Original Article

Off-pump CABG Attenuates Myocardial Enzyme Leakage but Not Postoperative Brain Natriuretic Peptide Secretion

Munetaka Masuda, MD, Shigeki Morita, MD, Hiroyuki Tomita, MD, Kazuhiro Kurisu, MD, Takahiro Nishida, MD, Rhuji Tominaga, MD, and Hisataka Yasui, MD

Background: Off-pump coronary artery bypass surgery is considered to be less invasive compared with a conventional coronary artery bypass surgery, while objective assessment of its invasiveness has not been well established. The grade of invasiveness of off-pump CABG was evaluated by biochemical markers released from the myocardium.

Methods: Perioperative serial changes of myocardial enzyme leakage (creatine kinase-MB isoenzyme and troponin T) were evaluated in 217 patients who underwent coronary artery bypass surgery (28 off-pump CABG patients and 189 conventional CABG patients). Serial changes of atrial natriuretic peptide and brain natriuretic peptide secretion as markers of heart failure were also evaluated in 12 off-pump CABG patients and 49 conventional CABG patients.

Results: Myocardial enzyme leakage was significantly less in the off-pump CABG group, while increase of brain natriuretic peptides secretion were similar in both groups with its peak at the first postoperative day (246±46 pg/ml in the off-pump CABG group and 312±57 pg/dl in the conventional CABG group).

Conclusions: Although off-pump CABG seems to be less invasive to the myocardial cells from the aspect of enzyme leakage, ischemic stress to the heart assessed by brain natriuretic peptide secretion was similar to that of conventional CABG. Careful monitoring and management throughout postoperative period is mandatory even in off-pump CABG procedure. (Ann Thorac Cardiovasc Surg 2002; 8: 139–44)

Key words: off-pump CABG, brain natriuretic peptide, atrial natriuretic peptide, creatinine kinase-MB, troponin T

Introduction

Coronary artery bypass grafting surgery (CABG) is one of the most effective therapies for ischemic heart disease. The advance of the techniques of cardiopulmonary bypass and myocardial protection has made this procedure safe and popular. The bloodless and motionless operative field allows surgeons to accomplish this procedure with an excellent graft patency rate. However, morbidity associated with inflammatory response caused by cardiopulmonary bypass is still a problem to be solved.[1] These days, CABG without using extra-corporeal circulation is a matter of concern for worldwide cardiac surgeons, because this technique eliminates cardiopulmonary bypass to accomplish CABG. Recently, decreased operative mortality, reduced perioperative myocardial infarction, preservation of renal function, shortened hospital stays and economical advantages of off-pump CABG have been reported.[2-8] Although off-pump CABG is considered to be less invasive compared with conventional CABG, objective assessment of its invasiveness has not been well established.

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are hormones secreted from the heart. It is well known that these peptides have good correlation with

From the Department of Cardiac Surgery, Kyushu University Hospital, Fukuoka, Japan

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Address reprint requests to Munetaka Masuda, MD: Department of Cardiac Surgery, Kyushu University Hospital, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan.

the status of heart failure and they are good predictors for a patient's prognosis.[9-12] However, little is known about their perioperative changes in CABG, especially in off-pump CABG. Thus, we have measured their serial changes combined with myocardial enzyme leakage to assess the impact of CABG on the heart in both off-pump CABG and conventional CABG patients.

Patients and Methods

Two hundred seventeen patients underwent an isolated CABG at our institutes between January 1998 and April 2000. Among them, 189 patients underwent conventional CABG, and the other 28 patients underwent off-pump CABG. Indication for off-pump CABG in our institute was still strictly limited to the patients with significant cerebrovascular disease (severe stenosis/occlusion of carotid artery or intracranial arteries) or severe atheromatous changes of the ascending aorta. Seven patients underwent off-pump CABG through a lateral-anterior small thoracotomy (LAST) because they were good candidates for the LAST procedure.

Written informed consent was obtained from all patients. Analysis of myocardial enzyme leakage was performed in all patients. The mean value of preoperative left ventricular ejection fraction was 61.8±13.3% in the conventional CABG patients and 59.5±15.0% in off-pump CABG patients. Forty nine elective conventional CABG patients and 12 elective off-pump CABG patients who had accepted informed consent for natriuretic peptides study and had no sign of heart failure were enrolled in the study of natriuretic peptides analysis.

All patients except for the LAST patients underwent the operation through a median sternotomy. In conventional CABG, after systemic heparinization at 3 mg/kg, extracorporeal circulation using a membrane oxygenator was installed combined with moderate hypothermia (32˚C in bladder temperature). Myocardial protection was achieved by administration of cold hyperkalemic crystalloid cardioplegic solution (Kyushu University solution) combined with terminal blood cardioplegia. Distal coronary anastomosis was done with continuous running suture using 7-0 or 8-0 monofilament sutures. Seventy two percent of the conventional CABG patients had revascularized arterial grafts only.

In off-pump CABG, anastomosis was done using a commercially available stabilizing foot plate after systemic heparinization (1-2 mg/kg) to achieve activated clotting time over 300 seconds. All patients had revascularized arterial grafts only.

Mean operation time was 422±67 minutes in conventional CABG patients and 247±57 minutes in off-pump patients.

Blood samples were collected at different time points. The analysis of creatine kinase-MB isoenzyme (CK-MB): was carried out before induction of anesthesia, and 0.5, 1, 3, 6, and 18 hours after aortic unclamping in conventional CABG and after the completion of the last anastomosis in off-pump CABG. The analysis of troponin T: before induction of anesthesia and the first postoperative day. The analysis of ANP and BNP: before induction of anesthesia, 0.5, 1, 3 and 6 hours and 1, 3, 7, 14 days after surgery. Blood samples for ANP and BNP analysis were placed into EDTA-coated tubes containing 500 IU/ml aprotinine. Thereafter the plasma was immediately centrifuged at 4˚C and then stored at –80˚C until analysis.

CK-MB was measured with an immunoinhibition assay using a commercial kit (Boehringer Mannheim, Germany). Troponin T was measured with an enzyme immunoassay using a commercial kit (Boehringer Mannheim, Germany). Plasma ANP and BNP concentrations were measured with a specific immunoradiometric assay using a commercial kit (Shionogi, Tokyo, Japan).

All data were expressed as the mean±standard deviation in tables and as mean±standard error in figures. An analysis of differences was appropriately done by an unpaired Student's t test on continuous variables comparisons, or by the chi square contingency tables on discrete variable comparisons. Two way ANOVA for repeated measurements was used to assess group differences with interaction of time and treatment effects. Bonferroni test was used for post-hoc multiple comparisons. Analysis were performed using Statview (Abacus Concepts, Inc., Berkeley, CA).

Results

Preoperative and operative patient characteristics are shown in Table 1 and Table 2. The distribution of patient age, gender, body weight, history of old myocardial infarction, ratio of urgent status of surgery, and ratio of redo surgery between the treatment groups was identical, while conventional CABG patients had more diseased vessels. The mean number of grafts performed in the off-pump CABG group was significantly less than that of the conventional CABG group. All off-pump CABG patients and 72% of conventional CABG patients underwent CABG

Table 1. Preoperative patient characteristics

Variables	OPCAB (n=28)	CCAB (n=189)
Age (years)	68±8	65±11
Male	71%	75%
Body weight (kg)	58±12	60±9
OMI	32%	41%
Redo	7%	6%
Diseased vessels*		
1	11	6
2	6	37
3	6	86
LMT	5	59
Surgical policy		
Elective	75%	66%
Urgent	25%	34%

OPCAB: off-pump coronary artery bypass, CCAB: conventional coronary artery bypass, OMI: old myocardial infarction, LMT: left main trunk disease
*: p<0.05

Table 2. Operative and postoperative patient characteristics

Variables	OPCAB (n=28)	CCAB (n=189)
Number of grafts*	1.5±0.6	2.6±0.9
Arterial graft only	100%	72%
CPB time (minutes)		163±57
Cross clamp time (minutes)		74±46
PMI	0%	1.6%
Stroke	0%	1.6%
Mortality	3.5%	2.6%

OPCAB: off-pump coronary artery bypass, CCAB: conventional coronary artery bypass, CPB: cardiopulmonary bypass, PMI: perioperative myocardial infarction
*: p<0.05

without usage of a vein graft.

There was one operative death in the off-pump CABG group (3.5%) and five deaths in the conventional CABG group (2.6%), and the difference was not statistically significant. The incidence of perioperative myocardial infarction, as assessed by a new onset of Q-waves on the postoperative electrocardiogram, was 0% in the off-pump CABG group and 1.6% in conventional CABG group. The incidence of permanent stroke in the perioperative period was 0% in the off-pump CABG group and 1.6% in the conventional CABG group.

Perioperative changes of CK-MB were shown in Fig. 1. The levels of CK-MB were significantly lower in the off-pump CABG group throughout the postoperative period. Postoperative peak value of CK-MB shown in Fig. 2 was also significantly lower in the off-pump CABG group (14±2 IU/L in the off-pump CABG group versus 45±3 IU/L in the conventional CABG group). The level of troponin T on the first postoperative day was also significantly lower in the off-pump CABG group (0.5±0.2 ng/ml in the off-pump CABG group versus 2.2±0.3 ng/ml in the conventional CABG group).

No significant changes were observed in the ANP level throughout the perioperative period in both groups (Fig. 3). An increase of BNP level was observed with its peak at the first postoperative day in both groups (246±46 pg/ml in the off-pump CABG group and 312±57 pg/ml in the conventional CABG group). The BNP level tends to decline more rapidly in the off-pump CABG group, albeit not significantly.

Discussion

There has been increasing interest in off-pump CABG because it is thought to be less invasive compared with

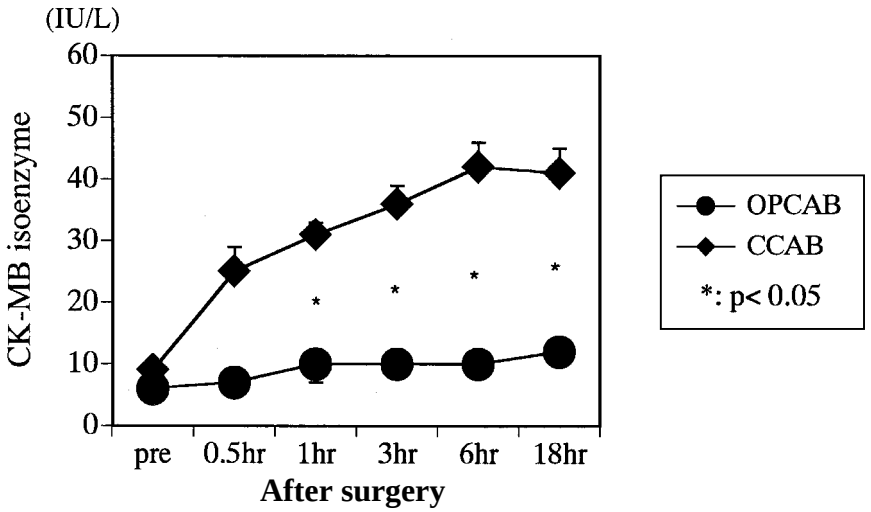

Fig. 1. Serial changes of CK-MB isoenzyme level. A closed circle indicates off-pump coronary artery bypass, and closed square indicates conventional coronary artery bypass.

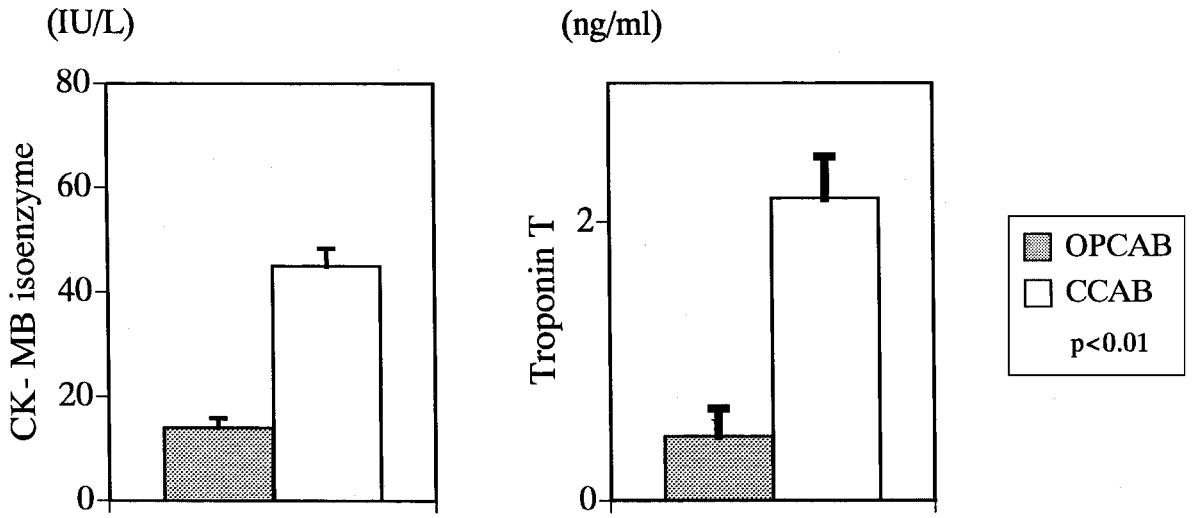

Fig. 2. Left: Postoperative peak value of CK-MB isoenzyme level. Right: Troponin T level on the first postoperative day. The dotted column indicates off-pump coronary artery bypass, and white column indicates conventional coronary artery bypass.

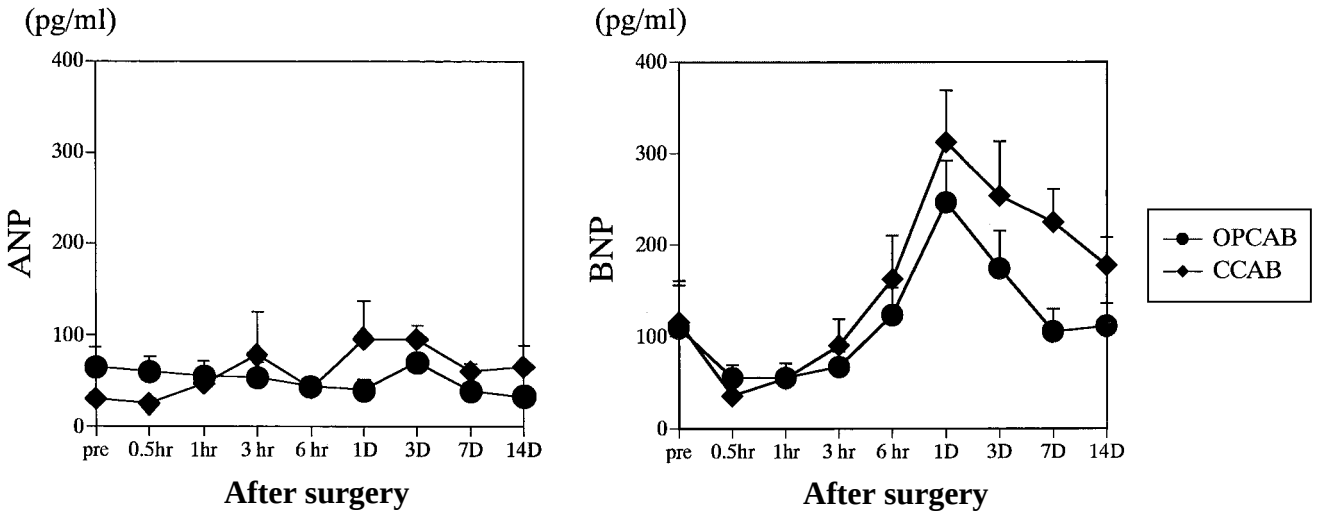

Fig. 3. Left: Serial changes of plasma atrial natriuretic peptide level. Right: Serial changes of plasma brain natriuretic peptide level. The closed circle indicates off-pump coronary artery bypass, and closed square indicates conventional coronary artery bypass.

conventional CABG using extra-corporeal circulation and cardioplegic arrest. Cardiopulmonary bypass causes systemic inflammatory reaction which may result in postoperative morbidity after cardiac surgery.[1)] The activation of complement cascade and neutrophils are a well known phenomenon after extra-corporeal circulation.[13,14)] The increase of proinflammatory cytokines and the production of oxygen free radicals[13,15)] are considered to lead to injury of organs such as the heart, lung, brain, kidney and liver. These inflammatory reactions can be attenuated by omission of cardiopulmonary bypass.

The recent development of operative techniques and instruments has made off-pump CABG a safe and effective method for revascularization of diseased coronary vessels.[2-4,7)] Reported shorter stays in intensive care units and in hospital, with off-pump CABG compared with that of conventional CABG might be the result of less morbidity of off-pump CABG derived from elimination of extracorporeal circulation.[7,8)] However, there are still some arguements about the superiority of off-pump CABG against conventional CABG in operative mortality and morbidity, such as an incidence rate of perioperative myocardial infarction and stroke,[2-4,7,8)] because many other factors affect operative mortality and morbidity. The objec-

tive assessment of less invasiveness of off-pump CABG against conventional CABG has not been fully established concerning myocardial protection, except for creatine kinase analysis,[7] thus, we have constructed a comparative study to measure the perioperative course of biochemical markers of myocardial injury.

ANP is a hormone which has a wide range of potent biological effects including diuresis, vasodilatation and inhibition of the renin-angiotensin-aldosterone system. ANP is secreted from the atria in normal humans and also from the left ventricle in patients with left ventricular dysfunction. BNP forms a peptide family with ANP, and is thought to be involved in the regulation of blood pressure and fluid volume. BNP is secreted mainly from the left ventricle in normal humans as well as in patients with left ventricular dysfunction.[16] These peptides, especially BNP, are reported to have a good correlation with left ventricular function, and are good prognostic predictors for patients with left ventricular dysfunction.[9-12,16] However, little is known about their perioperative changes in CABG, especially in off-pump CABG.

In our study, BNP, a more sensitive marker of heart failure than ANP, increased after CABG with its peak at the first postoperative day, while we could not find significant changes of ANP throughout the perioperative period up to two weeks after the operation. Our result of BNP measurements was compatible to the result of Morimoto et al.[17] who reported elevation of BNP at 12 to 48 hours after the cardiac operation. Although postoperative myocardial enzyme leakage was less in the off-pump CABG group, the postoperative peak value of BNP was similar in both the off-pump CABG group and conventional CABG group, and were more than double of its preoperative value. Because peak value of BNP was independent of myocardial enzyme leakage, peak value of BNP may reflect the left ventricular dysfunction in CABG.

Recently, we have reported the decrease of cyclic variation of integrated backscatter measured by transesophageal echocardiography during the procedure of off-pump CABG.[18] The change of cyclic variation is considered to reflect an ischemic stimuli to the myocardium. Kyriakides et al.[19] reported the elevation of the BNP level after balloon angioplasty in patients with good left ventricular function. The increase of the BNP level in off-pump CABG patients may reflect an ischemic stimuli to the myocardium caused by the short period of regional ischemia during the procedure.

The BNP level seems to return to near the preoperative level one week after the operation in the off-pump CABG group, while the elevation of BNP level lasted longer in the conventional CABG group, albeit not significantly. Morita et al.[20] reported two patterns of time course of the BNP level in patients with acute myocardial infarction: monophasic and biphasic patterns. The second peak of the BNP level occurred 4 to 7 days after onset of infarction. The patients with a the biphasic pattern were associated with a higher peak of CK-MB isoenzyme than those with the monophasic pattern. The late phase of the BNP change may reflect the myocardial cell damage which is correlated with myocardial enzyme leakage, although further examination is required to get a definitive conclusion.

Because of our strict indications of off-pump CABG in the selected patients, this study is not a randomized or patient matched study. We also have not been convinced of the long term superiority of off-pump CABG against conventional CABG, however, we may conclude that off-pump CABG is a less harmful procedure to the myocardial cells compared with conventional CABG. Although damage of myocardial cells assessed by enzyme leakage was less in the off-pump CABG, ischemic stimuli to the myocardium assessed by the increase of BNP in the early postoperative period was similar in off-pump CABG and in conventional CABG. Careful monitoring and management throughout the postoperative period is mandatory even in off-pump CABG.

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