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Release of Brain Natriuretic Peptide during the Perioperative Period of Cardiac Surgery

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Brain natriuretic peptide (BNP) is well known as a cardiac hormone. To examine the release of BNP in patients undergoing cardiac surgery with cardiopulmonary bypass and to investigate the relationships between plasma BNP concentrations and various clinical parameters, we measured the arterial plasma BNP level in 17 consecutive adult patients during the perioperative period, and compared it with the level from another cardiac hormone, atrial natriuretic peptide (ANP). The mean preoperative plasma BNP level (baseline) was 63.8 ± 34.4 pg/mL (mean ± SD). A slight decrease in the mean plasma BNP level was observed during cardiopulmonary bypass (CPB) surgery. After the cessation of CPB, however, the mean plasma BNP level gradually increased, and a significant increase was observed 12, 24 and 48 h after the cessation of CPB (mean ± SD; 149.5 ± 43.0 pg/mL, 175.2 ± 93.6 pg/mL and 146.2 ± 59.4 pg/mL, respectively; $P < 0.01$, $P < 0.01$ and $P < 0.01$, respectively). The mean value 3 weeks after the operation was similar to that before the operation. The plasma ANP levels did not significantly change during the same time course. The plasma BNP as opposed to the ANP concentration 12 h after CPB significantly correlated with the cardiac index ($r = -0.52$, $P < 0.05$), current injection rate of dopamine hydrochloride ($r = 0.51$, $P < 0.05$), aortic crossclamp time ($r = 0.55$, $P < 0.05$) and peak postoperative serum creatine phosphokinase level ($r = 0.82$, $P < 0.01$). We conclude that plasma levels of BNP are markedly elevated in the acute phase after cardiac surgery requiring bypass and reflect the left ventricular function at the same time. Furthermore, myocardial damage due to ischemia may participate in the mechanism of synthesis and secretion of BNP.

Key words: atrial natriuretic peptide; brain natriuretic peptide; cardiac surgery; cardiopulmonary bypass

The heart does not only play the role of a pump, but also as an important endocrine organ that secretes 2 natriuretic peptides. One of these peptides is atrial natriuretic peptide (ANP), which is primarily derived from the atrium (Arai et al., 1988; Ogawa et al., 1991). The other is brain natriuretic peptide (BNP), which was originally isolated from the porcine brain (Sudoh et al., 1988), and subsequently found in the heart (Kambayashi et al., 1990). A higher concentration of BNP is present in the heart rather than in the brain (Ogawa et al., 1990), and BNP is known as a novel cardiac hormone that is mainly synthesized in, and secreted from, the ventricle (Mukoyama et al., 1991). These 2 cardiac hormones perform biologic actions including natriuresis, diuresis, vasorelaxation and inhibition of renin and aldosterone secretion (Nakao et al., 1992). Although the physiologic plasma level of BNP is lower than that of ANP, it markedly increases along with the severity of congestive heart failure (CHF) and

Abbreviations: ANP, atrial natriuretic peptide; AP; angina pectoris; AR, aortic valve regurgitation; AS, aortic valve stenosis; ASD, atrial septal defect; AXCl, aortic crossclamp; BNP, brain natriuretic peptide; CHF, congestive heart failure; CPB, cardiopulmonary bypass; CPK, creatine phosphokinase; LA, left atrial; MR, mitral valve regurgitation; mRNA, messenger RNA; MS, mitral valve stenosis; TR, tricuspid valve regurgitation

Table 1. Clinical variables and patient demographics

Patient No.	Age (year)	Gender	Diagnosis	Procedure	Time (min) AXCl	Time (min) CPB
1	42	Male	MS	MVR	64	105
2	73	Female	MS, atrial fibrillation	MVR	61	100
3	51	Male	MS, atrial fibrillation	MVR	57	88
4	58	Female	MR, TR	MVR, tricuspid annuloplasty	148	231
5	52	Female	MR, atrial fibrillation	MVR, maze operation	151	217
6	69	Female	MR	MVR	90	203
7	58	Male	AP	Coronary artery bypass grafting	74	118
8	76	Female	AS, AP	AVR, coronary artery bypass grafting	169	202
9	63	Female	Ebstein's anomaly	ASD repair, tricuspid annuloplasty	72	106
10	66	Male	AR	AVR	75	110
11	52	Male	AP	Coronary artery bypass grafting	111	197
12	52	Female	ASD	ASD repair	30	48
13	60	Female	AR	AVR	68	91
14	59	Male	MR, atrial fibrillation	MVR, maze operation	117	216
15	51	Male	AS	AVR	86	114
16	54	Male	AP	Coronary artery bypass grafting	117	186
17	73	Female	LA myxoma, atrial fibrillation	Resection	80	185

AP, angina pectoris; AR, aortic valve regurgitation; AS, aortic valve stenosis; ASD, atrial septal defect; AVR, aortic valve replacement; AXCl, aortic crossclamp; CPB, cardiopulmonary bypass; LA, left atrial; MR, mitral valve regurgitation; MS, mitral valve stenosis; MVR, mitral valve replacement; TR, tricuspid valve regurgitation.

exceeds the plasma ANP concentration in severe cases (Mukoyama et al., 1990, 1991; Yoshida et al., 1991). Previous studies have shown changes in plasma ANP concentrations associated with cardiac surgery (Greeley et al., 1986; Hedner et al., 1986; Nicklas et al., 1986). However, changes in plasma BNP in adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) have not been identified. In this study, we investigated the changes in plasma BNP during the perioperative period of cardiac surgery and the relationships between plasma BNP concentrations and various clinical parameters.

Subjects and Methods

Patients

After approval by the local ethics committee, 17 consecutive adult patients (8 males and 9 females) (Table 1) who were undergoing cardiac surgery with CPB were prospectively selected for the study. Their ages ranged from 42 to 76 years (mean ± SD; 59.4 ± 9.5 years). The preoperative diagnosis included mitral valve regurgitation (MR) in 3 patients, mitral valve stenosis (MS) in 3, angina pectoris (AP) in 3, aortic valve regurgitation (AR) in 2, aortic valve stenosis (AS) in 1, MR and tricuspid valve regurgitation (TR) in 1, AS and AP in 1, atrial septal defect (ASD) in 1, Ebstein's anomaly in 1 and a left atrial (LA) myxoma in 1. The surgical procedure and length of aortic crossclamp (AXCl) and CPB are summarized in Table 1. There were no patients with metabolic diseases or primary lung diseases. Preoperative routine biochemical examinations for liver and renal function revealed no abnormalities in any patients.

Intraoperative anesthetic management was uniform for all patients, and the operation was performed through median sternotomy. The superior and inferior vena cava and ascending aorta were cannulated separately to institute the bypass circuit. The circuit was primed with 800 mL of Ringer's lactate solution, 1000 mL of hydroxyethylated starch and 20% D-mannitol (4 mL/kg body weight). Mannitol also was

added to the circuit (2 mL/h/kg body weight) during the CPB. Heparin (2.5 mg/kg body weight) was administered to maintain an activated clotting time of more than 400 s during CPB. The CPB flow used during AXCl was generated with a roller pump, motor control (model 6501) (PEMCO Inc., Cleveland, OH) at a pump flow rate of 2.2 L/min per square meter of body surface area. In addition to moderate systemic hypothermia, a cold blood cardioplegic solution was administered continuously via the aortic root or coronary sinus. Oxygenation was provided by a membrane oxygenator in all cases. Protamine sulfate was administered at a ratio of 1:1 to the total heparin dose to neutralize the effects of heparin following termination of CPB.

Plasma electrolytes were maintained within the normal range during the study. Serum creatine phosphokinase (CPK) was measured by an autoanalyzer immediately at the end of the operation, and then 6, 12, 24, 36, 48 and 72 h after the operation by the autoanalyzer. After weaning the patient from CPB, dopamine hydrochloride was administered as needed to achieve a systolic arterial pressure greater than 90 mmHg.

Hemodynamic measurements

Hemodynamic measurements included the heart rate, systemic arterial blood pressure, central venous pressure, pulmonary artery blood pressure, pulmonary capillary wedge pressure and cardiac output. A balloon-tipped thermodilution catheter, Swan-Ganz thermodilution catheter (model 93A-171H-7F or 746H-8F) (Baxter, Irvine, CA) was inserted via the jugular vein or the femoral vein and was positioned in the pulmonary artery, and a cannula was placed in the radial artery or the femoral artery. Heart rate was monitored throughout the examination by standard electrocardiographic leads, and blood pressures were measured by a transducer (model JH-180H) (Nihon Kohden, Tokyo, Japan), color memory scope (model VM-185G) (Nihon Kohden), controller (model RMC-1200M) (Nihon Kohden), bedside monitor (model BSM-8500) (Nihon Kohden) and thermal array recorder (model WS-180G) (Nihon Kohden). Cardiac output was measured by the thermodilution method. All hemodynamic measurements were done at the following times: i) before the operation; ii) 30 min after AXCl (during CPB); iii) 1 h after; iv) 6 h after; v) 12 h after; vi) 24 h after and vii) 48 h after cessation of CPB; and viii) 3 weeks after the operation. Other hemodynamic parameters were calculated using standard formulas. Preoperative left ventriculography was performed to determine the left ventricular end-diastolic and end-systolic volumes and left ventricular ejection fraction.

Blood sampling and measurements of plasma BNP and ANP concentrations

At the same time as the hemodynamic measurements were taken, arterial blood samples for measurements of plasma BNP concentration were drawn from a peripheral artery. For measurements of plasma ANP concentrations, peripheral arterial blood samples were drawn at the following times: i) before the operation; ii) 30 min after AXCl (during CPB); iii) 12 h after cessation of CPB and iv) 3 weeks after the operation. Furthermore, we examined plasma concentrations of BNP following the induction of anesthesia and the systemic administration of heparin and protamine sulfate in 5 of 17 patients in this study. The plasma BNP concentrations 15 min after the induction of general anesthesia and 5 min following the administration of heparin and protamine were measured. The samples were immediately placed into prechilled tubes containing EDTA sodium (5 mmol/L) and aprotinin (0.15 mmol/L), and centrifuged at 3000 rpm (4˚C) for 10 min. The plasma samples were then stored at –20˚C until assays could be performed. Plasma concentrations of ANP and BNP were determined using immunoradiometric assay kits, SHIONORIA ANP and SHIONORIA BNP (Shionogi, Osaka, Japan). Both kits include 2 kinds of monoclonal antibodies. One monoclonal antibody, coated on beads, recognizes the carboxyl terminus of the natriuretic peptide. The other antibody, labeled with iodine 125, recognizes the ring

portion of the natriuretic peptide. One hundred microliters of plasma were incubated with the 2 antibodies at 4˚C for 24 h. After washing, radioactivity in the beads was measured with a γ scintillation counter. The recovery of BNP during extraction was 104% as assessed by calculating the recovery of known quantities of standard BNP added to plasma. The antibody used in this study exhibited cross-reactivity of 100% with human BNP (4-32, 7-32, 10-32), and did not cross-react with human BNP (10-26) without the carboxyl terminus or human BNP (27-32) without the ring portion. The antibody did not cross-react with α- and β-human ANP, human endothelin, human angiotensin I, vasopressin and human vasoactive intestinal peptide. The intraassay and interassay coefficients of variation were 8.6 and 6.4%, respectively. The effect of hemodilution during CPB on plasma BNP concentration was corrected by the formula: corrected BNP concentration = measured BNP concentration during CPB × (hematocrit before the operation/hematocrit during CPB).

Statistical analysis

Results were expressed as mean ± SD. Comparisons of plasma natriuretic peptide levels at different times were performed by an analysis of variance with Scheffe's *F* correction. Correlations between natriuertic peptide concentrations and clinical or hemodynamic parameters were assessed by linear regression analysis. Significance was accepted at a *P* value less than 0.05.

Results

The total CPB time ranged from 48 to 231 min (mean: 148.1 ± 57.9 min) and the AXCl time ranged from 30 to 169 min (mean: 92.4 ± 37.7 min). The minimum hematocrit during CPB ranged from 18.0 to 24.2% (mean: 20.8 ± 2.0%) and the minimum rectal temperature ranged from 27.7 to 33.2˚C (mean: 29.2 ± 1.4˚C). All patients recovered without incident and had no significant postoperative complications.

Changes in BNP and ANP

The mean corrected preoperative plasma BNP level (baseline) was 63.8 ± 34.4 pg/mL. A slight decrease in the mean plasma BNP and ANP levels (Table 2, Fig. 1) was observed 30 min after AXCl during CPB. After the cessation of CPB, however, the mean plasma BNP level gradually increased, and a significant increase (in the mean plasma BNP levels) was observed 12, 24 and 48 h after the cessation of

Table 2. Perioperative changes in BNP and ANP levels

	Plasma level corrected for hemodilution				BNP/ANP ratio	
	BNP (pg/mL)		ANP (pg/mL)		Range	Mean ± SD
	Range	Mean ± SD	Range	Mean ± SD		
Before operation	15–140	63.8 ± 34.4	15–280	79.4 ± 85.1	0.2–2.3	1.2 ± 0.7
30 min after AXCl	4–270	55.8 ± 58.1	19–203	52.2 ± 45.4	0.1–2.9	1.3 ± 0.7
1 h after CPB cessation	11–365	79.4 ± 80.1	ND	ND	ND	ND
6 h after CPB cessation	36–200	89.5 ± 42.8	ND	ND	ND	ND
12 h after CPB cessation	117–272	149.5 ± 43.0**	17–248	67.6 ± 63.5	0.5–11.3	4.1 ± 3.1**
24 h after CPB cessation	75–498	175.2 ± 93.6**	ND	ND	ND	ND
48 h after CPB cessation	65–263	146.2 ± 59.4**	ND	ND	ND	ND
3 weeks after operation	41–220	83.5 ± 45.1	22–33	75.0 ± 78.3	0.6–3.5	1.3 ± 0.8

ANP, plasma level of atrial natriuretic peptide corrected for hemodilution;AXCl, aortic crossclamping; BNP, plasma level of brain natriuretic peptide corrected for hemodilution; CPB, cardiopulmonary bypass; ND, not determined.

**$P < 0.01$ versus preoperative value.

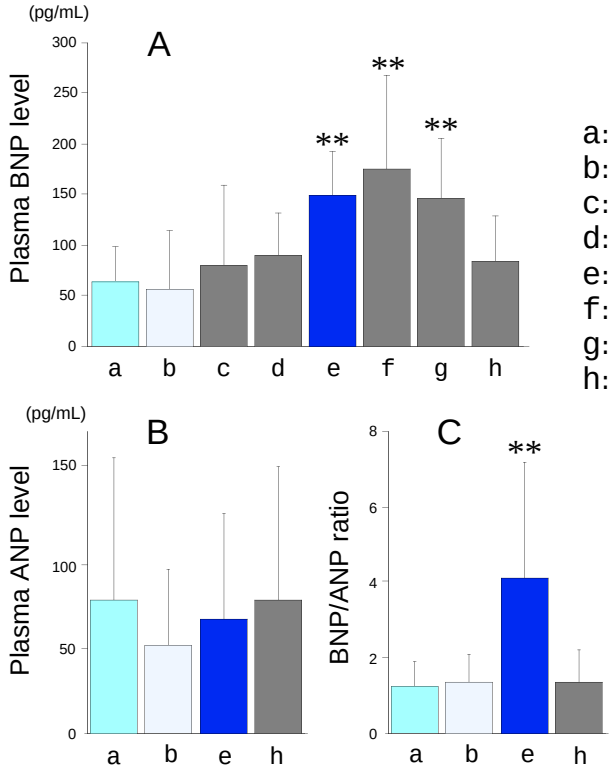

Fig. 1. Changes in plasma levels of (**A**) BNP, (**B**) ANP and (**C**) BNP/ANP ratio during the perioperative period in 17 patients undergoing CPB. Results are expressed as mean ± SD. $^{**}P < 0.01$ versus preoperative value.

CPB (149.5 ± 43.0 pg/mL, 175.2 ± 93.6 pg/mL and 146.2 ± 59.4 pg/mL; $P < 0.01$, $P < 0.01$ and $P < 0.01$, respectively). The mean value 3 weeks after the operation was similar to that before the operation. The corrected preoperative plasma level of ANP was 79.4 ± 85.1 pg/mL and there were no significant changes in the mean plasma ANP levels 12 h after CPB or 3 weeks after the operation. The mean preoperative BNP/ANP ratio was 1.2 ± 0.7 and did not significantly change during CPB. However, the mean ratio 12 h after the cessation of CPB (4.1 ± 3.1) was significantly higher than the mean preoperative ratio ($P < 0.01$). The mean ratio 3 weeks after the operation was not significantly above the mean preoperative ratio. These changes in the BNP/ANP ratio were similar to those in the BNP level.

Furthermore, we examined the plasma levels of BNP following the induction of anesthesia and the systemic administration of heparin and protamine sulfate in 5 of the 17 patients in this study. The corrected plasma BNP level 15 min after the induction of general anesthesia ranged from 13 to 58 pg/mL (mean: 45.3 ± 23.7 pg/mL), and did not significantly change (as opposed to the preoperative level). The plasma BNP levels 5 min after the administration of heparin and protamine were 11 to 58 pg/mL (mean: 39.2 ± 17.6 pg/mL) and 13 to 66 pg/mL (mean: 33.4 ± 24.2 pg/mL), respectively, and did not significantly differ from the levels 15 min after the induction of anesthesia or 30 min after AXCl (during CPB), respectively.

Correlations between plasma natriuretic peptide concentrations and hemodynamic or clinical data

Preoperatively, the plasma BNP concentration correlated significantly with the left ventricular ejection fraction ($r = –0.727$; $P = 0.017$); however, there was no significant correlation between the plasma BNP concentration or any other hemodynamic parameter assessed (Table 3). The preoperative plasma ANP concen-

Table 3. Correlations between plasma natriuretic peptide concentrations and preoperative hemodynamic parameters

Hemodynamic parameter			BNP		ANP	
Variable		Value	*r*	*P*	*r*	*P*
Heart rate	(beats/min)	70 ± 13	0.064	0.808	0.150	0.566
Mean systemic arterial pressure	(mmHg)	93 ± 21	0.165	0.540	0.037	0.893
Central venous pressure	(mmHg)	6 ± 4	0.179	0.507	0.165	0.541
Mean pulmonary arterial pressure	(mmHg)	23 ± 12	0.041	0.877	0.386	0.126
Pulmonary capillary wedge pressure	(mmHg)	13 ± 7	0.143	0.596	0.362	0.168
Left ventricular end-diastolic pressure	(mmHg)	14 ± 8	–0.154	0.634	0.064	0.843
Cardiac index	(L/min/m^2)	2.8± 0.4	–0.125	0.646	–0.606	0.013*
Stroke volume index	(mL/m^2)	46 ± 21	0.077	0.777	–0.246	0.359
Systemic vascular resistance	(dyne·s/cm^5)	1730 ± 590	0.074	0.803	0.449	0.107
Pulmonary vascular resistance	(dyne·s/cm^5)	168 ± 128	–0.027	0.928	0.015	0.959
Left ventricular end-systolic volume index	(mL)	31 ± 16	0.596	0.069	–0.021	0.954
Left ventricular end-diastolic volume index	(mL)	78 ± 39	0.258	0.472	–0.262	0.464
Left ventricular ejection fraction	(%)	60 ± 13	–0.727	0.017*	–0.468	0.172

ANP, atrial natriuretic peptide; BNP, brain natriuretic peptide.
All values are expressed as mean ± SD.
* $P < 0.05$.

tration correlated significantly with cardiac index ($r = –0.606$; $P = 0.013$), but did not significantly correlate with other parameters (Table 3).

The plasma BNP concentration 12 h after the cessation of CPB correlated significantly with the cardiac index at this time ($r = –0.520$; $P = 0.032$), the injection rate of dopamine hydro-

Table 4. Correlations between plasma natriuretic peptide concentrations and hemodynamic or clinical data 12 h after cessation of CPB

Hemodynamic or clinical data			BNP		ANP	
Variable		Value	*r*	*P*	*r*	*P*
Heart rate	(beats/min)	92 ± 10	–0.419	0.106	–0.222	0.428
Mean systemic arterial pressure	(mmHg)	77 ± 13	–0.397	0.128	–0.450	0.092
Central venous pressure	(mmHg)	11 ± 3	–0.315	0.235	–0.148	0.599
Mean pulmonary artery pressure	(mmHg)	21 ± 5	–0.146	0.589	0.336	0.222
Pulmonary capillary wedge pressure	(mmHg)	11 ± 4	0.053	0.845	0.370	0.175
Cardiac index	(L/min/m^2)	3.0± 0.9	–0.520	0.032*	0.017	0.949
Stroke volume index	(mL/m^2)	33 ± 9	–0.325	0.219	0.004	0.988
Systemic vascular resistance	(dynes·s/cm^5)	1330 ± 656	0.397	0.128	0.044	0.876
Pulmonary vascular resistance	(dynes·s/cm^5)	195 ± 89	0.204	0.449	0.192	0.494
Injection rate of DA	(μg/min/kg)	5.6± 1.8	0.510	0.036*	0.412	0.113
AXCl time	(min)	92 ± 38	0.547	0.023*	–0.106	0.696
Cardiopulmonary bypass time	(min)	148 ± 58	0.204	0.432	–0.277	0.300
Operation time	(min)	423 ± 109	0.223	0.390	0.067	0.805
Bleeding volume during operation	(mL)	924 ± 604	0.061	0.817	0.121	0.655
Peak CPK concentration	(mg/dL)	1035 ± 756	0.824	< 0.0001**	0.477	0.062

ANP, atrial natriuretic peptide; AXCl, aortic crossclamp; BNP, brain natriuretic peptide; CPK, creatine phosphokinase; DA, dopamine hydrochloride.
All values are expressed as mean ± SD.
* $P < 0.05$.
** $P < 0.01$.

chloride at this time (r = 0.510; P = 0.036), the AXCl time (r = 0.547; P = 0.023), and the peak postoperative serum creatine phosphokinase (CPK) level (r = 0.824; P < 0.0001) (Table 4, Fig. 2). However, there was no significant correlation between the plasma ANP concentration or any of these parameters (Table 4, Fig. 2). The plasma BNP concentration 12 h after CPB also correlated significantly with the preoperative plasma BNP concentration (r = 0.563; P = 0.019) (Fig. 3).

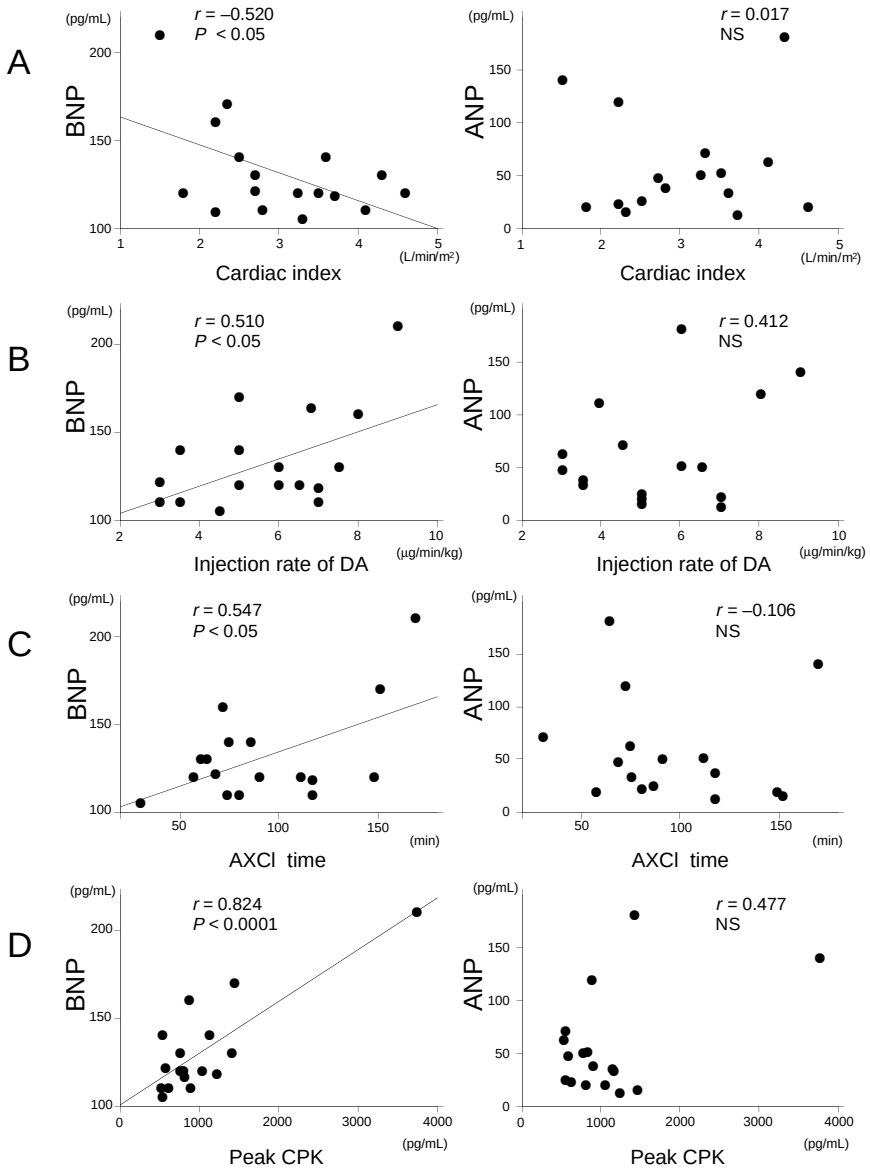

Fig. 2. Correlations between the plasma natriuretic peptide concentration at 12 post-CPB h and (**A**) the cardiac index (L/min/m^2) at this time; (**B**) the injection rate of dopamine hydrochloride (DA) at this time (μg/min/kg); (**C**) the aortic crossclamp (AXCl) time (min) and (**D**) the peak creatine phosphokinase (CPK) concentration (mg/dL). NS, not significant.

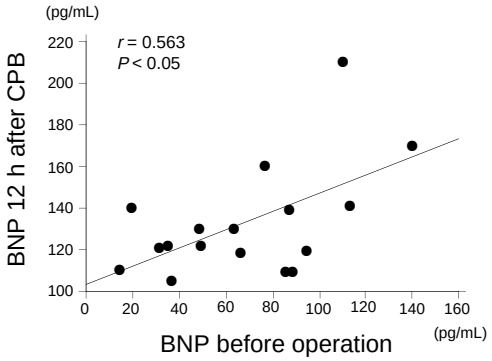

Fig. 3. Correlation of plasma BNP concentration between 12 h after CPB and before the operation.

Discussion

Preoperatively, plasma BNP and ANP concentrations negatively correlated significantly with the left ventricular ejection fraction and cardiac index, respectively. These results indicate that plasma BNP and ANP concentrations reflect cardiac function, and are consistent with findings in previous reports (Yoshimura et al., 1993; Yasue et al., 1994; Kohno et al., 1995; Matsumoto et al., 1995).

In vitro and in vivo, BNP and ANP are rapidly synthesized in, and secreted from, cardiac myocytes by acute stimulation, such as volume expansion (Wambach and Koch, 1995), atrial stretch (Bilder et al., 1986), vasoactive agents (Hu et al., 1988; Suzuki et al., 1992), cardiac pacing (Naruse et al., 1994), percutaneous balloon mitral valvuloplasty (Waldman et al., 1988) and exercise (Tanaka et al., 1986). These 2 hormones disappear rapidly from plasma because of their short half lives (Nakao et al., 1987; McGregor et al., 1990; Yoshimura et al., 1991; Kohno et al., 1992; Hashimoto et al., 1994). Therefore, plasma levels of BNP and ANP can be influenced by some stimuli. In this study, a slight decrease in the mean plasma BNP and ANP levels was observed 30 min after AXCl (during CPB). Flezzani and coworkers (1988) have reported that CPB does not appear to have an appreciable effect on ANP levels, and mentioned that neither hemodilution nor unloading of the atria caused by the institution of CPB alters ANP levels. Others have shown that there is a specific influence of temperature on ANP release, and that a reduction in temperature produces a marked decrease in ANP release in vitro (Bilder et al., 1986). In our study, the nonsignificant change in BNP and ANP levels during CPB may be due in part to a reduction in both synthesis-secretion and the clearance of these 2 natriuretic peptides because of cooling of the heart, cardiac arrest and generalized hypothermia during CPB. In addition, it has been reported that anesthesia has no significant effects on plasma ANP levels during CPB (Curello et al., 1991). In the present study, we also found that general anesthesia did not significantly affect plasma BNP levels. Furthermore, the peptide level during CPB was not changed by intraoperative surgical stress. It is possible that the suitable control of hemodynamics by anesthesia and use of vasoactive drugs may indirectly affect hormone levels, although systemic heparinization with subsequent neutralization did not significantly change plasma BNP levels in this study. Kharasch and coworkers (1989) have reported that systemic heparinization prior to CPB and neutralization of heparin following CPB also does not affect circulating ANP levels. In the present study, the plasma BNP levels expressed reflect a correction for hemodilution. Thus, we think that systemic heparinization and neutralization of heparin in cardiac surgery with CPB do not markedly affect the release of BNP.

The present study revealed that the plasma levels of BNP were significantly elevated 12, 24, and 48 h after the cessation of CPB, but that the plasma levels of ANP did not show any significant change. This difference in characteristic between BNP and ANP may have been produced by the differences in the mechanisms of synthesis and secretion or the difference in production between the 2 natriuretic peptides. For example, it has been reported that BNP messenger RNA (mRNA) is degraded more rapidly than ANP mRNA, and that BNP gene expression is regulated differently from ANP gene expression, while BNP gene expression may be turned on and off more rapidly than ANP gene expression (Nakao et al., 1992). In

addition, BNP is secreted predominantly from the ventricle in contrast to ANP, which is mainly derived from the atrium.

In this study, furthermore, the plasma BNP as opposed to the ANP concentration 12 h after the cessation of CPB correlated significantly with the cardiac index and injection rate of dopamine hydrochloride. We used the cardiac index and injection rate of dopamine hydrochloride as indices of postoperative cardiac function, that is, we considered a low cardiac index and a high injection rate of dopamine hydrochloride as indicating a state of heart failure. These findings indicate that the plasma level of BNP is markedly elevated in the acute phase after open heart surgery performed with CPB, which reflects the left ventricular function more appropriately than does the ANP concentration. In previous studies, it has been documented that the plasma BNP concentration markedly increases along with the severity of CHF, exceeding the plasma ANP concentration in severe cases (Mukoyama et al., 1990, 1991; Yoshida et al., 1993; Matsumoto et al., 1995). We suggest that the measurement of plasma BNP concentration is valuable for the estimation of postoperative cardiac functions in patients treated with open heart surgery.

It was also demonstrated that plasma ANP concentrations correlate with atrial pressures (Bates et al., 1986; Raine et al., 1986; Richards et al., 1986; Rodeheffer et al., 1986; Hirata et al., 1987), and that the most significant physiologic stimulus for the secretion of ANP is the atrial stretch (Dietz, 1984; Lang et al., 1985). Concerning BNP, it was reported that the plasma concentration is elevated in patients with hypertension, ventricular hypertrophy (Kohno et al., 1994, 1995), CHF (Yoshimura et al., 1993; Yasue et al., 1994; Matsumoto et al., 1995) and various cardiovascular diseases (Richards et al., 1993; Naruse et al., 1994). Very recently, it has been reported that exercise-induced increases in BNP and ANP are observed in patients with CHF (Matsumoto et al., 1995). Previous reports have shown that the plasma BNP level is more prominently elevated than the ANP level in patients with acute myocardial infarction (Mukoyama et al., 1991). This raises the possibility that the synthesis and secretion of BNP could be stimulated by myocardial necrosis and/or local mechanical stress on ventricular cardiomyocytes. Current studies reveal that the plasma BNP and not the ANP level is significantly elevated in the acute phase after cardiac surgery undergoing CPB, and that the elevated BNP concentration correlates significantly with the AXCl time and peak postoperative CPK level. The elevated BNP concentration did not significantly correlate with other parameters, such as duration of the CPB, duration of the operation, and bleeding volume during the operation. It is also well-known that the duration of AXCl and peak CPK level following cardiac surgery are indices of myocardial damage due to ischemia in patients treated with cardiac surgery. In the present study, there were no patients suffering from perioperative myocardial infarction. These facts suggest that BNP may be synthesized and secreted by the stimulus of myocardial damage due to ischemia during AXCl.

As mentioned above, the plasma BNP level reflects left ventricular dysfunction. In the present study, the plasma BNP concentration in the acute postoperative phase correlates with the preoperative plasma BNP concentration. This finding suggests that the severity of heart failure in the acute phase after cardiac surgery can be predicted by the preoperative plasma BNP concentration. Preoperative high plasma BNP concentration may be a risk factor for open heart surgery. A more definite conclusion about the estimation of prognosis after cardiac surgery will require further studies.

In conclusion, the present study has revealed that the plasma BNP level is markedly elevated in the acute phase following open heart surgery with CPB in adults, and that plasma BNP concentrations reflect current left ventricular functioning more appropriately than ANP concentrations. We hypothesize that injury of cardiomyocytes due to ischemia may participate in mechanisms of the synthesis and secretion of BNP.

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