Predictors of atrial fibrillation after off-pump coronary artery bypass graft surgery

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Background. Postoperative atrial fibrillation (AF) is one of the most common complications after cardiothoracic surgery and is associated with an increased risk of stroke, and longer hospital stay. The pathophysiology of postoperative AF is uncertain, and its prevention remains unsatisfactory. Many previous studies have examined the predictors of AF after on-pump coronary artery bypass graft surgery (CABG), but there are few reports after off-pump CABG.

Methods. The aim of the present prospective observational study, in which 296 consecutive patients were enrolled, was to elucidate the predictors of AF after off-pump CABG. The association of perioperative factors with AF was investigated using univariate analysis. Significant variables were included into a stepwise logistic regression model to ascertain their independent influence on the occurrence of AF.

Results. The incidence of AF was 32%. AF prolonged the time until patients were fit for discharge by 3 days (P<0.01). Stepwise multivariate analysis identified increasing age [odds ratio (OR) 1.44 per 10-yr increase; 95% confidence interval (CI) 1.06–1.95], intraoperative average core temperature (OR 1.64; 95% CI 1.05–2.56), the average cardiac index in the intensive care unit (OR 0.37; 95% CI 0.19–0.71), and intraoperative fluid balance (OR 0.96 per 100-ml increase; 95% CI 0.93–0.99) as independent predictors of postoperative AF.

Conclusion. Our present findings indicate that ageing, the intraoperative fluid balance, and postoperative cardiac index are associated with the onset of AF after off-pump CABG.


Keywords: anaesthesia, cardiovascular; atrial fibrillation, arrhythmia; complications, perioperative; surgery, cardiovascular

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Postoperative atrial fibrillation (AF) remains a common complication, especially after cardiovascular surgery. Over the last 20 yr, the incidence of AF after coronary artery bypass graft surgery (CABG) has been consistently reported to range between 10% and 50%. Postoperative AF is associated with an increased risk of stroke, congestive heart failure, myocardial infarction, and renal insufficiency and with increased short- and long-term mortality.¹ ²

The pathophysiology of postoperative AF is multifactorial. Whereas previous studies have implicated age-related degenerative change and electrophysiological abnormality of atrial cells as causes of AF,³ a recent article reported an association between perioperative inflammation and postoperative AF.⁴ Whether the off-pump CABG technique reduces the incidence of AF remains controversial, despite the fact that it is a less invasive approach associated with a less marked perioperative inflammatory response.⁵

The prevention of postoperative AF remains unsatisfactory.⁶ Prophylactic preoperative β-blocker administration is recommended to prevent postoperative AF, especially in...
patients with a history of β-blocker use, but whether prophylactic β-blocker administration reduces the length of hospitalization remains to be seen.\textsuperscript{7} Identifying the population most at risk of postoperative AF could lead to more targeted preventive or therapeutic interventions, while further reducing the potential for antiarrhythmic-related toxicity and drug costs.

Many previous studies have investigated the predictors of AF after conventional on-pump CABG, but there have been few papers examining AF after off-pump cardiac surgery.\textsuperscript{8} The goal of the present study was to identify perioperative predictors of AF after off-pump CABG.

**Methods**

A total of 296 consecutive patients who underwent off-pump CABG surgery between January 1, 2001 and December 31, 2004 in our institution were enrolled in this prospective observational study. The mean age of the study population was 69 yr (range 38–87 yr). Two hundred and twenty-four of the patients were male. The study was approved by the Review Board on Human Experiments at the Kyoto Prefectural University of Medicine. Written informed consent was obtained from all patients. Patients who had had previous cardiac surgery were excluded, as were patients having concomitant major surgery. All patients were in sinus rhythm at the outset of the study, including patients with a history of paroxysmal AF.

All preoperative medications except β-blockers, diuretics, angiotensin-converting enzyme inhibitors, and calcium channel blockers were routinely omitted on the day of surgery. Our routine AF prophylaxis strategy consisted of potassium and magnesium supplementation in the operating room and in the intensive care unit (ICU). No other drugs were continued routinely, and no other drugs were given for arrhythmia prophylaxis. Preoperative β-blockers were continued after operation to avoid withdrawal.

All surgical procedures were performed by the same surgical team. Anticoagulation was provided by i.v. heparin (1 mg kg\textsuperscript{-1}) which was given after graft harvesting. A mechanical stabilizer (Octopus, Medtronic Inc., Minneapolis, MN, USA) and a heart positioner (Starfish or Urchin, Medtronic Inc.) were used to control motion of the beating heart.

Intraoperative haemodynamic management was standardized. Hypotension (systolic blood pressure <90 mm Hg) was treated with volume replacement, ephedrine (0.05 mg kg\textsuperscript{-1}), or methoxamine (0.02 mg kg\textsuperscript{-1}) as indicated. Persistent hypertension (systolic blood pressure >140 mm Hg) was treated by increasing the depth of anaesthesia or by administration of nitroglycerin (initially 0.8 μg kg\textsuperscript{-1} min\textsuperscript{-1}). Tachycardia (heart rate >100 beats min\textsuperscript{-1}) was also treated by increasing the depth of anaesthesia or by using an ultra-short-acting β-blocker (lindoolol hydrochloride, 0.02 mg kg\textsuperscript{-1} min\textsuperscript{-1}) and edrophonium chloride (0.05 m kg\textsuperscript{-1}). Bradycardia (heart rate <50 beats min\textsuperscript{-1}) was treated with pericardial ventricular pacing.

Intraoperatively, both groups were given 12 ml kg\textsuperscript{-1} h\textsuperscript{-1} of lactated Ringer’s solution, and i.v. crystalloid fluids were not warmed. When blood loss exceeded 30% of the blood volume, albumin was administered. When patients’ haematocrit decreased to less than 25%, red blood cells were transfused. The ambient operating room temperature was maintained at approximately 23°C. Patients were extubated in the operating room or ICU. The extubation criteria were as follows: patient responsive to simple commands; body core temperature >35.0°C; haemodynamically stable; absence of uncontrolled arrhythmia; chest tube drainage <1 ml kg\textsuperscript{-1} over 30 min; and blood gas analysis (pH >7.30, arterial oxygen tension >8 kPa, P\textsubscript{CO\textsubscript{2}} <7.3 kPa) at an inspired oxygen fraction <0.4. The discharge criteria from ICU were as follows: alert and cooperative; no inotropic support; no significant arrhythmia; adequate ventilation; chest tube drainage <1 ml kg\textsuperscript{-1} over 120 min; urine output >0.5 ml kg\textsuperscript{-1} h\textsuperscript{-1}; no recent generalized seizures; and no active seizures.

The length of hospitalization for this procedure is generally longer in Japan than in the Europe or USA as the Japanese health-care system does not demand a short hospital stay, and allows patients to stay until a nursing home bed becomes available. Thus, we determined when patients met the discharge criteria rather than relying on the actual duration of hospitalization. The discharge criteria from the hospital were as follows: haemodynamically stable; stable cardiac rhythm; no infected incisions and afebrile; ability to void and have bowel movements; independent ambulation and feeding; and ability to walk upstairs. The physicians blinded to the predictive criteria being studied made all the clinical decisions.

Continuous ECG monitoring was performed for at least 72 h after surgery depending on the patient’s condition. Twelve-lead ECGs were recorded if arrhythmia was suspected. After discharge from the hospital, intermittent ECG assessments (once per week) were performed until 1 month after surgery. Each episode of arrhythmias was recorded and interpreted by an independent physician. AF, atrial flutter, and atrial tachycardia were defined according to previous studies.\textsuperscript{9} AF was defined as non-sustained if lasting between 10 beats and 10 min and sustained if persisting for more than 10 min.

The following data were prospectively collected, preoperative variables included age, gender, body mass index, medications, left ventricular fractional shortening, PR interval, and P-wave duration of ECG, history of paroxysmal AF, hypertension, diabetes mellitus, chronic obstructive pulmonary disease under medical treatment, neurological events (e.g. stroke, transient ischaemic attack, epilepsy), hepatic insufficiency (alanine amino transferase >50 IU litre\textsuperscript{-1}, or ICG retention rate at 15 min >20%), and renal insufficiency (creatinine >132.6 μmol litre\textsuperscript{-1}). Perioperative data included perioperative core temperature (in the operating room: average of readings taken every 30 min, and in the
ICU for the first 12 h: average of readings taken every 1 h), intraoperative total amounts of noradrenaline, dopamine, dobutamine, blood lactate concentration at the end of surgery, the base excess at the end of surgery, perioperative fluid balance (in the operating room, and in the ICU for the first 12 h), perioperative total blood loss (the sum of blood loss in the operating room and in ICU for the first 12 h), perioperative average cardiac index (in the operating room: average of readings taken every 30 min, and in the ICU for the first 12 h: average of readings taken every 1 h), intraoperative average central venous pressure (average of readings taken every 30 min), number of distal anastomoses, and postoperative pleural effusion.

Statistics
Atrial flutter, atrial tachycardia, and other arrhythmias were not included in the same group as AF because their mechanisms differ. Only sustained episodes of AF were considered. Univariate characteristics between patients with and without AF were compared using a Mann–Whitney U-test for continuous variables and $\chi^2$ tests with a Yates correction for categorical variables.

A model was built using stepwise logistic regression to identify the subset of variables that jointly predicted post-CABG AF risk. All variables whose univariate tests resulted in a P-value of <0.2 were considered in the multivariate analysis. A backward stepwise logistic regression analysis was used to identify the subset of variables that predicted postoperative AF. The area under the receiver operating characteristic curve was computed for use as a descriptive tool for measuring the bias of the model. A Hosmer–Lemeshow goodness-of-fit statistic was computed to examine the calibration of the model.

Results
Thirty-six patients were excluded due to a change in surgical procedures after informed consent was obtained. We thereafter analysed data from 260 patients. AF occurred in 83 patients, representing 32% of the overall population. Postoperative day 2 was most common for the initial occurrence of AF (Fig. 1).

Patient data and perioperative characteristics were compared between patients with and without postoperative AF (Table 1). Univariate analysis indicated age, history of paroxysmal AF, average core temperature in the operating room, intraoperative fluid balance, and the average cardiac index in the operating room and in the ICU were all associated with postoperative AF. Multivariate analysis identified advancing age [odds ratio (OR) 1.44 per 10 yr increase, 95% confidence interval (CI) 1.06–1.95], a lower cardiac index in the ICU for the first 12 h (OR 0.37, 95% CI 0.19–0.71), a lower intraoperative fluid balance in the operating room (OR 0.96 per 100 ml increase in intraoperative fluid balance, 95% CI 0.93–0.99), and a higher average core temperature in the operating room (OR 1.64, 95% CI 1.05–2.56) all to be independently associated with postoperative AF (Table 2). The predictive model based on these variables had an area under the receiver operating characteristic curve of 0.73, and the Hosmer–Lemeshow goodness-of-fit statistic suggested a good calibration ($P=0.10$).

Time to extubation after ICU did not show any significant difference between the patients who suffered postoperative AF [median (inter-quartile range) 4 (2.7–6) h] and those who did not [4 (2.5–5.5) h], $P>0.05$. Likewise, there was no difference in ICU duration of stay between those with and without AF [38 (20–67) and 30 (15–50) h, respectively, $P>0.05$]. Patients with postoperative AF took on average 3 days longer before meeting the hospital discharge criteria than those without postoperative AF [10 (7–13) days vs 7 (5–10) days, $P<0.01$].

Discussion
Many previous studies have investigated the clinical predictors of AF after on-pump CABG. Whereas age is the most consistent predictor of AF after on-pump CABG, other reported predictors vary between studies. Several recent meta-analyses reported that the incidence of postoperative AF was decreased by the use of the off-pump technique.$^{10–12}$ These findings suggest that the predictors of AF in off-pump procedures may be different from the ones of conventional on-pump procedure. The major findings in this study show that lower postoperative cardiac index, lower intraoperative fluid balance, relatively higher intraoperative core temperature, and older age contribute to the risk for postoperative AF.

Advanced age was a predictor of postoperative AF in our study. According to previous reports and meta-analyses study,$^2$ $^{10–12}$ age is the most consistent predictor of AF. Postoperative AF is thought to arise partially from

![Fig 1 Day of occurrence of postoperative AF after off-pump coronary artery bypass grafting. A total of 83 patients, representing 32% of the overall population (n=260), developed AF. The initial episode of AF most frequently occurred on postoperative day 2.](https://academic.oup.com/bja/article-abstract/98/5/575/246440/577)
the electrophysiological abnormality of the atrial substrate and age-related degenerative changes. Although the present study did not show a significant difference, preoperative electrocardiographic P-wave duration and PR interval were reported to be potential predictors of AF. 

**Table 2** Multivariate analysis of postoperative AF

<table>
<thead>
<tr>
<th></th>
<th>With AF (n=83)</th>
<th>Without AF (n=177)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 yr increase)</td>
<td></td>
<td></td>
<td>0.020</td>
</tr>
<tr>
<td>Average cardiac index in ICU for the first 12 h (l min⁻¹ m⁻²)</td>
<td>2.4 (0.4)</td>
<td>3.2 (0.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Fluid balance in ICU for the first 12 h (ml)</td>
<td>1750 (1150, 2200)</td>
<td>1600 (1000, 2150)</td>
<td>0.24</td>
</tr>
<tr>
<td>Perioperative total blood loss (ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average cardiac index in OR (l min⁻¹ m⁻²)</td>
<td>2.6 (0.4)</td>
<td>2.8 (0.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Fluid balance in OR (ml)</td>
<td>1700 [750–2050]</td>
<td>1700 [1200–2400]</td>
<td>0.002</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>296 (77)</td>
<td>297 (90)</td>
<td>0.9</td>
</tr>
<tr>
<td>Average core temp in OR (°C)</td>
<td>35.6 (0.8)</td>
<td>35.3 (0.7)</td>
<td>0.008</td>
</tr>
<tr>
<td>Average core temp in ICU for the first 12 h (°C)</td>
<td>37.2 (0.5)</td>
<td>37.2 (0.5)</td>
<td>0.6</td>
</tr>
<tr>
<td>Noradrenaline (g kg⁻¹)</td>
<td>14.1 (14.5)</td>
<td>16.4 (19.6)</td>
<td>0.34</td>
</tr>
<tr>
<td>Dopamine (μg kg⁻¹)</td>
<td>14.8 (12.2)</td>
<td>12.8 (11.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Dobutamine (μg kg⁻¹)</td>
<td>3.9 (5.5)</td>
<td>2.4 (5.0)</td>
<td>0.07</td>
</tr>
<tr>
<td>Lactate at the end of surgery (mmol l⁻¹)</td>
<td>2.1 (1.2)</td>
<td>1.9 (1.0)</td>
<td>0.24</td>
</tr>
<tr>
<td>Base excess at the end of surgery (mmol l⁻¹)</td>
<td>2.4 (2.5)</td>
<td>2.2 (2.9)</td>
<td>0.51</td>
</tr>
<tr>
<td>Fluid balance in ICU for the first 12 h (ml)</td>
<td>750 [1250, 0]</td>
<td>800 [1300, 100]</td>
<td>0.81</td>
</tr>
<tr>
<td>Perioperative total blood loss (ml)</td>
<td>1750 (1150, 2200)</td>
<td>1600 (1000, 2150)</td>
<td>0.24</td>
</tr>
<tr>
<td>Average core temp in ICU for the first 12 h (°C)</td>
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<td>3.2 (0.7)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Average CVP in OR (mm Hg)</td>
<td>8.6 (3.2)</td>
<td>9.3 (3.7)</td>
<td>0.12</td>
</tr>
<tr>
<td>Number of distal anastomoses</td>
<td>3 [2–4]</td>
<td>3 [2–4]</td>
<td>0.78</td>
</tr>
<tr>
<td>Postoperative pleural effusion (n)</td>
<td>33 (40)</td>
<td>55 (64)</td>
<td>0.0001</td>
</tr>
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</table>

The development of AF is often associated with a lower intraoperative fluid balance and age-related degenerative changes. Hypovolaemia increases the sympathetic nervous activity in order to maintain cardiovascular stability. Enhanced sympathetic nervous system activity is reported to increase susceptibility to postoperative AF, and this offers a plausible mechanism for β-adrenoreceptor blockade as prophylaxis. However, the evaluation of the cardiac sympathovagal balance before the onset of AF in patients recovering from CABG showed either a higher or lower heart rate variability. These findings indicate that in some patients heightened sympathetic tone is present, but in others, either higher vagal tone or dysfunctional autonomic heart rate control is present before arrhythmia onset. The contribution of intraoperative hypovolaemia to autonomic changes and postoperative AF, however, remains unclear.
inflammatory cytokine production due to cardiac dysfunction might also facilitate AF generation. Alternatively, in our study, lower cardiac output during the early postoperative period could be secondary to perioperative hypovolaemia, especially as we found, no difference in preoperative cardiac function (% fractional shortening), preoperative number of coronary vessels with significant stenosis (≥50%), number of distal anastomoses, and duration of surgery between patients with or without postoperative AF.

Intraoperative, relatively higher core temperature was associated with an increased risk of postoperative AF. Previous studies have reported that the incidence of AF is higher after moderate hypothermic cardiopulmonary bypass surgery between patients with or without postoperative AF. The incidence of postoperative AF has increased over the past 20 yr. This may reflect advances in ECG monitoring and the fact that older or has increased over the past 20 yr. This may reflect advances in surgical and medical engineering techniques, the incidence of AF has changed little, and perioperative hypothermia increases the risk of morbid cardiac events (unstable angina, cardiac arrest, and myocardial infarction). In our study, relatively higher intraoperative core temperatures are likely to reflect in intraoperative fluid balance, because perioperative hydration status affects core temperature. Appropriate hydration may account for the development of postoperative AF and mild perioperative core temperature changes may simply reflect the difference in fluid balance status in patients with and without postoperative AF.

In spite of the advances in surgical and medical engineering techniques, the incidence of AF has changed little, or has increased over the past 20 yr. This may reflect advances in ECG monitoring and the fact that older patients with one or more co-morbidities now routinely undergo cardiac surgery. The incidence of postoperative AF was 32% in our study. Our patients were relatively elderly, and medications other than β-blockers were not immediately started after surgery, which might account for a slightly higher incidence of AF, when compared with previous off-pump CABG studies. The initial episode of postoperative AF most frequently occurred on the second postoperative day, which is similar to previous studies. Although exaggerated perioperative inflammatory response might cause postoperative AF, the reason for the delayed onset of AF more than 2 days after operation is not clear.

A major limitation of the present study is that it is conducted in a single centre with comparatively small sample sizes. Multicentre studies associated with larger populations are thus recommended for future investigations.

In summary, we documented the predictors of AF after off-pump CABG. Our present findings indicate that some of the known postoperative AF predictors after on-pump CABG also apply to off-pump cases. Further large studies focusing on the postoperative AF predictors in off-pump CABG are needed.

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