) | 0.16 |
| Diabetes mellitus, medically treated | 38/162 (23.5) | 441/1,650 (26.7) | 0.37 |
| Chronic obstructive pulmonary disease | 18/162 (11.1) | 117/1,647 (7.1) | 0.06 |
| History of anemia | 23/161 (14.3) | 152/1,646 (9.2) | 0.04 |
| History of carotid artery disease | 9/160 (5.6) | 140/1,644 (8.5) | 0.20 |
| Peripheral vascular disease | 20/160 (12.5) | 157/1,646 (9.5) | 0.23 |
| Critical pre-operative state | 4/162 (2.5) | 24/1,649 (1.5) | 0.31 |
| Valve disease (moderate or less) | | | |
| Aortic stenosis | 5/150 (3.3) | 36/1,536 (2.3) | 0.40 |
| Mitral stenosis | 2/149 (1.3) | 9/1,529 (0.6) | 0.25 |
| Aortic regurgitation | 21/150 (14.0) | 162/1,527 (10.6) | 0.20 |
| Mitral regurgitation | 53/150 (35.3) | 435/1,531 (28.4) | 0.07 |
| Tricuspid regurgitation | 37/148 (25.0) | 383/1,517 (25.2) | 0.95 |
| Prior percutaneous coronary intervention | 34/162 (21.0) | 272/1,648 (16.5) | 0.15 |
| Previous cardiac surgery | 0/162 (0.0) | 8/1,650 (0.5) | 1.00 |
| Prior myocardial infarction | 36/161 (22.4) | 276/1,637 (16.9) | 0.08 |
| Clinical presentation | | | |
| Recent MI (within 7 days) | 29/162 (17.9) | 242/1,643 (14.7) | 0.28 |
| ST-segment elevation MI | 2/162 (1.2) | 24/1,637 (1.5) | 1.00 |
| Non-ST-segment elevation MI | 27/162 (16.7) | 210/1,637 (12.8) | 0.17 |
| Unstable angina | 35/162 (21.6) | 411/1,643 (25.0) | 0.34 |
| Body mass index, kg/m$^2$ | 29.3 ± 5.4 | 28.5 ± 4.9 | 0.14 |
| Left ventricular ejection fraction, % | 56.1 ± 9.1 | 57.4 ± 9.2 | 0.05 |
| SYNTAX score (core laboratory assessed) | 26.5 ± 9.6 | 26.6 ± 9.4 | 0.90 |
| Baseline laboratory values | | | |
| Creatinine clearance, ml/min | 87.1 ± 32.8 | 90.1 ± 32.2 | 0.16 |
| Hemoglobin, g/dl | 13.5 ± 1.6 | 13.6 ± 1.6 | 0.74 |
| Brain natriuretic peptide, units | 241.6 ± 427.3 | 224.7 ± 557.2 | 0.04 |
| $CHADS_2$ score | 1.7 ± 1.3 | 1.6 ± 1.3 | 0.45 |
| $CHA_2DS_2$-VASc score | 3.3 ± 1.4 | 3.2 ± 1.4 | 0.29 |

Values are mean ± SD or n/N (%).

$CHADS_2$ = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke, transient ischemic attack, or thromboembolism; $CHA_2DS_2$-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and stroke, transient ischemic attack, or thromboembolism; vascular disease, age 65 to 74 years, and female sex; MI = myocardial infarction; NOAF = new-onset atrial fibrillation or flutter; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

as-treated population, excluding patients with in-hospital AF before the index procedure and those who did not undergo revascularization procedures. Continuous variables are reported as mean ± standard deviation and were compared using the Student's *t*-test. Categorical variables are expressed as counts and percentages and were compared with the chi-square or Fisher exact test, as appropriate. Predictors of NOAF in patients undergoing CABG were determined in a Cox proportional hazards model including the following clinical and angiographic variables: age, sex, history of medically treated diabetes, history of hypertension, history of congestive heart failure, recent MI (<7 days), body mass index (BMI), baseline hemoglobin, baseline renal insufficiency (creatinine clearance <60 ml/min), left ventricular ejection fraction (LVEF), angiographic core laboratory-assessed SYNTAX score, off-pump versus on-pump CABG, number of bypass conduits, and bypass of the left circumflex artery. The same model was tested in patients who underwent off-pump surgery. A second Cox proportional hazards model was constructed in patients who underwent on-pump surgery including the foregoing covariates (except off-pump vs. on-pump surgery) in addition to bypass duration, cross-clamp duration, use of crystalloid cardioplegia, and retrograde cardioplegia.

Event rates at 30 days and 3 years were estimated using the Kaplan-Meier method, with comparisons made using the log-rank test. Multivariable Cox proportional hazard analyses were used to determine whether NOAF was an independent predictor of all-cause death, cardiovascular death, stroke, and the primary composite outcome measure of death, MI, or stroke at 3 years. The following covariates were included in the model: NOAF, age, sex, medically treated diabetes, history of hypertension, history of congestive heart failure, recent MI (<7 days), BMI, baseline renal insufficiency, LVEF, left main distal bifurcation lesion, and core laboratory SYNTAX score. Multivariable analyses were also performed in the CABG cohort alone with the same variables, in addition to on-pump versus off-pump surgery. A 2-sided p value <0.05 was considered to be statistically significant for all tests. All statistical analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, North Carolina).

## RESULTS

**BASELINE AND PROCEDURAL CHARACTERISTICS.** Among the 1,905 patients randomized in EXCEL, 70 had in-hospital AF before revascularization, and 23 did not undergo PCI or CABG. Thus 1,812 randomized patients with LMCAD without AF on presentation were included in the analysis, including 893 and 919 patients treated with CABG and PCI, respectively. NOAF developed at a mean of 2.7 ± 2.5 days after revascularization in 162 patients (8.9%), including 161 of 893 (18.0%) CABG-treated patients and 1 of 919 (0.1%) PCI-treated patients (p < 0.0001). All NOAF episodes consisted of AF; 1 patient had both AF and atrial flutter. Baseline characteristics of patients with and without NOAF are shown in Table 1. Patients with NOAF were older and were more likely to have a

history of anemia and MI and lower LVEF. Preprocedure laboratory values were similar between groups except for a slightly higher brain natriuretic peptide level in patients with versus without NOAF. Procedural characteristics were also similar in patients with versus without NOAF except for more frequent blood cardioplegia, retrograde cardioplegia, and grafting of the left circumflex artery during the index CABG (Table 2). Pre-operative amiodarone in the CABG group was administered to 3 of 160 (1.9%) patients and 12 of 727 (1.7%) patients, respectively, who had or did not have in-hospital post-CABG NOAF ($p = 0.11$).

By multivariable analysis, the independent predictors of NOAF in patients undergoing CABG were older age, greater BMI, and reduced LVEF (Table 3). The C-statistics for the relationships among age, BMI, LVEF, and the subsequent development of NOAF were 0.62, 0.53, and 0.55, respectively. In patients undergoing off-pump CABG, age (hazard ratio [HR]: 1.05; 95% confidence interval [CI]: 1.03 to 1.08; $p < 0.0001$), BMI (HR: 1.06; 95% CI: 1.01 to 1.09; $p = 0.03$), and LVEF (HR: 0.98; 95% CI: 0.96 to 0.99; $p = 0.03$) were confirmed as important predictors of NOAF. In patients undergoing on-pump surgery, age and retrograde cardioplegia independently predicted NOAF (Online Table 1).

By the time of hospital discharge, NOAF had resolved in 139 of 162 patients (85.8%), including 20 patients who underwent cardioversion. The duration of hospitalization was significantly longer in patients with versus without NOAF (14.3 ± 10.9 days vs. 8.3 ± 7.5 days; $p < 0.0001$). Discharge medications varied substantially according to the occurrence of NOAF (Table 4). Patients with NOAF were more frequently discharged with anticoagulant therapy with either warfarin or a novel oral anticoagulant agent, whereas dual antiplatelet therapy was more commonly prescribed to patients without NOAF. Aspirin was equally prescribed in both groups. Antiarrhythmic medications and diuretics were also more frequently used in patients with NOAF.

**CLINICAL OUTCOMES.** The development of in-hospital NOAF was associated with increased unadjusted 30-day rates of major and minor bleeding, but not with adverse cardiovascular events; after multivariable adjustment adjusted for differences in baseline characteristics, the 30-day risk for the composite outcome of death, MI, or stroke was higher in patients with NOAF compared with patients without NOAF (Online Table 2). At 3 years, in addition to major and minor bleeding, NOAF was associated with increased rates of all-cause death, cardiovascular death, stroke,

**TABLE 2 Procedural Characteristics According to the Development of In-Hospital New-Onset Atrial Fibrillation**

| | NOAF (n = 162) | No NOAF (n = 1,650) | p Value |
|---|---|---|---|
| PCI group (including staged procedures) | | | |
| Hemodynamic support device used | 0/2 (0.0) | 54/999 (5.4) | 1.00 |
| PCI of the distal left main bifurcation | 1/1 (100.0) | 516/908 (56.8) | 1.00 |
| Procedure duration, min | 103.0 ± 4.2 | 80.6 ± 42.4 | 0.24 |
| CABG group | | | |
| Revascularization priority | | | |
| Emergent | 15/161 (9.3) | 86/732 (11.7) | 0.38 |
| Urgent | 55/161 (34.2) | 235/732 (32.1) | 0.61 |
| Elective | 91/161 (56.5) | 411/732 (56.1) | 0.93 |
| Off-pump coronary artery bypass grafting | 43/161 (26.7) | 217/732 (29.6) | 0.46 |
| Intermittent cross-clamp | 36/118 (30.5) | 153/515 (29.7) | 0.86 |
| Crystalloid cardioplegia | 25/118 (21.2) | 158/513 (30.8) | 0.04 |
| Blood cardioplegia | 89/118 (75.4) | 332/513 (64.7) | 0.03 |
| Direction of cardioplegia | | | |
| Antegrade | 106/118 (89.8) | 450/515 (87.4) | 0.46 |
| Retrograde | 40/118 (33.9) | 112/515 (21.7) | 0.005 |
| Other surgical procedures performed | 106/118 (89.8) | 450/515 (87.4) | 0.46 |
| Number of conduits per patient | 2.6 ± 0.8 | 2.6 ± 0.8 | 0.71 |
| Internal mammary artery used | 157/161 (97.5) | 721/728 (99.0) | 0.12 |
| Pan-arterial revascularization | 41/161 (25.5) | 180/732 (24.6) | 0.82 |
| Vessels bypassed per subject | 2.3 ± 0.5 | 2.2 ± 0.6 | 1.00 |
| Coronary artery bypassed | | | |
| Left anterior descending | 158/160 (98.8) | 720/728 (98.9) | 0.70 |
| Left circumflex | 149/160 (93.1) | 636/728 (87.4) | 0.04 |
| Right | 54/160 (33.8) | 279/728 (38.3) | 0.28 |
| CABG duration, min | 252.6 ± 78.9 | 240.9 ± 67.7 | 0.11 |
| Bypass duration, min | 86.3 ± 45.4 | 82.7 ± 44.7 | 0.23 |
| Cross-clamp duration, min | 56.9 ± 28.5 | 54.7 ± 27.2 | 0.66 |

Values are mean ± SD or n/N (%).

CABG = coronary artery bypass grafting; NOAF = new-onset atrial fibrillation or flutter; PCI = percutaneous coronary intervention.

**TABLE 3 Independent Predictors of In-Hospital New-Onset Atrial Fibrillation in Patients Undergoing Coronary Artery Bypass Grafting**

| | Adjusted Hazard Ratio (95% Confidence Interval) | p Value |
|---|---|---|
| Age, per yr | 1.05 (1.03-1.07) | <0.0001 |
| Male | 1.31 (0.82-2.11) | 0.26 |
| Body mass index, per kg/m$^2$ | 1.05 (1.01-1.09) | 0.009 |
| Diabetes mellitus, medically treated | 0.71 (0.47-1.08) | 0.11 |
| Hypertension, medically treated | 0.92 (0.61-1.39) | 0.68 |
| Congestive heart failure | 0.58 (0.24-1.39) | 0.20 |
| SYNTAX score, per unit | 1.01 (0.99-1.03) | 0.30 |
| Creatinine clearance <60 ml/min | 1.09 (0.64-1.87) | 0.74 |
| Baseline hemoglobin, per g/dl | 1.00 (0.88-1.14) | 0.50 |
| Recent myocardial infarction | 1.12 (0.70-1.79) | 0.63 |
| Left ventricular ejection fraction, % | 0.97 (0.96-0.99) | 0.02 |
| On-pump surgery | 0.80 (0.54-1.20) | 0.29 |
| Total number of bypass conduits | 0.89 (0.70-1.14) | 0.36 |
| Bypass of the left circumflex artery | 1.67 (0.86-3.21) | 0.13 |

Abbreviation as in Table 1.

**TABLE 4 Medications at Discharge According to the Development of In-Hospital New-Onset Atrial Fibrillation**

| | NOAF (n = 162) | No NOAF (n = 1,650) | p Value |
|---|---|---|---|
| Aspirin | 155/157 (98.7) | 1,597/1,612 (99.1) | 0.66 |
| CABG group | 154/156 (98.7) | 711/717 (99.2) | 0.59 |
| PCI group | 1/1 (100.0) | 886/895 (99.0) | 0.91 |
| ADP antagonist | 54/158 (34.2) | 1,120/1,617 (69.3) | <0.0001 |
| CABG group | 53/157 (33.8) | 241/719 (33.5) | 0.95 |
| PCI group | 1/1 (100.0) | 879/898 (97.9) | 0.16 |
| Both aspirin and ADP antagonist | 53/158 (33.5) | 1,107/1,617 (68.5) | <0.0001 |
| CABG group | 52/157 (33.1) | 237/719 (33.0) | 0.97 |
| PCI group | 1/1 (100.0) | 870/898 (96.9) | 0.16 |
| Warfarin | 16/158 (10.1) | 19/1,617 (1.2) | <0.0001 |
| Novel oral anticoagulant agent | 0/158 (0.0) | 2/1,617 (0.1) | 1.00 |
| Warfarin or novel oral anticoagulant agent | 16/158 (10.1) | 21/1,617 (1.3) | <0.0001 |
| CABG group | 16/157 (10.2) | 15/719 (2.1) | <0.0001 |
| PCI group | 0/1 (0.0) | 6/898 (0.7) | 0.74 |
| Low-molecular-weight heparin | 3/158 (1.9) | 10/1,617 (0.6) | 0.10 |
| CABG group | 3/157 (1.9) | 5/719 (0.7) | 0.15 |
| PCI group | 0/1 (0.0) | 5/898 (0.6) | 0.94 |
| Antiarrhythmic agent | 72/158 (45.6) | 34/1,617 (2.1) | <0.0001 |
| CABG group | 72/157 (45.9) | 30/719 (4.2) | <0.0001 |
| PCI group | 0/1 (0.0) | 4/898 (0.4) | 0.95 |
| Beta-blocker | 144/158 (91.1) | 1,412/1,617 (87.3) | 0.16 |
| CABG group | 143/157 (91.1) | 667/719 (92.8) | 0.47 |
| PCI group | 1/1 (100.0) | 745/898 (83.0) | 0.65 |
| Calcium channel blocker | 16/158 (10.1) | 99/1,617 (6.1) | 0.051 |
| CABG group | 16/157 (10.2) | 45/719 (6.3) | 0.08 |
| PCI group | 0/1 (0.0) | 54/898 (6.0) | 0.80 |
| ACE inhibitor or ARB | 69/158 (43.7) | 809/1,617 (50.0) | 0.13 |
| CABG group | 69/157 (43.9) | 300/719 (41.7) | 0.61 |
| PCI group | 0/1 (0.0) | 509/898 (56.7) | 0.25 |
| Statin | 145/158 (91.8) | 1,532/1,617 (94.7) | 0.12 |
| CABG group | 144/157 (91.7) | 666/719 (92.6) | 0.70 |
| PCI group | 1/1 (100.0) | 866/898 (96.4) | 0.84 |
| Diuretic | 48/158 (30.4) | 196/1,617 (12.1) | <0.0001 |
| CABG group | 48/157 (30.6) | 165/719 (22.9) | 0.04 |
| PCI group | 0/1 (0.0) | 31/898 (3.5) | 0.85 |

Values are n/N (%).

ACE = angiotensin-converting enzyme; ADP = adenosine diphosphate receptor; ARB = angiotensin receptor blocker; other abbreviations as in Table 2.

and the primary composite endpoint of death, MI, or stroke (Table 5). By multivariable analysis, NOAF was an independent predictor of all-cause death, cardiovascular death, stroke, and the primary composite outcome of all-cause death, MI, or stroke at 3 years in the overall population and in the CABG-treated group (Table 6).

The increased 3-year rate of cardiovascular death in patients with versus without NOAF was driven by deaths adjudicated as stroke related and heart failure related (2.6% vs. 0.6%; p = 0.005; and 1.9% vs. 0.4%; p = 0.009, respectively). Among the 10 patients with in-hospital NOAF who had a stroke during follow-up, 5 (50%) were not taking warfarin or a novel oral anticoagulant agent at the time of the event. As shown in the Central Illustration, the rate of the 3-year composite primary endpoint of death, MI, or stroke was reduced in patients treated with PCI compared with patients treated with CABG who had NOAF development. In contrast, PCI and CABG had nonsignificantly different rates of the 3-year primary endpoint if NOAF did not occur.

## DISCUSSION

The major findings from the present analysis from the EXCEL trial, in which the incidence, predictors, and prognostic impact of in-hospital NOAF in patients with LMCAD undergoing PCI or CABG were examined, are as follows: 1) NOAF was frequent after CABG but extremely rare after PCI; 2) older age, greater BMI, and reduced LVEF were independent predictors of NOAF after CABG; 3) NOAF was associated with prolonged hospitalization and increased 30-day rates of bleeding; and 4) NOAF was a strong independent predictor of the 3-year rates of all-cause and cardiovascular death, stroke, and the primary composite endpoint of death, MI, or stroke after CABG.

Among patients with LMCAD and sinus rhythm who were enrolled in the EXCEL trial, in-hospital NOAF was much more likely to develop after CABG than after PCI. The 18% rate of NOAF after CABG for LMCAD in the present study is consistent with prior reports in which post-CABG AF developed in 11% to 40% of patients (7–10). The range of post-operative NOAF between studies likely reflects differences in patient populations (e.g., operative urgency, critical state, and hemodynamic stability), the use of preoperative prophylactic therapies (e.g., beta-blockers and amiodarone), and variability in the rigor and duration of detection. Patients enrolled in EXCEL were relatively stable and not high risk, with equipoise for revascularization by either PCI or surgery. Nonetheless, in-hospital NOAF occurred in only 1 patient after PCI, markedly less than after CABG, a finding reflecting in part the fact that relatively few patients in EXCEL presented with acute MI, a cohort more commonly affected by post-PCI AF (11–13).

NOAF was a powerful predictor of adverse outcomes during 3-year follow-up after CABG, in particular stroke, cardiovascular death, and all-cause death. Notably, NOAF was a stronger multivariable predictor of death after CABG than either diabetes or reduced LVEF. As shown in the Central Illustration, PCI had superior 3-year event-free survival compared with CABG if NOAF after surgery occurred. PCI may thus be preferred in selected patients who have a very high risk of NOAF after surgery. In this regard,

**TABLE 5 Clinical Outcomes at 3 Years According to the Development of In-Hospital New-Onset Atrial Fibrillation**

| | All Patients | | | CABG-Treated Patients | | |
|---|---|---|---|---|---|---|
| | NOAF (n = 162) | No NOAF (n = 1,650) | p Value | NOAF (n = 161) | No NOAF (n = 893) | p Value |
| Death, MI, or stroke | 19.3 (36) | 12.8 (208) | 0.02 | 22.6 (36) | 12.8 (93) | 0.002 |
| All-cause death | 11.3 (18) | 6.1 (99) | 0.01 | 11.4 (18) | 4.3 (31) | 0.0005 |
| Cardiovascular | 8.9 (14) | 3.4 (55) | 0.0007 | 9.0 (14) | 2.4 (17) | <0.0001 |
| Noncardiovascular | 2.6 (4) | 2.8 (44) | 0.94 | 2.6 (4) | 2.0 (14) | 0.61 |
| MI | 11.4 (18) | 8.0 (130) | 0.14 | 11.4 (18) | 8.0 (58) | 0.19 |
| Stroke or TIA | 7.9 (12) | 2.8 (44) | 0.0007 | 7.9 (12) | 3.0 (21) | 0.005 |
| Stroke | 6.5 (10) | 2.3 (37) | 0.002 | 6.6 (10) | 2.4 (17) | 0.009 |
| Ischemic | 5.3 (8) | 1.8 (28) | 0.004 | 5.4 (8) | 2.1 (15) | 0.03 |
| Hemorrhagic | 1.3 (2) | 0.7 (11) | 0.40 | 1.3 (2) | 0.4 (3) | 0.20 |
| TIA | 1.4 (2) | 0.4 (7) | 0.14 | 1.4 (2) | 0.6 (4) | 0.31 |
| Bleeding | | | | | | |
| TIMI major/minor | 16.8 (27) | 6.7 (109) | <0.0001 | 16.9 (27) | 8.6 (63) | 0.002 |
| TIMI major | 6.8 (11) | 2.8 (46) | 0.005 | 6.9 (11) | 4.0 (29) | 0.11 |
| TIMI minor | 10.6 (17) | 3.9 (64) | <0.0001 | 10.7 (17) | 4.7 (34) | 0.004 |
| BARC scale, any | 18.6 (30) | 12.9 (210) | 0.03 | 18.8 (30) | 15.4 (112) | 0.29 |
| Type 1 | 0.0 (0) | 2.4 (39) | 0.05 | 0.0 (0) | 2.1 (15) | 0.07 |
| Type 2 | 6.9 (11) | 5.5 (89) | 0.44 | 6.9 (11) | 5.0 (36) | 0.32 |
| Type 3 | 8.7 (14) | 4.1 (67) | 0.007 | 8.8 (14) | 5.2 (38) | 0.09 |
| Type 4 | 7.5 (12) | 2.9 (47) | 0.002 | 4.4 (7) | 3.3 (24) | 0.49 |
| Type 5 | 4.3 (7) | 1.5 (25) | 0.009 | 0.0 (0) | 0.1 (1) | 0.64 |

Values are Kaplan-Meier estimates, presented as % (n).

BARC = Bleeding Academic Research Consortium; CI = confidence interval; HR = hazard ratio; MI = myocardial infarction; TIA = transient ischemic attack, TIMI = Thrombolysis in Myocardial Infarction; other abbreviations as in Tables 1 and 2.

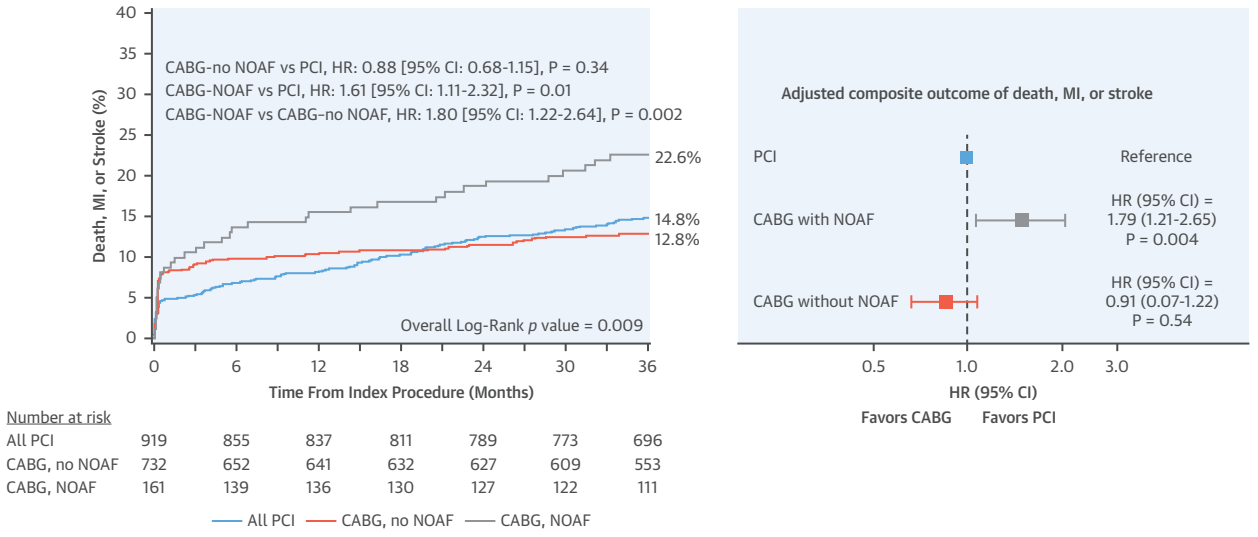
**TABLE 6 Independent Predictors of 3-Year Clinical Outcomes***

| | All Patients (n = 1,812) | | CABG Group (n = 893) | |
|---|---|---|---|---|
| | Hazard Ratio (95% Confidence Interval) | p Value | Hazard Ratio (95% Confidence Interval) | p Value |
| All-cause death | | | | |
| NOAF | 2.06 (1.21-3.50) | 0.008 | 3.02 (1.60-5.7) | 0.0006 |
| Age | 1.03 (1.01-1.06) | 0.02 | – | – |
| Left ventricular ejection fraction, % | 0.97 (0.96-0.99) | 0.008 | 0.97 (0.93-0.99) | 0.03 |
| Diabetes mellitus | 1.77 (1.16-2.69) | 0.008 | – | – |
| Congestive heart failure | – | – | 2.48 (1.00-6.12) | 0.049 |
| Cardiovascular death | | | | |
| NOAF | 3.25 (1.76-5.98) | 0.0002 | 4.86 (2.27-10.44) | <0.0001 |
| Diabetes mellitus | 1.92 (1.12-3.31) | 0.02 | – | – |
| Left ventricular ejection fraction, % | 0.97 (0.95-1.00) | 0.048 | – | – |
| Stroke | | | | |
| NOAF | 4.08 (1.89-8.78) | 0.0003 | 4.19 (1.74-10.11) | 0.001 |
| Renal insufficiency | 2.29 (1.02-5.13) | 0.045 | – | – |
| Diabetes mellitus | 2.52 (1.29-4.93) | 0.007 | 3.22 (1.32-7.87) | 0.01 |
| Male | 0.47 (0.24-0.92) | 0.03 | – | – |
| Body mass index | 0.91 (0.85-0.98) | 0.01 | – | – |
| Composite death, MI, or stroke | | | | |
| NOAF | 1.84 (1.26-2.68) | 0.002 | 2.13 (1.39-3.25) | 0.0004 |
| Diabetes mellitus | 1.55 (1.17-2.07) | 0.003 | 1.63 (1.08-2.44) | 0.02 |
| Hypertension | – | – | 1.68 (1.00-2.82) | 0.048 |
| Renal insufficiency | 1.51 (1.04-2.19) | 0.03 | – | – |

*The full list of covariates tested appears in the Methods section. Covariates not appearing in the table were not statistically significant in the final models.

Abbreviations as in Tables 1 and 2.

**CENTRAL ILLUSTRATION** **Atrial Fibrillation After Left Main Revascularization**




**Kosmidou, I. et al. J Am Coll Cardiol. 2018;71(7):739–48.**

Time-to-event curves and adjusted hazard ratios (HR) for the 3-year primary composite endpoint of death, myocardial infarction (MI), or stroke in patients with left main coronary artery disease without pre-procedural atrial fibrillation who underwent revascularization by percutaneous coronary intervention (PCI) (n = 919) versus coronary artery bypass grafting (CABG) with the subsequent development of new-onset atrial fibrillation (NOAF) before hospital discharge (n = 161) versus coronary artery bypass grafting without new-onset atrial fibrillation before hospital discharge (n = 732). The 3-year adverse event rates were highest in coronary artery bypass grafting–treated patients with new-onset atrial fibrillation and similar in coronary artery bypass grafting–treated patients without new-onset atrial fibrillation and in percutaneous coronary intervention–treated patients. CI = confidence interval.

advanced age, increased BMI, and reduced LVEF were independent clinical predictors of NOAF after CABG for LMCAD, consistent with previous reports (7,14,15). However, although these associations were statistically significant, the C-statistics for the correlations between these risk factors and NOAF were modest, and many patients who may benefit from CABG have these characteristics (16). Thus, although the increased periprocedural risk of NOAF should be recognized in patients with advanced age, increased BMI, and/or reduced LVEF, rather than avoiding CABG in these patients, effective pre-operative and perioperative measures (prophylactic beta-blockers or amiodarone) (17,18) should be considered to prevent the post-surgical occurrence of NOAF. Consistent with previous reports (19,20), the strategy of surgical revascularization (on-pump vs. off-pump) in EXCEL was not a predictor of NOAF.

In patients undergoing on-pump CABG, the use of retrograde cardioplegia was a strong predictor of NOAF. Potential adverse effects of retrograde cardioplegia have been previously reported (21), and they may in part be related to the delay in cardiac arrest and subsequent myocardial protection with retrograde compared with antegrade cardioplegia. However, total bypass duration and cross-clamp duration were not associated with an increased risk for AF, a finding suggesting that alternate mechanisms may underlie the increased rate of NOAF with retrograde cardioplegia.

The higher periprocedural rates of stroke with CABG compared with PCI that has been noted in most prior trials (22,23) may in part be explained by the greater rate of NOAF after surgical revascularization (24). Although a recent large registry-based analysis suggested that post-operative AF was a predictor only of early stroke (25), in the present study the increased rate of stroke with in-hospital NOAF emerged not within 30 days, but during long-term follow-up. A low proportion (10.2%) of patients with NOAF after CABG in EXCEL was discharged with long-term oral anticoagulant therapy (reflecting the high in-hospital rate of conversion to sinus rhythm), and although the 3-year post-CABG rate of stroke was relatively low compared with prior studies, 50% of the post-CABG NOAF patients who developed a stroke during follow-up were not being treated with anticoagulant therapy at the time. Future studies are warranted to determine the extent to which recurrent AF during long-term follow-up contributed to the late stroke

risk (26,27). Alternatively, in-hospital NOAF that resolves may be a marker of high-risk patients' characteristics, systemic inflammation, and diffuse vascular atherosclerosis (28), thus predisposing patients with NOAF to thrombotic or atheroembolic events (29), with or without recurrent AF. Continuous monitoring may elucidate whether recurrent AF episodes precede cerebrovascular events in this patient population.

In addition to affecting long-term prognosis, NOAF was strongly associated with prolonged hospitalization, likely attributable to its management (rate control and attempted pharmacological or electrical cardioversion, diuresis, and initiation of anticoagulation in some patients), and with bleeding complications (in part from anticoagulation) that may have contributed to the poor prognosis of patients with NOAF (30,31). The ongoing formal EXCEL cost substudy will assess the extent to which NOAF increased costs in CABG-treated patients.

**STUDY STRENGTHS AND LIMITATIONS.** As a large randomized trial of patients with LMCAD who were undergoing revascularization, EXCEL provides clinically relevant insights regarding the relative frequency of NOAF after PCI and CABG and of its association with long-term cardiovascular outcomes. However, several limitations should be considered. First, the present analysis was post hoc, and it should thus be considered hypothesis generating. Second, the absolute number of events (NOAF, stroke, and death) was modest, and not all confounders in their described relationships may have been identified. Third, although we excluded patients with in-hospital AF before revascularization from the present analysis, a history of prior AF was not captured in the case report form and systematic screening for pre-operative AF was not done; as such, pre-procedure episodes of AF may have been missed. Fourth, pre-CABG use of amiodarone was uncommon, and data on the rate of perioperative beta-blocker use were not collected. We thus cannot speak to the efficacy of these measures in preventing NOAF or influencing prognosis. Finally, data on arrhythmias during follow-up (including AF recurrence) were not systematically collected in the present study.

## CONCLUSIONS

In the randomized EXCEL trial comparing PCI and CABG for the treatment of LMCAD in patients with low and intermediate SYNTAX scores, NOAF occurred almost exclusively following CABG and was a powerful predictor of all-cause death, cardiovascular death, stroke, and the composite endpoint of death, MI, or stroke at 3 years. Further studies are needed to identify patients at high risk for NOAF after CABG to guide prophylactic measures, to examine the potential role of implantable monitors to detect AF recurrence in patients with NOAF who convert to sinus rhythm before hospital discharge, and to determine whether the routine use of long-term oral anticoagulation in patients with in-hospital NOAF improves long-term prognosis after CABG for LMCAD.

**ADDRESS FOR CORRESPONDENCE:** Dr. Gregg W. Stone, Columbia University Medical Center, Cardiovascular Research Foundation, 1700 Broadway, 9th Floor, New York, New York 10019. E-mail: gs2184@columbia.edu.

## PERSPECTIVES

**COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:** AF occurs much more commonly after CABG surgery than after PCI. Patients developing AF after CABG for LMCAD face elevated risks of stroke, cardiovascular mortality, and all-cause mortality during the subsequent 3 years than do patients without AF.

**TRANSLATIONAL OUTLOOK:** Additional studies are needed to determine whether long-term monitoring for detection of AF after CABG and oral anticoagulant therapy could improve the prognosis of patients undergoing CABG for LMCAD.

## REFERENCES

**1.** Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. N Engl J Med 2016;375:2223–35.

**2.** Makikallio T, Holm NR, Lindsay M, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. Lancet 2016;388:2743–52.

**3.** Kaw R, Hernandez AV, Masood I, Gillinov AM, Saliba W, Blackstone EH. Short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting: a systematic review and meta-analysis. J Thorac Cardiovasc Surg 2011;141:1305–12.

**4.** Knotzer H, Dunser MW, Mayr AJ, Hasibeder WR. Postbypass arrhythmias: pathophysiology, prevention, and therapy. Curr Opin Crit Care 2004;10:330–5.

**5.** Min SY, Park DW, Yun SC, et al. Major predictors of long-term clinical outcomes after coronary revascularization in patients with unprotected left main coronary disease: analysis from the MAIN-COMPARE study. Circ Cardiovasc Interv 2010;3:127–33.

**6.** Kappetein AP, Serruys PW, Sabik JF, et al. Design and rationale for a randomised comparison of everolimus-eluting stents and coronary artery bypass graft surgery in selected patients with left

main coronary artery disease: the EXCEL trial. EuroIntervention 2016;12:861–72.

**7.** Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. J Am Coll Cardiol 2008;51:793–801.

**8.** Chelazzi C, Villa G, De Gaudio AR. Post-operative atrial fibrillation. ISRN Cardiol 2011; 2011:203179.

**9.** Mathew JP, Parks R, Savino JS, et al. Atrial fibrillation following coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. JAMA 1996;276: 300–6.

**10.** Ommen SR, Odell JA, Stanton MS. Atrial arrhythmias after cardiothoracic surgery. N Engl J Med 1997;336:1429–34.

**11.** Kudaiberdieva G, Gorenek B. Post PCI atrial fibrillation. Acute Card Care 2007;9:69–76.

**12.** Chan W, Ajani AE, Clark DJ, et al. Impact of periprocedural atrial fibrillation on short-term clinical outcomes following percutaneous coronary intervention. Am J Cardiol 2012;109: 471–7.

**13.** Lopes RD, Elliott LE, White HD, et al. Antithrombotic therapy and outcomes of patients with atrial fibrillation following primary percutaneous coronary intervention: results from the APEX-AMI trial. Eur Heart J 2009;30: 2019–28.

**14.** Echahidi N, Mohty D, Pibarot P, et al. Obesity and metabolic syndrome are independent risk factors for atrial fibrillation after coronary artery bypass graft surgery. Circulation 2007;116 Suppl: I213–9.

**15.** Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk index for atrial fibrillation after cardiac surgery. JAMA 2004;291:1720–9.

**16.** Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. Lancet 2013;381: 639–50.

**17.** Giri S, White CM, Dunn AB, et al. Oral amiodarone for prevention of atrial fibrillation after open heart surgery, the Atrial Fibrillation Suppression Trial (AFIST): a randomised placebo-controlled trial. Lancet 2001;357: 830–6.

**18.** Khan MF, Wendel CS, Movahed MR. Prevention of post-coronary artery bypass grafting (CABG) atrial fibrillation: efficacy of prophylactic beta-blockers in the modern era: a meta-analysis of latest randomized controlled trials. Ann Noninvasive Electrocardiol 2013;18:58–68.

**19.** Almassi GH, Pecsi SA, Collins JF, Shroyer AL, Zenati MA, Grover FL. Predictors and impact of postoperative atrial fibrillation on patients' outcomes: a report from the Randomized On Versus Off Bypass trial. J Thorac Cardiovasc Surg 2012; 143:93–102.

**20.** Kuss O, von Salviati B, Borgermann J. Off-pump versus on-pump coronary artery bypass grafting: a systematic review and meta-analysis of propensity score analyses. J Thorac Cardiovasc Surg 2010;140:829–35, 835.e1–13.

**21.** Arom KV, Emery RW, Petersen RJ, Bero JW. Evaluation of 7,000+ patients with two different routes of cardioplegia. Ann Thorac Surg 1997;63: 1619–24.

**22.** Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. J Am Coll Cardiol 2011; 58:1426–32.

**23.** Palmerini T, Biondi-Zoccai G, Reggiani LB, et al. Risk of stroke with coronary artery bypass graft surgery compared with percutaneous coronary intervention. J Am Coll Cardiol 2012;60: 798–805.

**24.** Horwich P, Buth KJ, Legare JF. New onset postoperative atrial fibrillation is associated with a long-term risk for stroke and death following cardiac surgery. J Card Surg 2013;28: 8–13.

**25.** Whitlock R, Healey JS, Connolly SJ, et al. Predictors of early and late stroke following cardiac surgery. CMAJ 2014;186:905–11.

**26.** Melduni RM, Schaff HV, Bailey KR, et al. Implications of new-onset atrial fibrillation after cardiac surgery on long-term prognosis: a community-based study. Am Heart J 2015;170: 659–68.

**27.** Reiffel JA, Verma A, Kowey PR, et al. Incidence of previously undiagnosed atrial fibrillation using insertable cardiac monitors in a high-risk population: the REVEAL AF study. JAMA Cardiol 2017;2: 1120–7.

**28.** Healey JS, Alings M, Ha AC, et al. Subclinical atrial fibrillation in older patients. Circulation 2017;136:1276–83.

**29.** Violi F, Pastori D, Pignatelli P. Mechanisms and management of thrombo-embolism in atrial fibrillation. J Atr Fibrillation 2014;7:1112.

**30.** Schwann TA, Habib JR, Khalifeh JM, et al. Effects of blood transfusion on cause-specific late mortality after coronary artery bypass grafting: less is more. Ann Thorac Surg 2016;102:465–73.

**31.** Stone GW, Clayton TC, Mehran R, et al. Impact of major bleeding and blood transfusions after cardiac surgery: analysis from the Acute Catheterization and Urgent Intervention Triage strategY (ACUITY) trial. Am Heart J 2012;163:522–9.

**KEY WORDS** atrial fibrillation, coronary artery bypass grafting, left main disease, mortality, percutaneous coronary intervention, prognosis, stroke

**APPENDIX** For supplemental tables, please see the online version of this paper.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