

REVIEW

The significance of preoperative atrial fibrillation in patients undergoing cardiac surgery: preoperative atrial fibrillation—still underestimated opponent

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Atrial fibrillation (AF) has been described as an 'epidemic' due to its increasing prevalence in the ageing population. The prevalence of AF in the UK has risen from 0.78% in 1994 to 1.42% in 2006. The pathogenesis of AF seems to be multifactorial, and includes electrical and structural remodelling, and inflammation. As a result of recent developments in invasive cardiology together with improved pharmacological treatments, cardiac surgeons are increasingly operating on elderly patients with very advanced heart disease and other co-existent diseases. Therefore, AF is often present before cardiac surgery, increasing the risk of surgery and the occurrence of postoperative complications. According to available data, preoperative AF (pre-AF) should be considered as a high-risk marker of postoperative complications, which also significantly reduces long-term patient survival. However, although some multivariate models have concluded that pre-AF seems to be an independent predictor of outcome, this does not prove a cause–effect relationship. Therefore, such a link would need to be proven in prospective randomized studies, yet to be undertaken.

Introduction

Atrial fibrillation (AF) has been described as an 'epidemic' due to its increasing prevalence in our ageing population.¹ The prevalence of AF in the UK has risen from 0.78% in 1994 to 1.31% in 2003, and 1.42% in 2006.^{1–3} A similar prevalence is observed in Poland and other Central European countries.^{2,3} In another epidemiological study carried out in USA, the incidence of age- and gender-adjusted AF rose from 3.04 to 3.68 per 1000 person-years, between 1980 and 2000.⁴ A prevalence model structured by the same group estimated a three-fold increase in the number of patients with AF in the next 50 years.⁴

Atrial fibrillation before cardiac surgery

As a result of recent developments in invasive cardiology together with improved pharmacological treatments,

cardiac surgeons are increasingly operating on elderly patients with very advanced heart disease and other co-existent diseases.⁵ Therefore, AF is often present before cardiac surgery, increasing the risk of surgery and the occurrence of postoperative complications.^{5–7}

Preoperative AF (pre-AF) significantly worsens the postoperative haemodynamic function of the heart.⁷ This increases the chance of developing postoperative complications which could result in death and prolonged length of intensive care unit (ICU) and hospital stay.^{7,8} While ~30% of patients undergoing cardiac surgery will develop postoperative atrial fibrillation (POAF), if patients have co-existing preoperative supraventricular arrhythmias, the risk can be as high as 60%.^{9,10} This was confirmed in the author's previous studies, where postoperative AF was diagnosed in almost 61% patients who underwent isolated surgical revascularization to 78.3% in consecutive patients subjected to different types of cardiac surgery that were included in the Consciousness Disorders After Cardiac Surgery trial (CODACS).^{10,11} Compared with patients

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without pre-AF, there was a three- to four-fold increase in the risk of developing POAF. In a recent meta-analysis, we reported that pre-AF was an independent and important risk factor in developing POAF, more than doubling that risk.¹² These results were in agreement with the results of other studies. Magee *et al.*¹³ designed a risk stratification model in order to predict the relative risk of developing POAF in patients undergoing coronary artery bypass grafting (CABG). They developed a regression model with 14 significant indicators, including preoperative arrhythmias as one of the most important risk factors.¹³

Preoperative atrial fibrillation and postoperative delirium

Preoperative AF increases the risk of other postoperative complications.⁵ Postoperative delirium quite commonly complicates cardiac surgery, and occurs with a frequency from 8.4 to 33.6%.¹⁴ This results in higher morbidity and mortality ratios, and prolongs hospital stay.¹⁴ Unfortunately, little is known about the natural history of psychiatric morbidity, postoperative delirium, cognitive decline, and health-related quality of life in cardiac surgery patients. There are several mechanisms by which AF prior to surgery may influence the occurrence of postoperative delirium. Preoperative AF may contribute to postoperative delirium by inducing cerebral emboli, brain hypoperfusion and provoke periods of arterial hypotension during and post-surgery.^{10,15} Many different risk factors for delirium following cardiac surgery have been described which has made it difficult to estimate risk of postoperative delirium using predictive scores. The following risk factors for postoperative delirium have been mentioned: advanced age, alcohol abuse/alcohol dependence, preoperative arrhythmias, heart failure, diabetes mellitus, history of peripheral arterial disease, neurological history, prolonged cardiopulmonary bypass exposure, and type of surgical procedure performed.^{10,14–16} In the preliminary results of the CODACS trial, we identified six independent predictors of postoperative delirium: cognitive impairment, AF before surgery, history of cerebrovascular disease, peripheral arterial disease, major depression, and advanced age. Preoperative AF was the strongest non-psychiatric predictor of postoperative delirium, with a seven-fold increase in risk (OR 7.2, 95% CL 2.3–22.7; $P = 0.007$).¹¹ Our results have been confirmed in other studies. Bucerius *et al.*¹⁴ analysed the predictors of

postoperative delirium. The overall prevalence of post-operative delirium was only 8.4%. Of 49 selected patient-related risk factors and treatment variables, 35 were highly associated with postoperative delirium. Stepwise logistic regression revealed that pre-AF was one of the most important independent risk factors of delirium after cardiac surgery.¹⁴ Besides AF, the authors also selected other independent predictors: history of cerebrovascular disease, peripheral arterial disease, diabetes mellitus, left ventricular ejection fraction (LVEF) <30%, preoperative cardiogenic shock, urgent operation, intraoperative haemofiltration, operation time of 3 h, or more and high perioperative transfusion requirement. The authors also identified two variables as having a significant protective effect against postoperative delirium: beating-heart surgery and younger patient age. This is probably because both off-pump coronary artery bypass (OPCAB) and younger age significantly decrease the risk of brain hypoperfusion and arterial hypotension.¹⁴ These results were also confirmed in other studies.^{16,17}

To the further analysis of CODACS trial, we included 565 consecutive patients undergoing cardiac surgery. We observed that pre-AF occurred in 49 (8.7%) and postoperative delirium in 92 patients (16.3%). The statistical analysis showed that pre-AF was still the strongest non-psychiatric predictor of postoperative delirium, with an over six-fold increase in risk (OR 6.4; 95% CL 3.4–11.9; $P < 0.001$).¹⁸

Preoperative atrial fibrillation and postoperative stroke

We previously showed that pre-AF significantly increases the risk of stroke irrespective of the type of surgery⁷ (Table 1). Most strokes in AF patients are thought to arise from thrombi in the left atrial appendage.⁷ In the study by Ngaage *et al.*,¹⁹ the authors evaluated the prognostic significance of pre-AF at the time of aortic valve replacement (AVR). They observed that if the patients were in AF, the patients had a worse late survival with 1-, 5-, and 7-year survival rates substantially reduced at 94, 87, and 50%, respectively, vs. 98, 90, and 61% for patients in sinus rhythm preoperatively ($P < 0.05$). Patients in AF also had a greater probability of subsequent rhythm-related intervention, more frequently developed congestive heart failure, and more often had a stroke (16 vs. 5%, $P = 0.005$).¹⁹ On the basis of this multi-variable analysis, it was felt that pre-AF was an independent

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Table 1 The studies evaluating the impact of preoperative atrial fibrillation on postoperative strokes

Study	No. of patients/kind of surgery	Outcomes
Orszulak <i>et al.</i> ²⁰	285/MVR and/or CABG	5-year freedom from stroke rate was 89.2%. Advanced NYHA class was the only significant variable associated with a greater risk of late stroke. Neither chronic pre-AF nor operative obliteration of the left atrial appendage increased or decreased the late risk of stroke in patients following MVR. The mean stroke rate over 12 years was only 2.5% and was more likely to occur in older and more compromised patients
Ngaage <i>et al.</i> ¹⁹	381/AVR	Patients with pre-AF had a greater probability of postoperative stroke (16 vs. 5%, $P = 0.005$). On the basis of this multivariable analysis, pre-AF was an independent predictor of late adverse cardiac and cerebrovascular events
Banach <i>et al.</i> ¹¹	3000/CABG or OPCAB	In the study of patients undergoing isolated surgical revascularization, it was demonstrated that pre-AF increased the risk of stroke by two-fold (from 4.4 to 9.2%; $P < 0.001$)

predictor of late adverse cardiac and cerebrovascular events.¹⁹ In our study of 3000 patients undergoing isolated surgical revascularization, we demonstrated that pre-AF increased the risk of stroke by two-fold (from 4.4 to 9.2%; $P < 0.001$).⁷ However, Orszulak *et al.*²⁰ were unable to show a correlation between pre-AF and stroke after surgery. Patients ($n = 285$) who had undergone mitral valve replacement (MVR) and/or CABG were included in the study. Overall, the 5-year survival rate was 58.9% which included a 62.7% survival for MVR and 50.1% survival for MVR + CABG patients, respectively. The 5-year freedom from stroke rate was 89.2% which includes rates of 89.1% for MVR and 90.2% for MVR + CABG, respectively.²⁰ Advanced New York Heart Association (NYHA) class was the only significant variable associated with a greater risk of late stroke. Neither chronic pre-AF nor operative obliteration of the left atrial appendage increased or decreased the late risk of stroke in patients following MVR. The mean stroke rate over 12 years was only 2.5%, and strokes following MVR + CABG were more likely to occur in older and more compromised patients²⁰ (Table 1).

Preoperative atrial fibrillation and postoperative low cardiac output syndrome

Opinion is still divided as to whether pre-AF significantly predicts postoperative low cardiac output syndrome (LCOS).²¹ Low cardiac output syndrome is usually defined as the need for high dosages of inotropic medication and/or intra-aortic balloon pumping to sustain adequate haemodynamic status.²¹ Low cardiac output syndrome is a common complication following cardiac surgery, and significantly increases the length of ICU and hospital stay while worsening prognosis.^{21,22} There are few studies that investigated the predictors of LCOS in patients who have undergone cardiac surgery. Sato *et al.*²³ reported 145 cases including 76 patients who underwent MVR, 42 AVR, and 27 double valve replacement. They described the following predictors of postoperative LCOS: extracorporeal circulation time, aortic cross-clamping time, left ventricular myocardial mass index, heart failure, NYHA class, left ventricular end diastolic pressure, and left ventricular diastolic eccentricity ratio.²³ Rao *et al.*²² identified patients who would be at risk from the development of LCOS in 4558 consecutive patients who had had isolated CABG. The overall prevalence of LCOS was 9.1%. The operative mortality rate was higher in patients in whom LCOS developed than in those in whom it did not (16.9 vs. 0.9%, $P < 0.001$). Stepwise logistic regression analyses identified nine independent predictors of low output syndrome: LVEF $< 20\%$, repeat operation, emergency operation, female gender, diabetes, age older than 70 years, left main coronary artery stenosis, recent myocardial infarction, and triple-vessel disease. The authors concluded that patients at high risk for the development of LCOS should be the focus of trials using new techniques in myocardial protection to resuscitate the ischaemic myocardium.²² Maganti *et al.*²⁴ analysed the predictors of LCOS in patients undergoing isolated aortic valve surgery. They included 2255 patients who underwent aortic valve surgery with no other concomitant cardiac surgery. The overall prevalence of LCOS was 3.9%. The independent predictors of LCOS were: renal failure, earlier year of

operation, LVEF $< 40\%$, shock, female gender, and increasing age. Overall mortality was 2.9% and it was higher in patients who experienced LCOS (3.8 vs. 1.5%; $P < 0.001$).²⁴

These studies did not confirm the influence of pre-AF on postoperative LCOS. However, this could have been related to the low number of patients with pre-AF.^{21–24} In contrast, there are also studies that have shown that pre-AF was a significant predictor of postoperative LCOS.^{9,11} Similar results were seen in our study in 3000 patients who had isolated CABG. We showed that pre-AF was significantly associated with an increased risk of postoperative LCOS, occurring in 25.9% of patients with pre-AF and in 23.1% without AF before surgery ($P < 0.02$).⁷ However, there is still need to perform a study in a large group of patients undergoing cardiac surgery, with LCOS as a main endpoint, and pre-AF as a variable.

Preoperative atrial fibrillation and postoperative mortality

If one excludes postoperative complications, pre-AF has the greatest effect on survival rate (Table 2). This suggests the need for suitable preventive management of AF prior to surgery.⁷ Quader *et al.*²⁵ investigated almost 47 000 patients who underwent primary isolated CABG. Patients with pre-AF were older and were more likely to have left ventricular dysfunction and hypertension but had less severe angina. In propensity-matched patients, survival at 30 days and at 5 and 10 years for patients with pre-AF as opposed to no AF was 97 vs. 99%, 68 vs. 85%, and 42 vs. 66%, respectively. The survival difference at 10 years was 24%. Median survival in patients with AF was 8.7 vs. 14 years for those without it.²⁵ Ngaage *et al.*²⁶ analysed the independent effect of pre-AF on the outcome of CABG, including the causes of death. Patients with AF had significantly longer hospital stays with a trend to more frequent early and late readmissions. Risk of late mortality in patients with AF increased by 40% compared with patients in sinus rhythm preoperatively. The late cardiac death rate in the AF group was 2.8 times that of the sinus rhythm group. Major adverse cardiac events occurred in 70% of patients with pre-AF compared with 52% of patients in preoperative sinus rhythm.²⁶ Kvidal *et al.*²⁷ evaluated the predictors of mortality in 2359 patients who had undergone AVR. Early mortality after AVR (within 30 days) was 5.6% and relative survival rates after 5, 10, and 15 years were 94.6, 84.7, and 74.9%, respectively. Advanced NYHA functional class, pre-AF, and pure aortic regurgitation were independent risk factors for observed and relative survival.²⁷ We observed that pre-AF significantly worsened the postoperative condition with an increased risk of postoperative complications, and prolonged duration of ICU and hospital stay.⁷ There was a decrease in survival during the observation period in patients following surgical revascularization that was insignificant at 6 and 30 days (96.4 vs. 98.1%, 94.5 vs. 97.3%), respectively, in patients with preoperative AF when compared with patients without AF. However, by 6 and 12 months, the mortality was 86.2 vs. 93.0% ($P < 0.03$) and 74.7 vs. 91.0% ($P < 0.02$), respectively, and during the long-term observation (on average 3 years), the survival difference was almost 20% (70.7 vs. 90.6%, $P < 0.01$). Moreover, we showed that

Table 2 The studies evaluating the impact of preoperative atrial fibrillation on postoperative mortality

Study	No. of patients/kind of surgery	Outcomes
Kvidal <i>et al.</i> ²⁷	2359 / AVR	Early mortality after AVR (within 30 days) was 5.6% and relative survival rates after 5, 10, and 15 years were 94.6, 84.7, and 74.9%, respectively. Advanced NYHA functional class, pre-AF, and pure aortic regurgitation were independent risk factors for observed and relative survival
Quader <i>et al.</i> ²⁵	46 984 / CABG	The survival at 30 days and at 5 and 10 years for patients with pre-AF as opposed to no AF was 97 vs. 99%, 68 vs. 85%, and 42 vs. 66%, respectively. The survival difference at 10 years was 24%. Median survival in patients with AF was 8.7 vs. 14 years for those without it
Ngaage <i>et al.</i> ²⁶	526 / CABG	Patients with pre-AF had significantly longer hospital stays with a trend to more frequent early and late readmissions. Risk of late mortality in patients with pre-AF increased by 40% compared with patients in sinus rhythm preoperatively. The late cardiac death rate in the AF group was 2.8 times that of the sinus rhythm group
Banach <i>et al.</i> ²⁸	3000 / CABG or OPCAB	In patients with pre-AF when compared with patients without AF, it was observed a decrease in survival that was insignificant at 6 and 30 days (96.4 vs. 98.1%, 94.5 vs. 97.3%), respectively; however, by 6 and 12 months the mortality was 86.2 vs. 93.0% ($P < 0.03$) and 74.7 vs. 91.0% ($P < 0.02$), respectively, and during the long-term observation (on average 3 years) the survival difference was almost 20% (70.7 vs. 90.6%, $P < 0.01$). It was also showed that preoperative AF was an independent predictor of postoperative death

preoperative AF was an independent predictor of postoperative death⁷ (Table 2).

Conclusions

We conclude that pre-AF in patients subjected for cardiac surgery should be considered as a high-risk marker of postoperative complications, including postoperative AF and reduced long-term survival.^{7,28}

However, it is necessary to emphasize that although some multivariate models have concluded that pre-AF seems to be an independent predictor of outcomes, this does not prove cause-effect relations. Therefore, this would need to be proven in prospective randomized studies, yet to be undertaken.^{7,29}

Conflict of interest: none declared.

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