Postoperative atrial fibrillation in patients undergoing aortocoronary bypass surgery carries an eightfold risk of future atrial fibrillation and a doubled cardiovascular mortality

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Received 12 October 2009; received in revised form 30 December 2009; accepted 31 December 2009

Abstract

Objective: This article presents a study of postoperative atrial fibrillation (AF) and its long-term effects on mortality and heart rhythm.

Methods: The study cohort consisted of 571 patients with no history of AF who underwent primary aortocoronary bypass surgery from 1999 to 2000. Postoperative AF occurred in 165/571 patients (28.9%). After a median follow-up of 6 years, questionnaires were obtained from 91.6% of surviving patients and an electrocardiogram (ECG) from 88.6% of all patients. Data from hospitalisations due to arrhythmia or stroke during follow-up were analysed. The causes of death were obtained for deceased patients.

Results: In postoperative AF patients, 25.4% had atrial fibrillation at follow-up compared with 3.6% of patients with no AF at surgery \(p < 0.001\). An episode of postoperative AF was the strongest independent risk factor for development of late AF, with an adjusted risk ratio of 8.31 (95% confidence interval (CI) 4.20—16.43). Mortality was 29.7% (49 deaths/165 patients) in the AF group and 14.8% (60 deaths/406 patients) in the non-AF group \(p < 0.001\). Death due to cerebral ischaemia was more common in the postoperative AF group (4.2% vs 0.2%, \(p < 0.001\)), as was death due to myocardial infarction (6.7% vs 3.0%, \(p = 0.041\)). Postoperative AF was an age-independent risk factor for late mortality, with an adjusted hazard ratio of 1.57 (95% CI 1.05—2.34).

Conclusions: Postoperative AF patients have an eightfold increased risk of developing AF in the future, and a doubled long-term cardiovascular mortality.

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Keywords: Atrial fibrillation; Bypass; Surgery; Follow-up studies; Survival

1. Introduction

Postoperative atrial fibrillation (AF) affects 20–40% of open-heart surgery patients and is associated with increased risk for postoperative stroke and increased length of hospital stay [1–3]. The median onset of AF is on the second postoperative day, and the median duration is 1–2 days [4,5]. In most cases, the arrhythmia is self-terminating, and the patient discharged is in sinus rhythm.

While the short-term consequences of postoperative AF are well known, the long-term effects are poorly understood. Recent studies have demonstrated an increased long-term mortality in patients with an episode of postoperative AF, due to an increased risk of cardiovascular death [6–8]. It has been suggested that late recurrence of AF could explain these findings, but no study so far has examined the long-term consequences of postoperative AF on heart rhythm.

This study investigates the relationships between mortality, heart rhythm and arrhythmia-related symptoms 6 years after coronary artery bypass graft (CABG) surgery in a large cohort of patients. Our hypothesis was that an episode of postoperative AF is a risk indicator for later development of AF.

2. Material and methods

2.1. Patients

All 648 consecutive patients who underwent primary aortocoronary bypass surgery at the Department of Cardiothoracic Surgery and Anesthesiology, Örebro University Hospital, Örebro, Sweden, between 1 January 1999 and 30 June 2000 were eligible for the study. Forty-six patients with a history of AF of any form (identified from patient history and previous ECGs) were excluded, as well as patients with preoperative pacemaker implants (seven patients) and those...
not surviving postoperative day 5 (three patients). From October 2005 to May 2006, all surviving patients were asked to take part in the study. Twenty-one patients declined, and the remaining 571 patients formed the study cohort (Fig. 1). The study complies with the declaration of Helsinki and was approved by the Regional Ethical Committee of Uppsala, Sweden (2004 M-409). Signed informed consent was obtained from each patient.

After aortocoronary bypass surgery, all patients were monitored by continuous five-lead telemetry (Sirecust 960; Siemens Medical Solutions Diagnostics, Tarrytown, NY, USA) until the second postoperative day. From day 2 until discharge, telemetry was re instituted in the presence of arrhythmia. A standard 12-lead electrocardiogram (ECG) was routinely performed on postoperative days 1, 2 and 5, and more often if an arrhythmia was detected. Episodes of arrhythmia were noted on patient surveillance charts, and assessed thrice daily and at discharge by the heart surgeon responsible for the case. Postoperative AF was defined as an ECG-verified episode lasting more than 1 min during the first seven postoperative days, and the onset and duration of AF were recorded in the patient’s record as well as in the clinical database at the time of discharge. Two independent observers each looked twice through all patients’ records and ECGs to collect AF episode data.

The clinical management of postoperative AF at the time of surgery was as follows: preoperative medication including β blockers and acetylsalicylic acid (ASA) was continued up to the day of surgery, with the exception of warfarin, which was discontinued 3 days before surgery. Unless contraindicated, all patients received β-blocker medication postoperatively. Following the diagnosis of AF, patients received one or more of the following therapies at the physician’s discretion: a β blocker (sotalol was preferred, if tolerated by the patient), amiodarone, digoxin or verapamil, which were maintained for at least 4 weeks. Cardioversion was considered if the AF was difficult to rate-control. At the end of this period, and coinciding with the first postoperative visit to the outpatient clinic, the medication was discontinued if the rhythm had reverted to sinus. If the patient was still in AF, cardioversion was considered. Patients in AF were given heparin or low-molecular-weight heparin for anticoagulation; warfarin medication was initiated if AF persisted beyond 7 days.

Anaesthetic management was similar in all patients, and included standard monitoring techniques (electrocardiography, central venous/pulmonary artery and arterial pressure monitoring, urinary output and nasopharyngeal and urinary bladder temperature monitoring). The aortocoronary bypass surgery was routinely performed with cardiopulmonary bypass using the left internal mammary artery to bypass the left anterior descending artery, and using the great saphenous vein to revascularise the circumflex and right coronary artery areas. In some patients with one-vessel disease, off-pump aortocoronary bypass surgery (OPCAB) was performed. After surgery, the patients were transferred to an intensive care unit, extubated after a few hours and transferred to the patient ward the morning after surgery.

2.2. Procedures

Patient baseline data, as well as perioperative and postoperative parameters, were prospectively entered into a clinical database. The study database comprised parameters from the clinical database, along with retrospectively collected data from patient records and laboratory data. The registered parameters included patient characteristics (age, sex and body mass index), comitant diseases, serum creatinine (μmol l⁻¹) obtained the day before surgery, and left ventricular ejection fraction obtained from preoperative echocardiography or angiography. Perioperative and postoperative data included surgical times, length of stay, the presence of postoperative neurological deficit of any kind (defined as a 'neurological event') and medication preoperatively and at discharge.

From October 2005 to May 2006, all patients in the study cohort were located using the Swedish Population Registry. Deceased patients in the cohort were identified, and surviving patients were sent a letter and a questionnaire. The hospitals in the counties were contacted, and each patient’s most recent ECG was obtained. If the ECG was older than 1 year, a new ECG was recorded at the local care centre. In deceased patients, the latest ECG recording prior to death was obtained from the electrocardiographic database at the local hospital. Hospitalisations due to heart rhythm problems or embolic events during the follow-up period, excluding the first postoperative year, were identified from questionnaires and health-care databases, and all relevant patient records and ECGs were obtained and evaluated.

All collected ECGs were evaluated by one observer (E.F.), who was blinded to postoperative AF data. The heart rhythm was classified into one of five categories: (1) ‘sinus rhythm (SR)’, if SR in all ECGs and no hospitalisations due to AF; (2) ‘atrial fibrillation (AF)’, if AF in one or more ECG recordings during follow-up; (3) pacemaker rhythm (PM); (4) ‘other heart rhythm’; and (5) ‘unknown’, if no ECG was available. The questionnaire enquired about symptoms of angina, irregular heart rhythm and current medication. Up to three
telephone reminders were used to encourage questionnaire completion and return; in some instances, patients answered questions by phone.

All patients in the study who were deceased as of October 2006 were identified in the Swedish Nation Cause of Death Register, which records the deaths of all Swedish residents. In this register, the underlying cause of death is recorded from the death certificate made out by the responsible doctor. The cause of death is classified according to revision 10 of the International Statistical Classification of Diseases and Related Health Problems (ICD-10). Death causes are obtained for 99.8% of all deaths (2005), and the coding error is estimated to be 0.3% [9]. The cause of death in the individual patient is established by different methods such as autopsy or clinical examination before death. The quality of the Cause of Death Register has been examined repeatedly [10].

Primary death causes were classified into three main groups and 10 subgroups: (1) ‘cardiac’: acute myocardial infarction, heart failure and sudden death; (2) ‘cerebral’: cerebral infarction, cerebral haemorrhage and cerebrovascular insult (due to either bleeding or infarction); and (3) ‘other’: malignancy, ruptured aortic aneurysm, infection and miscellaneous causes. In this classification scheme, no information was available regarding the patient’s heart rhythm or previous postoperative AF.

2.3. Statistics

Data were expressed as mean ± standard deviation (SD). Categorical variables were compared using the chi-square test or Fisher’s exact test, while continuous variables were compared using the Student’s t-test for independent samples or the Mann–Whitney test in case of discrete data. Where appropriate, skewed distributions were transformed to logarithms before application of the parametric tests. A p value <0.05 was considered statistically significant.

To illustrate the effect of postoperative AF on long-term survival, Kaplan–Meier cumulative survival curves were constructed and compared by the log-rank test. Factors determining survival were analysed through Cox proportional hazard analysis. Variables of interest were screened using univariate analysis, and those with a p value ≤0.10 or those that were considered of clinical importance were entered into a proportional hazard analysis with no variable selection used.

To test the hypothesis that postoperative AF is a risk indicator for later development of AF, logistic regression was used and an odds ratio was calculated. Several variables were tested pairwise together with postoperative AF; those that changed the estimated risk ratio more than 10% were included in the model as possible confounders, and an adjusted risk ratio was calculated. Statistical analysis was performed using version 14 of the SPSS software (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Baseline data

Of the 571 patients included in the study, 165 (28.9%) developed postoperative AF. The postoperative AF patients were older than the patients in stable sinus rhythm postoperatively (Table 1). There were no sex differences, and the left ventricular ejection fraction did not differ between the groups.

Perioperative and postoperative data are summarised in Table 2. There were no differences regarding techniques of revascularisation, but in postoperative AF patients the postoperative release of creatine kinase-MB (CK-MB) was elevated compared with non-AF patients. Hospitalisation was prolonged, and 30-day mortality higher in patients with an episode of postoperative AF.

3.2. Arrhythmia follow-up

(1) ECGs were obtained from 443 of 491 surviving patients (90.2%) and from 61 of 80 deceased patients (76.3%) with no differences between non-AF and postoperative AF patients (89.2% vs 86.1%). The median time from surgery to the latest ECG recording was 5.3 years. In total, 85 hospitalisations due to heart rhythm problems or embolic events were identified, and the median time from surgery to hospitalisation was 3.1 years. Multiple ECG recordings were available from 172/504 patients (34.1%).

(2) The number of patients with AF during follow-up was 13 of 362 patients (3.6%) without postoperative AF and 36 of 142 patients (25.4%) with an episode of postoperative AF at surgery (p < 0.001) (Fig. 2). Among the 80 deceased patients, none in the non-AF group (0/37) had AF at their most recent ECG, compared with 6/24 (25%) among postoperative AF patients (p < 0.001).

The unadjusted odds ratio for late development of AF when an episode of postoperative AF was documented was 9.12 (95% CI 4.66–17.82). Variables tested as possible confounders were age, sex, previous myocardial infarction, diabetes mellitus, hypertension, left ventricular ejection fraction, preoperative body mass index and medication with statins/β blockers/angiotensin-converting enzyme inhibitors/angiotensin receptor II blockers at follow-up. The only

<p>| Table 1 |
|---|---|---|---|</p>
<table>
<thead>
<tr>
<th>Patient characteristics (n = 571).</th>
<th>Non-AF group</th>
<th>AF group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>64.6 ± 9.4</td>
<td>69.2 ± 7.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender (%)</td>
<td>22.9</td>
<td>18.8</td>
<td>0.279</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>26.8 ± 3.8</td>
<td>27.0 ± 3.8</td>
<td>0.617</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>30.4</td>
<td>35.8</td>
<td>0.211</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>19.0</td>
<td>17.0</td>
<td>0.577</td>
</tr>
<tr>
<td>Previous AMI (%)</td>
<td>54.2</td>
<td>58.8</td>
<td>0.316</td>
</tr>
<tr>
<td>Previous PCI (%)</td>
<td>11.1</td>
<td>9.1</td>
<td>0.481</td>
</tr>
<tr>
<td>History of smoking (%)</td>
<td>38.2</td>
<td>43.0</td>
<td>0.282</td>
</tr>
<tr>
<td>History of CVD (%)</td>
<td>7.4</td>
<td>7.3</td>
<td>0.955</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>57.4 ± 14.5</td>
<td>55.7 ± 14.9</td>
<td>0.228</td>
</tr>
<tr>
<td>S-creatinine (μmol l⁻¹)</td>
<td>99.4 ± 69.1</td>
<td>109.8 ± 76.5</td>
<td>0.117</td>
</tr>
<tr>
<td>CCS angina class IV (%)</td>
<td>30.3</td>
<td>37.0</td>
<td>0.122</td>
</tr>
<tr>
<td>Higgins risk score*</td>
<td>1</td>
<td>2</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation (SD) for continuous variables, and as percentages for dichotomous variables. AF: atrial fibrillation; AMI: acute myocardial infarction; BMI: body mass index; CCS: Canadian Cardiovascular Society; CVD: cerebrovascular disease; PCI: percutaneous coronary intervention.

* Median value.
substantial change of the odds ratio was caused by age, and the adjusted odds ratio for development of late AF was 8.31 (95% confidence interval (CI): 4.20—16.43).

3.3. Cause of death

The median follow-up time was 6.9 years. The total mortality was 60 deaths/406 patients (14.8%) in the non-AF group and 49 deaths/165 patients (29.7%) in the AF group (Table 3).

There were no missing data regarding cause of death. Death due to cerebral ischaemia was more common in the postoperative AF group (4.2% vs 0.2%, \( p < 0.001 \)), as was undefined cerebrovascular death and death due to myocardial infarction. Sudden death and death due to heart failure also tended to be more common among postoperative AF patients. Non-cardiovascular death causes did not differ between the groups.

In patients who died from cardiac or cerebral causes, 12 of 43 (27.9%) of the available ECGs from before death showed AF, compared with 5 of 39 (12.8%) ECGs in patients who died from other causes (\( p = 0.052 \)) (data not shown).

The long-term survival in the two groups is illustrated with a Kaplan—Meier curve in Fig. 3. The Cox regression analysis of patients surviving the first postoperative 30 days is summarised in Table 4. Univariate predictors of late mortality were age, postoperative AF, diabetes and left ventricular ejection fraction, while sex and hypertension had no significant influence on late mortality. In the multivariable analysis, postoperative AF was an independent risk indicator for late mortality (\( p < 0.027 \)), with a hazard ratio of 1.57 (95% CI 1.05—2.34). Age, diabetes and left ventricular ejection fraction were also independent risk factors for late mortality.

3.4. Questionnaires

(1) Questionnaires were obtained from 450 of 491 surviving patients (91.6%). There were no differences between the groups regarding questionnaire collection (91.9% vs 90.9%). The patients who did not answer the questionnaires were

Table 2

Perioperative and postoperative data.

<table>
<thead>
<tr>
<th>Perioperative data</th>
<th>Non-AF group (n = 406)</th>
<th>AF group (n = 165)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPB time (min)</td>
<td>102 ± 33</td>
<td>108 ± 32</td>
<td>0.072</td>
</tr>
<tr>
<td>X-clamp time (min)</td>
<td>57 ± 18</td>
<td>60 ± 18</td>
<td>0.180</td>
</tr>
<tr>
<td>No. of grafts (mean)</td>
<td>3.6</td>
<td>3.7</td>
<td>0.147</td>
</tr>
<tr>
<td>Use of LIMA (%)</td>
<td>89.4</td>
<td>86.7</td>
<td>0.350</td>
</tr>
<tr>
<td>OPCAB (%)</td>
<td>7.1</td>
<td>3.6</td>
<td>0.113</td>
</tr>
<tr>
<td>Retrograde cardiology (%)</td>
<td>72.9</td>
<td>73.3</td>
<td>0.925</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Postoperative data</th>
<th>Non-AF group (n = 406)</th>
<th>AF group (n = 165)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK-MB day 1 (( \mu )g l(^{-1}))</td>
<td>45.0 ± 57.0</td>
<td>52.4 ± 56.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>7.4 ± 2.4</td>
<td>9.2 ± 5.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neurological event during hospital stay (%)</td>
<td>0.7</td>
<td>2.4</td>
<td>0.111</td>
</tr>
<tr>
<td>Death within 30 days (%)</td>
<td>0.2</td>
<td>2.4</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Data are presented as means ± standard deviation (SD) for continuous variables, and as percentages for dichotomous variables. AF: atrial fibrillation; AMI: acute myocardial infarction; BMI: body mass index; CK-MB: creatine kinase-muscular band; CPB: cardiopulmonary bypass; LIMA: left internal mammary artery; OPCAB: off-pump coronary artery bypass.

Fig. 2. Arrhythmia classification at follow-up. The data shown include all patients with any ECG recording at 5 years after CABG surgery divided into patients with postoperative AF (AF group) and patients with no AF at surgery (non AF group). Numbers of patients are shown. (AF: atrial fibrillation, PM: pacemaker rhythm, SR: sinus rhythm).

Table 3

Causes of death in the study cohort after a median follow-up of 6.9 years.

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Non-AF group (n = 406)</th>
<th>AF group (n = 165)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>12 (3.0)</td>
<td>11 (6.7)</td>
<td>0.041</td>
</tr>
<tr>
<td>Heart failure</td>
<td>5 (1.2)</td>
<td>6 (3.6)</td>
<td>0.058</td>
</tr>
<tr>
<td>Sudden death</td>
<td>3 (0.7)</td>
<td>4 (2.4)</td>
<td>0.097</td>
</tr>
<tr>
<td>Cerebral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral ischaemia</td>
<td>1 (0.2)</td>
<td>7 (4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cerebral bleeding</td>
<td>3 (0.7)</td>
<td>1 (0.6)</td>
<td>0.863</td>
</tr>
<tr>
<td>Cerebrovascular, undefined</td>
<td>0 (0.0)</td>
<td>2 (1.2)</td>
<td>0.026</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>19 (4.7)</td>
<td>9 (5.5)</td>
<td>0.698</td>
</tr>
<tr>
<td>Infection</td>
<td>4 (1.0)</td>
<td>1 (0.6)</td>
<td>0.639</td>
</tr>
<tr>
<td>Aortic rupture</td>
<td>1 (0.2)</td>
<td>2 (1.2)</td>
<td>0.148</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>12 (3.0)</td>
<td>6 (3.6)</td>
<td>0.673</td>
</tr>
<tr>
<td>Total mortality</td>
<td>60 (14.8)</td>
<td>49 (29.7)</td>
<td></td>
</tr>
</tbody>
</table>

Results are reported as number of patients, with percentages in parentheses. AF: atrial fibrillation.
slightly younger than patients who did, and were also more frequently female. The median time from surgery to our receipt of the completed questionnaire was 6.3 years.

(2) There were no differences in angina symptoms 6 years after coronary bypass surgery between the groups: a total of 209/330 patients (63.3%) in the non-AF group were free of angina compared to 73/120 patients (60.8%) in the postoperative AF group ($p = 0.552$). In total, 29/550 patients (5.3%) had angina symptoms in daily activities 6 years after surgery.

(3) The number of patients with hospitalisations due to cerebral ischaemic stroke during follow-up was 8/165 patients (4.8%) in the postoperative AF group and 11/406 patients (2.7%) in the non-AF group ($p = 0.196$). Notably, no patient had warfarin medication before the stroke, and AF at the time of stroke could be documented in 9/19 patients. Adding the patients who died due to cerebral ischaemia, the total number of ischaemic cerebral vascular events was 15/165 patients (9.1%) in the postoperative AF group and 12/406 patients (3.0%) in the non-AF group ($p = 0.002$).

3.5. Medication

At discharge and at follow-up, there were no significant differences between postoperative AF patients and non-AF patients regarding medication with statins, β blockers including sotalol and angiotensin-converting enzyme inhibitors (Table 5). At discharge, 3.6% of the AF patients and 1.2% of the non-AF patients received warfarin ($p < 0.058$). At follow-up, 8.3% of postoperative AF patients received warfarin, compared with 3.9% of non-AF patients ($p = 0.061$). Medication with digitals, diuretics and angiotensin II receptor blockers was also more common among postoperative AF patients after 6 years (Table 5). In total, 6.7% of postoperative AF patients received an anti-arrhythmic drug at follow-up, compared with 1.8% of non-AF patients.

4. Discussion

4.1. Development of atrial fibrillation

The most important finding in this study was that an episode of postoperative AF is a predictor of late recurrence
of AF. Postoperative AF has been considered to be a self-limiting arrhythmia with a median duration of 48 h and with 98% of patients regaining sinus rhythm after 2 months [4,11]. The present study of 571 consecutive CABG patients had a nearly 90% complete 5-year ECG follow-up. Analysing these data together with data from hospitalisations for heart rhythm problems or stroke, we found that approximately one-fourth of the postoperative AF patients developed AF of any form during late follow-up. They had a significantly higher risk of developing AF than non-AF patients, with an adjusted risk ratio of 8.31 (95% CI 4.20—16.43).

The impact of postoperative AF on late arrhythmia has been studied in a limited number of papers with conflicting results. In one study comprising 305 non-consecutive CABG patients seen in an outpatient clinic and followed for a median time of 2 years, symptomatic episodes of AF requiring medical care were more common during follow-up in postoperative AF patients (20.4%) than in non-AF patients (3.2%) [12]. However, in four studies with shorter follow-up times involving a total of 1286 CABG patients, postoperative AF was found to be self-limiting, with a total prevalence of AF of 1—4% at 1 year [11,13—15]. The present study is the largest study with the longest follow-up time so far, and it seems reasonable to state that the relation between postoperative AF and late AF is a new finding with clinical implications.

The mean patient age at surgery in this study was 66 years. At follow-up, the mean age was 69 years in non-AF patients and 74 years in AF patients. Epidemiological data from the Framingham Heart Study and the Rotterdam Study indicate that the overall prevalence of AF in this age group is 5—7% [16,17]. Since patients in these studies were followed with repeated controls, and AF in conjunction with open-heart surgery was excluded, it seems unlikely that the 25.4% prevalence of AF in this study reflects any ‘normal’ prevalence of AF in this age group.

It was beyond the scope of this study to determine why postoperative AF patients have a higher risk of developing AF. We speculate that major surgery may function as a ‘stress test’ that unmasks a tendency to develop AF. Coronary artery bypass surgery may thus reveal the risk of developing AF, which might otherwise not have been detected until later. Another explanation could be that the surgery causes permanent changes that increase the potential for AF, for example, by inducing inflammation and atrial scarring.

4.2. Postoperative AF and mortality

A second important finding of this study was that postoperative AF is an age-independent risk factor for late mortality, with an adjusted hazard ratio of 1.57 (95% CI 1.05—2.34). In this study, postoperative AF patients had a greater than twofold risk of death due to cerebral ischaemia and cardiac disease than non-AF patients. An unexplained increased risk of cardiovascular death and thrombo-embolism in postoperative AF patients has been demonstrated in two previous studies [6,7]. Can the development of late AF in postoperative AF patients explain these findings? In general, AF is a well-established risk factor for mortality, stroke and heart failure [18]. Recent studies have also demonstrated a link between AF and death due to acute myocardial infarction and sudden death [19]. It has been suggested that higher mortality in postoperative AF patients, especially a higher incidence of sudden death, may be related to the use of potentially harmful anti-arrhythmic drugs [20]. In the present study, the proportion of postoperative AF patients receiving sotalol or amiodarone was 69.1% at discharge (note that, in the typical case, anti-arrhythmic medication was discontinued after 4 weeks) and 6.7% at follow-up. Anti-arrhythmic medication may thus potentially increase the early mortality, but can hardly explain the increased long-term mortality in postoperative AF patients.

In our survival analysis, we included potential confounders like age, left ventricular ejection fraction, diabetes and hypertension. Since the use of statins, β blockers and angiotensin-converting enzyme inhibitors all have been shown to influence incidence of AF or mortality [21—24], these are all possible confounders. We can state that there were no differences between the groups regarding these medications at discharge and follow-up, but cannot control for any differences in treatment during the follow-up period.

To summarise, the findings of the present study suggest that the observed increased long-term mortality and cardiovascular morbidity seen in postoperative AF patients may be explained by an increased risk of late AF and AF-related disease. These findings may also shed some light on the stroke incidence in the Syntax trial [25], where percutaneous coronary intervention and coronary bypass surgery were compared. In the coronary surgery group, the stroke incidence during the first postoperative year was 2.2% compared with 0.6% in the coronary intervention group. The incidence of postoperative AF was not reported, and the anticoagulation protocol in the coronary surgery group was far less aggressive than in the coronary intervention group. Given the results from the present study, it seems possible that the higher stroke incidence in the coronary surgery group can at least partly be explained by postoperative AF and thrombo-embolic disease.

4.3. Clinical implications

The findings of this study suggest that an episode of postoperative AF after CABG surgery can be regarded as a risk marker for the development of late AF and late cardiovascular death. From a clinical point of view, these findings have several implications. The follow-up strategy in patients with postoperative AF should probably be more intense, with the goal of detecting late arrhythmias. Anticoagulation therapy should be initiated in high-risk patients with AF. Further studies are needed to confirm the benefits of this strategy and to determine whether prevention of postoperative AF can diminish future risk.

5. Conclusion

This study found that patients with an episode of postoperative AF have a higher risk of developing AF in subsequent years, and that postoperative AF is an independent risk factor for late mortality and cerebrovascular morbidity. The higher mortality in postoperative AF patients was mainly due to a higher risk of cardiovascular death. These findings suggest that development of AF may be
directly linked to the increased mortality in postoperative AF patients.

5.1. Limitations

The incidence of postoperative AF in this study was 28.9%, which is in accordance with earlier studies. There is, however, a possibility of undetected episodes of AF in the postoperative period.

The classification of AF at follow-up should be addressed. In some patients with several ECG recordings, a paroxysmal or persistent AF could be suspected, but since this was impossible to determine in the majority of patients, the definition of type of AF in this study was abandoned. It follows that the true prevalence of any AF at follow-up may still be underestimated, since cases of silent paroxysmal AF may be undetected. Likewise, some cases of clinically unknown (and thus unprotected) paroxysmal AF patients may have been revealed at follow-up. The present study is, however, the first long-term arrhythmia follow-up in postoperative AF patients.

The identification of hospitalisations due to heart rhythm problems and embolic disease was based on self-reporting and search in health-care databases. Thus, some events could have been missed and relevant information thereby not included in the analysis.

Data from the Swedish National Cause of Death Register were complete, but different methods were used to establish the cause of death, and thus causes of death could be wrongly assigned in this database. The observed difference between the groups concerning cardiovascular and non-cardiovascular death cannot, however, easily be explained by poor validity of the cause of death data.

Acknowledgement

We would like to thank personnel from Clinical Research Support at Örebro University Hospital for their valuable help in collecting data.

References