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Lower Survival After Coronary Artery Bypass in Patients Who Had Atrial Fibrillation Missed by Widely Used Definitions

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Abstract

Objective: To investigate the impact of limiting the definition of post-coronary artery bypass graft (CABG) atrial fibrillation (AF) to AF/flutter requiring treatment—as in the Society of Thoracic Surgeons' (STS) database— on the association with survival.

Patients and Methods: We assessed in-hospital incidence of post-CABG AF in 7110 consecutive isolated patients with CABG without preoperative AF at 4 hospitals (January 1, 2004 to December 31, 2010). Patients with ≥1 episode of post-CABG AF detected via continuous in-hospital electrocardiogram (ECG)/telemetry monitoring documented by physicians were assigned to the following: Group 1, identified as having post-CABG AF in STS data and Group 2, not identified as having post-CABG AF in STS data. Patients without documented post-CABG AF constituted Group 3. Survival was compared via a Cox model, adjusted for STS risk of mortality and accounting for site differences.

Results: Over 7 years' follow-up, 16.0% (295 of 1841) of Group 1, 18.7% (79 of 422) of Group 2, and 7.9% (382 of 4847) of Group 3 died. Group 2 had a significantly greater adjusted risk of death than both Group 1 (hazard ratio [HR]: 1.16; 95% confidence interval [CI], 1.02 to 1.33) and Group 3 (HR: 1.94; 95% CI, 1.69 to 2.22).

Conclusions: The statistically significant 16% higher risk of death for patients with AF post-CABG missed vs captured in STS data suggests treatment and postdischarge management should be investigated for differences. The historical misclassification of "missed" patients as experiencing no AF in the STS data weakens the ability to observe differences in risk between patients with and without post-CABG AF. Therefore, STS data should not be used for research examining post-CABG AF.

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Over the past 2 decades, evidence has shown that postoperative atrial fibrillation (AF) following cardiac surgery is not the minor, self-limiting complication it was previously considered to be[1-5] but, rather, is independently associated with poorer survival.[2,5-9] Risk-adjusted estimates of its impact on survival following isolated coronary artery bypass graft (CABG) have been reported as ranging from 21% to 35% increased risk of mortality with up to 5 to 12.5 years' follow-up,[2,5-7] to 96% with 1-year follow-up.[9] Furthermore, among isolated patients with CABG who survived to hospital discharge, 1 study found the adjusted risk of mortality during up to 7 years' follow-up was more than twice that of patients who did not experience post-CABG AF.[8] The mechanism underlying the relationship between post-CABG AF and late mortality has yet to be determined, but theories include that it might presage recurrent AF that carries risks for complications such as stroke[7,8] or the development of congestive heart failure,[2] or that patients may suffer adverse drug effects from prescribed treatments, such as proarrhythmia, with antiarrhythmic drugs or hemorrhage with anticoagulants[2].

Investigations into the association between post-CABG AF and late mortality (and the

underlying causative mechanism) are complicated by the fact that no standard definition of post-CABG AF has been agreed on, and the studies thus apply a variety of definitions, creating uncertainty about how great the risk posed to patients truly is. This, in turn, makes it difficult to determine whether the risks of potential prophylactic measures (eg, preoperative β-blockers or amiodarone) are outweighed by the benefits.

The Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database includes postoperative AF among the variables routinely collected from the participating cardiac-surgery programs. Given the quality of the clinical data it contains, and the fact that data regarding >95% of the cardiac surgery operations performed each year in the United States are included,[10,11] the STS database is considered a valuable resource for studies investigating postoperative AF. As such, it is influential in determining the definition of postoperative AF on which the evidence base regarding its prevention and management continues to be built. For example, the 2012 article describing trends in isolated CABG and its outcomes using the STS data[12] has been cited >230 times, earning the "highly cited" designation in the Web of Science Core Collection.[13] The STS defines postoperative AF as "atrial fibrillation/flutter requiring treatment," adding the clarification in the Adult Cardiac Surgery Database training manuals for versions 2.73 and later (corresponding to the years 2011, on) that this should include any event that "lasts longer than 1 hour and/or requires treatment."[14,15] However, neither the training manuals nor the data specifications provide criteria for determining when treatment is required, meaning it may vary according to differing indications for treatment among physicians and hospitals. Limiting the definition to events requiring treatment may also miss patients at increased risk for later mortality, as we have previously shown it to do for 30-day mortality.[16] We examined this possibility, using data from a large, multicenter observational study, to compare risk-adjusted incidence of new-onset post-CABG AF captured by the STS definition and data vs 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 assess the impact of the use of these different definitions on the association between new-onset post-CABG AF and late mortality.

METHODS

This multicenter observational study was conducted in all 7110 consecutive patients without histories of AF who underwent isolated CABG between January 1, 2004, and December 31, 2010, at Baylor University Medical Center (Dallas, Texas), The Heart Hospital Baylor Plano (Plano, Texas), Emory University (Atlanta, Georgia), or Washington University (St. Louis, Missouri).

The University of Virginia (Charlottesville, Virginia) was included in our previous investigation looking at the association between post-CABG AF events missed by the STS definition and data and increased risk of 30-day mortality[16] but had to be excluded here, as their institutional policy prohibited the sharing of the patient identifiers (eg, social-security numbers) needed for matching with the long-term vital status data. Patients were excluded if they had preoperative endocarditis or ventricular assist devices.

Data Sources

Each site provided the data they had submitted to the STS Adult Cardiac Surgery Database for patients who underwent isolated CABG from 2004 to 2010. The STS database was established in 1989 and contains more than 6.1 million surgical records, representing >95% of the cardiac surgery operations performed each year in the United States,[10,11] Annual audits, checking 75 variables submitted for CABG surgeries against patient medical records for a sample of patients, have shown a mean aggregate agreement rate across these variables of 96.1%.[17-19]

To augment the STS data with detailed data regarding AF events based on ECG findings, and to ensure data on all episodes of post-CABG AF (regardless of duration or need for treatment), hospital medical records were abstracted for each patient by trained study personnel, using a standardized data-collection form. These chart abstractions were validated through audits of 50 randomly selected charts every 6 months, in which those 50 charts were independently abstracted by all

TABLE. Patient Characteristics by Development of New-Onset Atrial Fibrillation (AF) per STS Definition or Physician-Assessed AF Not Captured by the STS Data

Characteristic:	No AF 4847 (68.2%)	STS AF[a] 1841 (25.9%)	AF missed by STS[b] 422 (5.9%)
Study site			
Baylor[c]	2644 (54.5%)	1053 (57.2%)	244 (57.8%)
Emory	1724 (35.6%)	449 (24.4%)	124 (29.4%)
Washington University	479 (9.9%)	339 (18.4%)	54 (12.8%)
Age [d]	61.1±10.6	67.6±9.4	65.8±10.1
Body mass index (kg/m^2)[d]	29.5±5.9	29.6±6.9	30.0±6.4
Male	3472 (71.6%)	1398 (75.9%)	293 (69.4%)
Female	1375 (28.4%)	443 (24.1%)	129 (30.6%)
Race			
White	3543 (75.1%)	1553 (84.4%)	326 (77.3%)
Black	823 (17.0%)	171 (9.3%)	65 (15.4%)
Hispanic	239 (4.9%)	65 (3.5%)	14 (3.3%)
Asian	124 (2.6%)	30 (1.6%)	5 (1.2%)
Other	118 (2.4%)	22 (1.2%)	12 (2.8%)
Diabetes mellitus	1997 (41.2%)	754 (41.0%)	201 (47.6%)
Renal failure	136 (2.8%)	57 (3.1%)	20 (4.7%)
Creatinine (mg/dL)[e]	1.0 (0.8, 1.2)	1.0 (0.9, 1.3)	1.0 (.9, 1.3)
Chronic lung disease	981 (20.2%)	467 (25.4%)	91 (21.6%)
Systemic hypertension	4230 (87.3%)	1617 (87.8%)	370 (87.7%)
Peripheral vascular disease	873 (18.0%)	460 (25.0%)	86 (20.4%)
Cerebrovascular disease	768 (15.8%)	376 (20.4%)	88 (20.9%)
Time from last myocardial infarction to surgery			
No myocardial infarction	2709 (55.9%)	962 (52.3%)	195 (46.2%)
≤6 hours	37 (0.8%)	19 (1.0%)	8 (1.9%)
>6 but <24 hours	96 (2.0%)	36 (2.0%)	15 (3.6%)
≥24 hours	2005 (41.3%)	824 (44.7%)	204 (48.3%)
Current smoker	1503 (31.0%)	421 (22.9%)	117 (27.7%)
Congestive heart failure	966 (19.9%)	456 (24.8%)	119 (28.2%)
Previous PCI	1424 (29.4%)	553 (30.0%)	139 (32.9%)
Previous coronary bypass	264 (5.5%)	96 (5.2%)	31 (7.4%)
Previous valve surgery	116 (2.4%)	63 (3.4%)	18 (4.3%)
Preoperative angina pectoris	3051 (63.0%)	1126 (61.2%)	253 (60.0%)
Preoperative ejection fraction (%)[d]	49.7±12.9	48.9±13.7	47.8±14.6
Left main disease	1309 (27.0%)	581 (31.6%)	130 (30.8%)
Operation			
Elective	2802 (57.8%)	1098 (59.6%)	242 (57.4%)
Nonelective	2045 (42.2%)	743 (40.4%)	180 (42.6%)

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TABLE. Continued

Characteristic:	No AF 4847 (68.2%)	STS AF[a] 1841 (25.9%)	AF missed by STS[b] 422 (5.9%)
Operation, continued			
Off-pump	2302 (47.6%)	712 (38.7%)	173 (41.1%)
On-pump	2536 (52.4%)	1127 (61.3%)	248 (58.9%)
Preoperative IABP	519 (10.7%)	289 (15.7%)	87 (20.6%)

[a]Patients identified as having postcoronary artery bypass graft (CABG) atrial fibrillation (AF), according to the Society of Thoracic Surgeons (STS) data/definition ("atrial fibrillation/flutter requiring treatment").[29]
[b]AF = patients who had at least 1 episode of post-CABG AF detected via continuous in-hospital ECG/ telemetry monitoring and documented by a physician in the chart, regardless of duration or need for treatment, but not identified within the STS data as having AF under the STS definition.
[c]Two Baylor sites participated: 1 academic medical center and 1 high-volume specialty cardiac hospital.
[d]Mean ± standard deviation.
[e]Median (interquartile range [IQR]).
IABP = intra-aortic balloon pump; PCI = percutaneous coronary intervention.

current study personnel engaged in data collection and cross-checked for consistency. Vital status data were obtained from a copy of the Social Security Death Master File archived before state-owned data were removed on November 1, 2011.[20]

Study Exposure

The study exposure, post-CABG AF status, was defined as follows:

Patients who had at least 1 episode of post-CABG AF, regardless of duration or need for treatment, documented by a physician in the chart, based on detection via continuous in-hospital electrocardiogram (ECG)/ telemetry monitoring, were assigned to 1 of 2 groups:

- Group 1, STS-definition post-CABG AF: those patients identified as having post-CABG AF according to the STS data (definition: "atrial fibrillation/flutter requiring treatment," Version 2.61)[21]
- Group 2, post-CABG AF missed by the STS data: those patients not identified as having AF according to the STS data

A third group comprised those patients who had no documented episodes of post-CABG AF (Group 3: no post-CABG AF).

The possibility that some patients identified in the STS data as having post-CABG AF might have no such episodes documented by physicians in the chart was considered, but we found no patients for whom this had occurred.

Study Outcome

The outcome of interest was survival, censored at October 31, 2011, and assessed using the archived copy of the Social Security Death Master File. The study was approved by the institutional review boards of all participating centers.

Statistical Analysis

Unadjusted frequencies and means (standard deviations) of preoperative patient characteristics were calculated for the 3 groups defined here. Differences in long-term mortality among the 3 groups were assessed using a Cox proportional hazards model, adjusted for the STS predicted risk of mortality (which is calculated from the patient characteristics presented in the Table),[21] modeled using restricted cubic spline functions to avoid assuming a linear relationship with the outcome.[22–26] The Cox model employed robust sandwich variance estimates to account for differences between study sites.[27] Model estimates were used to compute adjusted hazard ratios (HRs), 95% confidence intervals (95% CIs), and *P* values. Proportional hazards assumptions were assessed and confirmed through visual inspection of Schoenfeld's residuals plots.[28] No missing data were observed for any of the variables used in the model. All analyses were performed using SAS 9.3 (SAS Institute, Cary, North Carolina).

Patient Involvement

This was an observational study investigating the impact of applying different definitions of common complication of CABG to evaluations of its impact on outcomes. No patients were involved in setting the research question or selecting the outcome measures, nor were they involved in the design and implementation of the study, and there are no plans to involve patients in dissemination.

RESULTS

In our study cohort of 7110 isolated CABG patients without histories of AF, 2263 (31.8%) experienced post-CABG AF:

- Of the overall study population, 1841 (25.9%) experienced postoperative AF and were identified as having AF according to the STS data and definition
- Of the overall study population, 422 (5.9%) patients who experienced postoperative AF and were not identified as having AF in the STS data; accordingly, 18.5% of patients experiencing post-CABG AF were missed by the STS data and definition.

The remaining 4847 (68.2%) had no documented episodes of AF. The Table shows the patient characteristics for each of these groups. The Figure also reports length of follow-up for each of the study groups.

Over the 7-year follow-up, unadjusted cumulative mortality was 16.0% (295 of 1841) in Group 1 (post-CABG AF according to the STS data, median follow-up 2.28 years [25th percentile: 1.1, 75th percentile: 3.9]), 18.7% (79 of 422) in Group 2 (post-CABG AF missed by the STS data and definition, median follow-up 2.17 years [25th percentile: 1.1, 75th percentile: 3.8]), and 7.9% (382 of 4847) in Group 3 (no post-CABG AF, median follow-up 2.24 years [25th percentile: 1.1, 75th percentile: 3.6]). After adjustment, patients in Group 2 (post-CABG AF missed by the STS data and definition) had significantly greater risks of death than those in both in Group 1 (post-CABG AF according to the STS data) (HR: 1.16; 95% CI, 1.02 to 1.33; $P=.024$) and Group 3 (no post-CABG AF) (HR: 1.94; 95% CI, 1.69 to 2.22; $P<.001$) (Figure). Likewise, Group 1 (post-CABG AF according to the STS data) patients had significantly higher risks of mortality than Group 3 (no post-CABG AF) patients (HR: 1.67; 95% CI, 1.30 to 2.16; $P<.001$) (Figure).

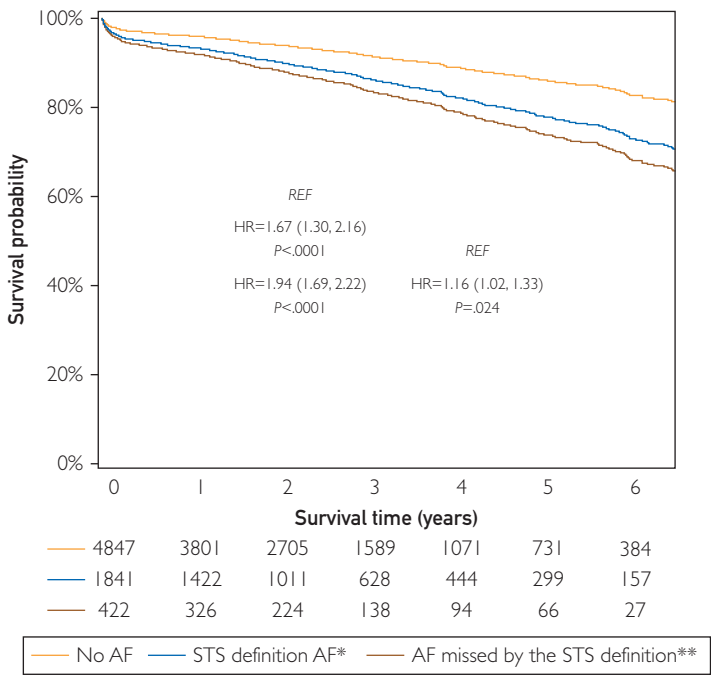

FIGURE. Adjusted (Society for Thoracic Surgeons [STS] risk of mortality) survival curves, hazard ratios (HRs) (95% confidence intervals [CIs]), and *P* value comparing patients experiencing new-onset postcoronary artery bypass graft (CABG) atrial fibrillation (AF), according to whether the AF events were captured by the STS data and definition. See Appendix A (available online at http://www.mayoclinicproceedings.org) for confidence intervals. *Patients identified as having post-CABG AF according to the STS data, which applies the definition "atrial fibrillation/flutter requiring treatment," Version 2.61. ** Patients identified as having post-CABG AF detected via continuous in-hospital ECG/telemetry monitoring and documented by a physician in the chart, but were not identified as having AF in the STS data. REF, reference

DISCUSSION

Our results show that more than 18% of patients undergoing isolated CABG who experience post-cardiac AF are missed by the STS data and definition and that these patients have poorer risk-adjusted survival than both patients who do not develop post-CABG AF and patients who developed new-onset post-CABG AF captured by the STS data and definition. This unexpected result demonstrates the urgency of establishing a standard

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definition of post-CABG AF that captures all patients who experience this complication.

The increase in risk of long-term mortality we observed among the patients with post-CABG AF according to the STS data (compared with patients who did not experience AF) was substantially greater than the 21% and 29% increases reported in 2 previous studies that applied this definition.[5,7] This is likely explained, at least in part, by the fact that in those studies the patients with post-CABG AF missed by the STS data and definition—who, our results indicate, have the poorest risk-adjusted survival of all—would have been included in the "no AF" comparison group. Studies that have applied time-based limits to the definition of AF, or no limits beyond the requirement that a physician document it based on ECG findings, have reported greater increases in risk of mortality (ranging from 35%, when only AF episodes lasting ≥30 minutes were included, to 213% in a study that included all AF episodes lasting >15 minutes).[2,8,9] The 94% greater risk of long-term mortality we observed in the post-CABG patients with AF missed by the STS data and definition (vs patients who did not develop AF) most closely corresponds to the 96% increase reported in a study looking at the impact of "transient" post-CABG AF, defined as AF episodes lasting ≥2 minutes but <7 days.[9]

The most intriguing of our results is the finding that patients with post-CABG AF missed by the STS data had a 16% greater risk of mortality over the 7-year follow-up than the patients who experienced new-onset post-CABG AF, according to the STS definition. Intuitively, as the STS defines post-CABG AF as events "requiring treatment," one expects the STS definition to capture the higher-severity events, making those patients more likely to have poor long-term outcomes. Our results show this is not the case, but further research is needed to understand why. One possibility is that patients who experience post-CABG AF events that their clinicians view as warranting treatment are consciously or subconsciously flagged as being at higher risk for adverse outcomes and are therefore more closely followed and managed in-hospital and postdischarge. Future studies should therefore include examination both of the characteristics (timing, duration, frequency) of the post-CABG AF experienced by patients captured by the STS definition and data vs not and of the in-hospital and postdischarge treatment and management the patients in these 2 groups receive. The results of this research could help establish standardized, evidence-based criteria for when treatment of post-CABG AF is required and the post-discharge medications and management that optimize survival.

Study Limitations

Some limitations should be kept in mind when interpreting our results. First, without cause of death data, we have little insight into the mechanisms mediating the association observed between a patient having post-CABG AF missed by the STS data and definition and increased risk for late mortality. Second, our cohort dates from 2004 to 2010; as such, we do not have data for the years following the clarification made in the STS training manual version 2.73 that the post-CABG AF variable is intended to capture not only events that required treatment but also any event lasting longer than 1 hour. Assuming that the sites submitting data to the STS have adopted this expanded definition from the training manual (an assumption that may be questionable, given that the data specifications for the variable have not been similarly updated), we would expect partial mitigation of the problem of patients who experienced post-CABG AF episodes being missed by the STS definition and data. For example, in our cohort, ~50% of the "missed" patients had at least 1 AF event that lasted at least 1 hour. However, it is important to note that the 1-hour duration cutoff the training manual update provides to the STS definition of post-CABG AF is not based on evidence showing that this is the duration at which post-CABG AF becomes associated with increased risk for mortality or other adverse outcomes. In fact, based on our previous analysis showing a positive association between the number of post-CABG AF events patient experience and their risk for 5-year mortality that was independent of the

total time spent in AF,[30] any duration-based definition of post-CABG AF can be expected to exclude at least some patients who experienced episodes of AF that carry an associated risk for adverse outcomes. As such, the broader AF data capture intended by the expanded definition in versions 2.73 and on of the Adult Cardiac Surgery Database training manual should help reduce the proportion of "missed" post-CABG AF cases but will not necessarily improve capture of patients who carry the associated increased risk of mortality. Lacking data from 2011 on, we cannot, unfortunately, evaluate the extent to which the problem has been mitigated.

CONCLUSIONS

Our results show that that "AF requiring treatment" is an inadequate definition of post-CABG AF because it misses a substantial number of isolated CABG patients who experience this serious complication and carry its associated risks. This has clinical implications in that it identifies a subgroup of CABG patients that may need to be targeted for more meticulous follow-up to manage their risk for adverse outcomes. It also has important policy and research implications: the historical "misclassification" of 18.5% of isolated CABG patients who experience post-CABG AF to the "no AF" group in the STS data means that studies using these data likely underestimate the impact of post-CABG AF on patient outcomes, which, in turn, threatens the validity of studies using STS data that include post-CABG AF among either the exposure or outcome variables. Additional research is needed to determine the extent to which STS data from the years following the 2011 update to the training manual capture the post-CABG AF events that carry an associated increased risk of death. To avoid missing any such events, the STS should revise its definition of postoperative AF to include all episodes of AF documented by physicians in patients' charts. Any other revision to the definition must wait for rigorous analyses of the assocition between the characteristics of AF (eg, number of events, duration of AF) and increased risk of late mortality. In the meantime, new studies investigating post-CABG AF as either an exposure or outcome variable should not rely on STS data — and results existing studies should be viewed and applied with caution.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **AF** = atrial fibrillation; **CABG** = coronary artery bypass graft'; **CI** = confidence interval; **ECG** = electrocardiogram; **HR** = hazard ratio; **STS** = Society of Thoracic Surgeons

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