Predictors of atrial fibrillation after coronary artery bypass graft: a meta-analysis

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Objectives Postoperative atrial fibrillation (AF) has been associated with less favorable outcomes in patients undergoing coronary artery bypass graft surgery (CABG) and may result in increased post-operative morbidity and mortality. A systematic review and meta-analysis of published studies was conducted to examine the risk factors of occurrence of AF after CABG. Methods Using the Medline database, the Cochrane clinical trials database and online clinical trial databases, we reviewed all randomized controlled trials (RCTs) and observational studies examining the risk factors of occurrence of AF after CABG. We searched for literature published April 2009 or earlier. Results Our review identified 8 studies (observational studies), involving 14548 patients, that examined the risk factors of occurrence of AF after CABG. Although studies provide conflicting results, the overall outcomes suggest that advanced age, previous hypertension, numbers of bridge vessels may increase the occurrence of AF after CABG, while no significant difference of diabetes, preoperative myocardial infarction, and preoperative medication of β-Blocker have been observed between the AF patients and no-AF patients. Conclusions Patients with advanced age, previous hypertension and more numbers of bridge vessels had higher risk for the occurrence of AF after CABG, and perioperative medication and care must be intensified to decrease the postoperative occurrence of AF (J Geriatr Cardiol 2009; 6:162-167).

Key words atrial fibrillation; coronary artery bypass graft; postoperative; meta-analysis; predictors

Introduction

Atrial brillation (AF) is the most common complication after cardiac surgery, which has important clinical and economic implications. Coronary artery bypass graft surgery (CABG) is widely used in the treatment of patients with coronary artery disease, which provides significant relief of anginal symptoms and improves survival.1-3 Although the procedure is very successful and mature, the post-operative AF is one of the most common complications with the incidence ranges from 25% to 50%.4 Evidence show that patients with post-operative AF after CABG is associated with increased post-operative morbidity and mortality and requires additional medical and nursing time and a prolonged hospital stay even intensive care unit stay.5

Although several studies have identified various baseline predictors of postoperative AF, the pathophysiological mechanisms remain unclear. The risk factors of AF after CABG have been studied by many studies, which showed different outcomes especially in the preoperative baseline characters. Therefore, we conducted a systematic review of the evidence obtained from observational studies to evaluate the predictors of AF recurrence rates after CABG, which can provide an useful clinical evidence for determination of the coronary artery disease treatment.

Methods

We performed this analysis according to the guidelines of the Meta-analysis of Observational Studies in Epidemiology group (MOOSE).6 Studies were considered eligible for this review if they met the following criteria: (1) had prospective or observational study design, patients were assigned into AF and no-AF group, (2) described the basic characteristics of patients involved in the study, and (3) evaluated the potential predictors for the occurrence of AF after CABG. Published and unpublished studies without language restriction were included. The databases of MEDLINE (January 1966 to November 2008), EMBASE (January 1980 to November 2008), and the Cochrane Controlled Trials Register (Cochrane Library Issue 4, 2007) were searched. The following keywords: “atrial fibrillation” “coronary artery bypass graft”, “risk factors”, “outcome”, “predictors” were used to help find the articles. Titles and abstracts as well as the reference lists of all of the identified reports were also independently examined. All analyses were
conducted using Review Manager version 4.2 (Revman, The Cochrane Collaboration, Oxford, United Kingdom).

**Results**

Twenty-four records were identified by the primary literature search. However, finally 8 studies were included in this analysis, 9,26-30,35 the other 16 studies were excluded because they were either laboratory studies, review articles, or irrelevant to the current analysis. The characteristics of each study are depicted in Table 1.

**Age**

To date, age was considered as a definite factor for AF after CABG.1,16 In all 8 studies included in this study, age of AF group was significant older than that of no-AF group. The heterogeneity test showed that there is significant differences between individual studies, and the random model will be used in the analysis to decrease the selective bias (P=0.007). Overall, age was much older in patients of AF group. The weighed mean difference (WMD) between the patients with, and those without AF after CABG was 5.04 units (95% confidence interval 4.16 to 5.91, Fig. 1), and the z-score for overall effect was 11.28 (P<0.001).

**Hypertension**

Hypertension was considered to play an important role in causing AF after CABG,1,11 but there has been no clinical evidence to verify that. In the included 8 studies after systematical analysis using Review Manager version 4.2, outcomes showed that prevalence of hypertension in AF group was significant higher than that in non-AF group. Random model was also be used in the analysis because of the significant heterogeneity between individual studies (P<0.001). Overall, the odds ratio/OR was 2.80 units (95% confidence interval 1.31 to 5.97, Fig. 2), and the z-score for overall effect was 2.67 (P=0.008).

**Diabetes mellitus**

Diabetes accelerates atherosclerosis of the blood vessels, leading to coronary heart disease, but whether it is a risk factor for AF is still not confirmed.14-17 In the included 8 studies, there are 7 studies with description of diabetes in patients. Because of the significant heterogeneity between individual studies random model was be used. Meta-analysis showed that there was no significant difference in diabetes percentage in these two groups (P<0.001). Overall, the OR was 2.36 units (95% confidence interval 0.87 to 6.39, Fig. 3), and the z-score for overall effect was 1.68 (P=0.09).

**Number of bridge vessels**

There are still arguments regarding wether the numbers of bridge vessels is a risk factor for AF in patients after CABG. Some studies showed that the more bridge vessels are, the more often the post-operative AF will be. We inte-

### Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>AF group</th>
<th>Non-AF group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerim, et al</td>
<td>2000</td>
<td>36</td>
<td>63±7</td>
</tr>
<tr>
<td>Soud A, et al</td>
<td>2001</td>
<td>100</td>
<td>58</td>
</tr>
<tr>
<td>Rollo P, et al</td>
<td>2004</td>
<td>994</td>
<td>73.3</td>
</tr>
<tr>
<td>Alberto Z, et al</td>
<td>2004</td>
<td>33</td>
<td>68±8.8</td>
</tr>
<tr>
<td>Keichi, et al</td>
<td>2006</td>
<td>11</td>
<td>70±6.4</td>
</tr>
<tr>
<td>Tongtong S, et al</td>
<td>2007</td>
<td>103</td>
<td>68.7±6.2</td>
</tr>
<tr>
<td>Giovanni M, et al</td>
<td>2008</td>
<td>1601</td>
<td>68.4±6.7</td>
</tr>
<tr>
<td>Akira S, et al</td>
<td>2009</td>
<td>73</td>
<td>72.1±7.07</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>AF Mean (SD)</th>
<th>Non-AF Mean (SD)</th>
<th>Weight (%)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wang et al</td>
<td>1003</td>
<td>62.9 (7.3)</td>
<td>61.6 (7.9)</td>
<td>26.1</td>
<td>25.6</td>
</tr>
<tr>
<td>Wang et al</td>
<td>1003</td>
<td>60.1 (7.3)</td>
<td>59.8 (7.9)</td>
<td>25.6</td>
<td>25.6</td>
</tr>
<tr>
<td>Saud et al</td>
<td>1000</td>
<td>66 (6.8)</td>
<td>66.5 (6.4)</td>
<td>25.6</td>
<td>25.6</td>
</tr>
<tr>
<td>Alberto et al</td>
<td>1000</td>
<td>66 (6.8)</td>
<td>66.5 (6.4)</td>
<td>25.6</td>
<td>25.6</td>
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<tr>
<td>Rozej et al</td>
<td>1000</td>
<td>62.5 (7.3)</td>
<td>61.9 (7.9)</td>
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<td>Nakazawa et al</td>
<td>1000</td>
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<tr>
<td>Chang et al</td>
<td>1000</td>
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<td>61.9 (7.9)</td>
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<td>25.6</td>
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<tr>
<td>Akira S, et al</td>
<td>1000</td>
<td>66 (6.8)</td>
<td>66.5 (6.4)</td>
<td>25.6</td>
<td>25.6</td>
</tr>
</tbody>
</table>

**Comparison of age of patients with and without AF after CABG.** Age in AF group was significantly older than that in no-AF group (Z=11.28, P<0.001).

**Fig.1** Comparison of age of patients with and without AF after CABG. Age in AF group was significantly older than that in no-AF group (Z=11.28, P<0.001).
grate 3 of the included studies, and there is no heterogeneity between individual studies (P=0.47), the fixed model was used. The Meta-analysis showed that the patients in AF group have more bridge vessels, the WMD was 0.17 units (95% confidence interval 0.03 to 0.71, Fig. 4), and the z-score for overall effect was 2.34 (P=0.02).

Preoperative myocardial infarction

The fact that atrial ischemia may induce AF has been established by several studies. Many patients who receive CABG have history of myocardial infarction, but whether preoperative myocardial infarction may increase the risk of post-operative AF is still controversial.19-20 In 5 of the included studies, 3 showed a result that preoperative myocardial infarction is a risk factor for AF after CABG, but the overall statistical result is that there was no significant difference in the prevalence of preoperative myocardial infarction between the 2 groups. The OR was 1.16 units (95% confidence interval 0.99 to 1.36, Fig. 5), and the z-score for overall effect was 1.78 (P=0.07).

Preoperative use of β-Blocker

The preoperative use of β-blocker was considered as a risk factors in causing AF after CABG.21,22 But in our analysis the result showed that in the 5 studies with description of preoperative use of medication there was no significant difference between the 2 groups in patients with preoperative medication of β-blocker, the overall statistical result is that the OR was 1.16 units (95% confidence interval 0.82 to 1.65, Fig. 6), and the z-score for overall effect was 0.86 (P=0.39).

Discussion

Postoperative AF remains a problem following cardiac surgery, especially in CABG which is associated with an increased hospital stay and may result in hypotension, congestive heart failure, stroke and et al.1,2,23 The mechanisms underlying are unknown, and thought to be multifactorial. It has been reported that AF after CABG most often develops between the second and fifth postoperative days,24 and it may increase the risk of thromboembolic complications.

Because relating to the risk factors of occurrence of AF, clinical evidence are not definitely supported, and the preoperative medication are not reliable.25,26 This systematical review searched published studies related to the occurrence of AF after CABG, in the 24 studies of which meet our criteria and included in this analysis. In this Meta-analysis we include age, hypertension, diabetes, numbers of bridge vessels, history of AF, preoperative myocardial infarction, preoperative medication as statistical evaluated risk factors of AF after CABG. After systematical analysis using Review Manager version 4.2 we demonstrated that in Fig. 2 Comparison of prevalence of hypertension in patients with and without AF after CABG. AF group has a significantly higher percentage of hypertension patients than that in no-AF group (Z=2.67, P=0.008).

Fig. 3 Comparison of prevalence of diabetes in patients with and without AF after CABG. There was no significant difference between AF group and no-AF group in percentage of diabetes patients (Z=1.68, P=0.09).
Fig. 4 Comparison of number of bridge vessels in patients with and without AF after CABG. Number of bridge vessels in AF group was significantly more than that in no-AF group (Z=2.34, P=0.02).

Fig. 5 Comparison of preoperative myocardial infarction in patients with and without AF after CABG. There was no significant difference between AF group and no-AF group in percentage of myocardial infarction patients (Z=1.78, P=0.07).

Fig. 6 Comparison of preoperative use of β-blockers in patient with and without AF. There was no significant difference between AF group and no-AF group in patients with preoperative medication of β-blocker, (Z=0.86, P=0.39).

AF group patients were much older than patients in non-AF group, possibly because older patients have atrial structural changes affecting susceptibility to postoperative AF. And previous hypertension in AF group has a more percentage that in non-AF group, and numbers of bridge vessels is also more in AF group, but because there is only 3 studies describing the numbers of bridge vessels, and the data is also not identified, the result may not be convincing in our analysis. As to diabetes, preoperative myocardial infarction, and preoperative medication of β-blocker, there is no significant difference between the 2 groups. The preoperative medication of β-blocker was considered as an independent risk factor in causing AF after CABG, but we got a different result, which still need prospective study to verified. Previous history of AF may increase the risk of occurrence of AF after CABG is reported by many studies, but in our search studies there is no one with description of that, so this is not included in our evaluated risk factors.

There are many factors causing AF in patients undergoing CABG, including the preoperative, intraoperative and postoperative factors. The preoperative characters of patients, such as age, weight, and diseases they got has an important pact on the recurrence of AF after CABG. The recent study find that there is a significant increase in risk of AF after CABG with obese patients. Studies related to the occurrence of AF after CABG have been studied from various perspectives, including age, preoperative cardiac function, renal function, use of β-Blocker and ACE-I, hypertension, cardiac failure, cerebrovascular disease, obesity, use of CPB, history of arrhythmia, but there is no definite consensus reached. Recently, in a observational study, Giovanni Filardo and his colleagues find that in-
creased body mass index (BMI) and body surface area (BSA) are associated with a higher risk of AF after CABG and that risk for men is higher. It was demonstrated that in patients with acute myocardial infarction there seems to be an independent positive association between elevated CRP and new-onset AF which suggests the role of previous myocardial infarction and inflammation in the occurrence of AF after CABG. Inflammation was recently reported as a new molecule mechanism inducing AF, and inflammation caused by CPB in CABG surgery may increase the occurrence of postoperative AF. But there is a paper of a randomized study which reported that neither off-pump CABG nor conventional CABG affected the occurrence of postoperative AF. In the prophylaxis in preventing AF after CABG, numerous trials used prophylactic antiarrhythmic therapies, such as β-blockers, amiodarone, and sotalol, but with various magnitudes of effectiveness. This review will provide a large-scale meta-analysis statistical outcome for reference of prophylactic antiarrhythmic therapies in preventing AF after CABG.

Study limitations
Our study adds to the current understanding of risk factors of AF occurrence after CABG. However, some potential limitations may be apparent. Firstly, our included studies are not enough and requires more related studies, which may be subjected to the potential biases of such studies. Second, in converting non-normally distributed statistics to normally distributed statistics, inevitably, there may be a cause of bias in this analysis. But in conclusion, our studies may be useful for preventing AF after CABG.

References


