Study of the factors related to atrial fibrillation after coronary artery bypass grafting: A search for a marker to predict the occurrence of atrial fibrillation before surgical intervention

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Objective: Atrial fibrillation after cardiac surgery is a frequent complication. In this study we studied various factors in addition to trying to identify a marker that would predict the potential for atrial fibrillation before surgical intervention to prevent its occurrence.

Methods: We targeted 234 cases in which isolated coronary artery bypass grafting had been performed. The items for study included age, EuroSCORE, and maximum values of creatine phosphokinase–MB, troponin I, and angiotensin II after surgical intervention and preoperative values of atrial natriuretic peptide, brain natriuretic peptide, and C-reactive protein. As fibrotic markers, we measured levels of the sialylated carbohydrate antigen KL-6 in the blood, hyaluronic acid, and pyridinoline cross-linked carboxyterminal telepeptide of type I collagen C. At the time of surgical intervention, a section of the right atrium was extracted, and atrial natriuretic peptide, the sialylated carbohydrate antigen KL-6, hyaluronic acid, and pyridinoline cross-linked telopeptide of type I collagen levels were measured.

Results: Atrial fibrillation was observed in 73 (31.2%) cases, and preoperative factors that showed statistically significant differences in the occurrence of atrial fibrillation included age, EuroSCORE, and preoperative values of atrial natriuretic peptide, angiotensin II, the sialylated carbohydrate antigen KL-6, hyaluronic acid, and pyridinoline cross-linked telopeptide of type I collagen in the blood. As for intraoperative and postoperative factors, statistically significant differences were observed in the postoperative maximum of angiotensin II, atrial natriuretic peptide of the right atrium, the sialylated carbohydrate antigen KL-6, hyaluronic acid, and pyridinoline cross-linked telopeptide of type I collagen levels.

Conclusion: The fibrosis of tissue associated with age is believed to be closely related to the occurrence of atrial fibrillation after coronary artery bypass grafting. This study suggests that the preoperative values of atrial natriuretic peptide, angiotensin II, the sialylated carbohydrate antigen KL-6, hyaluronic acid, and pyridinoline cross-linked telopeptide of type I collagen in the blood are useful as a new index for the occurrence of atrial fibrillation after coronary artery bypass grafting.

Atrial fibrillation (AF) after cardiac surgery is a frequent complication, with a rate of occurrence that has been reported to range from 18.3% to 33%.[1-4] Various studies regarding the causes of its occurrence have been conducted, including advanced age,[1-7] sex,[2] body mass index,[4,5] left atrial dimensions,[5] low cardiac function,[4,6] chronic respiratory failure,[4,7] and renal dysfunction,[6] but no definitive consensus has yet been reached. However, one fact that is common among the various reports in the past is that advanced age is believed to be one of the factors. The occurrence of postoperative AF also has an effect on a patient's prognosis, resulting in an increased hospital stay, and therefore prevention of its occurrence is important. In the elderly, in particular, it is important to predict and prevent postoperative AF before surgical intervention because complications occur in many cases as a result of a lengthy hospital stay, which strongly affects the patient prognosis.

In this study related to the occurrence of postoperative AF, we examined several factors. Many reports suggesting that age has a strong effect on the occurrence of postoperative AF have been presented in the past, and we measured levels of the sialylated carbohydrate antigen KL-6, hyaluronic acid, pyridinoline cross-linked telopeptide of type I collagen (I-CTP), and atrial natriuretic peptide (ANP) as indicators of the fibrosis of tissue to prevent the occurrence thereof. We thereafter examined whether any of these factors could be used as markers for predicting the occurrence of postoperative AF before surgical intervention.

MATERIALS AND METHODS

We targeted 234 consecutive cases in which isolated coronary artery bypass grafting (CABG) had been performed in our institute, but cases of acute myocardial infarction and patients who had a history of arrhythmia were excluded from this study. CABG with cardiopulmonary bypass (CPB) was

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Abbreviations and Acronyms

ACE-I = angiotensin-converting enzyme inhibitor
AF = atrial fibrillation
ANP = atrial natriuretic peptide
ARB = angiotensin II receptor blocker
BNP = brain natriuretic peptide
CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
CRP = C-reactive protein
I-CTP = pyridinoline cross-linked telopeptide of type I collagen
OR = odds ratio
RAAS = renin–angiotensin–aldosterone system

conducted in all cases by using the intermittent aortic crossclamp method, which does not use cardioplegia. The heart rate was monitored for a week after surgical intervention, and we studied its relationship to the occurrence of AF. In this study we defined AF as either cases that continued for more than 5 minutes or cases in which treatment was required due to the hemodynamic conditions. Regarding the treatment for AF, we administered 50 mg of pilsicainide hydrochloride (Sunrythm; AsubioPharma, Daiichi Sankyo, Tokyo, Japan) parenterally for 30 minutes, and then pilsicainide hydrochloride was administered internally as a first choice and amiodarone hydrochloride (Ancaron; Aventis Pharma, Tokyo, Japan) was administered internally for cases in which no effect was achieved.

The items for study included age, sex, incidence of emergency surgical intervention, body surface area, previous myocardial infarction, EuroSCORE, use of preoperative internal medicine (β-blockers, calcium antagonists, angiotensin II receptor blockers [ARBs], and angiotensin-converting enzyme inhibitors [ACE-Is]), diabetes mellitus, hypertension, hyperlipemia, history of smoking, use of hemodialysis, cerebrovascular disorders, cardiac function (left ventricular ejection fraction), and left atrial dimensions. We measured the ANP, brain natriuretic peptide (BNP), angiotensin II, and C-reactive protein (CRP) levels in the blood before surgical intervention. We also measured KL-6, hyaluronic acid, and I-CTP levels in the blood as markers of fibrosis. At the time of surgical intervention, a section of the right atrium was extracted, and we measured the levels of ANP (radioimmunoassay method; Shionogi, Co, Ltd, Tokyo, Japan), KL-6 (enzyme-linked immunosorbent assay method; Sanko Junyaku, Tokyo, Japan), hyaluronic acid (latex agglutination turbidimetric immunoassay; Mitsubishi Kagaku Latron, Inc, Tokyo, Japan), and I-CTP (radioimmunoassay method; TFB, Inc, Tokyo, Japan) therein. Regarding intraoperative and postoperative factors, aortic crossclamp time, CPB time, number of bypasses, operative mortality, complications (including cerebral infarction, respiratory failure, acute renal failure, acute cardiac failure, mediastinitis, and gastrointestinal complications), length of hospital stay, and, in a biochemical examination of the blood, creatinine phosphokinase–MB isoenzyme, troponin I, and CRP levels were measured immediately after surgical intervention, 3 hours after surgical intervention, and on the first, second, and third days after surgical intervention. ANP, BNP, and angiotensin II levels were measured immediately after surgical intervention and on the first and third days after surgical intervention. The maximum and minimum values of ANP were also measured and compared.

Results are expressed as the mean $\pm$ standard deviation. By using parametric and nonparametric data, statistically significant differences were determined by using the Student's t test and the Fisher's exact test, respectively. We compared patients with postoperative AF and those without AF regarding patient background, preoperative blood test findings, results during and after surgical intervention, and postoperative blood test findings by using the Fisher's univariate exact test or the unpaired Student's t test. Independent predictors for postoperative AF were examined by using a multivariate analysis with a logistic regression from the parameters detected by means of univariate analysis. All analyses were conducted with SPSS software (SPSS, Inc, Chicago, Ill).

TABLE 1. Postoperative complications

	AF (+)	AF (–)
Cerebral infarction	2	0
Acute cardiac failure	4	0
Mediastinitis	2	1
Acute renal failure	2	0
Respiratory failure	1	1
Gastrointestinal complication	1	1
Hemorrhage	1	0
Total	13	3

AF, Atrial fibrillation.

RESULTS

After CABG, AF was observed in 73 (31.2%) cases, and the time of occurrence averaged 2.42 $\pm$ 1.03 days (0–5 days). The sinus rhythm in all cases improved as a result of treatment. There were 2 cases of operative mortality, and both were cases of emergency surgical intervention for patients with unstable angina. These patients had perioperative myocardial infarction and died of cardiac failure. Postoperative AF was observed in both cases. The cases of postoperative complications were as follows: 2 cases of cerebral infarction, 4 cases of acute cardiac failure, 3 cases of mediastinitis, 2 cases of acute renal failure, 2 cases of respiratory failure, 2 cases of gastrointestinal complication, and 1 case of hemorrhage. Postoperative AF was observed in 2 cases of cerebral infarction, 4 cases of acute cardiac failure, 2 cases of mediastinitis, 2 cases of acute renal failure, 1 case of respiratory failure, 1 case of gastrointestinal complication, and 1 case of hemorrhage (Table 1).

The preoperative factors that showed statistically significant differences in the occurrence of AF included age, EuroSCORE, and preoperative values of ANP, angiotensin II, KL-6, hyaluronic acid, and I-CTP in the blood (Table 2). There were no differences in the risk factors, including sex, body surface area, hypertension, preoperative internal medicine treatment, previous incidence of myocardial infarction, incidence of emergency surgical intervention, preoperative ejection fraction, left atrial dimension, BNP, and CRP (Table 2).

Regarding intraoperative and postoperative factors, there were statistically significant differences observed in operative mortality, postoperative complications, length of hospital stay, maximum angiotensin II level after surgical intervention, ANP level in the right atrium, and KL-6, hyaluronic acid, and I-CTP levels. There were also no significant differences in the maximum postoperative value of