P-Wave Signal Averaging
High Tech or an Expensive Alternative to the Standard ECG?

Mark Seifert, MD, Mark E. Josephson, MD

Atrial fibrillation is the most common sustained arrhythmia treated by cardiologists and internists, occurring in 0.4% of the general population and in 2% to 4% of those over age 60 years.\textsuperscript{1,2} Several small studies of coronary artery bypass grafting (CABG) have shown an incidence of postoperative atrial fibrillation ranging from 5% to as high as 40%. Recent large studies by Taylor et al\textsuperscript{3} and Fuller et al\textsuperscript{4} reported 19% and 28.4% incidences of post-CABG atrial fibrillation, respectively, and these results may be more representative of the true incidence in the population undergoing CABG. Several investigators have noted a correlation between both increasing age and the lack of \(\beta\)-blockade and the incidence of post-CABG atrial fibrillation, but other clinical correlates have not been consistently demonstrated. Post-CABG atrial fibrillation usually occurs within 72 hours after surgery.\textsuperscript{4} Although often benign and self-limited, complications may occur in a small proportion of patients and may result in significant sequelae and increased length of hospitalization. Atrial fibrillation is more common in CABG patients who suffer postoperative stroke than in patients who do not,\textsuperscript{2} suggesting a possible causal relation. Hemodynamic compromise and/or the development of chronic atrial fibrillation resulting from post-CABG atrial fibrillation are rare.\textsuperscript{5}

See p 2618

The mechanism of maintenance of atrial fibrillation involves the presence of a number of independent wavelets of depolarization traveling through the atrium. The initiating events are multifactorial but can include enhanced vagal or sympathetic tone and hemodynamic alterations, with or without atrial premature complexes. In order to maintain a critical number of simultaneously circulating wavelets in the atria, the wavelength (a product of conduction velocity and refractory period) must be small. Studies in humans have demonstrated that intra-atrial conduction delays (more marked in the right atrium), and short right atrial refractory periods characterize patients with atrial fibrillation and flutter.\textsuperscript{6-8} Atrial conduction delays may result from active cell membrane abnormalities and nonuniform anisotropy caused by myofibril hypertrophy or interstitial fibrosis in dilated atria and possibly from other factors such as left atrial hypertension, atrial infarction, inflammation in pericarditis, or after cardiac surgery, atrial trauma. Autonomic tone also plays an important role in enhancing atrial vulnerability to fibrillation, but the interactions between vagal and adrenergic tone and their effects on atrial refractoriness, dispersion of refractoriness, and intra-atrial conduction delay are complex. Postoperative atrial fibrillation is more common in patients whose \(\beta\)-blockers have been discontinued than in those continuing to take \(\beta\)-receptor antagonists.\textsuperscript{9,10} This may be due to the observed upregulation of human cardiac \(\beta\)-adrenergic receptors as demonstrated by an increase in receptor density seen after the administration of \(\beta\)-blockers (Kempf FC, Hedberg A, Molinoff P, Josephson ME: unpublished observations; also see Reference 11). Additionally, post-CABG patients are occasionally treated with \(\beta\)-agonists and have an independent nonpharmacological increase in adrenergic tone as demonstrated by increased urine epinephrine and noradrenaline excretion, which may shorten the refractory period (a finding that would not be noted on signal-averaged ECG [SAECG]).\textsuperscript{12}

Although a number of prophylactic regimens for post-CABG atrial fibrillation including digoxin, digoxin plus a \(\beta\)-blocker, verapamil, and magnesium have been evaluated in controlled trials, \(\beta\)-blockers appear to be the safest and most effective. Magnesium, however, did reduce the incidence of post-CABG atrial fibrillation after replacement in one study.\textsuperscript{13} Given the high incidence of post-CABG atrial fibrillation, the associated increased morbidity and length of hospitalization, and the existence of reasonably safe and effective prophylactic therapy in the form of \(\beta\)-blockers (and possibly magnesium), the ability to accurately identify patients at risk for post-CABG atrial fibrillation noninvasively may allow prophylactic therapy for these patients.

Because intra-atrial conduction delay is a substrate for atrial fibrillation, analysis of the P wave on the surface ECG offers a readily available assessment of atrial conduction. Buxton and Josephson\textsuperscript{4} identified the total P-wave duration >110 milliseconds as measured in three simultaneous ECG limb leads (I, II, and III) as a significant predictor of atrial flutter or fibrillation in 99 patients undergoing CABG or valve surgery. While P-wave duration in lead II did not separate patients with
and without atrial fibrillation, total P-wave duration using all three leads did (126 versus 116 milliseconds; \(P < 0.001\)). However, considerable overlap existed; therefore, they used a derived isoelectric interval (IEI) obtained by subtracting the longest P-wave duration in a standard limb lead (lead II) from the total P-wave duration measured in three simultaneously recorded limb leads. The IEI was considered prolonged if IEI was ≥10 milliseconds. Using this operational definition, the IEI had a sensitivity of 72%, a specificity of 82%, and a positive predictive value of 39%. The presence of a prolonged P wave and IEI >10 milliseconds had a sensitivity of 66%, a specificity of 82%, and a positive predictive value of 48%.

Several groups have adapted the technology of SAECGs to the study of the P wave in an attempt to identify patients at risk for developing atrial fibrillation.\(^{14-18}\) The technique of SAECG for P-wave analysis involves ECG monitoring with three orthogonal lead pairs denoted X, Y, and Z. The fiducial point used to trigger the processing usually has been the QRS complex.\(^{14-16,18}\) The P-wave sampling area or “window” must be shifted to include 200 to 300 milliseconds before the QRS. Typically a template is used for the P wave to ensure that ectopic or aberrant beats are excluded according to a computer algorithm. Others have used a point on the P wave itself as the fiducial point,\(^7\) but this is more complex. The signals are digitized and averaged to eliminate random signal noise, high-pass filtered (or in some cases least-squares, fit-filtered) to remove ringing artifact, and finally combined into a vector sum (\(X^2 + Y^2 + Z^2\))\(^2\) referred to as the filtered complex. The resultant filtered complex is then subject to duration analysis, or less commonly for P-wave SAECG, frequency analysis. Although initial reports showed no difference in the incidence of atrial arrhythmias in patients with prolonged signal-averaged P waves,\(^{14}\) subsequent retrospective studies confirmed a statistically significant association between patients known to have a history of paroxysmal or chronic atrial fibrillation and the presence of a prolonged signal-averaged P-wave duration.\(^{15-17}\)

In this issue of Circulation, Steinberg et al\(^{18}\) report the first prospective use of P-wave SAECG to identify patients at risk for atrial fibrillation in 130 consecutive patients undergoing cardiac surgery. Patients undergoing elective surgery were screened, and those taking class I or class III antiarrhythmics or with a history of atrial fibrillation were excluded. The method of SAECG used standard orthogonal leads along with triggered acquisition and signal-averaging from the QRS complex. The window for analysis was shifted 300 milliseconds before QRS to expose the P wave. A computer algorithm excluded P waves that did not match a template P wave with a 99% correlation coefficient. P waves were acquired until background noise was <0.5 \(\mu\)V, which required 100 to 700 beats. A least-squares filter equivalent to a high-pass filter cutoff of 29 Hz was applied to the averaged signals in each bipolar lead, and the resulting filtered outputs were combined into a vector sum according to the above formula. Total P-wave duration then was measured visually by blinded observers. P-wave duration on the standard ECG was measured from lead II for comparison with the SAECG. Daily postoperative 12-lead ECGs were obtained, but telemetry monitoring was left to the discretion of the attending cardiologist and/or surgeon. The end point was the development of atrial fibrillation lasting at least 30 minutes. There was no difference in the use of \(\beta\)-blockers, inotropic agents or pressors, class I antiarrhythmic agents, and digoxin in the patients who developed atrial fibrillation and those who did not.

Thirty-three patients (25%) developed atrial fibrillation lasting at least 30 minutes. Examining ejection fraction, evidence of left ventricular hypertrophy on the ECG, P-wave duration in ECG lead II, and P-wave SAECG in a logistic regression model, only SAECG P-wave duration was an independent predictor of atrial fibrillation. The sensitivity, specificity, and positive predictive value for SAECG P-wave duration were 77%, 55%, and 37%, respectively.

Several important points regarding the study design and conclusions merit attention. The results of this study, with regard to the sensitivity, specificity, and positive predictive value of the technique, are remarkably similar to those of Buxton and Josephson, who used three simultaneous standard ECG leads.\(^3\) Prolonged IEI or a combination of prolonged P-wave duration and IEI >10 milliseconds had 39% and 48% positive predictive values, respectively. These measurements are readily available in all hospitals and offices. Additionally, the usual acquisition time for a 12-lead ECG required to calculate the P-wave duration and IEI is approximately 12 seconds, compared with the 20 to 30 minutes required for SAECG, and it is far less expensive. The failure of the P-wave duration on a single standard limb lead (lead II) to predict atrial fibrillation in the present study probably reflects the underestimated duration of the total P-wave duration on the standard ECG resulting from measurements in only a single lead rather than three simultaneous leads. This was noted by Buxton and Josephson,\(^4\) which is why they used three simultaneous ECG leads. Signal averaging of the P wave using the QRS as a trigger is somewhat limited by the frequent inability to separate the end of the P wave and the beginning of the QRS.

Of particular interest is the protocol for monitoring rhythm and the definition of atrial fibrillation used as the end point in this study. Without telemetry data available for all patients for the duration of the study, it is possible that short-lived episodes of atrial fibrillation occurred but were not diagnosed because of the single daily ECG used to screen for atrial fibrillation. Additionally, episodes of atrial fibrillation lasting less than 30 minutes were not considered an end point in the study but may still be associated with significant sequelae despite the short duration. These problems with protocol design could add to an overestimation of sensitivity and positive predictive value.

The inclusion of patients undergoing both valve surgery and CABG as a heterogeneous population makes the application of this data to any specific patient undergoing valve surgery difficult. Moreover, it is not necessarily applicable to predicting the occurrence of atrial fibrillation occurring under different circumstances.

Assuming that either the three-lead surface P-wave duration and IEI or the P-wave SAECG is adequately sensitive and specific for detecting the substrate for atrial fibrillation and that the positive predictive value is acceptable, the question remains as to how these tech-
nologies should be applied. Because studies of prophylaxis for post-CABG atrial fibrillation suggest that β-blockers are the safest and most effective agents, one might consider using them routinely in patients predicted to be at high risk.19 The data for other agents are equivocal, with the possible exception of magnesium, which deserves further study. Because of the high cost and low positive predictive value of the P-wave SAECG and the relative safety of β-blockers as empirical prophylaxis for atrial fibrillation after cardiac surgery, the technique of P-wave SAECG warrants further study, particularly with regard to cost-effectiveness, before it is considered a useful clinical tool. No acceptable data are available to attest to its usefulness in predicting patients at risk for atrial fibrillation occurring under other circumstances, particularly since the therapeutic agents generally used in these circumstances (eg, quinidine or flecainide) have significant side effects. Further work is required to evaluate the role of SAECG of the P wave in predicting atrial fibrillation. Use of atrial pacing to overcome some of the inherent limitations of the P-wave SAECG may make this technique more useful.

References
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