J Cardiol 2004 Jul; 44(1): 1–11

Influence of Paroxysmal Atrial Fibrillation Attack on Brain Natriuretic Peptide Secretion

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Abstract

Objectives. Plasma brain natriuretic peptide(BNP)concentration is higher during atrial fibrillation(Af) than sinus rhythm, based on studies of electrical defibrillation treatment of patients with chronic Af. However, the change in paroxysmal atrial fibrillation(PAf)is not well known. This study investigated such changes and the relationship between BNP and Af.

Methods. BNP levels were successfully measured at three time points: before Af attack, during Af attack, and after(spontaneous or pharmacological)termination of 68 consecutive Af attacks in 35 outpatients with PAf(23 men, 12 women, mean age 70.4±9.6 years). BNP was measured by immunoradiometric assay.

Results. BNP(median[quartiles])during PAf was increased by 66[25, 120]pg/m*l*(2.4-fold)compared to during sinus rhythm($p < 0.0001$), and fell to the former level after return to sinus rhythm(before attack = 39[18, 70], during attack = 102[52, 205], after attack = 35[20, 67]). BNP increased in 55(81%) of 68 attacks, did not change(within ±20 pg/m*l*)in 11(16%), and decreased in 2(3%). BNP was already elevated immediately(within 4 hr)after onset of Af, and BNP elevation(Δ BNP)showed no significant relationship with the time elapsed after onset. During the Af attack, 41% of PAf patients were asymptomatic although BNP increased significantly.

Conclusions. These results suggest that elevated amounts of BNP during Af are released from secretory granules in the atrium, and BNP elevation of unknown cause may be attributed to the presence of asymptomatic Af. Cardiac function evaluation using BNP during Af requires special consideration, unlike during sinus rhythm, even in patients with PAf or chronic Af, because BNP during Af is the sum of the BNP values from the ventricle(reflecting left ventricular function)and the atrium(due to Af).

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Key Words

Atrial fibrillation(paroxysmal) **Natriuretic peptide, brain**

INTRODUCTION

Brain natriuretic peptide(BNP)is mainly secreted by the heart in man, especially in the ventricle[1−3]. The plasma BNP concentration(BNP level)is also positively correlated with the left ventricular end-diastolic pressure and negatively correlated with the left ventricular ejection fraction[4−7], so BNP level should be measured to evaluate left ventricular function. Measurement of the BNP level during atrial fibrillation(Af)was made in patients with lone Af and patients with chronic heart failure and Af during Af rhythm and sinus rhythm after the Af was terminated with direct current shocks, showing that the BNP level was higher during Af than sinus rhythm[8,9]. However, the time course change in BNP level and the significance in paroxysmal atrial fibrillation(PAf)are unknown.

This study investigated the increase in BNP level during PAf in outpatients, and examined the relationship between BNP and Af.

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Manuscript received February 17, 2004; revised April 20, 2004; accepted April 20, 2004

SUBJECTS AND METHODS

Subjects

This study included 35 consecutive patients, 23 men and 12 women (mean age 70.4±9.6 years), treated for PAf in Tsuchida Clinic, whose BNP levels were successfully measured three times at the following times: 1) before Af attack (with documentation of sinus rhythm for at least 4 weeks prior to the attack), 2) during Af attack, and 3) during sinus rhythm at least 2 weeks and no more than 4 weeks after the spontaneous or oral pharmacological termination of Af. The measurements were made for 68 consecutive attacks in the 35 subjects.

The patient characteristics are summarized in **Table 1**. No underlying disease could be demonstrated in 6 patients, whereas underlying diseases were found in 29 patients: valvular disease in 1; ischemic heart disease in 8; hypertrophic cardiomyopathy in 2; hypertension in 25, including 5 with hypertensive heart disease; diabetes mellitus in 8; chronic obstructive pulmonary disease in 3; hyperthyroidism in 1; cerebrovascular accident in 2; including some patients with more than one disease. Forty of the 68 attacks were symptomatic with palpitations or anterior chest discomfort, and 28 were asymptomatic.

BNP was measured in 91 patients, 56 men and 35 women (mean age 71.3±8.9 years) with chronic Af as the control with a mean follow-up period in Af rhythm of 7.7±4.8 years. Underlying disease was present in 78 patients, valvular disease in 27 and non-valvular disease in 51, and lone Af in 13 patients.

Table 1 Characteristics of the study population

Number of patients	35 (68 attacks)
Age (yr, mean±SD)	70.4±9.6
Sex	
Men	23 (65.7)
Women	12 (34.3)
Underlying disease	
Valvular disease	1 (2.9)
Other diseases	28 (80.0)
Ischemic heart disease	8 (22.9)
Congestive heart failure	5 (14.3)
Hypertrophic cardiomyopathy	2 (5.7)
Hypertension	25 (71.4)
Diabetes mellitus	8 (22.9)
Chronic obstructive pulmonary disease	3 (8.6)
Hyperthyroidism	1 (2.9)
Cerebrovascular accident	2 (5.7)
None	6 (17.1)
Symptoms	
Present	40 (59)
Absent	28 (41)
Medication	
Digitalis	33 (94.3)
Beta-blocker	6 (17.1)
Disopyramide	3 (8.6)
Aprindine	13 (37.1)
Cibenzoline	8 (22.9)
Pilsicainide	2 (5.7)
Warfarin	9 (25.7)

( ): %.

Methods

BNP level was measured by the Immunoradiometric Assay method using a Shionoria BNP assay kit and blood samples taken in a sitting position. The change of BNP level (ΔBNP) was calculated as: ΔBNP = (BNP during attack) − (BNP before attack).

Statistical analysis

Values are shown as mean±standard deviation (SD) or as median (quartiles). The BNP values were transformed into natural logarithms to form a normal distribution for analysis (**Fig. 1**). Multicomparison analyses were performed at the three time points (before attack, during attack, after attack) with Scheffe's analysis after one-way analysis of variance. Analysis of factors affecting the BNP level increase during Af attack was performed using the unpaired *t*-test. Comparisons between patients with persistent PAf and those with PAf changed to chronic Af were analyzed with the unpaired *t*-test and chi-square analysis. $p < 0.05$ was considered significant.

RESULTS

Changes in brain natriuretic peptide during paroxysmal atrial fibrillation attacks

BNP level changes during the 68 PAf attacks are shown in **Fig. 1**. The mean (±SD) ΔBNP was 101±132 pg/m*l*, calculated from the values before attack of 61±75, during attack of 162±175, and after attack of 57±66. The median [quartile] value was 66 [25, 120] pg/m*l*, before attack 39 [18, 70], during attack 102 [52, 205], after attack 35 [20,

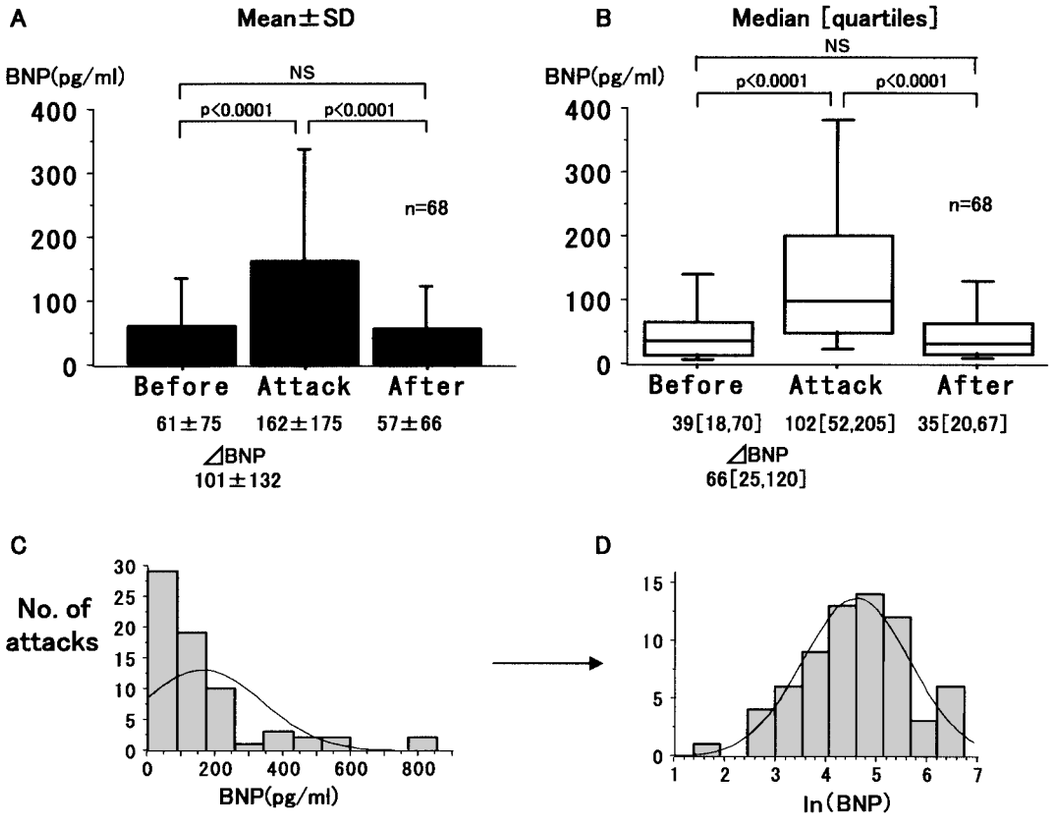

Fig. 1 Changes in levels of brain natriuretic peptide during an atrial fibrillation attack
A: Mean ± standard deviation (SD).
B: Box plots spanning the 25th to 75th percentiles and errors from the 10th to the 90th percentile points. Central lines represent distribution median.
C: Histogram of BNP levels during atrial fibrillation attack.
D: Natural logarithm of BNP levels during atrial fibrillation attack.
BNP = brain natriuretic peptide; Before = before attack; Attack = during attack; After = after attack; Δ BNP = BNP during attack − BNP before attack.

67], showing a significant increase ($p < 0.0001$) during attacks and resumption of the former levels after the attacks.

Distribution of Δ BNP for the 68 Af attacks is shown in **Fig. 2**. BNP increased during 55 attacks (81%) (Δ BNP $\geq$ 20 pg/m*l*), did not change during 11 (16%) (20 pg/m*l* $>$ Δ BNP $\geq -$ 20 pg/m*l*) and decreased in 2 (3%) (Δ BNP $\leq -$ 20 pg/m*l*). The increase in BNP was moderate in 18 attacks, mostly ranging from 50−100 pg/m*l*, and marked in 10 of more than 200 pg/m*l*. Decreased BNP occured during PAf attacks in patients with symptoms of heart failure during sinus rhythm before the attacks. Administration of diuretics in one patient and the discontinuance of β-blocker in another improved the symptoms of heart failure at the next visit, coincidentally with the PAf attack, and BNP levels decreased after termination of Af.

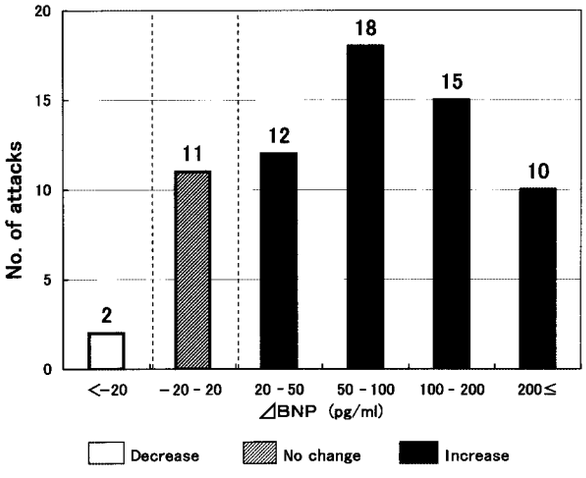

Fig. 2 Distribution of Δ BNP
Abbreviation as in Fig. 1.

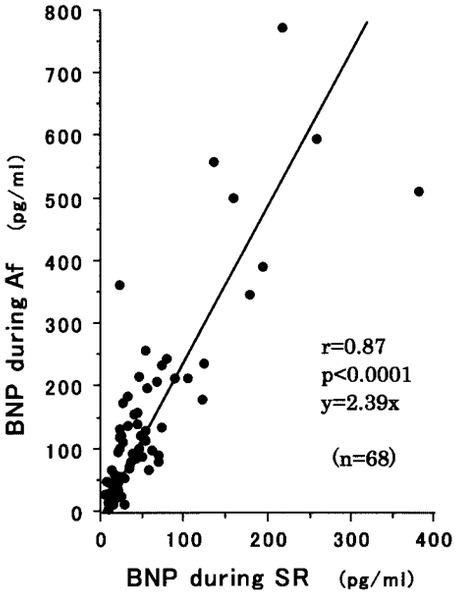

Fig. 3 Correlation of brain natriuretic peptide during atrial fibrillation and sinus rhythm
Af = atrial fibrillation; SR = sinus rhythm. Other abbreviation as in Fig. 1.

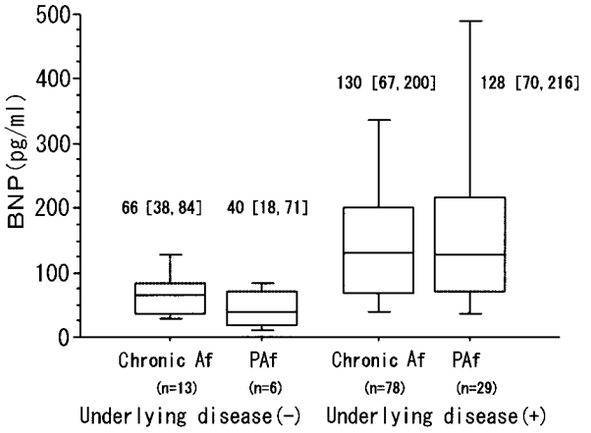

Fig. 4 Comparison of brain natriuretic peptide in patients with chronic atrial fibrillation and paroxysmal atrial fibrillation (during attack)
PAf = paroxysmal atrial fibrillation. Other abbreviations as in Figs. 1, 3.

Correlation of BNP levels during the PAf attacks and during sinus rhythm. These correlations were very good ($r = 0.87$; **Fig. 3**), increasing by about 2.4 times during Af over the sinus rhythm level before attack (95% confidence interval, 2.1−2.7). Furthermore, comparison of the BNP levels during Af attacks with chronic Af (**Fig. 4**) showed an elevation during PAf (PAf = 102 [52, 205] pg/m*l*) to the same level as in chronic Af (chronic Af = 110 [56, 190] pg/m*l*) in all patients. (Patients without underlying diseases had 40 [18, 71] during PAf and 66 [38, 84] in chronic Af, whereas patients with underlying diseases had 128 [70, 216] during PAf, and 130 [67, 200] in chronic Af).

Relationship between time elapsed after onset of paroxysmal atrial fibrillation attack and Δ BNP

BNP was measured in nine patients who visited the clinic within 4 hr after the onset of PAf attack as shown in **Fig. 5−A**. The BNP levels were already elevated at this early point of the PAf attack, with a Δ BNP of 44 [25, 93] pg/m*l* (before attack = 58 [23, 76], during attack = 100 [61, 160], after attack = 56 [29, 85], $p < 0.0001$). In addition, 17 attacks with exactly known onset time were analyzed to investigate the relationship between time elapsed after the onset and Δ BNP, but no significant correlation was seen ($r = 0.42$, $p = 0.09$; **Fig. 5−B**). These results suggested that the BNP level was immediately elevated at the onset of the PAf attack, and Af had no further effect on BNP levels during the time course.

Change in brain natriuretic peptide level after return to sinus rhythm

Five patients were followed up for 1 week after return to sinus rhythm. BNP had significantly returned to the former levels after 1 week (before attack = 14 [11, 23], during attack = 87 [57, 189], 1 week after attack = 14 [13, 37], $p = 0.012$).

Symptoms during paroxysmal atrial fibrillation attack and Δ BNP

Seventeen (25%) of 68 PAf attacks manifested as obvious symptoms (palpitations or anterior chest discomfort) noted by the patients, and in 23 attacks (34%) caused vague symptoms noted by the patients only after PAf was pointed out by a physician, totalling 40 symptomatic attacks (59%; **Fig. 6−A**). Twenty eight attacks (41%) remained asymptomatic even after PAf was pointed out. Symptomatic attacks were associated with marked elevation of BNP of 91 [44,184] pg/m*l* (before attack = 45 [19, 78], during attack = 135 [80, 236], after attack = 45 [23, 76], $p < 0.0001$), but asymptomatic attacks also showed substantial elevation of BNP of 48 [1, 65] pg/m*l* (before attack = 31 [16, 45], during attack = 71 [38, 119], after attack = 24 [18, 44], $p < 0.0001$).

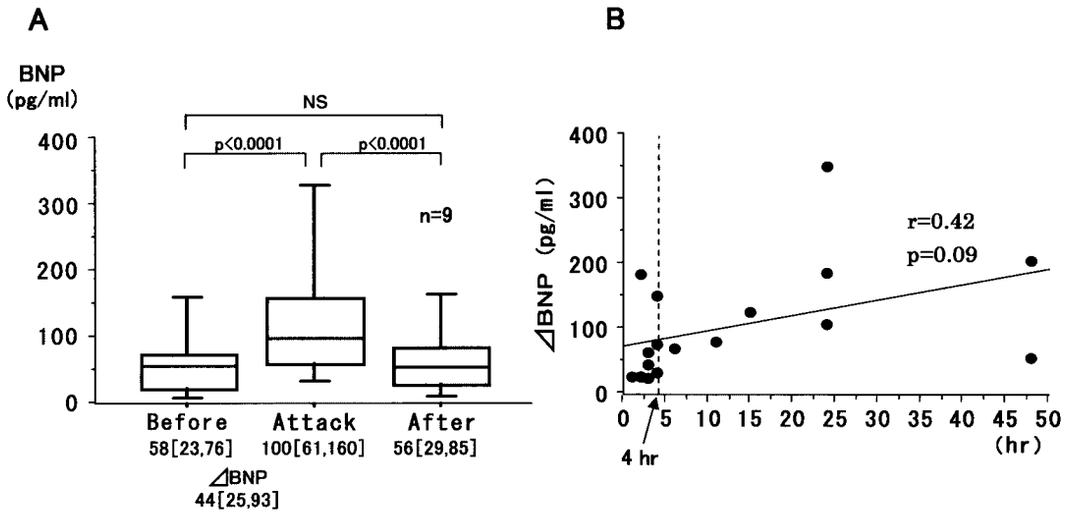

Fig. 5 Brain natriuretic peptide level changes in nine patients within 4 hr of the onset of paroxysmal atrial fibrillation attack (*A*) and correlation between time elapsed after paroxysmal atrial fibrillation attack onset and Δ BNP (*B*)
Abbreviations as in Figs. 1, 4.

Underlying diseases and Δ BNP

Patients with underlying diseases had marked elevation of BNP of 74 [31, 148] pg/m*l* (before attack = 43 [22, 75], during attack = 128 [70, 216], after attack = 42 [22, 73], $p < 0.0001$), but patients without underlying diseases (lone Af) also had significant elevation of BNP, of 31 [8, 49] pg/m*l* (before attack = 11 [7, 29], during attack = 40 [18, 71], after attack = 12 [8, 31], $p = 0.0106$; **Fig. 6−B**).

Factors affecting Δ BNP

Continuous values were divided using the median for analyzing the factors that affected Δ BNP (**Table 2**). Factors demonstrating significant correlations were the presence of symptoms ($p = 0.0379$), underlying diseases ($p = 0.0018$), BNP level over 40 pg/m*l* before Af attack ($p < 0.0001$), and age over 70 years ($p = 0.0030$). Left atrial dimension (LAD) greater than 41 mm also tended to be associated greater Δ BNP ($p = 0.0832$). On the other hand, Af heart rate, left ventricular fractional shortening (FS), and left ventricular diastolic dimension (LVDd) were not significant.

In addition, patients with and without symptoms showed no significant differences in Af heart rate, age, BNP levels before attack, FS, LVDd, and LAD. Patients with and without underlying diseases showed significant differences in Af heart rate ($p = 0.001$), age ($p = 0.037$) and BNP levels before attack ($p = 0.008$), but not in FS, LVDd, and LAD.

Factors influencing the change from paroxysmal atrial fibrillation to chronic atrial fibrillation rhythm (Table 3)

Prediction of change from PAf to chronic Af was studied by analyzing the 7 patients who later developed chronic Af and the 28 patients with persistent PAf. The mean follow-up period in all cases was 17.1 ± 10.5 months, and the mean duration of change from PAf to chronic Af was 9.4 ± 7.8 months. Analysis of the BNP data revealed no significant difference between these two groups in BNP level before attack, during attack, or after attack, or in Δ BNP. Other factors were also analyzed, and Af fixation was found to be significantly greater in older patients ($p = 0.004$), in those with larger LAD ($p = 0.044$) and in asymptomatic patients ($p < 0.001$), but no significant difference was seen in Af heart rate, FS, or LVDd.

Fig. 7 presents the data of monthly BNP measurements during changes from PAf to chronic Af in four representative cases. Patterns of BNP level changes during the course of change from PAf to chronic Af varied and no significant pattern was found.

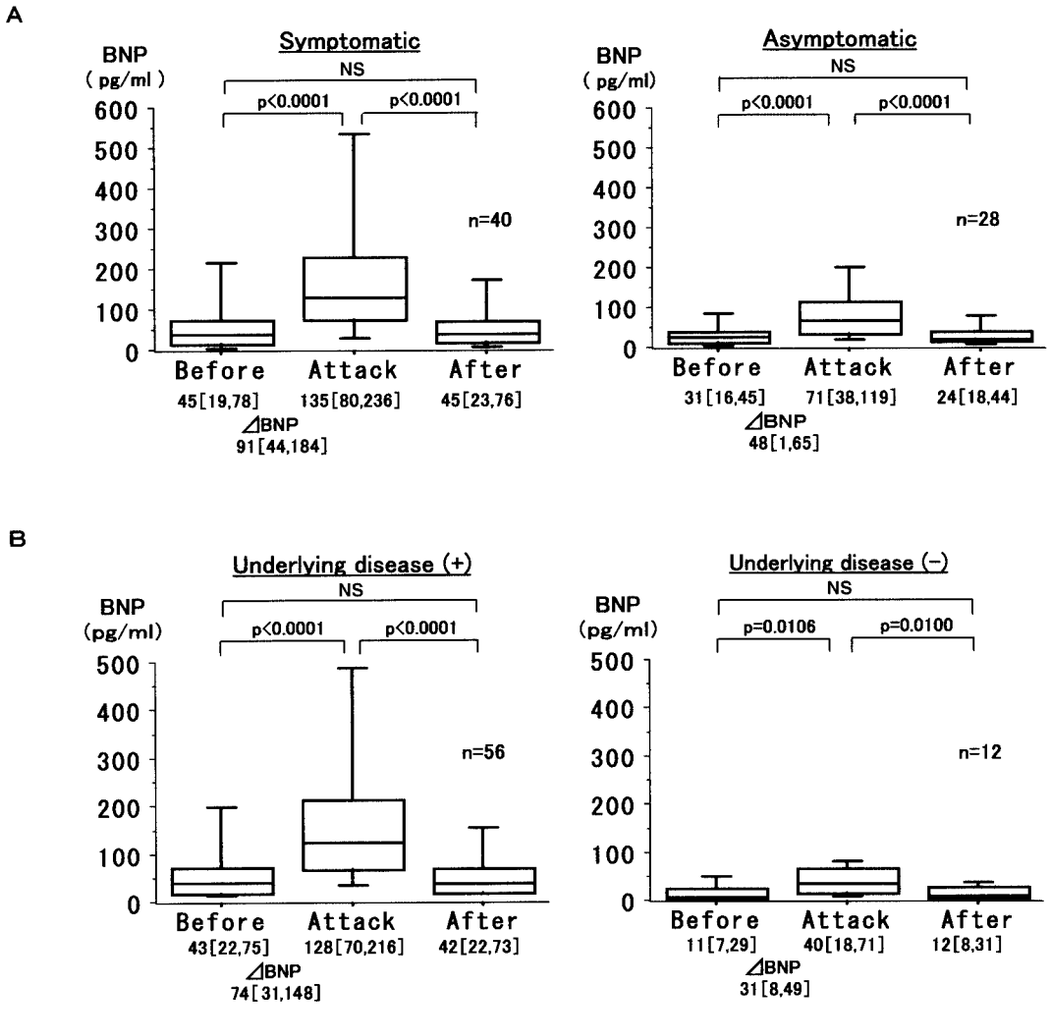

Fig. 6 Comparison between changes of brain natriuretic peptide in symptomatic and asymptomatic patients (*A*) and comparison between changes of brain natriuretic peptide in patients with and without underlying diseases (*B*)
Abbreviations as in Fig. 1.

DISCUSSION

Changes in brain natriuretic peptide levels with atrial fibrillation attacks

BNP measurement has recently become an essential method for the evaluation of heart function (left ventricular function). Studies of electrical defibrillation treatment with chronic Af have shown that BNP is significantly elevated in Af as compared with sinus rhythm[8,9]. Factors such as decreased cardiac function, atrial function and remodeling with a sustained period of Af rhythm can affect the BNP level in chronic Af, but the effect of an PAf attack that replaces sinus rhythm may simply be reflected in the BNP levels. The present study performed BNP measurements three times (before, during and after PAf attack), and showed that the values rose during attacks and returned to the former levels afterwards. This study may also have identified the only effect of Af, namely the atrial load, on BNP levels.

This study showed that BNP rose to 66 [25, 120] pg/m*l* during Af attack, an increase of about 2.4-fold (95% confidence interval, 2.1−2.7), which was the same as found in 91 patients with chronic Af used as the controls. A study on electrical defibrillation in patients with chronic lone Af showed an increase of about three times during Af (mean ± SD ; 137 ± 104 pg/m*l*) than in sinus rhythm (mean ± SD; 46 ± 44 pg/m*l*)[8], which was slightly

Table 2 Factors affecting ⊿BNP

	⊿ BNP	*p* value
Symptoms		
Present	91[44, 184]	0.0379
Absent	48[1, 65]	
History		
Underlying diseases	74[31, 148]	0.0018
None	31[8, 49]	
BNP levels at sinus rhythm		
≥40 pg/m*l*	102[53, 189]	<0.0001
<40 pg/m*l*	48[22, 74]	
Age		
≥70 years	74[48, 129]	0.0030
<70 years	48[19, 102]	
Heart rate at attack		
≥90 beats/min	74[25, 146]	NS(0.6226)
<90 beats/min	55[27, 100]	
LAD		
≥41 mm	74[30, 129]	NS(0.0832)
<41 mm	51[23, 100]	
FS		
<0.34	70[25, 145]	NS(0.9324)
≥0.34	55[26, 107]	
LVDd		
≥48 mm	74[25, 132]	NS(0.4761)
<48 mm	55[25, 86]	

Each continuous value is expressed as the median[quartiles]. LAD=left atrial dimension; FS=fractional shortening; LVDd=left ventricular diastolic dimension. Other abbreviations as in Fig. 1.

higher than that in our study.

The effect of Af on cardiac function or atrial contraction has been studied by analyzing the recovery processes of cardiac function in patients with chronic Af after electrical defibrillation. The atrial contribution to left ventricular filling recovered within 1 week, and the left ventricular ejection fraction and maximum oxygen consumption continued to increase for 1 month after the defibrillation[10]. On the other hand, atrial function recovery takes much longer, from several weeks up to several months[11]. Study of BNP change after electrical defibrillation in patients with chronic Af found that the elevated BNP rapidly decreased in the first week, and a gradual decrease followed for up to 1 month after the defibrillation[9]. This gradual decrease was inversely well correlated with the A wave height of the left ventricular inward blood flow, and indicated cardiac function recovery due to atrial contraction recovery.

The present study showed that elevated BNP associated with PAf attack returned to former levels 1 week after termination of Af. This suggests that BNP elevation caused by PAf attack resulted from atrial overload(elevation of atrial pressure, stretch of atrial wall, *etc.*)and lack of atrial contribution to left ventricular filling, and that no impairment of cardiac function or atrial contraction occurred during PAf attacks, although such impairment occurs in chronic Af.

Table 3 Comparison of parameters between patients who developed chronic atrial fibrillation and patients with persistent paroxysmal atrial fibrillation

	PAf-to-chronic Af (*n*=7)	Persistent PAf (*n*=28)	*p* value
BNP before attack(pg/m*l*)	41[25, 79]	39[15, 60]	NS(0.916)
BNP during attack(pg/m*l*)	93[47, 177]	123[55, 217]	NS(0.414)
BNP after attack(pg/m*l*)	36[21, 78]	34[19, 70]	NS(0.956)
⊿BNP(pg/m*l*)	60[15, 69]	67[36, 143]	NS(0.253)
Heart rate during attack(beats/min)	93±36	94±21	NS(0.878)
Age(yr)	76±8	67±10	0.004
LAD(mm)	45±7	40±6	0.044
FS	30±8	33±5	NS(0.259)
LVDd(mm)	47±40	48±25	NS(0.636)
No symptoms at attack	5/7	16/28	<0.001

Each continuous value is expressed as the median[quartiles]or mean±SD. Abbreviations as in Figs. 1, 3, 4, Table 2.

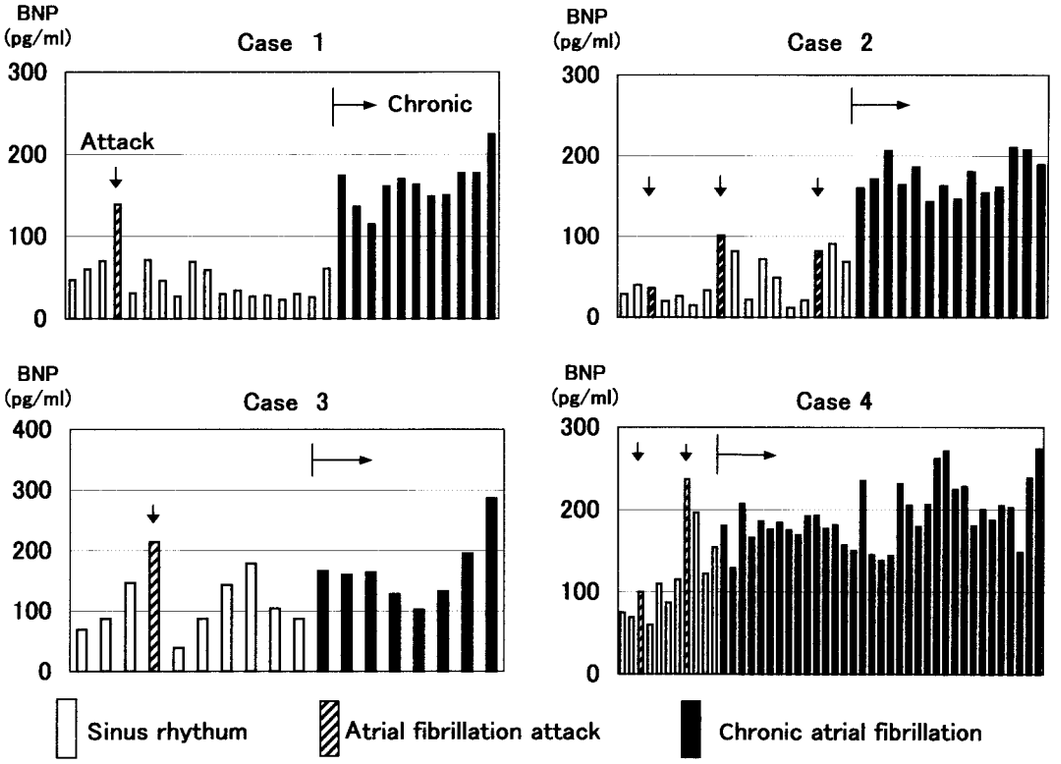

Fig. 7 Patterns of brain natriuretic peptide level with the fixation from paroxysmal atrial fibrillation to chronic atrial fibrillation
Attack = atrial fibrillation attack; Chronic = chronic atrial fibrillation. Other abbreviation as in Fig. 1.

Brain natriuretic peptide secretion during atrial fibrillation

Atrial natriuretic peptide(ANP)is released from secretory granules in the atrium under control of a regulated pathway, whereas BNP is released from the ventricle via a constitutive pathway after the detection of the stimulation.

However during Af, the BNP level in the coronary sinus is higher than in the anterior inter-ventricular vein in the patients with chronic lone Af, which indicates that BNP is released from the atrium[12]. The BNP level begins to decrease significantly 15 min after electrical defibrillation of Af in patients with chronic heart failure, suggesting that BNP is released from the atrium granules[13]. We previously studied the benefits of BNP measurement in cardiac disease screening, and found that BNP is not always elevated during a non-attack period of tachycardia or ischemic heart disease, as long as no depression of heart function is present, and also that the Af attack caused BNP elevation even immediately after the onset, but not in patients with acute myocardial infarction[14].

The present study demonstrated that the BNP level was already significantly elevated immediately(within 4 hr)after the Af attack onset, and this elevated BNP level was not significantly correlated with the time elapsed after Af onset. These facts seem to suggest that BNP is released from granules in the atrium during Af attack, unlike BNP released from the ventricle during myocardial infarction.

These findings indicate that we must be aware that the BNP level seen in Af is a combined value resulting from release from both the atrium and ventricle, which means that the evaluation of cardiac function using BNP in patients with PAf or chronic Af requires special consideration, unlike the situation in sinus rhythm.

Elevation of brain natriuretic peptide in asymptomatic cases

The substantial and significant BNP elevation in asymptomatic cases may indicate that patients with BNP elevation of unknown origin may be attributed to the occurrence of asymptomatic Af attack.

Δ BNP had no significant relationship with fractional shortening, left ventricular diastolic dimension

In this study, significant factors related to BNP increase included the presence of symptoms, underlying diseases, BNP level before attack, and age. On the other hand, FS and LVDd were not significant. In addition, analyses of the presence of symptoms and of underlying diseases revealed no significant correlation between the Δ BNP and the FS or LVDd, as indices of left ventricular function(particularly systolic function). These facts indicate that Δ BNP had no significant relationship with left ventricular systolic function. However, since ΔBNP is significantly related to BNP level during sinus rhythm before attack, the possibility cannot be excluded that Δ BNP may be related to other cardiac functions, such as atrial function or left ventricular diastolic function.

Atrial fibrillation fixation from paroxysmal atrial fibrillation to chronic atrial fibrillation

Low ANP and high BNP before electrical defibrillation in patients with chronic Af and congestive heart failure were independent predictive factors for Af recurrence[13]. The reason for the Af relapse in patients with low ANP and high BNP may be that the progression of fibrosis in the atrial tissue reflects a decrease in ANP production, and atrial and ventricular dysfunction reflects BNP elevation.

The present study analyzed BNP data to ascertain whether Af fixation from PAf to chronic Af could be predicted, but concluded that this is difficult with only BNP, because the BNP levels during an Af attack and during sinus rhythm, as well as ΔBNP, all showed non-significant differences. The reason for this lack of significance may be that the patterns of BNP levels varied during the course of changes from PAf to chronic Af(**Fig. 7**), which may be caused by the presence of asymptomatic Af attacks. Therefore, BNP was not very useful for prediction of Af fixation, but advancing age, large LAD, and asymptomatic Af attacks seemed to be useful.

Study limitations

This study showed that Δ BNP had no significant relationship to FS or LVDd, as indices of left ventricular systolic function, but had a significant relationship to BNP levels during sinus rhythm before Af. Further studies are needed to evaluate many other factors, such as atrial function or left ventricular diastolic function.

Examination of the prediction of change from PAf to chronic Af included a small number of patients, and the mean follow-up period was relatively short and not the same in all patients. Further studies in many more patients and longer follow-up periods are needed.

The present study was done during treatment with oral medications(digitalis, anti-arrhythmic drugs, *etc.*)in the outpatient clinic. Therefore, the possibility cannot be excluded that medication influenced the BNP levels, Af heart rate, symptoms, and so on. This is a limit of clinical research in the outpatient clinic.

CONCLUSIONS

BNP levels during Af attacks in patients with PAf showed an increase of 66[25, 120]pg/m*l*(= 2.4-fold)elevation compared to that in sinus rhythm, and the BNP level returned to normal after termination of Af. BNP levels were already elevated at the hospital visit, and occurred immediately (within 4 hr)after the onset of Af attack. ΔBNP showed no significant relationship with the time elapsed after the onset, which suggests that BNP was released from secretory granules in the atrium during Af attack. Forty-one percent of Af attacks were asymptomatic, and also demonstrated significant BNP increases, which suggests that some cases of BNP elevation of unknown cause may be attributed to the occurrence of asymptomatic Af attack. Finally, cardiac function evaluation using BNP in patients with Af, regardless of any PAf or chronic Af, requires special consideration, unlike in sinus rhythm, because BNP in Af is the sum of the releases from the ventricle(reflecting left ventricular function)and the atrium(due to Af).

Acknowledgements

We would like to thank Nobuo Shirahashi(Novartis Pharma K.K.) for statistical support, and Dr Naoki Matsumoto(St. Marianna University School of Medicine)for clinical suggestions, and Dr Joukichi Suzuki(Suzuki Clinic)and Dr Takashi Tomidokoro (Nagaoka Chuo General Hospital)for important advice.

要　　約

発作性心房細動による脳性ナトリウム利尿ペプチド分泌への影響

土田　桂蔵　　田辺　一彦

目　的: 脳性Na利尿ペプチド(BNP)は主に心室から分泌され左室機能を反映するが，慢性心房細動では洞調律時に比べてBNP値が高値を示すとされている．本研究では，発作性心房細動における発作時のBNP値の変動について検討し，さらに心房細動とBNP値の関係について検討した．

方　法: 発作性心房細動患者で，心房細動発作時，発作前(4週間以上)および発作後(自然停止あるいは内服による除細動後2−4週間)の洞調律時の計3回のBNP値を測定できた，35例(男性23例，女性12例，平均年齢70.4±9.6歳)の連続68発作を対象とした．BNP値は，外来受診時に座位で随時採血してイムノラジオメトリックアッセイ法で測定した．BNP値の代表値は中央値で表した．

結　果: 1) 全68発作の発作時のBNP値の変化(⊿BNP)は，66 pg/m*l*(発作前39→発作時102→発作後35 pg/m*l*)と有意の上昇が認められ，心房細動発作時BNP値は洞調律時BNP値の約2.4倍であった．そして発作後にまた発作前値に復した．2) 発作時BNP値上昇例は55発作(81%)で，不変例(⊿BNPが±20 pg/m*l*以内)は11発作(16%)，低下例は2発作(3%)であった．3) 発作出現直後(4時間以内)受診の9例全例において，すでに⊿BNPは44 pg/m*l*(58→100→56)と有意の上昇が認められた．また，心房細動発作経過時間と⊿BNPの間に有意な相関は認められなかった．4) 発作時の症状(動悸・前胸部不快など)の有無でみると，有症状40発作(59%)では⊿BNPは91 pg/m*l*(45→135→45)と有意の上昇が認められ，無症状28発作(41%)でも⊿BNPは48 pg/m*l*(31→71→24)と有意の上昇が認められた．

結　論: 心房細動発作時のBNP値は洞調律時のBNP値の約2.4倍であった．発作出現直後の受診でもすでにBNP値の上昇があり，心房細動時にはBNPが心房から顆粒分泌されている可能性が示唆された．また原因不明のBNP値の変動の中に，無症状の心房細動発作が関与している可能性も示唆された．最後に，心房細動時のBNP値による心機能評価においては，心房細動時のBNP値が，心室由来の(左室機能を反映する)BNPに心房由来の(心房細動による心房負荷で分泌された)BNPが加わった値であることを考慮する必要がある．

J Cardiol 2004 Jul; 44(1): 1−11

References

1) Sudoh T, Kangawa K, Minamino N, Matsuo H: A new natriuretic peptide in porcine brain. Nature 1988; **332**: 78−81
2) Ogawa Y, Nakao K, Mukoyama M, Hosoda K, Shirakami G, Arai H, Saito Y, Suga S, Jougasaki M, Imura H: Natriuretic peptides as cardiac hormones in normotensive and spontaneously hypertensive rats: The ventricle is a major site of synthesis and secretion of brain natriuretic peptide. Cir Res 1991; **69**: 491−500
3) Saito Y, Nakao K, Arai H, Nishimura K, Okumura K, Obata K, Takemura G, Fujiwara H, Sugawara A, Yamada T, Itoh H, Mukoyama M, Hosoda K, Kawai C, Ban T, Yasue H, Imura H: Augmented expression of atrial natriuretic polypeptide gene in ventricle of human failing heart. J Clin Invest 1989; **83**: 298−305
4) Mukoyama M, Nakao K, Hosoda K, Suga S, Saito Y, Ogawa Y, Shirakami G, Jougasaki M, Obata K, Yasue H, Kambayashi Y, Inoue K, Imura H: Brain natriuretic peptide as a novel cardiac hormone in humans: Evidence for an exquisite dual natriuretic peptide system, atrial natriuretic peptide and brain natriuretic peptide. J Clin Invest 1991; **87**: 1402−1412
5) Yoshimura M, Yasue H, Okumura K, Ogawa H, Jougasaki M, Mukoyama M, Nakao K, Imura H: Different secretion patterns of atrial natriuretic peptide and brain natriuretic peptide in patients with congestive heart failure. Circulation 1993; **87**: 464−469
6) Yasue H, Yoshimura M, Sumida H, Kikuta K, Kugiyama K, Jougasaki M, Ogawa H, Okumura K, Mukoyama M, Nakao K: Localization and mechanism of secretion of B-type natriuretic peptide in comparison with those of A-type natriuretic peptide in normal subjects and patients with heart failure. Circulation 1994; **90**: 195−203
7) Maeda K, Tsutamoto T, Wada A, Hisanaga T, Kinoshita M: Plasma brain natriuretic peptide as a biochemical marker of high left ventricular end-diastolic pressure in patients with symptomatic left ventricular dysfunction. Am Heart J 1998; **135**: 825−832
8) Ohta Y, Shimada T, Yoshitomi H, Inoue S, Murakami Y, Shimizu H, Nakamura K, Ohta T, Katoh H, Ishibashi Y: Drop in plasma brain natriuretic peptide levels after successful direct current cardioversion in chronic atrial fibrilla-

tion. Can J Cardiol 2001; **17**: 415−420
9) Nishimura T: Atrial fibrillation and natriuretic peptides. Naika 2002; **89**: 92−97(in Japanese)
10) van Gelder IC, Crijns HJGM, Blanksma PK, Landsman MLJ, Posma JL, Van Den Berg MP, Meijler FL, Lie KI: Time course of hemodynamic changes and improvement of exercise tolerance after cardioversion of chronic atrial fibrillation unassociated with cardiac valve disease. Am J Cardiol 1993; **72**: 560−566
11) Manning WJ, Leeman DE, Gotch PJ, Come PC: Pulsed Doppler evaluation of atrial mechanical function after electrical cardioversion of atrial fibrillation. J Am Coll Cardiol 1989; **13**: 617−623
12) Inoue S, Murakami Y, Sano K, Katoh H, Shimada T: Atrium as a source of brain natriuretic polypeptide in patients with atrial fibrillation. J Card Fail 2000; **6**: 92−96
13) Mabuchi N, Tsutamoto T, Maeda K, Kinoshita M: Plasma cardiac natriuretic peptides as biochemical markers of recurrence of atrial fibrillation in patients with mild congestive heart failure. Jpn Circ J 2000; **64**: 765−771
14) Tsuchida K, Tanabe K: Cardiac screening, evaluation and prediction of prognosis by plasma brain natriuretic peptide concentrations. Jpn Med J 2002; **4097**: 23−28(in Japanese)