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Predicting the risk of atrial fibrillation after coronary artery bypass surgery

Tapio Hakala[1] and Antti Hedman[2]

Atrial fibrillation (AF) is the most common arrhythmia, with an incidence of 17–33%, after coronary artery bypass grafting (CABG) and it increases the cost of operative treatment. β-Blocker therapy reduces markedly the incidence of postoperative AF. The more effective preventive methods, e.g. amiodarone therapy or atrial pacing, are not cost-effective for all the patients. Thus, identification of patients at high risk of AF after CABG would be helpful. This review summarizes the predictors of postoperative AF and the current methods for risk stratification. In summary, identification of the patients at high risk of postoperative AF remains a challenge. The clinical usefulness of most of the conventional factors, e.g. age or history of AF, is low. Even attempts to build logistic regression models based on the pre- and intraoperative variables have failed to provide powerful predictors for postoperative AF after CABG. From the new predictors, the P-wave duration in signal-averaged ECG looks promising. Sensitivity and negative predictive value are high, positive predictive value remains low, which limits its usefulness. Contrary, even detailed analysis of standard 12-lead ECG or measure of heart rate variability has failed to provide useful information for risk stratification. A new method for risk stratification has been developed in our centre. The diagnostic accuracy of high-rate atrial pacing seems to be sufficient to identify a group of patients to whom prophylactic treatment could be proactively targeted. Further experience is, however, warranted to verify significance of this method in everyday clinical practice.

Key Words: heart rate variability, postoperative atrial fibrillation, risk stratification, signal-averaged ECG

Atrial fibrillation (AF) is the most common arrhythmia after coronary artery bypass grafting (CABG). The reported incidence of AF after CABG varies widely depending on the particular definition used, the mode of postoperative monitoring of the patients, and the changing profile of the patients undergoing CABG. The incidence of post-CABG AF varied between 17 and 33% in the studies that included 300 patients or more (1–11). Patients undergoing CABG and combined valve surgery have a higher incidence of postoperative AF than patients having CABG alone (4, 12). The peak of AF incidence occurs between days 2 and 4 after the operation, with less than 10% on the first postoperative day (6).

AF after CABG is self-limiting in most cases, but, even when it is uncomplicated, it requires additional medical treatment and a prolonged hospital stay, and it consequently increases the costs of operative treatment (6, 12, 13). In some cases AF can cause haemodynamic compromise and increase the risk of stroke (4, 14).

Prophylactic medical therapy decreases the incidence of postoperative AF after CABG. A meta-analysis of 24 randomized, controlled trials demonstrated that therapy with a β-adrenergic blocker decreases the incidence of AF after CABG by 77% (15). Prophylactic therapy with amiodarone has been shown to be effective in decreasing the incidence of AF after CABG (16, 17). In addition to medical prevention, atrial pacing may play a significant role in the prevention of AF after CABG, especially when combined with medical therapy (18, 19).

The most effective preventive methods, either medical prevention or preventive pacing strategy, require additional nursing and medical resources and expense. Prophylactic treatment to prevent AF with intravenous amiodarone is not cost-effective if given to all patients (10). In addition, these treatments may have unfavourable side effects. Prophylaxis of the whole patient population undergoing CABG is not reasonable. Identification of patients who would be at high risk of AF after CABG would be very helpful. The aim of this review is to summarize the predictors of AF and the current knowledge how to identify preoperatively or intraoperatively the patients at high risk of AF after CABG.

PREOPERATIVE RISK FACTORS

Several demographic or preoperative factors, such as age, sex, history of previous AF, hypertension, chronic

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obstructive pulmonary disease (COPD), diseased right coronary artery, use or withdrawal of medication, have been shown to be risk factors for postoperative AF.

Age

Old age is the most often reported independent risk factor for post-CABG AF. The incidence of AF after cardiac surgery increases by at least 50% per 10 years of increased age (2, 5, 7, 10). Ageing causes cardiac dilatation, myocardial atrophy, decrease of conduction tissue, and fibrosis in atria (20, 21). These age-related changes may be responsible for increased risk of AF after CABG.

Sex

Men appear more likely to develop AF after CABG than women (1, 4–6, 9, 10). Sex differences in ion-channel expression and hormonal effects on autonomic tone may explain this difference between genders (1, 6, 7, 9, 10). However, data are inconsistent and there exist conflicting reports in which male gender was not an independent predictor of AF (3, 4).

History of AF

Preoperative history of AF is a factor which is consistently associated with AF after CABG. Patients with a history of AF appear to have the underlying substrate necessary for the development of AF, and they are thus susceptible to postoperative AF (3, 5, 8). The exclusion of patients with a history of AF is probably the reason why preoperative history of AF has not been found to predict postoperative AF in many studies.

Hypertension

Hypertension has been shown to predict postoperative AF, and this may be related to increased fibrosis and to dispersion of atrial refractoriness (6–8). However, in many well-conducted studies involving large numbers of patients, hypertension has not been found to be an independent predictor of AF after CABG (1, 3, 10).

Stenosis of the right coronary artery

The blood supply to the right atrium, the sinoatrial node and the atrioventricular node is mainly conveyed via the right coronary artery. Two studies have found that a total occlusion or severe stenosis of the proximal right coronary artery is an independent predictor of postoperative AF (22, 23). In other studies, obstructive disease specifically in the sinoatrial nodal and atrioventricular nodal arteries was more common in patients developing AF after CABG than in those who remained in sinus rhythm (SR) (24–26).

COPD

COPD is also a predictor of AF after cardiac surgery (2, 4, 7, 27). COPD patients have frequent premature atrial contractions that act as a trigger for the initiation of AF (2, 4, 7, 27).

Use of digoxin

Some authors have found preoperative use of digoxin as an independent risk factor for AF after cardiac surgery (4, 7). It is apparent that digoxin has been used for heart failure and less compellingly, for prophylaxis of AF as well. The use of digoxin is often associated with more advanced heart disease.

β-Blocking withdrawal effect

When long-term β-blocking medication is abruptly discontinued, a phenomenon called β-blocking withdrawal effect follows. It is characterized by increased catecholamine concentration in plasma. A withdrawal effect has been proposed as a possible cause of AF after cardiac operation when β-blocking medication has been stopped at the time of surgery (28, 29).

Other factors

Several other factors have been found independently to predict the risk of AF after CABG: previous congestive heart failure (5), previous myocardial infarction (10), resting pulse rate less than 80 bpm (7), precardiopulmonary heart rate over 100 bpm (5), peripheral vascular disease (4), smoking (4), three-vessel coronary artery disease (30), low body mass index (31), left atrial enlargement (30, 32) and large body surface area (33).

However, none of the above-mentioned factors are powerful enough to predict postoperative AF after CABG in any clinically meaningful extent. Thus, we created retrospectively a logistic regression model to predict the risk of postoperative AF in data of 3676 consecutive CABG patients in our centre (33). The model consisted of four preoperative (age, left ventricle ejection fraction, body surface area, digoxin use) and one postoperative variable (intra-aortic balloon pump or inotropic medication during the first 24 h). The discriminate power of the predictive model was not very good since the area under the receiver operating characteristic curve was no larger than 0.690. This suggests that even multifactorial models created from those risk factors have not enough power for clinical use.

INTRAOPERATIVE PREDICTORS

In addition to preoperative factors, some intraoperative factors have been suggested to be able to predict the risk of postoperative AF after CABG. However, data are not fully consistent.

Cardioplegia and aortic cross-clamp time

There are conflicting data studies that show that long cross-clamp time increases the risk of postoperative AF about the association between aortic cross-clamp time and postoperative AF. The correlation was found in some studies (4, 5, 10, 34) but not in others (1, 3, 6). The type of cardioplegia does not seem to have an effect on the incidence of postoperative AF (35–37), but in a recently published study, the total volume of cardioplegia was significantly less in patients with AF compared with patients with SR (38). A strong correlation was found between the duration of atrial activity during the cross-clamp time and the incidence of postoperative AF (39).

Off-pump vs on-pump surgery

During the last few years a growing number of coronary surgeries have been completed without using cardiopulmonary perfusion. From the theoretical standpoint, patients undergoing CABG without cardiopulmonary bypass (CPB) would not be subject to some precipitating factors of postoperative AF, i.e. atrial ischaemia, cannulation trauma to the atrium, and CPB itself (40). There is conflicting information about the incidence of postoperative AF among patients after off-pump CABG. Table I presents studies comparing postoperative AF incidence after off-pump and conventional CABG. Unfortunately most of these studies are retrospective and involve only a small number of patients.

Ascione et al. reported a prospective randomized study of 200 patients, with a postoperative AF incidence of 49% after conventional CABG, compared with 14% after off-pump CABG. The incidence of AF after conventional CABG was very high but the weakness of the study was that the use of β-blocking medication was not reported (41).

Despite few prospective studies, there are several retrospective studies looking at the effect of off-pump surgery on incidence of postoperative AF after CABG. Buffolo et al. reported a retrospective study involving 1067 patients. They also found the incidence of atrial arrhythmias significantly lower after off-pump CABG compared with conventional CABG (42). Allen et al. reported no postoperative arrhythmias in a small group of patients who underwent single vessel redo off-pump CABG with the left anterior thoracic artery (43). Subramanian et al. reported their experience of minimally invasive direct coronary artery bypass grafting (MIDCABG) (44). They used minithoracotomy, subxiphoid and lateral thoracotomy incisions, and the incidence of AF was only 8% (14/185 patients). No difference in the frequency of postoperative AF was found in a small case-controlled study after MIDCABG and conventional CABG (45). Similarly, no significant difference was found in a study comparing the incidences of AF after conventional CABG, MIDCABG and off-pump CABG (OPCABG) (46). In another study by Siebert et al., no difference was found between the incidence of AF after on-pump and off-pump CABG during ICU stay (47). There are also other negative studies, which did not reveal any difference in the incidence of AF after CABG with or without CPB (48–50). Tamis-Holland et al. compared 208 patients having MIDCABG or conventional CABG, and they concluded that the reason for low incidence of AF after MIDCABG is due to different clinical characteristics of patients compared with conventional CABG patients (51). In our opinion, current data suggest that off-pump surgery does not reduce incidence of postoperative AF as compared with on-pump surgery.

POSTOPERATIVE PREDICTORS

Some postoperative factors have been found to associate to postoperative AF after CABG. Postoperative pneumonia and mechanical ventilation longer than 24 h have been shown to be independent postoperative

Table I. *Studies comparing the incidences of postoperative AF after on-pump and off-pump CABG*

Study	Ref. no.	Total No. of patients	Type of study	On-pump AF (%)	Off-pump AF (%)	*p*-Value
Buffolo et al. 1996	(42)	1067	Retrospective, OFF-PUMP–ON-PUMP	12.6	5.5	<0.05
Allen et al. 1997	(43)	35	Retrospective, only LIMA–LAD REDO	58	0	<0.05
Cohn et al. 1999	(45)	110	Case-control, MIDCAB–CABG	20	24	NS
Saatvedt et al. 1999	(48)	704	Retrospective ON-PUMP–OFF-PUMP	36	37	NS
Ascione et al. 1999		80	Prospective randomized ON-PUMP–OFF-PUMP	38	15	<0.05
Abrey et al. 1999	(49)	781	Retrospective, OFF-PUMP–ON-PUMP	26	12	0.06
Tamis-Holland et al. 2000	(51)	209	Retrospective, MIDCABG–ON-PUMP	39	23	<0.05 but NS in multivariate
Ascione et al. 2000	(41)	200	Prospective randomized ON-PUMP–OFF-PUMP	49	14	0.001
Siebert et al. 2000	(46)	87	Retrospective ON-PUMP–OFF-PUMP	27	18	NS
Mueller et al. 2001	(50)	183	Retrospective, only LIMA–LAD	18	22	NS

AF = atrial fibrillation; CABG = coronary artery bypass grafting; LAD = left anterior descending artery; LIMA = left anterior mammarian artery; MIDCABG = minimally invasive direct coronary artery bypass grafting.

predictors of AF (6), as well as atrial pacing (5), and need of postoperative inotropic agents (7). Svedjeholm and Håkanson found that low postoperative mixed venous oxygen saturation and the need for postoperative mechanical circulatory support were independent predictors of post-CABG AF (8). In addition, a high central venous pressure at the time of admission to intensive care is predictive of a higher risk of AF (52). We think that these factors have, however, a minimal clinical value in selecting patients at high risk of postoperative AF for targeted preventive measures.

CURRENT METHODS TO PREDICT THE RISK OF POSTOPERATIVE AF

Signal-averaged P-wave ECG

Recent studies have demonstrated that signal-averaged P-wave ECG analysis is useful in identifying patients at high risk of developing AF after cardiac surgery. Specifically, abnormal atrial conduction, defined by a prolonged filtered P-wave duration in signal-averaged P-wave ECG analysis, has been shown to be an independent predictor of postoperative AF (53–58). Table II summarizes the studies of signal-averaged P-wave ECG analysis in predicting the risk of AF after cardiac surgery. In these studies the abnormal P-wave duration varied from 122 to 155 ms. Sensitivity of signal-averaged P-wave duration in identifying the patients who developed AF postoperatively was 68–86%, and specificity was 39–88%. The positive predictive value and negative predictive value varied from 34 to 76% and from 83 to 85%, respectively.

The predictive value of the signal-averaged P-wave duration is further enhanced when it is combined with ejection fraction. When P-wave duration was >140 ms and ejection fraction <40% the risk of postoperative AF was nearly nine times higher compared with the situation when both were normal (59). Similarly, the combination of P-wave duration (>155 ms) and low serum magnesium concentration (<0.7 mmol) on the first postoperative day increased the positive predictive value from 37 to 62% (55). When P-wave duration (>122.3 ms) and the presence of right coronary artery lesion were combined, the positive and negative predictive values were subsequently 81 and 76% (57).

These data seem rather consistent. Especially, when combined with some other risk factor, signal-averaged P-wave duration might have clinically significant power to select a subgroup of patients at high risk of postoperative AF. To these patients it might be, e.g. worthwhile to administrate postoperative amiodarone. The cost-effectiveness of such selection and treatment warrants further research.

Standard ECG

There are clearly conflicting data concerning the standard ECG as a tool for predicting the risk of AF after cardiac surgery. Buxton and Josephson first reported that patients developing AF after CABG had a significantly longer P-wave duration in the standard ECG (60). In a recently published study (61), the presence of prolonged P-wave duration (>100 ms in lead II) was an independent predictor of AF with 1.9-fold risk compared with a P-wave duration of less than 100 ms. The P-wave duration in both the signal-averaged ECG and in the surface ECG was prolonged in patients who had AF after CABG (62). In the latter study, a significant correlation was found between the P-wave duration in standard ECG and signal-averaged ECG. In a study published by Aytemir et al., lead II P-wave duration and left atrial enlargement in the electrocardiograph were determined from standard ECG. In multivariate analysis left atrial enlargement (relative risk 2.7-fold) but not the P-wave duration was an independent predictor of AF after CABG (57). Passman et al. found that P-wave duration in lead V1 was an independent predictor of AF after CABG (63). The age-adjusted odds ration (OR) for AF was 2.30 when P-wave duration in lead V1 was >110 ms. Tsikouris et al. measured P-wave dispersion and maximum P-wave duration on the 12-lead ECG preoperatively and on postoperative days 1–4 in patients undergoing open-heart surgery (64). They found that P-wave dispersion is greatest on days 2 and 3 and the longest atrial conduction time is greatest on day 3 after open-heart surgery, findings that coincide with the time of greatest risk of AF.

Stafford et al. analysed lead II P-wave duration, total P-wave duration, and P-terminal force in standard ECG. No significant differences were observed in any of these variables between patients who developed AF and those who did not after CABG (56). Similarly, no difference was reported on P-wave duration on standard ECG between the patients with AF and without AF after CABG in a recently published study (58).

We feel that, at the moment, an analysis of preoperative standard 12-lead ECG has no clinical value in risk stratification of postoperative AF after CABG.

Table II. *Comparison of signal-averaged P-wave studies for predicting the risk of AF after cardiac surgery*

Study	*N*	P-Duration (ms)	Specificity (%)	Sensitivity (%)
Steinberg et al. 1993	130	140	55	77
Klein et al. 1995	45	155	79	69
Hutchinson and Steinberg 1996	272	140	39	82
Zaman et al. 1997	102	155	45	86
Stafford et al. 1997	201	141	48	73
Aytemir et al. 1999	53	122	88	68
Caravelli et al. 2002	129	135	73	84

N = number of the patients studied; ms = milliseconds; P-duration = cut-off value of P-wave duration used in the study.

Heart rate variability

Two studies have evaluated heart rate variability (HRV) preceding onset of AF after CABG. Dimmer et al. found that the low frequency/high frequency (LF/HF) ratio was initially significantly lower in their AF group compared with the SR group and it was followed by a significant increase compared with the initial values in AF patients. This study showed that changes of autonomic tone rather than autonomic tone itself were important indicators before AF onset (65). Hogue et al. observed either lower or higher measures of HRV before AF after CABG, a finding consistent with divergent autonomic conditions before AF onset. They thought that in some patients heightened sympathetic tone is present before AF but in others, either higher vagal tone or dysfunctional autonomic heart rate control is present before AF onset (66). In order to find those patients at high risk of AF after CABG, postoperative assessment of HRV is not feasible. It shows the risk of AF just prior to its onset, when any prophylactic actions would be too late and, furthermore, it requires so many resources, that it is practically impossible to apply clinically.

Two studies evaluated preoperatively the risk of postoperative AF after CABG with HRV. Frost et al. analysed HRV of a 24-h preoperative Holter monitoring performed in 102 CABG patients (67). They calculated the percentage of successive RR interval differences >6% (vagal index) and found it significantly lower in patients developing AF while the overall HRV was the same between AF and SR groups. They concluded that isolated reduction in the basic vagal modulation causes an autonomic imbalance in patients prone to develop AF after CABG. Jideus et al. did not find any difference in preoperative time and frequency domain variables between the patients who went into AF and those who remained in SR (68). However, they found that a diminished circadian variation in HRV before surgery indicated propensity for AF. The above-mentioned studies were based on the 24-h monitoring of HRV. Long-term measures of HRV represent responses of cardiac autonomic regulation to challenges of daily life and a limitation to interpreting these findings is that these challenges are not controlled, the recordings are not stationary and the recording conditions cannot be standardized. These standardization problems could be solved by using an assessment of short-term HRV. In addition, in the risk assessment of post-CABG, AF long-term HRV measurement requires additional resources and, therefore, it is not clinically feasible.

We showed that a short-term preoperative analysis of HRV under standardized physiological conditions couldn't reliably identify patients at high risk of AF after CABG (69). Heart rate, standard deviation of normal-to-normal RR interval (SDNN) or square root of the mean squared differences of adjacent RR intervals (RMSSD) did not differ significantly between AF and SR groups when tested either with spontaneous or controlled breathing. None of the spectral analysis measures (total power, very low frequency power, low frequency (LF) power, and high frequency (HF) power) differed significantly either. In both groups, heart rate increased and SDNN decreased after tilting towards the upright position, but there was no statistical difference between the groups. In power spectral analysis, total power and all of its components decreased after tilting up both in AF and SR groups but there was no statistical difference between the groups. There was no statistical difference between the groups in LF/HF ratio in any of the differing conditions.

These current data suggest that preoperative HRV analysis has not any value in risk stratification of postoperative AF after CABG.

INTRAOPERATIVE SCREENING TESTS

Intraoperative testing to determine the local refractory period of a particular site in the atrium is not technically feasible (70). The value of intraoperative induction of AF has been studied in 50 patients who underwent CABG (71). The intraoperative induction of AF with alternating current had a sensitivity of 94% and a specificity of 41% for the occurrence of postoperative atrial arrhythmias. The negative and positive predictive values of the test were 93 and 47%, respectively.

We developed a new intraoperative high-rate atrial pacing to identify patients at risk of AF after CABG (72). After cannulation but before initiation of CPB, two pacing wires were placed on the lateral surface of the right atrium. The right atrium was paced with the rate of 200 beats per min for 10 s. If that did not induce AF, high-rate pacing was repeated with the rate of 250 and 300 beats per min. The high-rate atrial pacing test was performed in 80 patients undergoing CABG. High-rate atrial pacing induced AF in 27 patients (33.7%). Of the 28 patients who experienced AF during the post-operative period, 17 patients were inducible in the atrial pacing test (sensitivity 61%). Of the 52 patients who did not develop AF postoperatively, 42 patients were not inducible in the atrial pacing test (specificity 81%). Positive and negative predictive accuracy of the test were 63 and 79%, respectively.

In our experience, high-rate atrial pacing during CABG is a safe, simple and fast method with reasonable accuracy to predict postoperative AF. Further experience is, however, warranted to verify usefulness and cost-effectiveness of this method in targeting measures to prevent postoperative AF in contemporary CABG surgery.

CONCLUSIONS

Postoperative use of β-blockers significantly reduces the incidence of postoperative AF after CABG. However, identification of the patients at high risk of postoperative AF and to whom other prophylactic measures (amiodarone, atrial pacing) to prevent AF could be targeted, remains a challenge for modern heart surgery.

Several factors, most often advanced age and history of AF, have been reported to be independent predictors of AF. However, the positive predictive value or usefulness of those conventional predictors of post-operative AF in clinical practice has been low. Even attempts to build logistic regression models based on the pre- and intraoperative variables have failed to provide powerful predictors for postoperative AF after CABG.

Recently, new predictors based on new technology to analyse ECG or measure HRV have been searched for. Of those, the prolongation of P-wave duration in signal-averaged ECG looks promising. It reflects intra-atrial conduction abnormalities and thus, could predict a risk of postoperative AF. Sensitivity and negative predictive value are high, but specificity and positive predictive value remain quite low, which limits its usefulness in clinical practise. On the other hand, even detailed analysis of standard 12-lead ECG has failed to provide useful information for risk stratification. Similarly, preoperative measurement of short-term HRV has failed to identify patients at risk of postoperative AF after CABG, although changes in HRV have been documented shortly before postoperative AF.

A new method to identify the patients at high risk of postoperative AF has been developed in our centre. The diagnostic accuracy of high-rate atrial pacing during operation seems to be sufficient to identify a group of patients to whom prophylactic treatment could be proactively targeted. Further experience is, however, warranted to verify significance of this method in everyday clinical practice.

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