Does preoperative atrial fibrillation increase the risk for mortality and morbidity after coronary artery bypass grafting?

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Objectives: Preoperative atrial fibrillation has been associated with less favorable outcomes in patients undergoing coronary artery bypass grafting. However, it was never investigated in a large cohort of patients using a national database. This study aims to (1) identify the effect of atrial fibrillation on operative mortality and morbidity in patients undergoing isolated coronary artery bypass grafting and (2) identify the potential effect of atrial fibrillation on patients with decreased left ventricular ejection fraction ($\leq 40\%$).

Methods: The Society of Thoracic Surgeons National Adult Cardiac Surgery Database was used for patients with coronary artery disease undergoing isolated coronary artery bypass grafting ($n = 281,567$). The association between atrial fibrillation and outcomes was estimated within 3 categories of low (ejection fraction, $<40\%$), moderate (ejection fraction, $40\%–55\%$), or normal (ejection fraction, $>55\%$) systolic function.

Results: Patients with atrial fibrillation were found to be older and have a higher incidence of comorbidities. A higher incidence of all major complications and mortality after surgical intervention was documented. An interaction between atrial fibrillation and an ejection fraction of greater than 40% for mortality, stroke, prolonged ventilation, and prolonged length of stay was identified.

Conclusions: Our findings suggest that preoperative atrial fibrillation is associated with an increased risk for perioperative mortality and morbidity in patients undergoing coronary artery bypass grafting. The negative effect of atrial fibrillation might be more significant in patients undergoing coronary artery bypass grafting with an ejection fraction of greater than 40% . Both the EuroSCORE and, until recently, the Society of Thoracic Surgeons risk calculator do not include atrial fibrillation as a potential risk modifier; however, based on this study, it should be identified as a variable to be investigated and incorporated into future risk calculators.

Atrial fibrillation is a very common arrhythmia affecting several million patients with a median age of 70 years in the United States.¹ The average age for patients treated surgically for ischemic heart disease is increasing, and as a result, it is not uncommon to have candidates for cardiac surgery presenting with concomitant atrial fibrillation. A few large cohort studies have recently recognized atrial fibrillation as a marker for increased cardiovascular morbidity and mortality.² This, together with the increased prevalence of atrial fibrillation in patients undergoing cardiac surgery, makes it important to assess the potential effect of the arrhythmia on outcome after surgical intervention using a large surgical database. Preoperative atrial fibrillation among patients undergoing coronary artery bypass grafting (CABG) has been shown to be associated with higher mortality and morbidity.^{3,4} Nevertheless, atrial fibrillation was never intro-

duced as a variable in the most commonly used risk calculators for cardiac surgery, such as the EuroSCORE and the Society of Thoracic Surgeons (STS) risk score (as recently incorporated by STS version 2.61), and subsequently has rarely been considered to be a variable of significance when discussing the risk and benefits of the surgical procedure with the referring physicians, payers, and patients.

Theoretically, preoperative atrial fibrillation might pose a higher clinical relevance in patients who present for surgical intervention with a low ejection fraction (EF) and congestive heart failure. In addition, patients with pre-existing atrial fibrillation are at a higher risk for time-related mortality after CABG.^{2,4} However, one of the challenges is to determine whether atrial fibrillation is a marker or causally related factor in less favorable outcomes, and this might require a prospective clinical trial to compare matched groups of candidates for surgical intervention with and without atrial fibrillation. The current literature dealing with this question is based on retrospective reports, most of them based on a single institution's experience. Therefore by using data from the STS Adult Cardiac Surgery Database, the present study was designed to identify the potential effect of preoperative atrial fibrillation on the operative mortality and morbidity in a large cohort of patients with coronary artery disease undergoing isolated CABG to identify the potential association with reduced left ventricular function.

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Received for publication July 25, 2008; revisions received Sept 9, 2008; accepted for publication Sept 23, 2008.

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J Thorac Cardiovasc Surg 2009;137:901-6
0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2008.09.050

Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
EF	= ejection fraction
OR	= odds ratio
STS	= Society of Thoracic Surgeons

MATERIALS AND METHODS

This is a prospective cohort observational study using data from the STS National Adult Cardiac Surgery Database data collection platform for surgical data collected during the years 2002 and 2003. This platform allows prospective data collection from multiple institutions with agreed definitions.

Subjects were patients undergoing isolated CABG. The STS data collection versions used were 2.35 and 2.41. EF was classified as low (<40%), moderate (40%–55%), or normal (>55%). Outcomes of interest were operative mortality, reoperation, permanent stroke, prolonged ventilation (>24 hours), renal failure, and prolonged postoperative length of stay (>14 days).

Baseline demographic characteristics, preoperative risk factors, and outcomes of interest were compared between patients with and without preoperative atrial fibrillation. Continuous variables were categorized, and all variables were described as frequencies, with χ^2 tests for comparisons between groups. We used regression splines to model the association between EF and the outcome without assuming strict linearity. We first performed unadjusted comparisons and then adjusted for a broad range of patient preoperative characteristics, which included age, body mass index, EF, glomerular filtration rate/dialysis, male sex, white race, smoking status, family history of coronary artery disease, diabetes, hypercholesterolemia, hypertension, cerebrovascular accident, infectious endocarditis, chronic lung disease, immunosuppressive treatment, peripheral vascular disease/cerebrovascular disease, any previous cardiovascular interventions, triple-vessel disease, congestive heart failure, myocardial infarction/timing of myocardial infarction, angina/angina type, resuscitation, New York Heart Association class IV, left main disease, and status/cardiogenic shock. In the CABG combined with mitral valve surgery group, we also adjusted for whether patients had mitral stenosis, moderate-to-severe mitral insufficiency, or both. All adjusted analyses were performed with generalized estimating equation models to account for correlations among clustered responses (eg, within-hospital correlations). Patients without preoperative atrial fibrillation serve as the reference group for all odds ratio (OR) comparisons.

We further investigated whether significant interactions exist between atrial fibrillation and the following continuous variables: EF, age, and body mass index. On finding evidence of a significant interaction effect between atrial fibrillation and EF with respect to several outcomes in the isolated CABG group, we estimated unadjusted and adjusted ORs for the effect of atrial fibrillation (vs no atrial fibrillation) on complications and mortality within each EF group to serve as comparisons that demonstrate the change in effect caused by adjustment. A *P* value of less than .05 was considered statistically significant. All analyses were performed with SAS software (version 8.2; SAS Institute, Inc, Cary, NC).

RESULTS

The prevalence of preoperative atrial fibrillation in patients undergoing operations for isolated CABG was found to be between 2.7% in the younger age group to 22.3% for the 75- to 80-year-old patients (Table 1), with a 5.3% calculated prevalence for the entire group of patients undergoing isolated CABG and equal distribution between sexes.

Patients undergoing isolated CABG with preoperative atrial fibrillation presented as older, with decreased EF, and with increased rates of diabetes mellitus, hypertension, and congestive heart failure compared with patients without atrial fibrillation (Table 1).

Among patients undergoing isolated CABG, the presence of preoperative atrial fibrillation is associated with greater rates of all major complications (any reoperation, stroke, prolonged ventilation time, renal failure, prolonged length of stay, and mortality), as shown in Table 2. Patients with preoperative atrial fibrillation undergoing CABG had higher percentages of renal failure (6.0% vs 2.8%), prolonged hospital stay (ie, postoperative length of stay >14 days; 11.3% vs 5.1%), and mortality (5.2% vs 2.2%) than those with no atrial fibrillation (Table 2). Despite adjusting for preoperative patient characteristics, the odds of serious complications and death were all significantly greater for patients with preoperative atrial fibrillation as opposed to those with no preoperative atrial fibrillation (Table 3). Adjusted odds for prolonged length of stay and mortality for those with preoperative atrial fibrillation versus those with no atrial fibrillation were 1.41 (95% CI, 1.33–1.49) and 1.30 (95% CI, 1.20–1.41), respectively.

The relationship between preoperative atrial fibrillation and EF for postoperative complications and mortality in both the unadjusted and adjusted multivariate models is shown in Table 4. There was a significant interaction between atrial fibrillation and EF for mortality, stroke, prolonged ventilation, and prolonged length of stay (>14 days) after adjusting for other preoperative characteristics. The effect of preoperative atrial fibrillation (vs no atrial fibrillation) on outcome is greater among patients with an EF of greater than 40%. The adjusted odds of mortality for patients with atrial fibrillation are only 1.17 when compared with patients without atrial fibrillation among the group with an EF of 40% or less. However, the odds of death for patients with atrial fibrillation are 1.47 and 1.37 compared with patients without atrial fibrillation among those with EFs of 40% to 55% and greater than 55%, respectively.

Similarly, adjusted ORs for postoperative length of stay for those with preoperative atrial fibrillation versus those with no preoperative atrial fibrillation are 1.22 (95% CI, 1.12–1.33) among patients with EFs of 40% or less, 1.56 (95% CI, 1.42–1.72) among those with EFs of 40% to 55%, and 1.60 (95% CI, 1.43–1.79) among those with EFs of greater than 55%. There was no strong evidence of an interaction between atrial fibrillation and age or atrial fibrillation and body mass index.

DISCUSSION

The prevalence of atrial fibrillation among patients undergoing isolated CABG (5.3%) is consistent with the reported literature. Patients admitted for CABG with a history of

TABLE 1. Preoperative demographic and clinical characteristics, 2002–2003

Parameter		Isolated CABG						P value
		Total		No preoperative AF		Preoperative AF		
		N	%	N	%	N	%	
Age	<50 y	28,610	10.6	28,253	10.6	357	2.7	.001
	50–55 y	29,613	10.5	28,998	10.9	615	3.9	
	55–60 y	38,633	13.7	37,517	14.1	1116	7.8	
	60–65 y	41,856	14.9	40,171	15.1	1685	10.7	
	65–70 y	44,619	15.8	42,001	15.8	2618	16.6	
	70–75 y	44,905	15.9	41,469	15.6	3436	21.8	
	75–80 y	34,344	12.2	30,823	11.6	3521	22.3	
	>80 y	19,105	6.8	16,694	6.3	2411	15.3	
Sex	M	202,290	71.8	190,908	71.8	11,382	72.2	.251
	F	79,279	28.1	74,906	28.2	4373	27.8	
EF	>55%	99,840	35.5	95,527	35.9	4313	27.4	.001
	40%–55%	110,050	39.1	104,349	39.2	5701	36.2	
	30%–40%	42,081	15.0	39,136	14.7	2945	18.7	
	≤30%	29,716	10.6	26,916	10.1	2800	17.8	
DM		100,494	35.7	94,473	35.5	6021	38.2	.001
HTN		214,279	76.07	201,559	75.8	12,720	80.7	.001
H-Chol		199,580	70.85	189,353	71.2	10,227	64.9	.001
F Hx CAD		120,821	42.89	115,063	43.3	5758	36.5	.001
Smoke		173,481	61.59	164,149	61.7	9332	59.2	.001
CLD		53,929	19.2	49,963	18.8	3966	25.7	.001
PVD		44,926	16.0	41,432	15.6	3494	22.7	.001
CVD		38,263	13.6	34,984	13.2	3279	20.8	.001
CVA		20,421	7.5	18,525	7.0	1896	12.0	.001
Prv CAB		15,098	5.4	14,022	5.3	1076	6.8	.001
Prv PTCA		56,152	19.9	53,179	20.0	2973	18.9	.001
Prv valve		729	0.3	596	0.2	133	0.8	.001
MI	≤24	10,442	3.7	9886	3.7	556	3.5	.001
	1–7 d	54,705	19.4	51,007	19.2	3698	23.5	
	8–21 d	9922	3.5	8962	3.4	960	6.1	
	>21 d	51,739	18.4	48,687	18.3	3052	19.4	
CHF		39,556	14.0	34,692	13.1	4864	30.9	.001
NYHA	III	106,665	37.9	100,328	37.7	6337	40.2	.001
	IV	58,110	20.6	54,027	20.3	4083	25.9	
No. diseased vessels	1	12,183	4.3	11,668	4.4	515	3.3	.001
	2	56,103	19.9	53163	20.0	2940	18.7	
	3	212,321	75.4	200,065	75.2	12,256	77.8	
LM >50%		70,697	25.1	66,141	24.9	4556	28.9	.001
Status	Elective	143,094	50.8	135,970	51.1	7124	45.2	.001
	Urgent	126,755	45.0	118,834	44.7	7921	50.3	
	Emergency	10,946	3.9	10,283	3.9	663	4.2	

CABG, Coronary artery bypass grafting; AF, atrial fibrillation; EF, ejection fraction; DM, diabetes mellitus; HTN, hypertension; H-Chol, hypercholesterolemia; F Hx CAD, family history of coronary artery disease; CLD, chronic lung disease; PVD, peripheral vascular disease; CVD, cerebrovascular disease; CVA, cerebrovascular accident; Prv CAB, previous CABG; Prv PTCA, previous percutaneous transluminal cardiac arthroplasty; Prv valve, previous valve; MI, myocardial infarction; CHF, chronic heart failure; NYHA, New York Heart Association class; LM, left main descending.

atrial fibrillation represent, in general, a higher-risk group of patients based on their preoperative clinical variables. Patients with atrial fibrillation are older and have more risk factors for morbidity and mortality.

Previous reports, such as the Framingham Study and a study published by the Cleveland Clinic, documented the same trend in patient outcomes.^{2,4} Other studies published in the past have also identified preoperative atrial fibrillation

as a risk factor for early and late mortality, as well as an increased risk for stroke and bleeding.^{3,5-9}

Although there were statistically significant interactions between atrial fibrillation and EF with respect to mortality and several complications, it is questionable whether the interaction effects are clinically significant and truly meaningful. From Table 3, of adjusted ORs for atrial fibrillation versus no atrial fibrillation stratified by EF category, it seems

TABLE 2. Postoperative outcomes, 2002–2003

Outcome (% yes)	Patients undergoing CABG						P value
	All		No atrial fibrillation		Atrial fibrillation		
	N	%	N	%	N	%	
Any reoperation	17,358	6.2	15,915	6.0	1443	9.2	<.001
Stroke	4134	1.5	3729	1.4	405	2.6	<.001
Prolonged ventilation time	21,634	7.7	19,549	7.4	2085	13.2	<.001
Renal failure	7943	3.0	7086	2.8	857	6.0	<.001
Prolonged LOS >14 d	15,257	5.4	13,472	5.1	1785	11.3	<.001
Mortality	6759	2.4	5942	2.2	817	5.2	<.001

CABG, Coronary artery bypass grafting; LOS, length of stay.

that the effect of atrial fibrillation (versus no atrial fibrillation) on outcome is greater among patients with higher EFs (ie, EF >40%). Among patients undergoing CABG, the effect of preoperative atrial fibrillation on outcome was found to be significant, despite adjusting for patient risk factors. Atrial fibrillation is a common endpoint in the natural history of patients with significant mitral valve disease and left atrial enlargement. However, among patients with coronary artery disease and no mitral valve pathology, atrial fibrillation might represent a subset of patients with ischemic

TABLE 3. Unadjusted and adjusted odds ratios for complications and mortality by preoperative atrial fibrillation (versus none) adjusted for potential confounders, patients undergoing CABG only

	Total N	Unadjusted		Adjusted	
		OR	95% CI	OR	95% CI
Any reoperation	281,567	1.58	1.49–1.67	1.18	1.12–1.26
Stroke	281,567	1.85	1.67–2.05	1.20	1.08–1.33
Prolonged ventilation time	281,567	1.88	1.79–1.98	1.22	1.15–1.28
Renal failure	281,567	2.19	2.04–2.36	1.28	1.19–1.37
Prolonged LOS >14 d	281,567	2.38	2.25–2.51	1.41	1.33–1.49
Mortality	281,567	2.36	2.19–2.54	1.30	1.20–1.41

CABG, Coronary artery bypass grafting; OR, odds ratio; CI, confidence interval; LOS, length of stay.

heart disease who should be given special consideration during assessment and counseling on risk in addition to evaluation based on left ventricular EF.

It should be clear that the findings of this study do not suggest that the operative results in general were better among patients with low EFs. However, when comparing the effect of atrial fibrillation on mortality and morbidity within the EF subgroups, preoperative atrial fibrillation increases the odds of a negative effect in patients with EFs of greater than 40%. The addition of EF as a potential modifier for

TABLE 4. Unadjusted and adjusted odds ratios for complications and mortality by preoperative atrial fibrillation adjusted for ejection fraction status and potential confounders, patients with CABG only

	Total N	Unadjusted OR	95% CI	AF, EF interaction*	Adjusted OR	95% CI	AF, EF interaction*
Any reoperation							
EF ≤40%	71,766	1.46	1.33–1.60	.4562	1.18	1.07–1.29	.5997
EF 40%–55%	109,999	1.49	1.35–1.64		1.15	1.04–1.27	
EF >55%	99,802	1.60	1.43–1.78		1.25	1.11–1.40	
Stroke							
EF ≤40%	71,766	1.40	1.19–1.64	.0021	1.02	0.86–1.20	.0335
EF 40%–55%	109,999	2.08	1.74–2.48		1.37	1.14–1.64	
EF >55%	99,802	1.99	1.61–2.46		1.33	1.07–1.64	
Prolonged ventilation time							
EF ≤40%	71,766	1.52	1.42–1.63	<.0001	1.13	1.05–1.22	.0479
EF 40%–55%	109,999	1.92	1.75–2.10		1.30	1.19–1.43	
EF >55%	99,802	1.88	1.69–2.09		1.27	1.15–1.41	
Renal failure							
EF ≤40%	65,413	1.73	1.55–1.93	.0007	1.15	1.03–1.29	.0528
EF 40%–55%	104,537	2.27	2.02–2.55		1.35	1.19–1.52	
EF >55%	96,095	2.34	2.01–2.72		1.43	1.23–1.66	
Prolonged LOS >14 d							
EF ≤40%	71,766	1.79	1.66–1.94	<.0001	1.22	1.12–1.33	<.0001
EF 40%–55%	109,999	2.55	2.32–2.81		1.56	1.42–1.72	
EF >55%	99,802	2.59	2.32–2.90		1.60	1.43–1.79	
Mortality							
EF ≤40%	71,766	1.80	1.62–1.99	<.0001	1.17	1.04–1.31	.0344
EF 40%–55%	109,999	2.56	2.24–2.92		1.47	1.28–1.69	
EF >55%	99,802	2.41	2.03–2.86		1.37	1.16–1.63	

CABG, Coronary artery bypass grafting; OR, odds ratio; CI, confidence interval; AF, atrial fibrillation; EF, ejection fraction; LOS, length of stay. *P value for test of interaction score between preoperative atrial fibrillation and ejection fraction.

postoperative complications and mortality might be suggestive of a causal relationship between preoperative atrial fibrillation and subsequent morbidity. Among patients defined by EFs of greater than 55%, atrial fibrillation is significantly associated with morbidity after adjustment for preoperative risk factors compared with the association seen in patients without atrial fibrillation. In patients predisposed to subsequent postoperative morbidity (EF <55%), atrial fibrillation continues to have a significant interactive effect with EF, despite adjustments for traditional risk factors for postoperative morbidity.

The importance of this large-scale study was to establish the clinical association between preoperative atrial fibrillation and increased morbidity and mortality after CABG. However, is there any clinical relevance for these findings? Should preoperative atrial fibrillation be identified as a risk factor to be included in risk-prediction models, such as the STS score? Based on this study, no absolute answer can be given, but the results would suggest that special attention should be given to candidates for CABG when assessing the operative risk and the expected outcome. The results of the present study should encourage developers of preoperative risk algorithms to consider atrial fibrillation as a risk factor in cardiac surgery preoperative risk algorithms, as was done by the STS, which included preoperative arrhythmia in the risk model for STS version 2.61.

Surgical ablation of atrial fibrillation has been advocated as a useful adjunctive procedure in the care of patients undergoing cardiac surgery and having a documented significant history of atrial fibrillation. The results of the combined and isolated procedure have been very good, with relatively low mortality and morbidity, and have resulted in a significant reduction in the risk for long-term thromboembolic events and strokes.¹⁰⁻¹³ Recent developments in ablation technologies enhance the ability of surgeons to create the different lesions in a very precise and efficient way.¹⁴⁻¹⁶ Nevertheless, surgical ablation of atrial fibrillation is far from being applied in all cases in which there is an indication for the procedure. Theoretically, ablation of atrial fibrillation in patients undergoing CABG alone should improve the outcome of the patients and reduce the risk for late strokes. Unfortunately, there are no surgical data stratified by risk factors that can support this assumption. In the electrophysiology literature there are scattered studies to support ablation of atrial fibrillation in patients with low EF, such as the study by Chen and colleagues,¹⁷ which documented significant improvement in left ventricular function and functional class in patients with low EFs after successful percutaneous ablation. The positive effect of surgical ablation on early outcome is questionable. A meta-analysis of the literature for patients with valve disease and atrial fibrillation revealed improvement in the perioperative results for those patients with a concomitant ablation procedure.¹⁸ A recent publication from the Mayo Clinic¹⁹ suggested that preoperative atrial fibrillation that was not addressed at the time of CABG is associated with increased risk for late mortality

and morbidity and less favorable long-term survival and therefore recommended surgical correction of atrial fibrillation at the time of CABG.

The question of whether preoperative atrial fibrillation is a marker of sicker patients or causally related to less favorable outcomes after CABG as a standalone procedure or combined with mitral valve surgery is very important. However, such a causal relationship can only be determined through prospective clinical trials. Lastly, the type of atrial fibrillation is not a variable that is currently being collected by the STS, and therefore the variability in the definition of the arrhythmia by the data collectors in the different centers is uncontrolled. Thus the potential effect of the type of atrial fibrillation could not be determined and should be considered a limitation of the study.

In this study we were able to show, in a large cohort of patients, that preoperative atrial fibrillation is associated with an increased risk for perioperative mortality and morbidity in patients undergoing CABG. Given all the familiar limitations associated with retrospective studies, we can carefully claim that in the low-EF group atrial fibrillation might signal a high-risk patient, and attention should be given when approaching such patients before surgical intervention for discussion of the risks of the surgical procedure. As for patients with good left ventricular function presenting for CABG, the presence of preoperative atrial fibrillation alone might be related to increased morbidity and mortality in which ablation of atrial fibrillation might theoretically improve the outcome. However, such a statement can be supported only after a prospective randomized study. Cardiac surgeons should be familiar with the association between atrial fibrillation and patients' outcome after CABG and also be able to apply modern techniques proved to be effective in treating atrial fibrillation. We also encourage ongoing outcomes studies and clinical research to evaluate developing techniques and their applications and indications to help build the necessary evidence to guide surgeons in their clinical decision making.

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