

Prediction of Atrial Fibrillation via Atrial Electromechanical Interval After Coronary Artery Bypass Grafting

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Background—We assessed the validity of the atrial electromechanical interval, measured by transthoracic tissue Doppler echocardiography, in determining patients at risk of post-coronary artery bypass graft atrial fibrillation (AF).

Methods and Results—This prospective study recruited 355 patients in sinus rhythm who were candidates for coronary artery bypass grafting. The patients underwent a preoperative transthoracic echocardiography with a tissue Doppler evaluation and were monitored with continuous ECG telemetry during their hospital stay. Sixty-eight patients had postoperative AF (19.2%), with the incident occurring 2.3 ± 0.7 days after surgery. The median length of hospitalization was 7.0 days for the AF patients and 6.0 days for the non-AF patients ($P < 0.0001$). The subjects with postoperative AF differed from the sinus rhythm patients in that the former had a lower ejection fraction ($40.4 \pm 8.5\%$ versus $48.4 \pm 9.4\%$), a reduced maximal A-wave transmitral Doppler flow velocity (44.3 ± 4.6 versus 53.3 ± 10.9 cm/s), an increased total atrial volume (68.7 ± 12.6 versus 55.3 ± 11.8 mL), and a prolonged atrial electromechanical interval (141.9 ± 13.4 versus 100.3 ± 10.3 ms, respectively; $P < 0.0001$ for all). In addition, the AF patients were older than the sinus rhythm group (66.0 ± 8.0 versus 59.8 ± 8.5 years). The atrial electromechanical interval was the best independent discriminator of the history of AF. We defined a cutoff point for the atrial electromechanical interval and chose 120 milliseconds for categorization, which yielded 100% sensitivity and 94.8% specificity for the prediction of AF.

Conclusions—The atrial electromechanical interval by transthoracic tissue Doppler echocardiography could be a valuable method for identifying patients vulnerable to post-coronary artery bypass graft AF. (*Circulation*. 2007;116:2012-2017.)

Key Words: arrhythmia ■ fibrillation ■ grafting ■ sensitivity ■ specificity

Atrial fibrillation (AF) is the most common arrhythmia after coronary artery bypass grafting (CABG), with a rate of occurrence of 17% to 33% in different studies.¹ Patients undergoing CABG and combined valve surgery have a higher incidence of postoperative AF than do patients having CABG alone.^{2,3} The peak of AF incidence occurs between 2 and 4 days after operation, with <10% happening on the first postoperative day.⁴

Clinical Perspective p 2017

AF after CABG is self-limiting in most cases, but even when it is uncomplicated, it requires additional medical treatment and a prolonged hospital stay and has the concomitant extra costs of operative treatment.³⁻⁵ Post-CABG AF is known to be a potential risk of systemic thromboembolism, hemodynamic compromise, and even stroke^{2,6}; therefore, it is advisable that prophylactic therapy with amiodarone or atrial pacing be administered to decrease its incidence.^{7,8} However, prophylactic treatment to prevent AF with intravenous amiodarone is not cost-effective if given to all patients.⁹ In addition, such treatments may have unfavorable side effects. On balance, the fact that the prophylaxis of the whole patient

population undergoing CABG is not reasonable renders the identification of at-risk patients of post-CABG AF very helpful.

To that end, several studies have used different ECG and echocardiographic parameters (eg, P-wave duration and left atrial [LA] volume). They all, however, have limitations.¹ Using M-mode Doppler tissue, Omi and colleagues¹⁰ have recently evaluated the ability of the atrial electromechanical coupling to detect atrial impairment in paroxysmal AF. They found that the time intervals from the onset of the P wave to the beginning of the backward motion of the mitral and tricuspid were prolonged in paroxysmal AF.

In light of the above-mentioned studies, we hypothesized that the atrial electromechanical interval (AEMI) as a measure of atrial impairment could be helpful in detecting patients facing the risk of post-CABG AF. Thus, this study sought to assess the validity of an echocardiographic index, namely the AEMI, in predicting post-CABG AF.

Methods

Patient Population

This prospective study recruited 587 consecutive patients who underwent CABG at the Day General Hospital (Tehran, Iran)

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between February 2005 and December 2005. The inclusion criteria were (1) the presence of significant coronary artery disease with an indication for CABG, (2) no need for associated surgery, (3) the absence of rhythm other than normal sinus rhythm, (4) the absence of a history of AF, (5) acceptable echocardiography image quality, and (6) the absence of valvular heart disease. In total, 365 patients met these criteria and were included in the study. Six patients died in hospital, and 4 patients had to undergo another surgical operation in the operating room; they were excluded from the study. Informed written consent was obtained from all patients, and the study protocol was approved by our institutional Ethics Committee on Human Study.

ECG Assessment

Until the day of discharge, all the patients were monitored with continuous ECG telemetry and had a standard 12-lead ECG recorded every day. AF was defined as AF requiring treatment and lasting >5 minutes. Brief isolated nonsustained episodes of AF were excluded. In the cardiovascular intensive care unit, automated detection of AF was obtained via the bedside arrhythmia monitor Solar 9500 (GE Medical Systems, Milwaukee, Wis). The diagnosis was confirmed by the cardiovascular intensive care unit physician, who also initiated treatment as appropriate. In the step-down units, AF was detected by means of continuous ECG telemetry monitoring (Eagle 4000, GE/Marquette Medical Systems, Milwaukee, Wis). The diagnosis of each patient was confirmed by a cardiologist, who led this project. In addition, the cardiologist who made the diagnosis of AF had no information about the AEMI and other parameters. The well-known difficulties in defining the P-wave onset and offset may restrict the accuracy and reproducibility of the measurements. Some of these restrictions are overcome via a computer-based ECG system.

The 30-second ECG signals were acquired and stored on the hardware of the data acquisition system. The ECG waves were then displayed on the computer screen, with the waves enlarged 2 to 4 times and paper speed increased to 50 to 100 mm/s.

Echocardiography

All patients underwent a preoperative transthoracic echocardiography with a tissue Doppler imaging analysis (GE Medical System, Vivid 7, Horton, Norway) during the week leading up to surgery. Tissue Doppler imaging is a relatively new technology that allows direct noninvasive measurements of myocardial velocities and displacement. A single experienced investigator took the recordings.

The left ventricular dimensions and wall thickness were determined in the parasternal long-axis view with the M-mode cursor positioned just beyond the mitral leaflet tips perpendicular to the long axis of the ventricle according to the recommendations of the American Society of Echocardiography. LA volume was determined by tracing the endocardium from the 4-chamber view at the maximal atrial dimension. The left ventricular ejection fraction by 2-dimensional echocardiography was obtained via a modified biplane Simpson method from the apical 4- and 2-chamber views.

From the transmitral Doppler spectra of 5 consecutive cardiac cycles, average values were calculated for late atrial filling velocity (A wave). Myocardial velocities obtained with tissue Doppler were recorded using a standard pulsed-wave Doppler technique with the sample volume placed at the junction of the left ventricle lateral wall with the mitral lateral annulus from the 4-chamber view. Peak velocities during the atrial systole (Am) also were measured, the final value representing the average of at least 5 cardiac cycles. The AEMI was measured in milliseconds as time intervals from the onset of the P wave to the beginning of the atrial systole (Am) at the lateral side of the left atrium (left side) (Figures 1 and 2).

Operative Technique

A median sternotomy was performed in all the patients. Standard cardiopulmonary bypass was established by ascending aortic cannulation and with a single 2-stage venous cannulation of the right atrium. Myocardial protection was achieved by antegrade intermit-

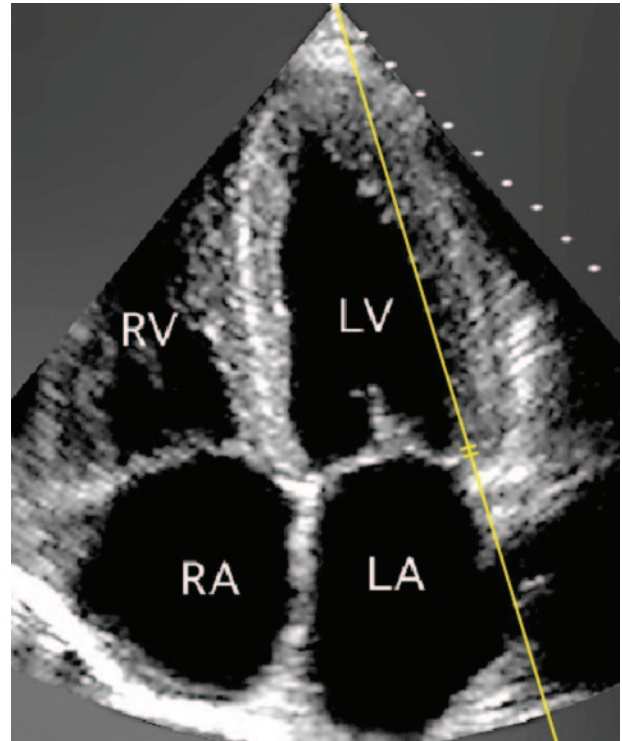


Figure 1. The AEMI was measured as time intervals from the onset of the P wave to the beginning of the atrial systole at the lateral side of the LA (left side). RV indicates right ventricle; LV, left ventricle; and RA, right atrium.

tent warm blood cardioplegia every 15 minutes. All the patients received total revascularization.

Statistical Analysis

Data are presented as mean \pm SD, percent, and total number when necessary. Comparisons were made between the continuous variables by a *t* test and between the categorical variables by a χ^2 test. A multiple logistic regression was applied to evaluate the independent risk factors for AF. All the independent variables (ie, both significant and nonsignificant variables in the single-variable analysis) were included in the models using a backward selection method. A value of $P > 0.1$ was used to reject variables from the model. The R^2 was used to assess the goodness of fit of the models. A value of $P < 0.1$

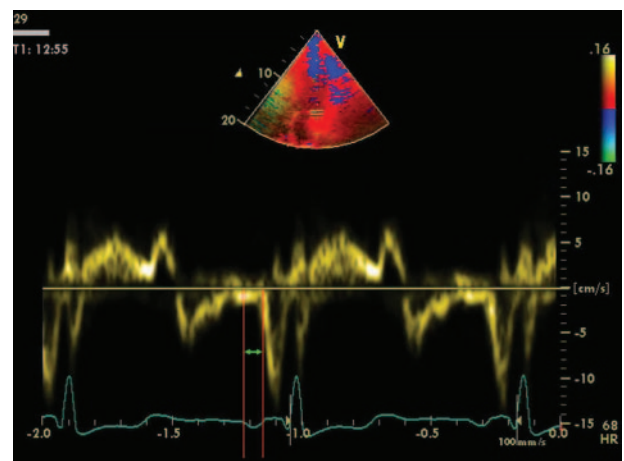


Figure 2. Four-chamber view. The sample volume was placed at the junction of the left ventricle lateral wall with the mitral lateral annulus.

Table 1. Demographic Data, Clinical Variables, and Drugs for Patients With and Without AF

Clinical Features	AF (n=68)	Without AF (n=287)	P
Age, mean±SD, y	66.0±8.0	59.8±8.5	<0.0001
Male sex, n (%)	44 (64.7)	191 (66.6)	0.772
Diabetes mellitus, n (%)	21 (30.9)	91 (31.7)	0.895
COPD, n (%)	31 (45.6)	107 (37.3)	0.206
Hypertension, n (%)	38 (55.9)	150 (52.3)	0.591
Grafts, mean±SD, n	3.2±1.0	3.3±1.0	0.770
BMI, mean±SD, kg/m ²	27.0±2.3	26.0±2.3	0.003
Drugs, n (%)			
Before surgery			
ACE inhibitors	49 (72.1)	212 (73.9)	0.761
Diuretics	26 (38.2)	109 (38.0)	0.969
β-Blockers	34 (50.0)	140 (48.8)	0.856
Calcium channel blockers	8 (11.8)	37 (12.9)	0.802
Digoxin	5 (7.4)	14 (4.9)	0.415
After surgery, n (%)			
β-Blockers	60 (88.2)	260 (90.6)	0.558
Calcium channel blockers	7 (10.3)	32 (11.1)	0.839

COPD indicates chronic obstructive pulmonary disease; BMI, body mass index; and ACE, angiotensin-converting enzyme.

was applied to select variables in the model. The best cutoff point for the AEMI to predict the possibility of postoperative AF was defined via a receiver-operating characteristics curve analysis. The statistical analyses were performed with the SPSS software package, version 13.0 (SPSS Inc, Chicago, Ill). A value of $P<0.05$ was considered statistically significant.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Of a total of 355 patients, 68 patients (19.2%) had postoperative AF, with the incident happening 2.3 ± 0.7 days after surgery. Sinus rhythm was restored in all patients with antiarrhythmic medical therapy. The median length of hospitalization was 7.0 days for the AF patients and 6.0 days for the non-AF patients ($P<0.0001$). The demographic data, clinical variables, and drugs are shown in Table 1. The preoperative echocardiographic parameters are listed in Table 2. The inclusion of all the variables (both significant and nonsignificant) in Tables 1 and 2 in the multiple logistic regression analysis revealed that AF correlated only with sex, A wave, AEMI, and cardiopulmonary bypass time (Table 3). The R^2 was equal to 0.58. The receiver-operating characteristics curve of the 3 continuous variables is shown in Figure 3; the area under the curve was 0.99 (95% confidence interval, 0.98 to 1.00) for the increase in AEMI, 0.64 (95% confidence interval, 0.56 to 0.72) for the increase in cardiopulmonary bypass time, and 0.77 (95% confidence interval, 0.72 to 0.81) for the decrease in A wave.

Receiver-operating characteristics curve for 3 variables: AEMI, cardiopulmonary bypass (CPB), and A wave.

Table 2. Preoperative Echocardiographic Parameters for Patients With and Without AF

	AF (n=68)	Without AF (n=287)	P
EF, %	40.4±8.5	48.4±9.4	<0.0001
AT volume	68.7±12.6	55.3±11.8	<0.0001
A wave, cm/s	44.3±4.6	53.3±10.9	<0.0001
P-wave duration	94.3±12.0	86.8±9.6	<0.0001
AEMI, ms	141.9±13.4	100.3±10.3	<0.0001
ACC, min	83.6±11.6	80.1±11.9	0.029
CPB, min	101.5±9.8	94.3±17.6	0.001
TDI A wave	10.7±1.8	12.7±2.8	<0.0001

Values are expressed as mean±SD. EF indicates ejection fraction; AT volume, left atrial volume; A wave, late atrial filling velocity; ACC, aortic cross-clamp time; CPB, cardiopulmonary bypass time; and TDI A wave, tissue Doppler imaging atrial contraction.

Multiple logistic regression analysis demonstrated that the AEMI not only was significant even in the presence of the other variables but also was strongly predictive of the occurrence of AF and that the area under the curve was the best. Our analysis to define a cutoff point for the AEMI (Figure 4) advised the use of 120 ms for categorization, which yielded 100% sensitivity, 94.8% specificity, 81.9% positive predictive value, and 100% negative predictive value for the prediction of postoperative AF. We opted for the cutoff point of 120 ms because we did not want to miss any patient with a possibility of developing postoperative AF, even at the cost of including some patients who did not face the risk of developing this postoperative complication.

Discussion

M-mode Doppler tissue echocardiography enabled us to evaluate the validity of the AEMI as a predictor of post-CABG AF. This user-friendly index, which is inexpensive and accessible, showed that patients with a larger AEMI were prone to develop AF rather than remain in sinus rhythm after CABG.

Preventing the onset of AF in lieu of treating its complications is of great significance from the standpoint of public health. Postoperative intravenous amiodarone, followed by oral amiodarone, appears to be effective in the prevention of new-onset postoperative AF. It also reduces the ventricular rate and duration of AF after CABG.¹¹ Despite these benefits, amiodarone has some serious side effects¹² that limit its application, hence the necessity to administer amiodarone only to patients at high risk of post-CABG AF. Nonetheless, identifying such patients at whom a prophylactic measure (including amiodarone, β-blockers, and atrial pacing) for preventing AF could be targeted remains a challenge for modern heart surgery.

To date, several demographic and preoperative factors such as age, sex, history of previous AF, hypertension, chronic obstructive pulmonary disease, diseased right coronary artery, and use or withdrawal of medication have been shown to be risk factors for postoperative AF. Unfortunately, none of these factors is powerful enough to predict postoperative AF after CABG to any clinically meaningful extent.¹ On the other

Table 3. Multiple Logistic Regression Analysis of the Risk of AF

B	B	SE	Wald	df	P	Odds Ratio (95% CI)
Male	-1.943	1.054	3.395	1	0.065	0.143 (0.018–1.132)
A wave	-0.176	0.069	6.573	1	0.010	0.838 (0.733–0.959)
AEMI	0.314	0.067	21.850	1	<0.001	1.370 (1.200–1.563)
CPB	0.079	0.029	7.689	1	0.006	1.083 (1.024–1.145)

A wave indicates late atrial filling velocity; CPB, cardiopulmonary bypass time; and CI, confidence interval. Variables were chosen by backward selection.

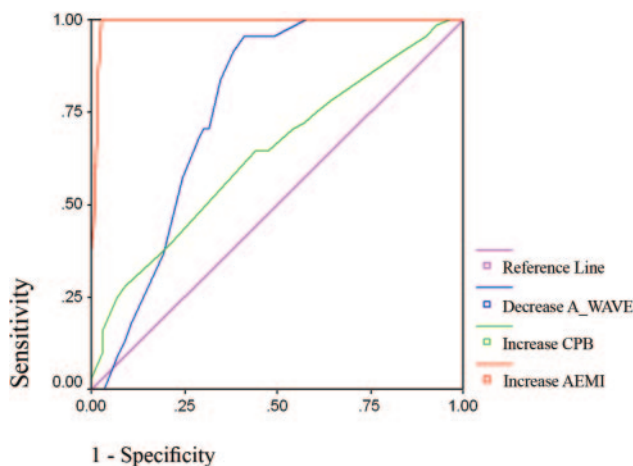
hand, several echocardiographic approaches to nonrheumatic AF have been previously reported,^{13–16} but one must not lose sight of the fact that conventional echocardiographic parameters have their own limitations. The LA volume has an independent predictive value for determining the risk of AF. Nevertheless, several studies have reported that the LA dimensions in patients with paroxysmal AF are not necessarily larger than those in control subjects.^{17,18} Furthermore, the relationship between the LA chamber size estimated by echocardiography and lone paroxysmal AF is controversial. Echocardiographic LA chamber size usually is measured as a short-axis dimension in the parasternal and apical views, but this method possibly is insensitive in the detection of LA enlargement.¹⁹ Transmitral flow velocity during early diastolic filling (E), atrial contraction (A), and E/A ratio are affected in paroxysmal AF.²⁰ Decreased A velocity is correlated with reduced atrial contraction.²¹ Decreased E/A ratio is related mainly to left ventricular diastolic dysfunction and not directly to atrial impairment.²² Both parameters are less sensitive and less specific because they are influenced by such cardiac conditions as heart rate, preload, and afterload.²³

There has been a search for new predictors based on new technology to analyze ECG or to measure heart rate variability.¹ Of these predictors, the prolongation of P-wave duration in signal-averaged ECG looks the most promising. According to the existing literature, the sensitivity of the signal-averaged P-wave duration in identifying patients developing AF postoperatively is 68% to 86%, and the specificity ranges from 39% to 88%. Moreover, the positive predictive and negative

predictive values vary from 34% to 76% and from 83% to 85%, respectively.^{24–29} Obviously, the fact that sensitivity and the negative predictive value are high but specificity and the positive predictive value remain quite low limits its usefulness in clinical practice. On the other hand, even a detailed analysis of a standard 12-lead ECG has failed to provide useful information for risk stratification. An analysis of lead II P-wave duration and P-terminal force in a standard ECG has been reported to show no significant difference in any of these variables between AF patients and non-AF patients after CABG.^{27,29} Changes in heart rate variability before postoperative AF have already been documented, yet Hakala and coworkers³⁰ showed that a short-term preoperative analysis of heart rate variability under standardized physiological conditions could not reliably identify patients at high risk of AF after CABG.

Benedetto and coworkers³¹ showed a correlation between preoperative LA dysfunction assessed by tissue Doppler and postoperative AF after CABG. They explained that a peak atrial systolic mitral annular tissue Doppler velocity of ≤ 9 cm/s ($P=0.03$; odds ratio, 1.8) was independently related to the incidence of postoperative AF.

As mentioned earlier, in the present study, a prolonged AEMI was detected in patients who showed post-CABG AF compared with those who remained in sinus rhythm after CABG (141.9 ± 13.4 versus 100.3 ± 10.3 ms, respectively; $P<0.0001$). Our data support a previous comprehensive study by Omi and colleagues,¹⁰ who evaluated the AEMI via M-mode Doppler tissue to test its clinical feasibility for detecting atrial abnormalities in paroxysmal AF. Using Doppler tissue, Omi and associates measured the time intervals from the onset of the P wave until the backward motions of



Diagonal segments are produced by ties.

Figure 3. Receiver operating characteristic for 3 variables (AEMI, CPB, and A wave).

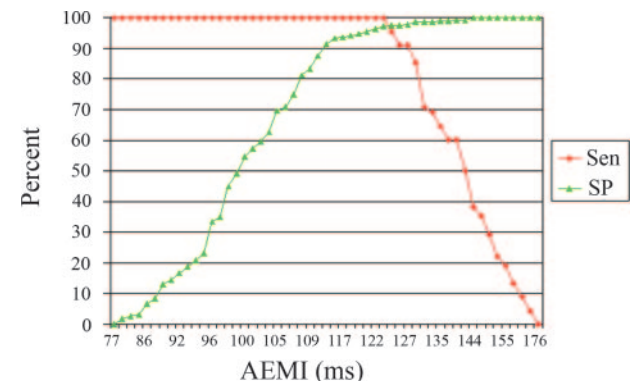


Figure 4. Analysis for the identification of a good cutoff point for the prediction of post-CABG AF by AEMI. Sen indicates sensitivity; SP, specificity.

the right (R-PC) and left (L-PC) atrioventricular rings in the apical 4-chamber view corresponding to the atrial contractions. They demonstrated that both R-PC and L-PC intervals in the paroxysmal AF group were significantly longer than those in the control group (74 ± 11 versus 61 ± 11 ms, $P < 0.005$; and 120 ± 15 versus 90 ± 11 ms, $P < 0.0001$, respectively). Using the criterion of L-PC interval > 112 ms as an atrial impairment of paroxysmal AF yielded sensitivity, specificity, and a positive predictive value of 73%, 93%, and 93%; using an L-PC interval > 104 ms (the value with the largest sum of sensitivity and specificity) yielded values of 87%, 93%, and 93%, respectively. Omi and colleagues also showed that L-PC interval was correlated positively with the LA long-axis dimension ($r = 0.499$, $P < 0.005$) and filtered P-wave duration ($r = 0.735$, $P < 0.0001$) but not with the short-axis dimension ($r = 0.264$, $P = 0.159$). These data support the notion that L-PC interval is determined by the atrial electric conduction disturbance and LA enlargement.

Surprisingly, some of the demographic factors that have been reported as predictors of post-CABG AF can increase fibrosis and lead to consequent atrial refractoriness and conduction delay. Because the prolongation of the AEMI can be explained not only by LA enlargement but also by increased time delay from electric activation in the atrium to atrial myocardial contraction,³ the AEMI can totally and significantly reflect the atrial impairment and predict post-CABG AF. In the present study, the patients who showed post-CABG AF were older than patients in sinus rhythm (66.0 ± 8.0 versus 59.8 ± 8.5 years). Aging causes cardiac dilatation, myocardial atrophy, decreased conduction tissue, and fibrosis in the atria.^{32,33} These age-related changes may partially affect the AEMI and may be responsible for an increased risk of AF after CABG. Likewise, hypertension has been shown to predict postoperative AF; it may be related to increased fibrosis and to the dispersion of atrial refractoriness, both of which influence the AEMI.

The results of our study are in line with those of some previous studies showing that the AEMI was a useful parameter for detecting atrial impairment. Therefore, the AEMI can be used as a reliable index to determine patients at high risk of post-CABG AF, with a larger AEMI denoting a higher probability of post-CABG AF. Consequently, effective prophylactic measures can be targeted only at patients with a prolonged AEMI.

Disclosures

None.

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CLINICAL PERSPECTIVE

Postoperative atrial fibrillation, one of the most common complications of coronary artery bypass grafting, is associated with prolonged hospital stay. Prophylactic therapies with medications such as amiodarone and β -blockers have been advocated but have risks. Identifying patients at high risk for atrial fibrillation is therefore of interest. The atrial electromechanical interval, measured from the onset of the P wave to echocardiographic detection of left atrial motion, reflects atrial conduction and contraction timing. We prospectively assessed whether the preoperative atrial electromechanical interval predicts postoperative atrial fibrillation. An atrial electromechanical interval of >120 ms was very sensitive (100%) and specific (94.8%) for identifying at-risk patients. These findings suggest that prophylactic therapy for atrial fibrillation can be specifically targeted to high-risk patients and that use of atrial electromechanical interval should be considered for trials of prophylactic therapy.