Clinical Investigations

Postoperative Atrial Fibrillation Is Not Associated With an Increase Risk of Stroke or the Type and Number of Grafts: A Single-Center Retrospective Analysis

Address for correspondence: Amir Lotfi, MD Division of Cardiology Springfield 4, Room 4641 Baystate Medical Center 759 Chestnut Street Springfield, MA 01199 amir.lotfi@bhs.org

Amir Lotfi, MD; Siddharth Wartak, MD; Pradheep Sethi, MD; Jane Garb, MS; Gregory R. Giugliano, MD, SM Department of Cardiology, Baystate Medical Center, Springfield, Massachusetts; Tufts University

School of Medicine, Boston, Massachusetts

Background: Atrial fibrillation (AF) and atrial flutter are the 2 most common types of dysrhythmia in patients undergoing coronary artery bypass graft (CABG) surgery and are associated with increased morbidity and mortality. We sought to explore the association between the type and quantity of bypass grafts and cardiovascular outcomes in patients with postoperative AF (POAF).

Hypothesis: The type and quantity of bypass grafts is associated with POAF.

Methods: We queried the Society of Thoracic Surgery National Database for CABG operations, both with and without valve procedures, performed at Baystate Medical Center between January 2002 and July 2007. We used multivariable logistic regression modeling to identify predictors of POAF and to explore the impact of AF on major adverse cardiac outcomes in this post-CABG population.

Results: A total of 3068 patients received CABG surgery, 187 (6.1%) of whom received concurrent valve replacement or repair. The incidence of POAF was 38.3%. POAF was significantly associated with readmission within 30 days (P < 0.009), increased length of stay ($P \ll 0.0001$), and a strong trend toward increased 30 day mortality (P = 0.058). There was no association between POAF and postoperative stroke (P = 0.92), graft type (P = nonsignificant) or number of grafts (P = nonsignificant).

Conclusions: Patients with POAF experienced increased morbidity and mortality as demonstrated by previous studies. Neither the number of grafts nor type of grafts was associated with POAF. Furthermore, the rate of stroke was not associated with POAF.

Introduction

ABSTRAC

Atrial fibrillation (AF) and atrial flutter are the 2 most common arrhythmias that develop in patients postoperatively following coronary artery bypass graft (CABG) surgery. Despite advances in surgical techniques and improved outcomes, the incidence of AF after surgery remains high, ranging from 15% to $40\%^{1-4}$ and carries significant morbidity and mortality.⁵ It is more common in patients undergoing combined CABG surgery and valve replacement.

Several studies have examined for predictors of postoperative AF (POAF),^{1,3,4,6–12} although each study supports a different array of predictive variables. Combining prior knowledge from 11 studies, a modern meta-analysis comprising 40 112 patients post-CABG surgery identified the predictors of POAF as older age, lower ejection fraction, history of hypertension, heart failure, prior stroke, peripheral arterial disease, and aortic clamp time.¹³ In addition, abrupt withdrawal of β -blockers has been associated with an increased risk of POAF.¹⁴ CABG surgery done off-pump appears to decrease the risk of POAF compared to conventional bypass surgery. 15,16

It has been previously demonstrated that graft flow is significantly affected after inducing atrial fibrillation.¹⁰ In particular, the flow in arterial grafts appeared to be more compromised than the flow within venous grafts in patients who developed AF.¹⁰ Given these 2 findings, one might then hypothesize that there may be an association between POAF and myocardial infarction (MI).

The objectives of the present study were to: (1) determine the predictors of POAF in our population with particular attention to the impact of the number of bypass grafts and the type of grafts implanted, and (2) examine the association between POAF and major adverse cardiovascular events.

Methods

This was a retrospective cross-sectional study of all patients undergoing coronary artery bypass surgery with or without valve repair or replacement performed at Baystate Medical Center between January 2002 and July 2007. Patients age 18 years and above were included. The data were obtained from the Society of Thoracic Surgery (STS) National Database, supplemented by data from the Baystate

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Table 1. Society of Thoracic Surgery Definitions for Perioperative Outcomes

Outcomes	Definition
Atrial fibrillation	New onset AF requiring treatment
Stroke	If the patient had a central neurological deficit persisting postoperatively for >72 hours
Perioperative MI	o-24 hours postoperatively: the CK-MB (or CK if MB not available) must be ≥5 times the upper limit of normal, with or without new Q waves present in 2 or more contiguous ECG leads; no symptoms required
	 > 24 hours postoperative: indicate the presence of a perioperative MI (>24 hours postoperatively) as documented by at least 1 of the following criteria: (1) evolutionary ST-segment elevations, (2) development of new Q waves in 2 or more contiguous ECG leads, (3) new or presumably new LBBB pattern on the ECG, and (4) the CK-MB (or CK if MB not available) must be ≥3 times the upper limit of normal
Abbreviations: Al	F, atrial fibrillation/flutter; CK-MB, creatine kinase-

Abbreviations: AF, atrial hbrillation/flutter; CK-MB, creatine kinasemyocardial band; ECG, electrocardiograph; LBBB, left bundle branch block; MI, myocardial infarction.

Cardio-Thoracic Surgery Research Department. Baseline demographic information, clinical characteristics, and operative data were gathered from the 2 databases. Outcome measures included the STS-defined incidence of POAF, stroke, perioperative MI, and 30-day mortality (Table 1). This study was approved by the institutional review board.

Statistical Analysis

We examined patient demographic, clinical, and operative risk factors for the development of POAF using multivariable logistic regression (MLR) modeling.¹⁷ Patients with a prior history of AF were excluded from analysis. Prior to MLR, univariable analysis was conducted to identify potential predictors of POAF to be tested in the model. In addition, the previously known predictors of POAF based on the meta-analysis by Kaw et al¹³ were forced into the model. Continuous variables were evaluated using a t test if normally distributed and Wilcoxon rank sum if non-normally distributed. Discrete variables were tested using the χ^2 statistic. All factors with a P value <0.2 on univariable analysis were entered into the MLR in addition to the predictors from Kaw et al.¹³ A forward stepwise procedure was used. A maximum likelihood procedure was used to calculate the regression coefficients. The likelihood ratio criterion¹⁸ was used to determine the significance of individual factors in the regression model. The association of POAF with other outcomes, including 30-day mortality, MI, stroke, length of stay, and readmission was also explored.

Results

A total of 3068 patients received CABG surgery, 187 (6.1%) of whom received concurrent valve replacement or repair (Table 2). The incidence of POAF was 38.3%. Multivariable modeling identified a significantly increased risk of POAF in patients with increased age (P < 0.001), history of hypertension (P = 0.041), history of peripheral arterial disease

Table 2. Population Baseline Characteristics

	N = 3068
Age, y	66.5 ± 10.8
Female	29.1
Weight, kg	$\textbf{84.3} \pm \textbf{17.5}$
African American	2.4
Asian	0.4
Hispanic	3.8
Previous stroke	7.4
Dialysis	1.5
Hypertension	79.1
Diabetes mellitus	39.0
Family history of CAD	21.2
Previous MI	57.2
History of CHF	19.6
PAD	17.2
Active smoking	20.3

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; MI, myocardial infarction; PAD, peripheral artery disease. Values in the table are reported as a mean \pm standard deviation for continuous variables or as a percentage for dichotomous variables.

(P = 0.012), and longer cross-clamp time (P < 0.001), after adjusting for the other factors listed in Table 3. Patients classified as Hispanic appeared to have a lower incidence of POAF (P < 0.001). Neither the type (arterial or venous) of bypass graft nor number of conduits used were associated with POAF (arterial, P = 0.25; venous, P = 0.66) (Table 3).

POAF was significantly associated with several important clinical endpoints and outcome metrics. Compared to patients who did not develop POAF, patients with POAF were more likely to have readmission within 30 days (P < 0.009), increased length of stay ($P \ll 0.0001$), and perioperative MI (P = 0.033). Patients with POAF demonstrated a strong trend toward increased 30-day mortality (3.2% vs 2.1%, P = 0.058). POAF did not result in a higher frequency of postoperative stroke (P = 0.92) (Table 4).

Patients with POAF were much more likely to be discharged on warfarin and less likely to receive either aspirin or β -blocker (Table 5). POAF did not result in higher rates of 30-day readmission for acute coronary syndromes (ACS). Of the 8 patients readmitted within 30-days for ACS, 4 had an ST-segment elevation MI, 2 patients had a non–ST-segment elevation MI, and 2 patients had unstable angina. Five of these 8 patients underwent cardiac catheterization, with 1 having a percutaneous intervention and 1 undergoing repeat CABG surgery.

Discussion

POAF has been associated with an increased incidence of stroke, congestive heart failure, respiratory failure, shock, multiorgan failure, cardiac arrest, use of intraaortic

⁷⁸⁸ Clin. Cardiol. 34, 12, 787–790 (2011) A. Lotfi et al: POAF association with risk of stroke or grafts Published online in Wiley Online Library (wileyonlinelibrary.com) DOI:10.1002/clc.21001 © 2011 Wiley Periodicals, Inc.

Table 3. Predictors of Postoperative Atrial Fibrillation

	No POAF (N = 1890)	POAF (N = 1178)	Univariable (P Value)	Multivariable (P Value)
Age, y	$\textbf{64.1} \pm \textbf{10.8}$	$\textbf{70.3} \pm \textbf{9.7}$	≪0.001	≪0.001
Male	70.8	71.1	0.838	
White	87.9	92.7	≪0.001	0.60
Hispanic	5.3	1.4	≪0.001	≪0.001
Current smoker	22.9	16.1	≪0.001	0.557
Family history of CAD	23.9	16.9	≪0.001	0.092
DM	40.0	37.3	0.13	0.264
Dyslipidemia	84.7	84	0.6	0.367
Renal failure	4.4	5.7	0.122	0.366
Dialysis	1.3	1.7	0.922	
HTN	77.1	82.3	0.001	0.041
Prior stroke	7.0	8.0	0.332	
PAD	15.1	20.1	≪0.001	0.0123
Prior MI	56.8	57.7	0.62	
History of CHF	17.4	23.2	≪0.001	0.623
Ejection fraction	$\textbf{49.0} \pm \textbf{13.7}$	$\textbf{48.6} \pm \textbf{13.7}$	0.436	0.643
Arterial graft	91.2	85.1	≪0.001	0.169
Venous graft	92.2	94-7	0.008	0.721
Mitral valve surgery	4.9	8.0	0.001	0.253
No. of arterial grafts	1.3 ± 0.7	$\textbf{1.2}\pm\textbf{0.7}$	≪0.001	0.298
No. of venous grafts	$\textbf{2.0}\pm\textbf{1.1}$	2.1 ± 1.0	0.0021	0.085
Cross clamp time	$\textbf{83.8} \pm \textbf{37.7}$	$\textbf{91.2} \pm \textbf{42.2}$	≪0.0001	≪0.001

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; DM, diabetes mellitus; HTN, hypertension; MI, myocardial infarction; PAD, peripheral arterial disease; POAF, postoperative atrial fibrillation. Values in the table are reported as a mean \pm standard deviation for continuous variables or as a percentage for dichotomous variables.

Table 4. Postoperative Outcomes in Patients With and Without Postoperative Atrial Fibrillation

	No POAF (N = 1890)	POAF (N = 1178)	P Value
30-day mortality	2.1	3.2	0.058
Postoperative stroke	5.8	5.7	0.92
Perioperative MI	11.3	13.9	0.033
Readmission within 30 days for ACS	0.4	0	0.025
Readmission within 30 days	8.6	11.5	0.009
Length of stay	$\textbf{7.2} \pm \textbf{4.7}$	$\textbf{11.7} \pm \textbf{11.2}$	<0.0001

Abbreviations: ACS, acute coronary syndrome; MI, myocardial infarction; POAF, postoperative atrial fibrillation. Values in the table are reported as a mean \pm standard deviation for continuous variables or as a percentage for dichotomous variables.

Table 5. Selected Medications at Discharge in Patients With and Without Postoperative Atrial Fibrillation

Medication	No POAF	POAF	P Value
Aspirin, n (%) ^a	1570 (92)	929 (87)	<0.0001
β-Blocker, n (%) ^{<i>a</i>}	1506 (89)	860 (80)	<0.0001
Warfarin, n (%) ^b	76 (8)	300 (46)	<0.0001

Abbreviation: POAF, postoperative atrial fibrillation. Values in the table are reported as a mean \pm standard deviation for continuous variables or as a percentage for dichotomous variables. ^{*a*} The Society of Thoracic Surgery database began recording aspirin and β -blocker prescription at discharge on July 1, 2002. ^{*b*} The Society of Thoracic Surgery database began recording warfarin prescription at discharge on July 1, 2004.

balloon pump, antiarrhythmic therapy, and anticoagulation use.^{4,7,12,19–21} These complications all have potential impact on the length of hospital stay, and in turn the overall cost of treatment.² In addition, POAF has been shown to decrease long-term survival.⁴

In the present study we have confirmed the POAF results in worse in-hospital and 30-day outcomes including perioperative MI, readmission, and length of stay. We demonstrated a strong trend toward increased mortality in patients with POAF. Interestingly, there was no associated increased risk of stoke in patients with POAF. Postoperative stroke has been associated with the extent of cerebral artery atherosclerosis,²² extent of atherosclerotic ascend-ing aortic disease,²³ older age, on-pump CABG surgery with hypothermia circulatory arrest,²⁴ increased cardiopulmonary bypass duration,²⁵ and POAF.^{25,20} However, the historical association between POAF and stroke has been inconsistent.26 The lack of association between POAF and stroke was recently supported in another large, 45 000patient post-CABG study.²⁴ Possible explanations for these discrepant findings include the STS definition of POAF, variable duration of POAF, anticoagulation treatment, and ascertainment of outcome bias.

Our study demonstrated that patients with POAF had a significantly higher rate of perioperative MI compared to those without POAF. We hypothesized that this might be attributable to the type or number of bypass grafts given the potential for flow compromise in grafts as previously described.¹⁰ However, we found no association between the incidence of POAF and graft type or number. Although perioperative MI is frequently related to technical anastomotic issues,²⁷ this does not explain the relationship to POAF. It is possible that POAF may lead to demand-related ischemic infarction.

There are several limitations to our study. This is a retrospective and observational analysis from a high-volume single center of patients post-CABG surgery, which makes it subject to well- known bias. Participation in the STS database is voluntary, STS data are not verified through an audit process, and the STS definition for POAF is subjective. The choice of graft type and number was not controlled for and was left to the discretion of the surgeon.

Conclusion

Patients with POAF experienced increased morbidity and mortality compared to postoperative patients without POAF. Neither the number of grafts nor type of grafts were associated with POAF. Importantly, the rate of stroke was not associated with POAF. Future research should be directed at identifying approaches to reduce POAF given the significant relationship between POAF and worse clinical outcomes.

References

- Elahi M. Hadjinikolaou L. Galinanes M. Incidence and clinical 1. consequences of atrial fibrillation within 1 year of first-time isolated coronary bypass surgery. Circulation. 2003;108(suppl 1):II207-II212
- Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. Ann Intern Med. 2001;135:1061-1073.
- Mathew JP, Fontes ML, Tudor IC, et al. A multicenter risk 3. index for atrial fibrillation after cardiac surgery. JAMA. 2004;291:1720-1729.
- Villareal RP, Hariharan R, Liu BC, et al. Postoperative atrial 4 fibrillation and mortality after coronary artery bypass surgery. I Am Coll Cardiol. 2004;43:742-748.

graft. J Am Coll Cardiol. 2010;55:1370-1376. 6 Asher CR, Miller DP, Grimm RA, et al. Analysis of risk factors for development of atrial fibrillation early after cardiac valvular surgery. Am J Cardiol. 1998;82:892-895.

5

7. Creswell LL, Schuessler RB, Rosenbloom M, et al. Hazards of postoperative atrial arrhythmias. Ann Thorac Surg. 1993;56: 539 - 549

El-Chami MF, Kilgo P, Thourani V, et al. New-onset atrial fibrillation predicts long-term mortality after coronary artery bypass

- Mathew IP. Parks R. Savino IS, et al. Atrial fibrillation following 8 coronary artery bypass graft surgery: predictors, outcomes, and resource utilization. MultiCenter Study of Perioperative Ischemia Research Group. JAMA. 1996;276:300-306.
- 9 Mendes LA, Connelly GP, McKenney PA, et al. Right coronary artery stenosis: an independent predictor of atrial fibrillation after coronary artery bypass surgery. JAm Coll Cardiol. 1995;25:198-202.
- 10 Shin H, Hashizume K, Iino Y, et al. Effects of atrial fibrillation on coronary artery bypass graft flow. Eur J Cardiothorac Surg. 2003:23:175-178.
- Zaman AG, Archbold RA, Helft G, et al. Atrial fibrillation after 11. coronary artery bypass surgery: a model for preoperative risk stratification. Circulation. 2000;101:1403-1408.
- 12 Aranki SF, Shaw DP, Adams DH, et al. Predictors of atrial fibrillation after coronary artery surgery. Current trends and impact on hospital resources. Circulation. 1996;94: 390 - 397
- 13. Kaw R, Hernandez AV, Masood I, et al. Short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting: a systematic review and metaanalysis. J Thorac Cardiovasc Surg. 2011;141:1305-1312.
- 14. Ali IM, Sanalla AA, Clark V. Beta-blocker effects on postoperative atrial fibrillation. Eur I Cardiothorac Surg. 1997:11:1154-1157.
- 15. Angelini GD, Taylor FC, Reeves BC, et al. Early and midterm outcome after off-pump and on-pump surgery in Beating Heart Against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomised controlled trials. Lancet. 2002;359:1194-1199.
- 16. Wijeysundera DN, Beattie WS, Djaiani G, et al. Off-pump coronary artery surgery for reducing mortality and morbidity: meta-analysis of randomized and observational studies. JAm Coll Cardiol. 2005;46:872-882.
- 17. Cox DR. The Analysis of Binary Data. London, UK: Methuen; 1970.
- 18 Lee ET. Statistical Methods for Survival Data Analysis. 2nd ed. New York, NY: Wiley; 1992.
- 19. Almassi GH, Schowalter T, Nicolosi AC, et al. Atrial fibrillation after cardiac surgery: a major morbid event? Ann Surg. 1997;226:501-511; discussion 511-503.
- Lahtinen J, Biancari F, Salmela E, et al. Postoperative atrial 20. fibrillation is a major cause of stroke after on-pump coronary artery bypass surgery. Ann Thorac Surg. 2004;77:1241-1244.
- 21. Stamou SC, Dangas G, Hill PC, et al. Atrial fibrillation after beating heart surgery. Am J Cardiol. 2000;86:64-67.
- 22 Lee EJ, Choi KH, Ryu JS, et al. Stroke risk after coronary artery bypass graft surgery and extent of cerebral artery atherosclerosis. I Am Coll Cardiol. 2011:57:1811-1818.
- 23. van der Linden J, Hadjinikolaou L, Bergman P, et al. Postoperative stroke in cardiac surgery is related to the location and extent of atherosclerotic disease in the ascending aorta. J Am Coll Cardiol. 2001;38:131-135.
- Tarakji KG, Sabik JF III, Bhudia SK, et al. Temporal onset, risk 24. factors, and outcomes associated with stroke after coronary artery bypass grafting. JAMA. 305:381-390.
- 25. Likosky DS, Leavitt BJ, Marrin CA, et al. Intra- and postoperative predictors of stroke after coronary artery bypass grafting. Ann Thorac Surg. 2003;76:428-434; discussion 435
- 26Kaireviciute D, Aidietis A, Lip GY. Atrial fibrillation following cardiac surgery: clinical features and preventative strategies. Eur Heart J. 2009;30:410-425.
- 27 Poirier NC, Carrier M, Lesperance J, et al. Quantitative angiographic assessment of coronary anastomoses performed without cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1999;117:292-297.
- Clin. Cardiol. 34, 12, 787–790 (2011) A. Lotfi et al: POAF association with risk of stroke or grafts Published online in Wiley Online Library (wileyonlinelibrary.com) DOI:10.1002/clc.21001 © 2011 Wiley Periodicals, Inc.