P-Wave Signal-Averaged Electrocardiogram Predicts Atrial Fibrillation After Coronary Artery Bypass Grafting

Paolo Caravelli, M.D., Marco De Carlo, M.D., Giuseppe Musumeci, M.D.,
Giuseppe Tartarini, M.D., Gherardo Gherarducci, M.D.,
Uberto Bortolotti, M.D., Massimo A. Mariani, M.D.,
and Mario Mariani, M.D.

From the Cardiothoracic Department, University of Pisa, Pisa, Italy

Background: AF is one of the most common complications after CABG. The aim of the study was to identify the risk factors for postoperative AF.

Methods: Between June and December 2000, 129 consecutive patients (72 men, 47 women; mean age 67 ± 6 years) underwent preoperative signal-averaged electrocardiogram (SAECG) with assessment of filtered P-wave duration (fPWD) and of the root mean square voltage of the last 10 and 20 ms of atrial depolarization (RMSV10 and RMSV20, respectively) before CABG.

Results: Fifty-six (43%) patients developed one episode of AF lasting > 30 seconds at a mean distance of 2.6 ± 1.8 days after surgery (group A), while 73 patients remained in sinus rhythm (group B). No differences between the two groups were found in terms of age, sex, P-wave duration on the standard ECG, left atrial dimensions, and operative characteristics. In contrast, group A patients showed a significantly longer fPWD (138 ± 10 vs 111 ± 9 ms; $P < 0.001$) and smaller RMSV10 and RMSV20 (2.8 ± 1.0 vs 4.3 ± 1.1 μ V, $P < 0.001$; 4.2 ± 2.1 vs 6.2 ± 2.0 μ V, $P < 0.001$). Multivariate analysis indicated only fPWD as an independent predictor of AF ($P = 0.009$). With a cut-off value of 135 ms for fPWD, the occurrence of AF could be predicted with a sensitivity of 84%, a specificity of 73%, a negative predictive value of 85%, and a positive predictive value of 70%.

Conclusion: Preoperative SAECG is a simple exam that correctly identifies patients at higher risk of AF after CABG. A more widespread use of this technique can be suggested. **A.N.E. 2002;7(3):198–203**

signal-averaged ECG; atrial fibrillation; coronary artery bypass grafting

Despite continuous improvement in surgical and anesthesiological techniques, atrial fibrillation (AF) remains one of the most common complications after coronary artery bypass grafting (CABG) with a reported incidence rate between 20% and 40%.^{1–4} Although postoperative AF usually is a benign, self-limiting condition, it increases the risk of embolic stroke^{1,5} and, in certain circumstances (e.g., in the presence of an impaired left ventricular function or in the case of incomplete myocardial revascularization) may cause hemodynamic instability. Moreover, the occurrence of AF requires

additional medications and often determines a prolongation of hospital stay, even when it is uncomplicated.^{1–4,6,7} Thus, the identification of preoperative and intraoperative parameters that predict the occurrence of AF after CABG could allow a pharmacologic prophylaxis in patients who are at higher risk.

Researchers have repeatedly tried to identify predictors of AF after CABG with conflicting results. Clinical features like advancing age,^{3,4,8–10} postoperative withdrawal of beta-blocking agents,^{3,11,12} low serum magnesium,¹³ and right coronary artery

Address for reprints: Paolo Caravelli, M.D., Dipartimento CardioToracico, Ospedale Cisanello, Via Paradisa 2, 56124 Pisa, Italy. Fax: +39-050-995308; E-mail: marcocodecarlo@interfree.it

stenosis¹⁴ have been reported to predict postoperative AF.

Signal-averaged electrocardiogram (SAECG) has been successfully used for the study of atrial conduction and for prediction of the occurrence of paroxysmal AF.¹⁵⁻¹⁷ More recently, a prolonged filtered P-wave duration (fPWD) has been demonstrated to predict the development of AF in patients undergoing CABG.^{10,13,18,19} Conversely, others have reported age, body weight, left ventricular ejection fraction, P-wave duration on the standard ECG (sPWD), and postoperative withdrawal of beta-blockers, but not fPWD, to be significant predictors of AF after CABG.^{9,12}

The aim of the present study was to evaluate the role of SAECG in the prediction of AF after CABG.

METHODS

The study included 143 consecutive patients who underwent CABG with cardiopulmonary bypass at the Cardiothoracic Department from June to December 2000, and who underwent preoperative SAECG. Of these, 12 patients were excluded because of high noise levels on the SAECG. Two more patients who died within 24 hours of surgery were excluded. The remaining 129 patients (72 men, 57 women; mean age 67 ± 7 years) form the basis of the present report. Patients with history of paroxysmal AF, with arrhythmia at rest, and with thyroid dysfunction, as assessed by preoperative clinical evaluation, standard ECG, and thyroid hormone plasma levels determination were excluded. P-wave duration in the surface ECG (sPWD) was measured by two operators on the bipolar leads I, II, and III with a paper speed of 50 mm/s. Total P-wave duration was defined as the time interval between the earliest onset of the P wave in any of the leads I, II, and III and the latest offset in any of the leads I, II, and III.

All patients underwent coronary angiography and transthoracic two-dimensional color Doppler echocardiography. Patients with any degree of mitral stenosis or with more than trivial mitral regurgitation were excluded. The left atrial diameter was measured from the parasternal long-axis view, while left ventricular end-diastolic volume (LVEDV), end-systolic volume (LVESV), and ejection fraction (LVEF) were measured from the apical four-chamber view.

P-Wave SAECG

The day before surgery all patients underwent signal-averaged P-wave analysis with a commercially available instrument (HIPEC 2000 Mortara Rangoni analyzer, Mortara Rangoni SpA, Casalecchio di Reno, Italy) provided with specific software. Recordings were taken with the patient supine and in a silent well-heated environment to minimize the artefacts due to muscular contraction. An orthogonal X, Y, Z lead system was used with the QRS as the trigger for the signal-averaging process. However, the fiducial point was shifted to the extreme right side of the 300-ms window, so as to expose the P wave and the PR interval. Input signals were sampled at 1 kHz and converted from analog to digital in 12 bits. A P wave selected by the operator was used as a template for P-wave recognition; P-wave complexes not matching the template with a 99% correlation coefficient were automatically rejected, thus ensuring that atrial ectopic beats and beats shifted because of autonomic tone were not averaged. The averaging procedure was a bidirectional filtering with a fourth-order Butterworth design set at a bandwidth of 30–250 Hz. Averaging was protracted until the background noise in the TP segment was $< 0.3 \mu\text{V}$, usually requiring 200–400 beats.

Atrial conduction delay was also assessed in all patients by measuring the root mean square voltage (RMSV) of terminal 10, and 20 ms of the signal-averaged P wave (RMSV10 and RMSV20, respectively).¹⁵

Surgical Data and Postoperative Care

The operative variables examined were aortic cross-clamp time, cardiopulmonary bypass time, and the number and type (arterial or venous) of conduits used for myocardial revascularization.

All patients were under continuous ECG monitoring after operation. A 12-lead ECG was recorded whenever a change in rhythm was observed on the telemetry. Episodes of AF lasting more than 30 seconds and which could be documented on a standard 12-lead ECG, both spontaneously and pharmacologically ceased, were considered relevant. Time of presentation, duration, and mode of interruption (spontaneous or pharmacologic) of each episode were recorded.

Plasma electrolyte concentrations were assessed at least once daily during the first week of hospital stay.

Statistical Analysis

Categorical data are presented as absolute values and percentages, whereas continuous data are summarized as mean value $\pm$ SD. The chi-square test was used for comparison of categorical variables. Student's *t*-test or Mann-Whitney test were used to compare continuous variables, as appropriate. All variables with a *P* value < 0.10 at univariate analysis were included in a logistic regression analysis. *P* values < 0.05 were considered statistically significant. The cut-off point for fPWD was identified by means of receiver operating characteristic (ROC) curves. Analysis was performed using NCSS 2000 Software (Statistical Solutions Ltd., Cork, Ireland).

RESULTS

Two (1.5%) patients died within 24 hours of surgery and were excluded from the study. Two more patients died on postoperative days 3 and 8, respectively; neither developed AF.

Episodes of AF, as previously defined, were observed in 56 (43%, group A) patients at a mean distance of 2.6 ± 1.8 days after operation (range 0–10 days). The remaining 73 (57%, group B) patients remained in sinus rhythm during hospital stay (48 men, 25 women; mean age 65 ± 6 years). Group A consisted of 34 men and 22 women with

a mean age of 67 ± 7 years. The mean duration of AF episodes was 106 ± 64 minutes, with a mean of 1.8 ± 0.4 episodes per patient. Sinus rhythm spontaneously recovered in four patients (7% of group A), while in 50 patients (89% of group A) sinus rhythm was restored with drug therapy, consisting of standard amiodarone intravenous infusion in 41 patients and of propafenone infusion in 9. AF persisted in spite of antiarrhythmic therapy in the remaining two patients (4% of Group A) who were discharged from the hospital with normofrequent ventricular response and good hemodynamic performance. The occurrence of AF was hemodynamically well tolerated in all patients, but significantly prolonged hospital stay (11.6 ± 4.0 vs 7.8 ± 1.4 days in groups A and B, respectively, $P < 0.001$). No episodes of cerebral embolism were observed in group A patients.

At univariate analysis, patients who developed postoperative AF did not significantly differ from patients who remained in sinus rhythm with respect to sex, age, body weight, systolic and diastolic blood pressure, and resting heart rate (Table 1). No significant differences between the two groups were found concerning sPWD (125 ± 3 vs 123 ± 2 ms in groups A and B, respectively) nor echocardiographic LVEF (51% in group A vs 52% in group B) and left atrial diameter (39 ± 7 vs 38 ± 6 mm in groups A and B, respectively). In addition,

Table 1. Clinical and Operative Characteristics

	Group A	Group B	P
Age (years)	67 ± 7	65 ± 6	> 0.2
Sex (M/F)	34/22	48/25	> 0.2
Body mass index	25 ± 3	24 ± 3	> 0.2
Resting heart rate (beats/min)	65 ± 7	66 ± 8	> 0.2
Systolic blood pressure (mmHg)	133 ± 11	135 ± 14	> 0.2
Diastolic blood pressure (mmHg)	76 ± 8	79 ± 9	> 0.2
Left ventricular end diastolic volume (mL)	105 ± 13	102 ± 14	> 0.2
Left ventricular end systolic volume (mL)	51 ± 9	49 ± 8	> 0.2
Left ventricular ejection fraction (%)	51 ± 6	52 ± 5	> 0.2
Left atrial diameter (mm)	39 ± 7	38 ± 6	> 0.2
NYHA class	1.6 ± 0.7	1.4 ± 0.8	> 0.2
Cardiopulmonary bypass time (min)	98 ± 46	86 ± 24	> 0.2
Aortic cross-clamp time (min)	63 ± 33	59 ± 22	> 0.2
sPWD (ms)	125 ± 3	123 ± 2	> 0.2
fPWD (ms)	138 ± 10	111 ± 9	< 0.001
RMSV10 (μ V)	2.8 ± 1.0	4.3 ± 1.1	< 0.001
RMSV20 (μ V)	4.2 ± 2.1	6.2 ± 2.0	< 0.001

fPWD = filtered P wave duration; RMSV10 = root mean square voltage of the last 10 ms of the P wave; RMSV20 = root mean square voltage of the last 20 ms of the P wave; sPWD = P wave duration on the standard electrocardiogram.

Figure 1. Comparison of filtered P-wave duration (black bars), root mean square voltage of the last 10 ms (RMSV10; white bars), and 20 ms (RMSV20; gray bars) of the P wave between patients who developed episodes of postoperative atrial fibrillation (group A) and those who remained in sinus rhythm (group B).

plasma potassium, sodium, calcium, magnesium, and chloride concentrations on the day of onset of AF were similar in the two groups of patients.

Aortic cross-clamp time and cardiopulmonary bypass time were slightly longer in group A patients, but the difference was not statistically significant (63 ± 33 minutes in group A vs 59 ± 22 minutes in group B and 92 ± 36 minutes in group A vs 86 ± 24 minutes in group B, respectively). The mean number of conduits used for myocardial revascularization was also not significantly different.

P-wave duration on the standard ECG was not significantly different between patients who developed AF and those who remained in sinus rhythm. In contrast, signal-averaged P-wave analysis showed significant differences between group A and group B patients, fPWD being significantly longer in group A than in group B (138 ± 10 vs 111 ± 9 ms, $P < 0.001$; Fig. 1). Moreover, RMSV10 and RMSV20 of the P wave were significantly lower in group A than in group B (RMSV10: 2.8 ± 1.0 vs 4.3 ± 1.1 μ V, $P < 0.001$; RMSV20: 4.2 ± 2.1

vs 6.2 ± 2.0 μ V, $P < 0.001$; Fig. 1). The cut-off value for fPWD with the highest sensitivity and specificity in predicting the occurrence of AF was a fPWD of 135 ms. This cut-off value allowed prediction of postoperative AF with a sensitivity of 84%, a specificity of 73%, a negative predictive value of 85%, and a positive predictive value of 70% (Table 2).

At multivariate analysis, only fPWD was found to be an independent predictor of the occurrence of postoperative AF ($P = 0.009$).

DISCUSSION

The incidence of episodes of AF in patients undergoing CABG has been reported to vary from 20% to 40%.¹⁻⁴ In the present study, an incidence of 43% was observed with most first episodes occurring within 72 hours from operation and lasting < 48 hours, in agreement with the most recent reports.^{7,9,10,19-22} The occurrence of AF did not significantly impair the hemodynamic performance in the population; however, it significantly prolonged hospital stay ($P < 0.05$), as previously reported.^{2-4,6,7}

Among the preoperative and perioperative variables considered, only signal-averaged P-wave duration appeared to be an independent predictor of the development of postoperative AF. The observed association between episodes of AF after CABG and P-wave abnormalities on SAECC may be due to the electrophysiological substrate of this arrhythmia. Cardiac surgery procedures (like cannulation of the right atrium or of the venae cavae, atriotomy, aortic cross-clamp, and cardiopulmonary bypass) can produce an ischemic injury that can trigger an intraatrial reentry circuit. Moreover, obstructive disease in the sinoatrial nodal and atrioventricular nodal arteries is more common in patients developing AF following CABG than in those who remain in sinus rhythm.²³ The mechanism by which ischemia may determine the reentry phenomenon²⁴ is probably related to the opening of potassium channels determined by the

Table 2. Predictivity of Filtered P-Wave Duration > 135 ms on Occurrence of Postoperative Atrial Fibrillation

	Atrial Fibrillation	Sinus Rhythm	
fPWD ≥ 135 ms	47	20	Positive predictive value: 70%
fPWD < 135 ms	9	53	Negative predictive value: 85%
	Sensitivity: 84%	Specificity: 73%	

fPWD = filtered P-wave duration.

decrease in cellular adenosine triphosphate (ATP) content, leading to a reduction of the refractory period.²⁵ Dispersion of refractoriness and fragmented activation of the atria are probably main factors in the pathophysiology of postoperative AF.^{26,27} Patients with this arrhythmic substrate show a prolonged P-wave duration at SAECC, while P-wave duration on the standard ECG has a lower accuracy in identifying such patients.

Male sex has been reported to be an independent predictor of postoperative AF.^{3,10,19} In the report by Zaman et al.¹⁰ the small number of women and the absence of gender-related differences in the occurrence of postoperative AF at univariate analysis prompted the authors to be cautious on any conclusion concerning the role of patient sex. In the present and other⁶ studies, male sex was not found to be a risk factor for the occurrence of AF.

Zaman et al.¹⁰ reported that patients ≥ 60 years had a 3.8 odds ratio for postoperative AF compared with patients < 60 years. The predictive value of advancing age had been reported also by others;^{3,8,9,12} in particular, Klöter Weber et al.¹² defined an algorithm based on age, preoperative beta-blockers, LVEF, and P-wave duration on 12-lead ECG, which could effectively predict the occurrence of postoperative AF. The relatively short age range in the population may explain why no association was found between advancing age and the development of postoperative AF.

Left atrial enlargement, as assessed by M-mode and two-dimensional echocardiography, is associated with AF in the general population and has been reported to be an independent predictor of AF after CABG.²¹ In agreement with the reports by Mathew et al.³ and Zaman et al.,¹⁰ correlation between left atrial diameter and development of postoperative AF could not be identified. Such finding may be due to the relatively small number of patients included in the study. In addition, it can be hypothesized that the occurrence of AF after CABG is prevalently influenced by factors other than left atrial size.

In the present report fPWD was the only independent predictor of postoperative AF, in agreement with the report by Steinberg et al.¹⁸ However, in the latter study that included patients with mitral valve disease, patients who postoperatively developed AF also had a significantly lower ejection fraction and a higher incidence of left ventricular hypertrophy. More recently, the role of fPWD as a predictor of the occurrence of AF in patients after

cardiac operations has been confirmed.^{10,19,22,28} The cut-off values for fPWD in the reports by Steinberg et al.,¹⁸ Stafford et al.,¹⁹ and Zaman et al.¹⁰ were 140, 141, and 155 ms, respectively. In the present study, the retrospectively defined cut-off value was 135 ms. Filtering techniques for P-wave analysis on SAECC were different, since Steinberg and Zaman used a least-squares-fit filter, Stafford a finite impulse response filter, while bidirectional filtering was used in the present study. Moreover, Stafford's and Zaman's cut-off values were determined in a prospective manner and not retrospectively, as in Steinberg's report and the present study.

In the present population a fPWD > 135 ms predicted occurrence of postoperative AF with a sensitivity of 85%, a specificity of 73 %, a negative predictive value of 85%, and a positive predictive value of 70%. These values are better than those reported by the others, possibly because of the smaller number of patients studied, compared to Stafford's and Zaman's reports.

The use of fPWD in the prediction of AF after CABG has been questioned by Frost et al.,⁹ who reported that the P-wave duration on the standard ECG was longer in patients who developed postoperative AF, whereas signal-averaged P-wave duration was not significantly different. In addition, Frost reported only age > 60 years and body weight > 80 kg to be independent predictors of AF after CABG. Such conflicting results may be due to different signal-averaging techniques. Moreover, in the authors' opinion, assessment of P-wave duration on the standard 12-lead ECG is operator-dependent and lacks accuracy.

CONCLUSION

The present study showed that assessment of fPWD by means of SAECC allows accurate prediction of the occurrence of AF after coronary surgery. A more widespread use of preoperative SAECC in patients undergoing CABG can be suggested to provide an effective risk stratification that may warrant prophylactic therapy.

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