Atrial Fibrillation After Coronary Artery Bypass Surgery
A Model for Preoperative Risk Stratification

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Background—Atrial fibrillation (AF) occurs in 20% to 40% of patients after CABG. Identification of patients vulnerable for arrhythmia will allow targeting of those most likely to benefit from prophylactic therapy. The aim of the present study was to evaluate accuracy of a prospectively defined signal-averaged P-wave duration (SAPD) cutoff and additional preoperative characteristics for the prediction of AF after CABG.

Methods and Results—Patients undergoing elective isolated CABG were recruited to the present prospective study. SAPD was measured in all patients. Filtered signals from 3 orthogonal leads were combined in a vector analysis, and total SAPD was measured preoperatively. Postoperative in-hospital AF occurred in 92 (28.2%) of 326 patients. Patients who developed AF were older (65.9 versus 61.7 years of age; \( P < 0.0005 \)) and had longer SAPD (158 versus 145 ms; \( P < 0.0005 \)) than non-AF patients. Incidence of AF increased in patients \( \geq 75 \) years of age and increased progressively throughout the range of SAPD. Stepwise logistic regression analysis of preoperative variables identified that SAPD \( > 155 \) ms (odds ratio, 5.37; 95% CI, 3.10 to 9.30; \( P < 0.0005 \)), advanced age (odds ratio, 1.53; 95% CI, 1.26 to 1.86 per 5-year increase in age; \( P < 0.0005 \)), and male sex (odds ratio, 2.88; 95% CI, 1.30 to 6.40; \( P < 0.01 \)) independently predicted AF. Prospectively defined SAPD \( > 155 \) ms predicted AF with positive and negative predictive accuracy of 49% and 84%, respectively.

Conclusions—A combination of prolonged SAPD, advanced age, and male sex identifies patients at high risk for development of AF after CABG. (Circulation. 2000;101:1403-1408.)

Key Words: fibrillation ■ arrhythmia ■ surgery ■ men ■ sex ■ aging

Atrial fibrillation (AF) occurs in 20% to 40% of patients after CABG.1–3 Incidence of arrhythmia has not changed, despite improvements in anesthetic and surgical techniques, and evidence suggests its incidence may be increasing.1 AF after CABG is self-limiting in most cases. However, even when AF is uncomplicated, its treatment requires additional medical and nursing time and a prolonged hospital stay.1–6 In a minority of cases, arrhythmia can cause hemodynamic compromise and increase risk of postoperative stroke.1,7,8 Consequently, AF after CABG leads to increased use of resources.2–4

Numerous studies have sought to identify predictors of AF after CABG. Their number is testament to the failure to prevent arrhythmia by prophylactic measures in unselected patients. Only increased age has consistently been associated with AF after CABG.1–3,9–11 Several workers, including those in our group, have demonstrated that prolonged preoperative signal-averaged P-wave duration (SAPD) is associated with AF after CABG.12–15 The present study was designed to evaluate prospectively accuracy of predefined SAPD for prediction of AF after CABG. The cutoff figure of 155 ms was derived from a previous study of 102 patients who underwent CABG.12 A secondary aim of the present study was to stratify patients at risk of AF on the basis of simple preoperative variables.

Results

Of 358 eligible patients, 30 (8.4%) were excluded as a result of signal interference or high noise levels on SAPD recordings. Two patients who died within 72 hours of surgery were excluded. The remaining 326 patients form the basis of our results. Of these, 3 died before discharge: 1 each on postoperative days 8, 11, and 25. All 3 developed AF, on days 6, 1, and 2, respectively. Mean patient age was 63 years, and 268 (82%) were male. Preoperatively, 218 (67%) were taking \( b \)-blockers. After surgery, 8 (2.5%) returned to theater for sternal rewiring and 7 (2.1%) for bleeding.

Ninety-two (28.2%) patients developed AF, at 2.8 ± 1.7 (mean; range, 0 to 11) days after operation. Five patients were
noted to have brief (<30-s) episodes of irregular rhythm on Holter monitor; these episodes were not recorded on 12-lead ECG, and these patients were not included in the AF group. These patients did not develop AF during hospital stay, and their postoperative course was unremarkable. Demographic data are presented in Table 1, and distribution of AF is illustrated in Figure 1.

Low serum magnesium on the first postoperative day was not associated with AF. Levels <0.7 mmol/L were seen in 57% of patients who received cross-clamp fibrillation for myocardial protection, 22% who received cold-crystalloid cardioplegia, 14% who received whole blood, and 0% after CABG on the beating heart.

Univariate Predictors
No differences were seen between AF and non-AF patients in left ventricular ejection fraction, Q waves on preoperative ECG, and left atrial diameter. Surgical techniques were similar between groups.

With univariate analysis, preoperative variables significantly associated with development of postoperative AF were age and SAPD. Use of preoperative β-blockers was more prevalent (70% versus 59%; P<0.05) in younger patients and those who remained in sinus rhythm. Weaker associations were noted between perioperative and postoperative variables of cardiopulmonary bypass time, units of blood transfused, and elevated postoperative plasma urea (>7 mmol/L) and creatinine (>125 μmol/L) concentrations. No difference was seen between groups in preoperative or postoperative magnesium concentrations. Postoperative β-blockers were used less commonly (26% versus 44%; P<0.005) in those who developed AF. β-Blocker withdrawal was significantly different (35% in the AF group versus 29% in those without AF; P=0.03). Postoperative hospital stay was significantly longer in patients with AF than in those without (9.2 versus 7.3 days; P<0.0005).

Age
Advanced age was strongly associated with postoperative AF. Mean age was 65.9 years in the AF group compared with 61.7 years in the non-AF group (P<0.0005). Incidence of AF increased progressively in patients aged ≤75 years (Figure 2), such that 1 of 29 (3.4%) patients aged 50 to 54 years versus 19 of 45 (42.2%) aged 70 to 74 years developed AF. Odds of developing AF increased 1.48 (95% CI, 1.24 to 1.77)-fold for each 5-year increase in age and 3.80 (2.00 to 7.23)-fold for those aged ≥60 years compared with patients <60 years of age.

No correlation existed between age and SAPD (R²=0.1; P=0.9). When incidence of SAPD >155 ms was documented within each 5-year age band, a small, nonsignificant differ-

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**TABLE 1. Clinical Characteristics of Patients With and Without AF After CABG**

<table>
<thead>
<tr>
<th>Variables</th>
<th>AF (n=92)</th>
<th>Non-AF (n=234)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>65.9</td>
<td>61.7</td>
<td>1.07 (1.04–1.11)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>SAPD, ms</td>
<td>158</td>
<td>145</td>
<td>1.06 (1.04–1.08)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>56</td>
<td>56</td>
<td>1.00 (0.98–1.02)</td>
<td>0.751</td>
</tr>
<tr>
<td>Left atrial size, cm*</td>
<td>3.8</td>
<td>3.9</td>
<td>0.90 (0.42–2.39)</td>
<td>0.831</td>
</tr>
<tr>
<td>CPB time, min</td>
<td>81</td>
<td>74</td>
<td>1.01 (1.00–1.02)</td>
<td>0.025</td>
</tr>
<tr>
<td>Clamp time, min</td>
<td>45</td>
<td>43</td>
<td>1.01 (0.99–1.03)</td>
<td>0.306</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>81 (88)</td>
<td>187 (80)</td>
<td>1.85 (0.91–3.75)</td>
<td>0.084</td>
</tr>
<tr>
<td>Pre-operative Q-waves, n (%)</td>
<td>31 (34)</td>
<td>70 (30)</td>
<td>1.19 (0.71–1.99)</td>
<td>0.506</td>
</tr>
<tr>
<td>RCA stenosis, n (%)</td>
<td>55 (60)</td>
<td>122 (52)</td>
<td>1.36 (0.84–2.23)</td>
<td>0.212</td>
</tr>
<tr>
<td>Grafts &gt;3, n (%)</td>
<td>31 (34)</td>
<td>53 (23)</td>
<td>1.74 (1.02–2.95)</td>
<td>0.040</td>
</tr>
<tr>
<td>Preoperative β-blocker, n (%)</td>
<td>54 (59)</td>
<td>164 (70)</td>
<td>0.61 (0.37–1.00)</td>
<td>0.049</td>
</tr>
<tr>
<td>Postoperative β-blocker, n (%)</td>
<td>24 (26)</td>
<td>103 (44)</td>
<td>0.45 (0.26–0.76)</td>
<td>0.003</td>
</tr>
<tr>
<td>β-Blocker withdrawal, n (%)</td>
<td>32 (35)</td>
<td>68 (29)</td>
<td>1.30 (0.78–2.18)</td>
<td>0.313</td>
</tr>
<tr>
<td>Preoperative urea &gt;7 mmol/L, n (%)</td>
<td>30 (33)</td>
<td>56 (24)</td>
<td>1.53 (0.90–2.60)</td>
<td>0.114</td>
</tr>
<tr>
<td>Preoperative creatinine &gt;125 μmol/L, n (%)</td>
<td>22 (23)</td>
<td>43 (18)</td>
<td>1.40 (0.84–2.33)</td>
<td>0.260</td>
</tr>
<tr>
<td>Postoperative urea &gt;7 mmol/L, n (%)</td>
<td>39 (42)</td>
<td>61 (26)</td>
<td>2.09 (1.26–3.46)</td>
<td>0.004</td>
</tr>
<tr>
<td>Postoperative creatinine &gt;125 μmol/L, n (%)</td>
<td>34 (37)</td>
<td>47 (20)</td>
<td>2.33 (1.37–3.96)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; CPB time, cardiopulmonary bypass time; RCA stenosis, proximal right coronary artery stenosis >70%; and creatinine, serum creatinine concentration.

*n=64.

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*Figure 1. Distribution of AF onset.*
ence was seen between groups. Those in the 55–to-69–years age band had lowest incidence of prolonged SAPD, 25.4%, and those in the 70-to-74-years age band, highest, 44.4% (P<NS).

Signal-Averaged P-Wave Duration
Mean SAPD was significantly longer (158 versus 145 ms; P<0.0005) in patients who developed AF after CABG. Incidence of AF increased progressively with increases in SAPD (Figure 3), such that 3 of 50 (6%) patients with SAPD <130 ms developed AF compared with 8 of 13 (61.5%) with SAPD >155 ms. Odds ratio (OR) for AF was 2.11 (95% CI, 1.62 to 2.74) per 15-ms increase in SAPD and 4.95 (2.96 to 8.28) for SAPD >155 ms.

In the 64 patients in whom preoperative echocardiograms were recorded (18 developed postoperative AF), no association existed between left atrial size (measured at the level of the aortic valve leaflets in the parasternal long-axis view) and AF. Furthermore, no significant difference was seen between AF and non-AF groups in mean body weight (82.2 and 77.6 kg, respectively) or body mass index (27.7 and 26.5 kg/m², respectively). We found no association between SAPD and either body weight or body mass index or with left atrial diameter. No significant difference was seen between the sexes in SAPD (148.9 ms for men versus 147.9 ms for women) and no significant difference in percentage of males (35.4%) versus females (39.7%) with SAPD >155 ms.

Multivariate Analysis
Stepwise logistic regression analysis of preoperative variables showed that age (P<0.0005), SAPD (P<0.0005), and male sex (P<0.01) were independently associated with development of AF (Table 2). When all (preoperative and postoperative) variables were entered into analysis, >3 grafts (OR, 2.22; 95% CI, 1.17 to 4.21; P<0.02) and elevated postoperative plasma creatinine concentration (OR, 1.93; 95% CI, 1.04 to 3.60; P<0.04) were additionally associated with AF. β-Blockade use was not associated with AF preoperatively (P=0.098) or postoperatively (P=0.057).

Predictive Accuracy of Preoperative Variables
SAPD >155 ms predicted AF with a sensitivity of 63%, specificity of 74%, and positive and negative predictive accuracy of 49% and 84%, respectively. The combination of SAPD >155 ms and age ≥60 years increased positive predictive accuracy to 57%, with a negative predictive accuracy of 82%. Age of ≥60 years alone had a positive and negative predictive accuracy of 35% and 87%, respectively. When combined with male sex, respective values were 39% and 87%.

Risk Profile
Table 3 stratifies patients by SAPD >155 ms and aged ≥60 years. Table 3 shows that the incidence of AF after CABG for patients aged <60 years with SAPD ≤155 ms was 6.8%, versus 56.8% for patients aged ≥60 years with SAPD >155 ms.

Similarly, Table 4 is a risk stratification table that includes gender. Interestingly, 0 of 35 women with SAPD ≤155 ms developed AF, irrespective of age, whereas 11 of 23 (47.8%) women with SAPD >155 ms developed AF. Highest incidence was in males ≥60 years with SAPD >155 ms, who had a 58.8% chance of AF after CABG.

Discussion
The present study confirms both high incidence of AF after CABG and its strong association with increases in age and SAPD. The present study is the largest to evaluate SAPD for the prediction of AF after CABG and the first to validate a cutoff value prospectively defined from a study of patients undergoing CABG. We have described incidence of AF in a population undergoing elective, isolated CABG and quantified the risk from SAPD, age, and sex, thereby to allow preoperative identification of vulnerable patients.

### TABLE 2. Multivariate Preoperative Predictors of AF

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 5-y increase)</td>
<td>1.53 (1.26–1.86)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>SAPD &gt;155 ms</td>
<td>5.37 (3.10–9.30)</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.88 (1.30–6.40)</td>
<td>0.0092</td>
</tr>
</tbody>
</table>

### TABLE 3. Incidence of AF After CABG in Patients Stratified by SAPD and Age

<table>
<thead>
<tr>
<th>Age, y</th>
<th>SAPD, ms</th>
<th>AF, n (%)</th>
<th>No AF, n (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60</td>
<td>≤155</td>
<td>5 (6.8)</td>
<td>68 (93.2)</td>
<td>73</td>
</tr>
<tr>
<td>&gt;155</td>
<td>8 (26.7)</td>
<td>22 (73.3)</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>≥60</td>
<td>≤155</td>
<td>29 (21.5)</td>
<td>106 (78.5)</td>
<td>135</td>
</tr>
<tr>
<td>&gt;155</td>
<td>50 (56.8)</td>
<td>38 (43.2)</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>
TABLE 4. Incidence of AF After CABG in Patients Stratified by SAPD, Age, and Sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>SAPD, ms</th>
<th>AF, n (%)</th>
<th>No AF, n (%)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;60 y</td>
<td>=155</td>
<td>0 (0)</td>
<td>7 (100)</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>&gt;155</td>
<td>1 (33)</td>
<td>2 (66)</td>
<td>3</td>
</tr>
<tr>
<td>Age ≥60 y</td>
<td>=155</td>
<td>0 (0)</td>
<td>28 (100)</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>&gt;155</td>
<td>10 (50)</td>
<td>10 (50)</td>
<td>20</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;60 y</td>
<td>=155</td>
<td>5 (7.6)</td>
<td>61 (92.4)</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>&gt;155</td>
<td>7 (25.9)</td>
<td>20 (74.1)</td>
<td>27</td>
</tr>
<tr>
<td>Age ≥60 y</td>
<td>=155</td>
<td>29 (27.1)</td>
<td>78 (72.9)</td>
<td>107</td>
</tr>
<tr>
<td></td>
<td>&gt;155</td>
<td>40 (58.8)</td>
<td>28 (41.2)</td>
<td>68</td>
</tr>
</tbody>
</table>

Despite improvements in surgical and anesthetic techniques, incidence of AF after CABG remains stubbornly unchanged. Little doubt exists that this is, at least in part, a reflection of increased age of patients undergoing surgical revascularization,1,16 itself a consequence of the aforementioned improvements.

Patients who develop AF have a prolonged postoperative hospital stay compared with patients who remain in sinus rhythm; this finding was confirmed in the present study. Recent evidence shows that prolonged hospitalization is attributable to arrhythmia rather than clinical characteristics of AF patients.6 The financial burden that results from prolonged hospitalization is considerable.2–4

We failed to confirm our previously reported association of AF with postoperative hypomagnesemia. One reason could be the different strategies of myocardial protection used in the 2 studies. In the earlier study12 post hoc analysis revealed 59% of patients received cross-clamp fibrillation and 41% cold-crystalloid cardioplegia. Patients in the former group had a significantly lower serum magnesium level on the first postoperative day (P<0.005; unpublished data). In the present study, although cross-clamp fibrillation was again associated with postoperative hypomagnesemia, most patients received whole-blood cardioplegia supplemented with magnesium. However, prevalence of AF in the 2 studies was similar, which suggests that postoperative magnesium is not causally related to arrhythmia development.

**Age**

Advanced age increases risk of AF in the general population.17,18 Therefore, it is not surprising that incidence of AF after CABG also increases with age. Dilatation and fibrosis of the atria have been shown to increase with age,19 with a loss of side-to-side electrical coupling between groups of atrial muscle fibers.20 Consequent slowing of electrical conduction within the atria provides a substrate for arrhythmogenesis. Of interest, the increase in AF was not sustained in patients >75 years of age, a finding previously reported in patients >80 years of age.3

**SAPD Duration**

AF is generally accepted to be reentrant in origin.21–23 Therefore, sustained AF requires that the depolarizing wave fronts continuously encounter excitable tissue, a circumstance favored by slow atrial conduction and a short atrial refractory period.24 SAPD has been established to be prolonged in patients who develop AF after CABG, and this is thought to reflect slow atrial conduction in patients with the arrhythmia substrate.25–29 Absence of a relation between SAPD and age or body weight in the present study suggests that the former is an independent marker of the arrhythmia substrate.

Prolonged SAPD merely identifies patients with the arrhythmia substrate. The trigger for development of AF is probably multifactorial. Cox proposed that vulnerability to development of AF after cardiac surgery is increased by nonuniformity of local refractory period distribution within the atrium.30 This dispersion of atrial refractoriness may be promoted by perioperative factors such as atrial ischemia, imbalance in autonomic tone, or electrolyte imbalance. That an additional trigger is necessary to initiate AF in those with the arrhythmia substrate is a possible explanation for the moderate positive predictive accuracy of SAPD. Those without the arrhythmia substrate and, hence, at low risk for AF after CABG are identified more accurately.

**Gender**

Several studies have found an increased incidence among males, 1–3,9 whereas others have reported no difference.6,31,32 In our study, the number of women was small, and any conclusion should be treated with caution. We found no differences on univariate analysis, but male sex was an independent predictor of AF after CABG on multivariate analysis and improved the accuracy of SAPD in identification of vulnerable patients.

**Left Atrial Size**

We did not find a relation between AF and left atrial size or between SAPD and left atrial size in a subset of patients. This is consistent with results from other studies.3,33 Given the strong association between left atrial size and AF in the general population, this result is surprising and may indicate that a different mechanism underlies arrhythmia induction in the postoperative group.

**β-Blocker Therapy**

Use of β-blockers preoperatively protected against arrhythmia on univariate analysis, but this effect was lost when stepwise logistic regression with other significant preoperative variables was performed. Previous reports suggest that β-blockers suppress AF after surgery.34,35 However, in our study, β-blocker use was confounded by age in multivariate analysis. Younger patients were given β-blockers more commonly than older patients, and age was more strongly associated with AF. We emphasize that the present study was not designed to establish drug efficacy. Our sole aim was to identify preoperative variables in risk stratification.
Clinical Relevance
Pharmacological intervention to reduce AF incidence in unselected patients has proved disappointing. Daoud et al reported amiodarone to be of benefit, but the study had major limitations and the in-hospital benefit was marginal. The ability to identify patients at increased risk for AF after CABG will increase the statistical power of studies to detect a meaningful reduction in AF in the treated group. Conversely, recognition of low-risk patients indicates those who will not benefit from preventive therapy and allows better planning of hospital resources in patient management after cardiac surgery. Given that the additional cost of AF after CABG in the United States is estimated to be $153 million, information on likely risk and possible increased hospital stay is useful to both providers and purchasers of health care.

Signal-averaged ECG is a noninvasive test that takes 20 minutes to record. The machine is portable and allows bedside recording, and it is thus suitable for outpatient use. By use of additional preoperative clinical variables, we have significantly improved the ability of high-resolution ECG to identify patients at risk of AF after CABG.

Study Limitations
As with all similar studies, one limitation of the present study is the method used to record arrhythmias. We continuously monitored rhythm on all patients for 72 hours and recorded 12-lead ECGs if arrhythmia was suspected clinically. Our AF prevalence of 28% is within the 25% to 30% range reported in the majority of such studies.

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References


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