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Use of Intraoperative Transesophageal Echocardiography to Predict Atrial Fibrillation after Coronary Artery Bypass Grafting

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Background: **Postoperative atrial fibrillation in coronary artery bypass graft surgery occurs in 10–40% of patients. It is associated with a significant degree of morbidity and results in prolonged lengths of stay in both the intensive care unit and hospital.**

Methods: **The authors prospectively evaluated patients undergoing coronary artery bypass with detailed transesophageal echocardiography examinations conducted before and after cardiopulmonary bypass to study whether risk factors for atrial fibrillation could be identified. Demographic and surgical parameters were also included in the analysis. Selected variables were subjected to univariate and subsequent multivariate analyses to test for their independent or joint influence on atrial fibrillation.**

Results: **Seventy-nine patients had assessable transesophageal echocardiography examinations. Significant univariate predictors of atrial fibrillation included advanced age (P = 0.002), pre–cardiopulmonary bypass left atrial appendage area (P = 0.04), and post–cardiopulmonary bypass left upper pulmonary vein systole/diastole velocity ratio (P = 0.03). When these three factors were considered together in a multiple logistic regression analysis, left upper pulmonary vein systole/diastole velocity ratio was a significant predictor (P < 0.05), as was the joint effect of age plus pre–cardiopulmonary bypass left atrial appendage area (P = 0.005). The probability of developing atrial fibrillation for the combination of age = 75 yr, post–cardiopulmonary bypass left upper pulmonary vein systole/diastole velocity ratio = 0.5, and left atrial appendage area = 4.0 cm was 0.83 (95% confidence interval, 0.51–0.96).**

Conclusions: **Early identification of patients at risk for postoperative atrial fibrillation may be feasible using the parameters identified in this study.**

POSTOPERATIVE atrial fibrillation (PostAF) in coronary artery bypass graft (CABG) surgery occurs in 10–40% of patients.[1–3] It is associated with a significant degree of morbidity in the form of hemodynamic instability and embolic phenomena such as stroke. It also may result in prolonged stays in both the intensive care unit and the hospital, and thus frequently leads to increased healthcare costs.[1,2,4]

Previous studies have examined demographic and surgical factors and have attempted to identify perioperative risk factors that would predict a patient's likelihood of developing PostAF.[1–3] By defining a subset of patients at high risk, it may be possible to offer prophylaxis, and thereby decrease the morbidity associated with PostAF, and to decrease the overall cost associated with CABG surgery.

The literature offers few prospective reports, and there is a great deal of inconsistency in the reported results.[5,6] One of the few consistent risk factors identified as a predictor for PostAF is older age.[2,7–12] Other identified parameters have included prolonged aortic cross clamp time, inadequate atrial protection resulting in atrial ischemia,[13] preoperative P-wave abnormalities, electrical inducibility of the atrium,[3] right coronary artery disease,[14] and interruption of perioperative β-blocker therapy.

Few studies have focused on the use of transesophageal echocardiography (TEE) to identify patients at risk for PostAF. Because many patients undergoing CABG have TEE monitoring performed as a routine standard of care, it would be beneficial to identify quantitative and easily measurable TEE parameters that are associated with an increased risk. Therefore, we prospectively monitored CABG patients and measured multiple variables using intraoperative two-dimensional TEE and Doppler echocardiographic techniques as well as demographic data to define a group of patients who are at increased risk for developing atrial fibrillation after CABG surgery.

Materials and Methods

Patient Population

Adult patients undergoing CABG surgery requiring cardiopulmonary bypass (CPB) from 1995 to 1997 were prospectively enrolled. Informed consent was obtained from all patients, in accordance with the hospital's institutional review board. Patients were not eligible for the study if any of the following preoperative criteria existed: (1) cardiac surgical procedures in addition to the planned CABG surgery; (2) history of atrial or ventricular dysrhythmias or baseline rhythm other than sinus rhythm; (3) presence of antidysrhythmic medication other than digoxin or β blockers; and (4) conditions contraindicating the placement of a TEE probe. Patients

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were excluded from the analysis if there was intraoperative atrial fibrillation or an intraoperative change in the planned CABG procedure. No patient received pharmacologic prophylaxis for atrial fibrillation, with the exception of continuation of preoperative β-blocker therapy.

Study Design

Patients were monitored prospectively from the time of surgery until hospital discharge. After placement of standard monitoring and induction of anesthesia, a pulmonary artery catheter was inserted, followed by placement of a 3.5–7 MHz phased array multiplane or biplane TEE probe (Acuson, Mountainview, CA).

Standard views of the heart were obtained using multiple imaging planes from 0–120° (multiplanar probes) or the transverse and the longitudinal imaging planes (biplanar probes).[15] At the time of TEE examination, pulmonary capillary wedge pressure or pulmonary artery diastolic pressure was recorded. TEE examinations were conducted before sternotomy (pre-CPB) and after sternal closure (post-CPB) during periods of hemodynamic stability. Pulmonary vein and transmitral flow velocity patterns were obtained during brief periods of apnea and were measured during multiple cardiac cycles. The examinations were recorded on VHS videotape and evaluated later by two independent investigators who were blinded to the patients' PostAF status. Final values represent the average of the two investigators' results (each of which was the average of three individual measures). If the two investigators' measurements differed by more than 5%, a third independent investigator performed the measurements, and the average of the three investigators' values was used. The TEE views used to obtain the measurements included the midesophageal four-chamber view, the midesophageal two-chamber view, the midesophageal bicaval view, and the transgastric mid–short axis view. All Doppler recordings were conducted using electrocardiogram timing.

The measured parameters were left and right atrial size, left atrial appendage area (LAAA), left atrial (LA) appendage outflow velocity, pulmonary vein inflow velocities, mitral and tricuspid inflow velocities,[16] and left ventricular ejection fraction (LVEF).

Criteria for Atrial Fibrillation

Electrocardiogram criteria for PostAF were defined as the presence of an irregular heart rate (R wave to R wave interval) with either the absence of electrical P-wave activity, or the presence of atrial fibrillatory waves. Patients were considered to have experienced an episode of PostAF if they had any electrocardiogram or telemetric documentation of PostAF for at least 1 min, as noted on the medical record, or if they required medical therapy for the dysrhythmia. Dysrhythmias were confirmed using 12-lead electrocardiogram when possible. Patients with dysrhythmias that could not be identified were not considered to have had atrial fibrillation. Patients were monitored until the time of discharge from the hospital using bedside electrocardiographic monitoring in the intensive care and step-down units, telemetry on the cardiac wards, and daily electrocardiogram when telemetry was discontinued.

Statistical Analysis

Univariate analyses were conducted to identify potentially important predictors of risk of PostAF. This was performed with chi-square tests for binary predictors. Continuous variables were grouped into quartiles and analyzed using the chi-square test to determine evidence of trend. Apparent linear associations were confirmed in univariate logistic regression analyses. The variables with $P < 0.2$ in the univariate analysis were then entered in a multiple logistic regression analysis to study their joint influence on the occurrence of PostAF. The statistical significance of the factors in the multivariate model was tested using likelihood ratio tests comparing the model that included, with those that excluded, the relevant factor or factors. If a significant interaction term was identified, we report the significance level of the combined effect of the factors and their interaction. To further illustrate the joint effect of the factors and their interaction, we also report the probability estimates arising from our model for selected combinations of factor levels.

Results

Of the 99 patients enrolled, 79 completed the study and had assessable examinations. Patients were excluded for the following reasons: intraoperative atrial fibrillation (n = 3) and missing preoperative data (n = 17). To be entered into the multivariate analysis, all of the measurements that were predefined had to be available in every patient.

Patient Demographics

The demographic data for the 79 subjects are presented in table 1. Of the 79 subjects studied, 28 (35.4%) experienced PostAF. The occurrence of PostAF in the 17 patients who were excluded for lack of preoperative data was 41%, which does not differ appreciably from the incidence in this study or in the general post-CABG population. Patients with PostAF had a median hospital length of stay of 10 days (range, 3–22 days) as compared with 8 days (range, 5–20 days) for those who did not have PostAF.

Preoperative Predictors

For dichotomous data, no demographic variable was significantly associated with PostAF. Of the continuous variables analyzed, only age was found to be a significant predictor for the development of PostAF ($P = 0.001$ by

Table 1. Demographic and Preoperative Parameters

	No. of Patients (% of Total)* (N = 79)
Hypertension	47 (59)
Age	
Mean ± SD	64.1 ± 10.5
≤ 56.4 yr	19 (24)
56.5–63.6 yr	20 (25)
63.7–70.7 yr	20 (25)
> 70.7 yr	20 (25)
Gender	
Male	60 (76)
Female	19 (24)
Preoperative β blocker	48 (61)
Ca^{2+} channel antagonist	21 (27)
ACE inhibitor	20 (25)
Digoxin	10 (13)
History of myocardial infarction	
None	45 (57)
Recent (≤ 21 days)	14 (18)
Distant (> 21 days)	20 (25)
Congestive cardiac failure	5 (6)
Angina	
None	30 (38)
Stable	21 (27)
Unstable	28 (35)

* Unless otherwise noted.

Ca^{2+} = calcium; ACE = angiotensin-converting enzyme.

chi-square test for trend). Table 2 shows the proportions of patients who developed PostAF for the demographic and preoperative variables studied.

Intraoperative and Transesophageal Echocardiography Predictors

None of the intraoperative parameters we studied was significantly associated with the development of PostAF. A comparison of mean values of specific intraoperative variables for patients who developed PostAF and those who did not is shown in table 3. A comparison of mean values of specific TEE variables for patients who developed PostAF and those who did not is shown in table 4.

Table 2. Demographic Variables and the Occurrence of Atrial Fibrillation

Demographics	n	Atrial Fibrillation [No. (% of Total)]
Hypertension	47	16 (34.0)
No hypertension	32	12 (37.5)
Age*		
≤ 56.4 yr	19	1 (5.3)
56.5–63.6 yr	20	6 (30.0)
63.7–70.7 yr	20	8 (40.0)
≥ 70.8 yr	20	13 (65.0)
Gender		
Male	60	19 (31.7)
Female	19	9 (47.4)
β Blockers	48	19 (39.6)
Calcium antagonists	21	9 (42.9)
ACE inhibitors	20	8 (40.0)
Digoxin	10	5 (50.0)
No medications	12	2 (16.7)

* $P < 0.001$ for chi-square test for trend. No other significant differences found. All P values ≥ 0.2.

ACE = angiotensin-converting enzyme.

Table 3. Intraoperative Variables by Occurrence of Atrial Fibrillation

Intraoperative Factors	Atrial Fibrillation (N = 28)	Nonatrial Fibrillation (N = 51)
CPB time (min)	122.8 ± 34.8	118.8 ± 30.5
Cross-clamp time (min)	94.7 ± 30.2	92.5 ± 28.7
Minimum temperature (°C)	22.4 ± 3.82	23.06 ± 3.32
PAD, pre-CPB (mmHg)	13.82 ± 4.73	13.44 ± 4.04
PAD, post-CPB (mmHg)	11.4 ± 4.46	11.06 ± 3.52

Data are mean ± SD. No parameter had a significant association with atrial fibrillation.

CPB = cardiopulmonary bypass; PAD = pulmonary arterial diastolic pressure.

Logistic Regression Analysis

The results of the univariate logistic regression analyses for parameters with $P < 0.20$ as predictors for PostAF are shown in table 5. These were age, pre-CPB LAAA, and post-CPB left upper pulmonary vein systolic to diastolic velocity (LUPVSD) ratio. Other TEE variables had P values > 0.20.

Multivariate Analysis

Age, pre-CPB LAAA, and post-CPB LUPVSD ratio were entered in a multiple regression model to assess their combined influence on PostAF. In developing this model, it became apparent that the influence of increasing age was demonstrated primarily in association with increasing values of pre-CPB LAAA (table 5). This is evident from the statistically significant interaction term representing the product of pre-CPB LAAA and age ($P < 0.05$). In this model, the joint effect of pre-CPB LAAA and

Table 4. TEE Parameters by Occurrence of Atrial Fibrillation

Intraoperative Factors	Atrial Fibrillation (N = 28)	Nonatrial Fibrillation (N = 51)
LUPVSD ratio, post-CPB	1.298 ± 0.394	1.568 ± 0.50
LAAA, pre-CPB (cm^2)	3.890 ± 1.048	3.323 ± 1.140
LUPVSD ratio, pre-CPB	1.477 ± 0.604	1.532 ± 0.444
LAA maximum velocity, post-CPB	0.455 ± 0.186	0.543 ± 0.196
LA transverse axis (0°), pre-CPB	4.256 ± 0.586	4.303 ± 0.474
LA longitudinal axis (0°), pre-CPB	4.845 ± 0.883	5.002 ± 0.895
LA longitudinal axis (90°), pre-CPB	4.833 ± 0.703	4.852 ± 0.739
LVEF, pre-CPB	41.36 ± 13.17	42.80 ± 12.49
LVEF, post-CPB	42.13 ± 12.88	45.77 ± 12.45

Data are mean ± SD unless otherwise noted.

TEE = transesophageal echocardiography; LUPVSD = left upper pulmonary vein systolic-to-diastolic velocity ratio; CPB = cardiopulmonary bypass; LAAA = left atrial appendage area; LAA = left atrial appendage; LA = left atrium; LVEF = left ventricular ejection fraction.

Table 5. Predictors of Atrial Fibrillation—Continuous Variables

Factor	*P* Value	
	Univariate	Multivariate
LUPVSD ratio, post-CPB	0.03	< 0.05
LAAA, pre-CPB	0.04	0.005
Age	0.002	0.005
Age–LAAA interaction	—	0.005

LUPVSD = left upper pulmonary vein systolic-to-diastolic velocity ratio; CPB = cardiopulmonary bypass; LAAA = left atrial appendage area.

Table 6. Model-based Probabilities of Developing Atrial Fibrillation

Age (yr)	LAAA (cm^2)	LUPVSD Ratio		
		1.5	1.0	0.5
65	3.0	0.23 (0.13–0.37)	0.37 (0.20–0.58)	0.54 (0.22–0.83)
65	4.0	0.31 (0.19–0.47)	0.47 (0.28–0.67)	0.64 (0.31–0.87)
75	3.0	0.32 (0.15–0.55)	0.48 (0.23–0.73)	0.64 (0.27–0.90)
75	4.0	0.56 (0.33–0.76)	0.71 (0.46–0.88)	0.83 (0.51–0.96)

Values are probability (95% confidence interval).

LAAA = left atrial appendage area; LUPVSD = left upper pulmonary vein systolic-to-diastolic velocity ratio.

age is statistically significant ($P < 0.005$) as compared with a model that omitted the factors of age and pre-CPB LAAA and their synergistic effect. Post-CPB LUPVSD ratio is also significant, independently of these other factors ($P < 0.05$). To help interpret the meaning of this model, it was used to generate estimates of the probability of PostAF for various combinations of age, LAAA, and LUPVSD ratio, as shown in table 6. Note that the probability of PostAF as the LAAA increases from 3.0 to 4.0 cm is greater for the 75-yr-old patient than for the 65-yr-old patient at each level of LUPVSD ratio (table 6).

Discussion

The incidence of atrial fibrillation after CABG surgery ranges from 10 to 40%.[1–3] Multiple perioperative risk factors have been identified for the development of PostAF[1–14] and the redevelopment of atrial fibrillation after conversion to sinus rhythm.[17–19] Some of these risk factors include hypertension, CPB time, reduced LVEF, inadequate atrial protection, hypothermia, the type of surgical procedure performed, and advanced age. With the exception of advanced age, no consistent pattern of risk has emerged from these studies. TEE parameters have not been extensively evaluated.

By more specifically defining the population at increased risk for PostAF, we may be able to offer prophylactic pharmacologic therapy in a more discriminative manner. Class III antidysrhythmia agents, when given before CABG, have been shown to significantly reduce the occurrence of postAF. In randomized controlled trials, Daoud *et al.*[20] administered amiodarone orally for 7 days before CABG, and Hohnloser *et al.*[21] and Guarnieri *et al.*[22] administered amiodarone postoperatively. Both showed significant reductions in the incidence of atrial fibrillation in the study group. Gomes *et al.*[23] showed that prophylactic sotalol prevents the occurrence of postAF, and VanderLugt *et al.*[24] showed similar results using prophylactic ibutilide. Because prevention seems possible, we sought to study preoperative, surgical, and TEE-derived data to identify parameters that would indicate an increased risk for developing PostAF.

The current study yielded an incidence of PostAF of 35.4%, which is consistent with other investigations. We found that age ($P = 0.002$), pre-CPB LAAA ($P = 0.04$), and post-CPB LUPVSD ratio ($P = 0.03$), when considered one at a time, were each associated with an increased risk of developing PostAF. The constellation of risk factors with the highest incidence of atrial fibrillation was high pre-CPB LAAA, in conjunction with older age, and low post-CPB LUPVSD ratio.

We did not find a significant relation between PostAF and a number of other factors that have been previously shown to be associated with PostAF. These include hypertension, CPB time, aortic cross clamp time, LA size, LA appendage outflow velocity, and LVEF.

Age

In accordance with published literature, when age was considered alone, it was found to be a significant predictor of PostAF.[1,7,8,10,12] The current multivariate analysis indicates that increased age is a risk for PostAF when in association with a large LAAA. This may be the result of age-related disease processes involving the myocardium (ischemia, valvular heart disease, congestive heart failure, and cardiomyopathy), which result in both mechanical and electrical atrial remodeling.[16,19,25] These changes in atrial loading conditions manifest as atrial dilation and hypertrophy,[26] which have been associated with PostAF.[19]

Left Atrial Appendage Area

Several studies in outpatient populations with longitudinal follow-up have demonstrated an association between LA size and PostAF.[19,25,27,28] However, the direction of causality is still speculative.[18,19,29] Some investigators suggest that changes in LA loading conditions lead to LA enlargement and an increased predisposition to develop atrial fibrillation.[25,27] Others propose that atrial fibrillation itself maybe the primary cause for the noted changes in LA size.[26,27]

The LA is a three-dimensional chamber, and it is difficult to quantify its size accurately with TEE because of the proximity of the posterior LA wall to the esophagus and near-field measurement inaccuracies. Measurement

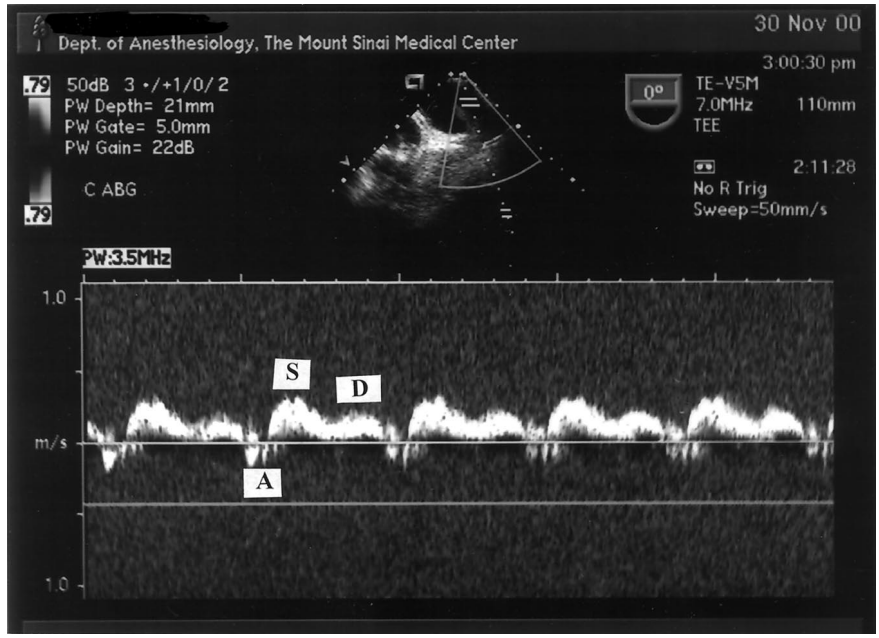

Fig. 1. Velocity components in Doppler recordings of pulmonary venous flow. During ventricular systole, there are two velocities (S1 and S2) that are often fused during normal atrioventricular conduction andform one wave, the S wave (S). Ventricular diastolic velocity, the D wave (D) is normally 20% smaller than S. Late ventricular diastole is marked by flow in the opposite direction caused by the atrial contraction, the A wave (A).

of the LAAA does not pose this specific limitation. Pre-CPB LAAA was associated with an increased incidence of PostAF in univariate analysis, the multivariate analysis indicating its strongest influence was evident in older patients. Because patients with a previous history of atrial fibrillation were excluded from our study, we can effectively rule out that atrial fibrillation led to enlarged LAAA in these patients.[29]

Left Upper Pulmonary Vein Systolic/Diastolic Ratio

There are four potentially measurable velocity components in Doppler recordings of pulmonary venous flow.[30] There are two ventricular systolic velocities, one ventricular diastolic velocity, and an atrial systolic velocity (flow reversal; fig. 1). With normal atrioventricular conduction, the two ventricular systolic velocities are often fused, and a single systolic velocity is seen in 70% of cases.[31] We showed that after CPB, a decreased LUPVSD ratio was associated with an increased incidence of PostAF. In situations of left ventricular diastolic dysfunction, early closure of the mitral valve occurs, LA pressure increases, and a subsequent increase in the diastolic velocity with a reduction in systolic velocity occurs. This reduction in the systolic to diastolic forward flow ratio[32] (decreased LUPVSD ratio) may be seen as an indicator of LA noncompliance and could be associated with an increased incidence of PostAF. Other conditions that result in a loss of LA compliance result in atrial remodelling[16,19] and would have the same effect on pulmonary vein inflow velocities.

Left Atrial Appendage Maximum Outflow Velocity

Previous studies have shown that a reduced LA appendage maximum outflow velocity is associated with atrial fibrillation and that this velocity increases when patients convert to sinus rhythm.[17] Omran *et al.*[18] showed that during sinus rhythm, peak emptying velocity of the LA appendage after cardioversion was significantly lower in those who would revert back to atrial fibrillation after cardioversion. However, our data and that of other investigators have not consistently shown LA appendage maximum outflow velocity to be a marker for atrial fibrillation.[33] Because LA appendage maximum outflow velocity has been associated with recurrence of atrial fibrillation, it may be a result of reduced atrial function rather than a marker for new onset or post–cardiac surgery atrial fibrillation.

Left Ventricular Ejection Fraction

We were unable to demonstrate a significant association between LVEF and PostAF. Other studies have shown that a decreased ejection fraction is associated with an increased incidence of PostAF.[7,9] Vaziri *et al.*[9] showed that reduced left ventricular fractional shortening was a predictor of nonrheumatic atrial fibrillation in an elderly population. Mathew *et al.*[7] identified congestive heart failure as an independent predictor of PostAF in patients undergoing coronary artery bypass surgery.

A decreased ejection fraction may be associated with ventricular and atrial noncompliance with resultant electromechanical dysfunction of the atrium leading to PostAF.[19] This may have been masked in our study by the relative small number of patients with low LVEF and inclusion of only 6% of patients with congestive heart failure. A larger cohort may reveal an association between low LVEF and PostAF.

Surgical Techniques

Several studies have found a relation between intraoperative techniques (duration of aortic cross clamp,

CPB time, minimum temperature) and the incidence of PostAF.[5,6,34,35] In the current study, we did not observe a significant relation between these factors and the incidence of PostAF. This may be a result of standard and consistent myocardial preservation techniques used among the surgeons at our institution.

Resource Utilization

Consistent with previous reports, PostAF is associated with longer overall hospital length of stay. It has been shown that pharmacologic therapy can reduce the occurrence of PostAF.[36] However, before prophylaxis can be offered, those at risk need to be identified. We used our model to estimate the probabilities of PostAF for various combinations of patient parameters, as shown in table 6.

Study Limitations

Several methodologic limitations of the current study exist and may make it difficult to generalize our findings to broader populations. The study was conducted on a specific population undergoing a relatively standard surgical protocol. In addition, the surgical techniques and myocardial preservation used in this study may differ from those at other institutions. A large number of potential risk factors were analyzed to identify important trends. We considered almost 50 potential factors and report the ones with significance levels less than $P = 0.2$. Thus, our findings should be considered the results of exploratory analyses and should be confirmed in a larger study.

Patients did not undergo any additional monitoring other than that which is used after CABG surgery. Thus, patients were not monitored with continuous electrocardiogram monitoring while in their regular hospital beds and may have had episodes of PostAF that went undetected. Nevertheless, the incidence of PostAF in our study is in keeping with that reported in the literature.

In conclusion, this study has identified large LAAA, increased age in conjunction with large LAAA, and low LUPVSD ratio as potentially important predictors of PostAF in CABG patients with no previous history of atrial dysrhythmia. If confirmed in larger studies, a model such as ours could be used to develop algorithms for identifying patients who are at high risk for developing PostAF. Prophylactic therapy could then be administered in the perioperative period with the aim of preventing PostAF, decreasing hospital length of stay, and reducing the overall cost of care.

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