Original Article

Sex Differences in the Epidemiology of New-Onset In-Hospital Post–Coronary Artery Bypass Graft Surgery Atrial Fibrillation

A Large Multicenter Study

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Background—New-onset atrial fibrillation (AF) after coronary artery bypass graft surgery (CABG) is associated with increased morbidity and poorer long-term survival. Although many studies show differences in outcome in women versus men after CABG, little is known about the sex-specific incidence and characteristics of post-CABG AF.

Methods and Results—Overall, 11 236 consecutive patients without preoperative AF underwent isolated CABG from 2002 to 2010 at 4 US academic medical centers and 1 high-volume specialty cardiac hospital. Data routinely collected for the Society of Thoracic Surgeons database were augmented with details on new-onset post-CABG AF events detected via continuous in-hospital ECG/telemetry monitoring. Unadjusted incidence of post-CABG AF was 29.5% (3312/11 236) overall, 30.2% (2485/8214) in men, and 27.4% (827/3022) in women. After adjustment for Society of Thoracic Surgeons–recognized risk factors, women had significantly lower risk for post-CABG AF (odds ratio [95% confidence interval]=0.75 [0.64–0.89]), shorter first, longest, and total duration of AF episodes (mean difference [95% confidence interval]=−2.7 [−4.7 to −0.8] hours; −4.1 [−6.9 to −1.2] hours; −2.4 [−2.5 to −2.3] hours, respectively). At 48 hours, AF-free probabilities were 77% for women and 72% for men ($P<0.001$). Number of episodes ($P=0.18$), operative mortality ($P=0.048$), stroke ($P=0.126$), and discharge in AF ($P=0.234$) did not differ significantly by sex.

Conclusions—These novel data on sex-specific characteristics of new-onset AF after isolated CABG show that women had lower adjusted risk for post-CABG AF and experienced shorter episodes. Investigation of sex-specific impacts on outcomes is needed to identify optimal strategies for prevention and management to ensure all patients achieve the best possible outcomes. **(*Circ Cardiovasc Qual Outcomes*. 2016;9:723-730. DOI: 10.1161/CIRCOUTCOMES.116.003023.)**

Key Words: atrial fibrillation ■ coronary artery bypass ■ epidemiology ■ morbidity ■ risk factor ■ women

New-onset atrial fibrillation (AF) after coronary artery bypass graft surgery (CABG) is associated with poorer long-term survival[1,2] and increased morbidity.[3,4] Because greater age is associated with higher risk of new-onset post-CABG AF,[5] the trend toward increasing age and risk profiles in the population of patients undergoing CABG[6] makes understanding this common complication of cardiac surgery a high priority, so that effective means of prevention and management can be identified and developed. Because women undergoing CABG are typically older and have higher risk profiles than their male counterparts,[7–11] such research may be particularly important to improving outcomes for women, even though some studies suggest that women have lower risk-adjusted odds of developing post-CABG AF.[12] One study investigating the impact of post-CABG AF on long-term survival found that it affected women more significantly;[1] another identified it as an independent risk factor for in-hospital mortality.[13]

Although previous studies have looked at the incidence of post-CABG AF in men and women—with some showing it to occur more frequently in women (although not to a statistically significant degree)[14,15] and others showing similar rates[16] or even lower risk for women[5,12,17,18]—it is not known how patterns of type, timing, duration, or frequency compare between men and women. We collected detailed data on post-CABG AF events (detected via continuous in-hospital ECG/telemetry monitoring) that occurred in patients who underwent isolated CABG surgery at 4 large academic medical centers and 1 high-volume specialty cardiac hospital in the United States during a period of 9 years. Here, we describe and compare the

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WHAT IS KNOWN

- New-onset AF after CABG is associated with poorer long-term survival and increased morbidity.
- There is limited population-based data available on the sex-specific incidence and characteristics (timing, duration, and frequency) of post-CABG AF episodes.

WHAT THE STUDY ADDS

- This study provides novel sex-specific data on the timing, duration, and frequency of new-onset post-CABG AF (defined as any episode detected via continuous in-hospital ECG/telemetry monitoring and documented by a physician, regardless of duration or need for treatment) from a large population-based multicenter cohort of >11 000 isolated CABG patients and compares these between women and men.
- It shows that, after adjustment for Society of Thoracic Surgeons–recognized risk factors, women had significantly lower risk for post-CABG AF and shorter durations of first and longest AF episodes and total time in AF.
- Further research is needed to investigate the sex-specific impacts of post-CABG AF on outcomes to identify optimal strategies for prevention and management to ensure all patients achieve the best possible outcomes.

epidemiology of post-CABG AF and its characteristics in men versus women, based on these data.

Methods

Study Setting and Design

This large, multicenter observational study included 11 236 consecutive patients (8214 men; 3022 women) without a history of AF who underwent isolated CABG between January 1, 2002, and December 31, 2010, at Baylor University Medical Center (Dallas, TX), The Heart Hospital at Baylor Plano (Plano, TX), Emory University (Atlanta, GA), University of Virginia (Charlottesville, VA), or Washington University (St Louis, MO). Patients were excluded if they had previous AF, previous valve surgery, preoperative endocarditis, or a ventricular assist device.

The study was approved by the institutional review boards of all centers.

Study Data

Data on patient and operative characteristics (Table 1) routinely collected for the Society of Thoracic Surgeons (STS) database were augmented with detailed data on AF events detected via continuous in-hospital ECG/telemetry monitoring.

Exposure and Outcomes of Interest

The exposure of interest was patient's sex.

The primary outcome measures were (1) the adjusted incidence of new-onset in-hospital post-CABG AF, defined as any episode detected via continuous in-hospital ECG/telemetry monitoring and documented by a physician in the chart, regardless of duration or need for treatment and (2) adjusted time (in hours) from end of CABG surgery to first episode of AF.

Table 1. Patient Characteristics by Sex

Characteristics	Men (n=8214, 73.1%)	Women (n=3022, 26.9%)
Study site		
Baylor*	4005 (48.8%)	1421 (47.0%)
Emory	1597 (19.4%)	698 (23.1%)
University of Virginia	1531 (18.6%)	508 (16.8%)
Washington University	1081 (13.2%)	395 (13.1%)
Age†, y	62.5±10.4	64.8±11.1
Body mass index†, kg/m^2	29.3±5.8	30.0±6.9
Race		
White	6732 (82.0%)	2217 (73.4%)
Black	826 (10.1%)	606 (20.1%)
Hispanic	314 (3.8%)	111 (3.7%)
Asian	160 (2.0%)	38 (1.2%)
Other	182 (2.1%)	50 (1.6%)
Diabetes mellitus	3060 (37.3%)	1471 (48.7%)
Renal failure	223 (2.7%)	102 (3.4%)
Creatinine†, mg/dL	1.26±1.18	1.14±1.17
Chronic lung disease	1531 (18.6%)	696 (23.0%)
Systemic hypertension	6843 (83.3%)	2686 (88.9%)
Peripheral vascular disease	1479 (18.0%)	677 (22.4%)
Cerebrovascular disease	1253 (15.3%)	644 (21.3%)
Time from last myocardial infarction to surgery, h		
No MI	4455 (54.2%)	1630 (53.9%)
≤6	69 (0.9%)	23 (0.8%)
>6 but <24	187 (2.3%)	67 (2.2%)
≥24	3503 (42.6%)	1302 (43.1%)
Current smoker	2322 (28.3%)	808 (26.7%)
Congestive heart failure	1722 (21.0%)	798 (26.4%)
Previous PCI	2322 (28.3%)	832 (27.5%)
Previous coronary bypass	418 (5.1%)	125 (4.1%)
Previous valve surgery/procedure	230 (2.8%)	94 (3.1%)
Preoperative angina pectoris	5173 (63.0%)	1931 (63.9%)
Preoperative ejection fraction†, %	48.4±13.4	51.2±13.3
Left main disease	2084 (25.4%)	706 (23.4%)
Operation		
Elective	5067 (61.7%)	1736 (57.4%)
On-pump	5393 (65.7%)	1825 (60.4%)
Preoperative IABP	1133 (13.8%)	392 (13.0%)

*Two Baylor sites participated in the study: one academic medical center and one high-volume specialty cardiac hospital.

†Mean±SD.

IABP indicates intra-aortic balloon pump; and PCI, percutaneous coronary intervention.

Secondary outcomes included duration (in hours) of the first AF episode, duration (in hours) of the longest AF episode, total time (in hours) spent in AF during hospitalization, and total number of post-CABG AF episodes experienced during hospitalization. Operative deaths (applying the STS definition[19]: death during CABG or any in-hospital death during a continuous post-CABG stay or any death within 30 days of post-CABG discharge), stroke, and discharge in unresolved AF were also assessed.

Statistical Analysis

To assess the association between sex and new-onset post-CABG AF, we used a propensity-adjusted generalized estimating equations model approach,[20–22] whereas a propensity-adjusted generalized estimating equation–like marginal approach using robust sandwich estimates on a Cox proportional hazards model was used to assess the association between sex and time to first AF.[20,22]

The propensity adjustment accounted for risk factors recognized by the STS[19] (Table 1); these were modeled as independent variables into a multivariable logistic regression model with sex as the outcome. All continuous variables in the propensity model were fitted using restricted cubic splines with 5 knots.[20,23] Likewise, a restricted cubic spline function with 5 knots was used to fit the propensity score as an independent variable in:

(1) a generalized estimating equation model with new-onset post-CABG AF as the dependent variable and sex, time of surgery (incremental month starting from January 2002 [month 1] to December 2010 [month 108]), and the sex×time of surgery interaction term as the independent variables. To avoid assuming a linear association of time of operation with the outcome of interest and to avoid the bias inherent

Table 2. Adjusted AF Outcomes by Sex and Year

	2002 (n=803, 7.1%)	2003 (n=1020, 9.1%)	2004 (n=984, 8.8%)	2005 (n=942, 8.4%)	2006 (n=921, 8.2%)	2007 (n=1124, 10.0%)	2008 (n=1997, 17.8%)	2009 (n=1875, 16.7%)	2010 (n=1573, 14.0%)	Total (N=11 236)
Adjusted new-onset AF*										
Male	37 (31–44)	36 (30–43)	34 (37–41)	35 (29–42)	31 (25–39)	34 (28–40)	32 (27–37)	32 (27–37)	30 (25–35)	33 (28–38)
Female	38 (28–48)	33 (24–43)	22 (15–32)	22 (14–33)	25 (16–35)	28 (20–38)	27 (21–35)	28 (21–35)	23 (17–30)	27 (22–32)
Adjusted time to reach 20% AF incidence, h†										
Male	11 (3–19)	14 (4–26)	18 (5–36)	19 (5–40)	16 (4–31)	14 (4–26)	15 (4–28)	16 (4–30)	26 (6–74)	15 (4–28)
Female	17 (5–34)	23 (6–57)	32 (7–179)	36 (7–305)	29 (6–113)	25 (6–69)	27 (6–89)	29 (6–114)	71 (9–437)	26 (6–80)
Adjusted 48-h AF-free (first episode) probabilities (95% CI)										
Male	0.68 (0.50–0.71)	0.71 (0.68–0.73)	0.73 (0.71–0.76)	0.74 (0.72–0.77)	0.73 (0.70–0.76)	0.71 (0.69–0.74)	0.71 (0.69–0.74)	0.72 (0.70–0.75)	0.77 (0.73–0.80)	0.72 (0.71–0.74)
Female	0.73 (0.69–0.77)	0.76 (0.73–0.79)	0.78 (0.075–0.81)	0.79 (0.76–0.81)	0.77 (0.75–0.80)	0.76 (0.74–0.79)	0.77 (0.75–0.80)	0.77 (0.75–0.80)	0.81 (0.79–0.85)	0.77 (0.76–0.79)
Adjusted time to first AF, mean, h‡										
Male	53 (46–60)	54 (48–59)	55 (48–61)	51 (45–57)	48 (41–55)	51 (45–57)	50 (45–56)	48 (42–54)	45 (35–54)	52 (50–54)
Female	54 (45–63)	55 (47–63)	56 (48–64)	52 (45–60)	50 (42–57)	53 (46–60)	52 (45–59)	50 (42–57)	47 (36–57)	54 (50–58)
Adjusted number of AF episodes‡										
Male (all)	1.3 (1.0–1.6)	1.1 (0.9–1.3)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	1.0 (0.7–1.2)	1.0 (0.8–1.3)	1.0 (0.8–1.2)	1.0 (0.7–1.2)	0.8 (0.5–1.2)	0.9 (0.8–1.0)
Male (≥1 episode of AF)	3.5 (2.7–4.2)	3.0 (2.4–3.5)	2.5 (1.8–3.2)	2.6 (1.9–3.2)	3.0 (2.3–3.7)	3.1 (2.5–3.7)	3.1 (2.5–3.7)	2.9 (2.3–3.6)	3.0 (2.0–4.1)	2.9 (2.6–3.1)
Female (all)	1.2 (0.9–1.6)	1.0 (0.7–1.3)	0.8 (0.5–1.0)	0.7 (0.5–1.0)	0.9 (0.6–1.2)	0.9 (0.7–1.2)	0.9 (0.7–1.2)	0.8 (0.6–1.1)	0.7 (0.3–1.1)	0.8 (0.6–0.9)
Female (≥1 episode AF)	3.6 (2.6–4.6)	3.1 (2.3–4.0)	2.7 (1.8–3.5)	2.8 (2.0–3.6)	3.2 (2.4–4.1)	3.4 (2.6–4.1)	3.4 (2.7–4.1)	3.2 (2.4–4.0)	3.4 (2.2–4.6)	3.1 (2.7–3.6)
Adjusted first AF duration, mean, h‡										
Male	7.7 (4.9–10.6)	8.3 (6.2–10.5)	9.0 (6.4–11.6)	10.3 (7.9–12.7)	11.1 (8.3–13.9)	10.1 (7.8–12.5)	9.6 (7.4–11.8)	10.0 (7.6–12.5)	6.7 (2.9–10.6)	9.0 (8.1–10.1)
Female	5.1 (1.4–8.8)	5.7 (2.6–8.8)	6.3 (3.0–9.5)	7.6 (4.7–10.5)	8.4 (5.3–11.5)	7.4 (4.6–10.1)	6.8 (4.1–9.5)	7.3 (4.3–10.2)	3.4 (0.1–8.3)	6.3 (4.6–7.9)
Adjusted longest AF duration, h‡										
Male	14 (10–18)	13 (10–16)	12 (8–16)	14 (11–18)	17 (13–21)	15 (11–18)	13 (10–17)	14 (10–17)	10 (4–15)	14 (12–15)
Female	8 (3–14)	8 (3–12)	7 (2–12)	10 (5–14)	12 (8–17)	11 (7–15)	10 (6–14)	10 (6–15)	7 (1–13)	10 (7–12)
Adjusted total AF duration, median, h§										
Male	23 (21–24)	21 (19–22)	20 (19–21)	23 (21–24)	27 (24–28)	24 (22–26)	22 (20–23)	21 (20–23)	20 (18–22)	22 (20–24)
Female	20 (19–21)	19 (18–20)	18 (17–19)	20 (19–21)	24 (23–25)	20 (21–22)	20 (19–21)	19 (18–20)	17 (16–19)	19 (18–21)

Time to first AF, duration of first AF, duration of longest AF, and total AF duration were calculated for the 3312 subjects with ≥1 AF episode; number of AF episodes was calculated for all 11 236 study subjects and for the subgroup of 3312 patients who experienced ≥1 AF episode. AF indicates atrial fibrillation.

*Percent (95% CI).

†80th percentile AF-free probability (90th, 75th).

‡95% CI.

§IQR.

with categorization of continuous variables, time of surgery was also modeled as a continuous covariate with a 5-knot restricted cubic spline;[20,23]

(2) a Cox proportional hazards model using robust sandwich estimates with time to new-onset post-CABG AF as the dependent variable and the same covariates and covariate structures listed in bullet (1).

Additionally, both models were tested to assess sex differences between sites using the appropriate interaction terms; no interactions among sites were found (models' P>0.95). Multiple imputation of all covariates used in the propensity model was done by Markov Chain Monte Carlo simulation,[24,25] to account for missing data (ejection fraction: 7.3% missing and left main disease: 0.4% missing).

The same model framework with the appropriate link function was used to assess adjusted sex differences for the other outcomes of interest. Likewise, models were tested for sex differences and site interaction; no interactions among sites were found (all models' P>0.5).

Estimates from all models were used to compute adjusted odds ratios, hazard ratios, mean differences, median differences, confidence intervals (CIs), and adjusted plots and curves. Model findings were also summarized to describe adjusted sex-specific time to reach 20% AF incidence and probability of remaining AF free for the first 48 hours post CABG.

Results

The overall unadjusted incidence of post-CABG AF was 29.5% (3312/11 236); in men, it was 30.2% (2485/8214), and in women, it was 27.4% (827/3022). Table 1 shows the clinical and demographic characteristics of the study population by sex.

The adjusted new-onset AF-related patient outcomes by year and sex are presented in Table 2. Adjusted differences in AF characteristics between women and men are presented in Table 3, whereas Table 4 summarizes differences between the sexes for other adverse outcomes considered, overall and stratified by new-onset post-CABG AF status.

Figure 1 shows the risk-adjusted predicted probability of new-onset post-CABG AF for men and women over time, as well as the risk-adjusted odds ratios (and 95% CIs) for men versus women developing new-onset post-CABG AF in each year. New-onset post-CABG AF significantly decreased from 2002 to 2010 overall (P=0.007) and in both men and women and was lower in women in all years. During the whole study period, women's risk-adjusted odds of developing post-CABG AF were significantly lower than men's (odds ratio [95% CI] for women versus men=0.75 [0.64–0.89]).

The adjusted mean (95% CI) number of episodes were similar in men (all men: 0.9 [0.8–1.0]; men with ≥1 episode: 2.9 [2.6–3.1]) and women (all women: 0.8 [0.6–0.9]; women with ≥1 episode: 3.1 [2.7–3.6]).

Overall, on average, during their hospital stay, men had a statistically significantly greater risk for developing new-onset post-CABG AF than women (hazard ratio [95% CI] for men versus women=1.16 [1.06–1.28]; Figure 2). Results were similar over the years (Figure 2). Adjusted time to reach 20% post-CABG AF incidence was 26 hours in women and 15 hours in men (Table 2), whereas at 48 hours, women had a 77% probability of being AF free compared with 72% for men (P<0.001; Table 2).

Among those who experienced ≥1 episode of AF, the adjusted mean (95% CI) duration of the first episode was significantly shorter in women (6.3 [4.4–7.9] hours) than in men (9.0 [8.1–10.1] hours; difference [95% CI]: −3.1 [−5.1 to −1.2] hours). Likewise, in these patients, the adjusted mean (95% CI) duration of the longest AF episode was significantly shorter in women (9 [7–12] hours) than in men (14 [13–15] hours; difference [95% CI]: −4.6 [−7.3 to −2.0] hours). Adjusted median (95% CI) total time in AF was significantly lower in women

Table 3. Adjusted* Comparison of Post-CABG Atrial Fibrillation Characteristics in Women Vs Men by Year

	2002 (n=803, 7.1%)	2003 (n=1020, 9.1%)	2004 (n=984, 8.8%)	2005 (n=942, 8.4%)	2006 (n=921, 8.2%)	2007 (n=1124, 10.0%)	2008 (n=1997, 17.8%)	2009 (n=1875, 16.7%)	2010 (n=1573, 14.0%)	Total (N=11 236)
Adjusted number of AF episodes (all), mean difference (95% CI)†	−0.1 (−0.4 to 0.3)	−0.1 (−0.4 to 0.2)	−0.1 (−0.3 to 0.2)	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.1)	−0.1 (−0.3 to 0.1)	−0.1 (−0.4 to 0.2)	−0.1 (−0.3 to 0.1)
adjusted P value (all)	…	…	…	…	…	…	…	…	…	P=0.18
Adjusted number of AF episodes (≥1 episode AF), mean difference (95% CI)†	0.2 (−0.8 to 1.1)	0.2 (−0.7 to 1.0)	0.2 (−0.5 to 0.9)	0.2 (−0.4 to 0.8)	0.2 (−0.3 to 0.8)	0.3 (−0.3 to 0.8)	0.3 (−0.3 to 0.9)	0.3 (−0.4 to 1.0)	0.3 (−0.5 to 1.2)	0.3 (−0.3 to 0.8)
P value (≥1 episode AF)	…	…	…	…	…	…	…	…	…	P=0.23
Adjusted 1st AF duration, mean difference (95% CI)†	−2.6 (−6.3 to 1.0)	−2.7 (−5.8 to 0.4)	−2.7 (−5.7 to −0.1)	−2.7 (−4.9 to −0.5)	−2.7 (−4.7 to −0.8)	−2.8 (−4.7 to −0.8)	−2.8 (−4.9 to −0.6)	−2.8 (−5.3 to −0.3)	−2.8 (−5.8 to 0.2)	−2.7 (−4.7 to −0.8)
P value	…	…	…	…	…	…	…	…	…	P=0.02
Adjusted longest AF duration, mean difference (95% CI)†	−5.5 (−11 to −0.1)	−5.2 (−9.8 to −0.6)	−4.9 (−8.7 to −1.0)	−4.6 (−7.8 to −1.3)	−4.3 (−7.2 to −1.4)	−4.0 (−6.8 to −1.1)	−3.7 (−6.8 to −0.5)	−3.4 (−7.0 to 0.3)	−3.1 (−7.4 to 1.3)	−4.1 (−6.9 to −1.2)
P value	…	…	…	…	…	…	…	…	…	P=0.02
Adjusted total AF duration, median difference (95% CI)‡	−2.7 (−3.0 to −2.4)	−2.4 (−2.5 to −2.1)	−2.3 (−2.5 to −2.2)	−2.4 (−2.7 to −2.0)	−3.0 (−3.3 to −2.7)	−3.1 (−3.4 to −2.8)	−2.5 (−2.7 to −2.4)	−2.4 (−2.6 to −2.2)	−2.5 (−2.8 to −2.3)	−2.4 (−2.5 to −2.3)
P value	…	…	…	…	…	…	…	…	…	P<0.0001

Time to first AF, duration of first AF, duration of longest AF, and total AF duration were calculated for the 3312 subjects with ≥1 AF episode; number of AF episodes was calculated for all 11 236 study subjects and for the subgroup of 3312 patients who experienced ≥1 AF episode. AF indicates atrial fibrillation; CABG, coronary artery bypass graft; and CI, confidence interval.

*Adjusted analyses used a propensity-adjusted model controlling for recognized STS risk factors (Table 1) in generalized estimating equations models by study site, with an interaction term between sex and month of surgery to allow mean differences to vary over time.

†Mean and (95% CIs).

‡Median (95% CIs).

Table 4. Risk-Adjusted Nonatrial Fibrillation Outcomes by Sex, Overall, and New-Onset Post-CABG AF Status

Outcome	Overall, % (95% CI)	Male (95% CI)	Female (95% CI)	Odds Ratio (95% CI)	*P* value
All patients (N=11 236)					
Operative mortality					
Unadjusted	1.7 (1.4–1.9)	1.3 (1.1–1.6)	2.5 (2.0–3.1)	1.9 (1.4–2.6)	<0.0001
Adjusted	1.5 (0.9–2.3)	1.3 (0.9–1.8)	2.2 (1.4–3.4)	1.8 (1.0–3.0)	0.048
Stroke					
Unadjusted	1.6 (1.3–1.8)	1.3 (1.0–1.5)	2.3 (1.8–2.9)	1.8 (1.4–2.5)	<0.0001
Adjusted	1.4 (0.8–2.4)	1.3 (0.9–1.7)	1.8 (1.2–2.8)	1.4 (0.8–2.5)	0.126
AF patients only (n=3312)					
Operative mortality					
Unadjusted	3.4 (2.8–4.1)	2.7 (1.8–4.0)	5.8 (3.7–9.0)	2.2 (1.2–4.1)	0.027
Adjusted	3.3 (2.2–5.0)	2.6 (1.7–3.9)	5.4 (3.2–8.9)	2.1 (1.1–4.3)	0.040
Stroke					
Unadjusted	2.5 (2.0–3.1)	2.0 (1.3–3.2)	3.8 (2.2–6.6)	1.9 (0.9–4.0)	0.070
Adjusted	2.2 (1.3–3.7)	1.8 (1.1–2.9)	3.3 (1.7–6.3)	1.9 (0.8–4.4)	0.094
Discharge home in AF					
Unadjusted	0.8 (0.7–1.0)	0.9 (0.7–1.1)	0.7 (0.4–1.0)	0.8 (0.5–1.3)	0.317
Adjusted	0.7 (0.4–1.3)	0.8 (0.5–1.3)	0.5 (0.2–1.2)	0.7 (0.3–1.6)	0.234
Non-AF patients (n=7924)					
Operative mortality					
Unadjusted	0.8 (0.6–1.1)	0.7 (0.4–1.2)	1.3 (0.7–2.4)	1.8 (0.8–3.9)	0.098
Adjusted	0.8 (0.4–1.4)	0.7 (0.4–1.1)	1.0 (0.4–2.1)	1.4 (0.6–3.8)	0.312
Stroke					
Unadjusted	1.1 (0.9–1.4)	1.0 (1.0–1.5)	1.8 (0.0–2.9)	1.8 (0.9–3.7)	0.063
Adjusted	1.0 (0.6–1.6)	0.9 (0.6–1.4)	1.2 (0.6–2.2)	1.3 (0.6–2.8)	0.332

AF indicates atrial fibrillation; CABG, coronary artery bypass graft; and CI, confidence interval.

(19 [18–21] hours) than in men (22 [20–24] hours; difference [95% CI]: −2.4 [−2.5 to −2.3] hours; *P*<0.0001).

Discussion

Ours is the first large (>11 200 patients), multicenter study to assess both the incidence and characteristics of new-onset AF after isolated CABG and to compare these in women versus men. Using detailed clinical data for patients who underwent CABG during a period of 9 years and including data for all episodes of AF detected via continuous in-hospital ECG/telemetry monitoring to provide an enhanced, comprehensive picture of new-onset AF after isolated CABG, our results reveal important differences between the sexes.

The novel sex-specific data presented here show that after robust risk adjustment to account for patients' clinical and nonclinical risk factors, women undergoing isolated CABG are not only less likely to develop new-onset post-CABG AF than their male counterparts but, among those who do suffer this common complication, they experience shorter first and longest episodes of AF, and spend shorter total amounts of time in AF during the hospital stay.

To our knowledge, this is the first study not only to describe the sex-specific characteristics of post-CABG AF but also to examine all of these (timing, duration, and frequency) and incidence simultaneously, giving a complete picture of both the risk for and clinical course of post-CABG AF in women and men.

Our finding of a lower adjusted incidence of post-CABG AF in women is consistent with the results reported from a relatively large study investigating patients who underwent CABG from 1995 to 2009.[12] Although that study used a slightly different AF definition (episodes of any duration during the hospitalization for the index surgery deemed to be clinically significant by the treating physician) from ours, the propensity-matched odds ratio reported for women versus men of 0.76 (95% CI: 0.65–0.90)[12] was similar to our risk-adjusted result of 0.75 (95% CI: 0.64–0.89). These results are also consistent with previous studies that have identified male sex as an independent risk factor for post-CABG AF.[17,26,27] Although other studies comparing incidence of post-CABG AF between men and women report finding no significant differences, they examined only unadjusted incidence.[14–16]

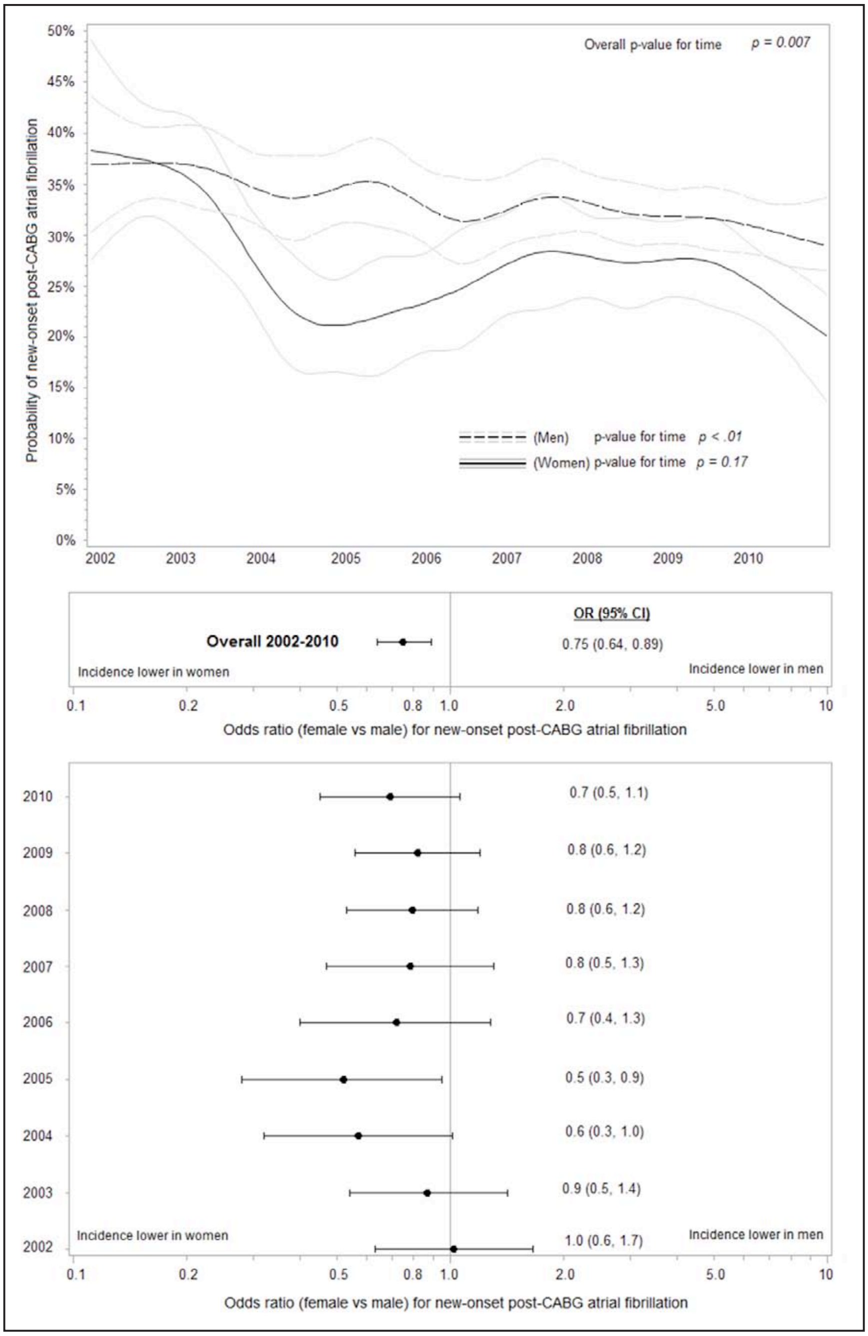

Figure 1. Adjusted* predicted probability, odds ratios comparing sex, and 95% confidence intervals of new-onset post-CABG atrial fibrillation according to sex by year. *Society of Thoracic Surgeons factors listed in Table 1, time of surgery (incremental month starting from January 2002 [month 1] to December 2010 [month 108]), and interaction between sex and time of surgery.

With respect to the significantly shorter duration of AF episodes we observed in women versus men, we found no previous studies with which to compare our results. Although 2 small studies have previously reported on the duration of post-CABG episodes,[28,29] neither reported sex-specific results. Furthermore, they applied different definitions of AF and patient inclusion/exclusion criteria, limiting the value of comparisons to our findings. We similarly found no previous studies comparing frequency or timing of onset of the first episode of AF between men and women. However, the adjusted mean of 52 hours for men and 54 hours for women we observed for time from CABG to first AF episode among patients who developed AF (Table 2) is consistent with previous observations that post-CABG AF onset tends to peak on days 2 to 3 post surgery.[18,30]

As described elsewhere (article currently under review), the characteristics (including the STS-recognized risk factors) of our study cohort are similar to those reported for isolated CABG patients from 2000 to 2009 in the national STS adult cardiac surgery database.[31] Given that >95% of the US cardiac surgery programs contribute to the database, this indicates that our results are likely generalizable to the broader population of US CABG patients. The significantly greater age and higher prevalence of comorbidities such as diabetes mellitus, hypertension, and congestive heart failure among the women in our cohort is also typical of the population of CABG patients;[9,10,32,33] and the borderline statistically significant higher risk-adjusted operative mortality we observed among the women in our study cohort is consistent with the

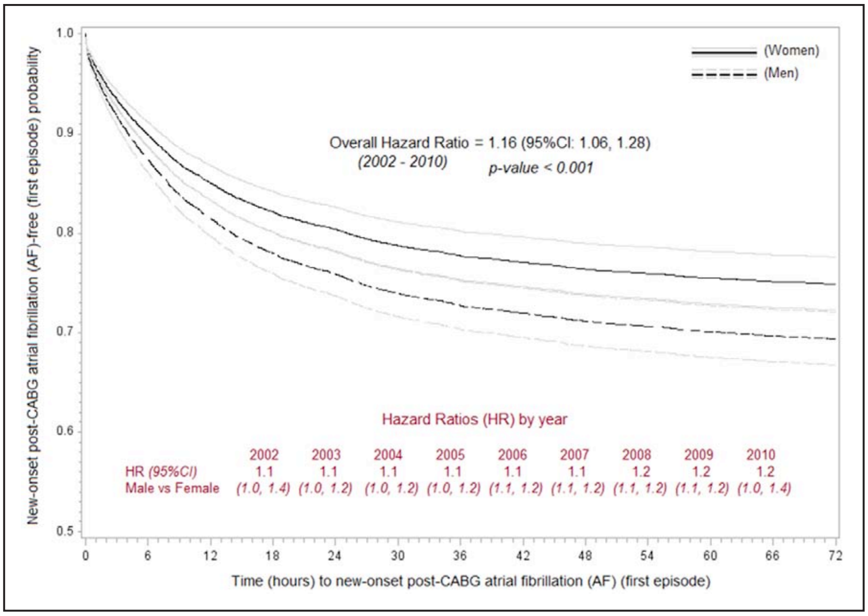

Figure 2. Adjusted* probability and hazard ratios (with 95% confidence intervals) for freedom from new-onset post-CABG atrial fibrillation (AF), by sex (2002–2010). *Society of Thoracic Surgeons factors listed in Table 1, time of surgery (incremental month starting from January 2002 [month 1] to December 2010 [month 108]), and interaction between sex and time of surgery.

results reported by several previous studies.[12,34–38] As with any observational study, we cannot rule out the possibility that unknown factors that confound the association between exposure (sex) and outcome (post-CABG AF) exist. However, the propensity-adjusted generalized estimating equations model approach developed to conduct the statistical analysis considered an extensive list of risk factors recognized by the STS in addition to other important variables, providing a rigorous adjustment for potential confounders.

Future research should investigate how the differences in incidence and duration of post-CABG AF observed here between women and men play out in terms of long-term outcomes. Although it is well established that post-CABG AF is associated with poorer long-term survival,[1,2,39] it is not yet known whether the magnitude of this association is consistent across sex. It is also not known how the characteristics of post-CABG AF affect long-term survival—nor whether such affects (including their magnitudes) are similar across sex. Given the inconsistencies in the existing evidence about whether (and why) women experience worse, equivalent, or better long-term outcomes after CABG,[40–44] this is a fertile area for research.

Our results showing significant differences in both the risk-adjusted incidence and duration of AF events between women and men provide important groundwork for future investigations of the sex-specific impacts on survival and of the sex-specific effectiveness of strategies for preventing and managing post-CABG AF. Teasing out differences in the impact of postoperative complications and their management on long-term outcomes between men and women could identify opportunities to improve care for both sexes—and help address the current dearth of information on the effectiveness of treatments for cardiovascular disease specifically in women,[45,46] something which has been called for to achieve health equity.[47]

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Disclosures

None.

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Sex Differences in the Epidemiology of New-Onset In-Hospital Post–Coronary Artery Bypass Graft Surgery Atrial Fibrillation: A Large Multicenter Study

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