Estimation of B-type Natriuretic Peptide Values from N-Terminal proBNP Levels

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Abstract: Both brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are established biomarkers that are necessary in the diagnosis and management of heart failure (HF). However, it is difficult to infer BNP concentration from NT-proBNP concentration for a clinician who is familiar with BNP. We investigated whether estimated BNP concentration from NT-proBNP has an equivalent prognostic strength compared with the actual BNP concentration in the prediction of future outcomes. We created a formula for estimating BNP concentration using multivariate analysis in a derivation cohort with known or suspected HF (n = 374). We determined whether the estimated BNP level had a similar prognostic power compared with the actual BNP and NT-proBNP levels in a validation cohort (n = 375). There was a strong correlation between log-transformed BNP and log-transformed NT-proBNP (r = 0.90) in the derivation cohort. We created two types of equation from the derivation cohort. During a median of 1 year of follow up, 49 major adverse cardiac events developed in the validation cohort. Cox proportional analysis revealed that the actual and estimated BNP levels represented equivalent and significant predictors of the future cardiovascular outcome. The estimated BNP levels calculated by our new formula showed a prognostic power similar to the actual BNP levels. This equation will be useful, especially for a physician who is not familiar with NT-proBNP testing.

Keywords: natriuretic peptide, prognosis, heart failure.

Introduction

Brain natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are reliable cardiac biomarkers with comparable accuracy in predicting future prognosis of patients with ischemic heart disease, heart failure (HF) and valvular heart disease [1–9]. The stretching of myocardium by volume or pressure overload activates the BNP encoding gene in cardiomyocytes especially in both ventricles. At first, preproBNP, a 134 amino acid residues long intracellular precursor propeptide, is created, then ProBNP is formed after the cleavage of the signal peptide of preproBNP. Some proBNPs are further processed into biologically
inactive NT-proBNP and biologically active BNP. ProBNP, NT-proBNP and BNP are released into the bloodstream via the coronary sinus mainly. Some of the physiological effects of BNP are the reduction of systemic vascular resistance and the facilitation of natriuresis. Due to their predominant clearance by renal excretion and longer biological half-life, NT-proBNP concentrations vary more widely than BNP concentrations in patients with renal dysfunction [10]. BNP has a shorter biological half-life, and this may cause the underestimation of BNP concentration if some time has elapsed before the measurement of a blood sample. Thus, there are both strong and weak points of each, and this is why which is used in daily examinations is not unified. Although previous studies have reported a close correlation between the relative concentrations of BNP and NT-proBNP [11–13], it is quite difficult for physicians using BNP testing in daily clinical practice to intuitively predict BNP concentrations from NT-proBNP concentrations. Thus, there is significant merit in re-evaluating a direct comparison between BNP and NT-proBNP in patients with known or suspected HF. Accordingly, the aims of this study were: 1) to compare plasma BNP concentration and NT-proBNP concentration; 2) to create an equation including NT-proBNP concentration as an independent variable to predict BNP concentration in a derivation cohort; and 3) to compare the prognostic strength of the actual and estimated natriuretic peptide levels for future cardiovascular events in a validation cohort.

Methods

Study population

This was a retrospective observational study carried out in a single center in Japan. Between September 2015 and December 2016, we selected 749 patients (mean age: 70 ± 13 years, 491 men) who had received clinically-indicated BNP measurements and whose plasma sample had been stored at −80°C. The study population consisted of approximately 24% (749/3,093) of the total population in which BNP tests had been ordered during the same time window in our hospital. Patients were divided into two groups according to whether their study identification (ID) number was an odd number or an even number. The group of patients whose ID was an odd number was allocated to the derivation cohort (n = 374), and the group of patients with an even number was allocated to the validation cohort (n = 375). The study protocol was approved by the Human Ethics Committee in the University of Occupational and Environmental Health, Japan, and the need for informed consent was waived.

BNP/NT-pro BNP measurements

At the time of ordering, blood was simultaneously collected in ethylenediaminetetraacetic acid (EDTA) tubes for BNP and serum separator tubes for NT-proBNP. The specimens in the EDTA tubes were centrifuged and the plasma was separated into plastic tubes immediately. The specimens in the serum separator tubes were also centrifuged immediately after clotting. The serum was then frozen and stored.

Using the separated plasma, BNP was measured with a commercially available assay (Centaur XP, Siemens Inc., Tokyo, Japan). The intra-assay coefficients of variation were 2.4%, 0.9%, and 0.9% for concentrations of 32, 323, and 1,262 pg/ml, respectively. After storage for a median of 329 days (interquartile range [IQR]: 271 to 538 days), the frozen serum specimens were allowed to thaw at room temperature, and the NT-proBNP concentration was determined (ECLIA Modular E-170, Roche Diagnostics Inc., Tokyo, Japan). The intra-assay coefficients of variation were 1.5% and 1.0% at 131 and 4,360 pg/ml, respectively. At the time of BNP examination, we also acquired blood examination parameters from electronic medical records. Estimated glomerular filtration rate (eGFR) was determined by the following equation: [eGFR = 194 × serum creatinine\(^{-1.094} \times \text{age}^{-0.287} \times 0.739 \text{ (if female)}\)] [14].

Follow up

Follow-up information was obtained from either clinical visits or telephone interviews. The primary end point was cardiac death, and the secondary end point was a composite of major cardiovascular events (MACEs), including cardiac death, non-fatal myocardial infarction, and HF requiring admission. The total follow-up time was calculated to the first event or the maximum length of follow-up in those without an endpoint.
Statistical methods

Continuous data are expressed as mean ± standard deviation (SD) or median and IQR according to the data distribution. Categorical data are presented as an absolute value or percentage. Paired comparison was performed using the t-test or Wilcoxon Signed Rank test. BNP and NT-proBNP concentrations were log-transformed. We performed univariate linear regression analysis, and the variables that were associated with log-transformed BNP and log-transformed NT-proBNP were determined by using the least squares method. Then, multivariate linear regression analysis was performed to determine the variables which were independently associated with log-transformed BNP by using the least squares method. Stepwise regression analysis was performed using those variables to generate an equation. The algorithm of stepwise regression analysis was forward selection based on Bayesian information criterion. BNP and NT-proBNP values were stratified into 4 groups, according to a statement of the Japanese Heart Failure Society (BNP: <100 pg/ml, 100–200 pg/ml, 200–600 pg/ml and >600 pg/ml; NT-proBNP: <400 pg/ml, 400–900 pg/ml, 900–4,000 pg/ml and >4,000 pg/ml). Concordance rate was calculated between groups stratified by the actual BNP level and those categorized by estimated BNP level with the use of this equation. Survival analysis was performed using the Kaplan-Meyer analysis. Cox proportional hazard regression analysis was used to calculate hazard ratios (HRs) and 95% confidence interval (95% CI). All statistical analyses were performed with commercial software (JMP version 13.1, SAS Institute Inc., Cary, NC, USA; SPSS version 24, IBM Inc., Chicago, IL).

Results

Characteristics of derivation cohort

The clinical characteristics of the derivation cohorts are summarized in Table 1.

Correlation between BNP level and NT-pro BNP level in the derivation cohort

In the derivation cohort, the median concentration of BNP was 154 pg/ml (IQR: 47 to 417 pg/ml), and the corresponding values for NT-proBNP were 1,230 pg/ml (IQR: 187 to 5,291 pg/ml). The Pearson coefficient of correlation between BNP and NT-proBNP was 0.75 (P<0.001); the corresponding value between log-transformed BNP and NT-proBNP was 0.90 (P<0.001). Table 2 shows the results of univariate linear regression analysis of log-transformed BNP and NT-proBNP with anthropometric factors and eGFR. Both log-transformed BNP and NT-proBNP were significantly associated with age, body surface area (BSA) and eGFR. Since BSA and BMI were co-linear, age, sex, BSA, log-transformed NT-proBNP and eGFR were entered into a multivariate regression model to allow us to predict log-transformed BNP. Log-transformed NT-proBNP, eGFR and age were identified as significant variables (intra-class correlation coefficient (ICC): 0.91, P<0.001) by the forward stepwise method, and the following equation was obtained.

\[
\log \text{BNP} = 0.71 \times \log \text{NT-proBNP} + 0.01 \times \text{eGFR} + 0.009 \times \text{age} - 1.17 \quad \text{(Equation 1)}
\]

For simplicity, however, we also created another equation using NT-proBNP and eGFR (ICC: 0.91, P<0.001) as follows.

\[
\log \text{BNP} = 0.72 \times \log \text{NT-proBNP} + 0.01 \times \text{eGFR} - 0.53 \quad \text{(Equation 2)}
\]

By using both equations, we calculated the estimated BNP concentrations for each patient in the validation cohort.

Characteristics of validation cohort

The clinical characteristics of the validation cohort are shown in Table 1. Overall, there were no significant differences between the deviation cohort and the validation cohort in the majority of parameters except for a lower prevalence of hypertension and hypercholesterolemia in the validation cohort. No significant differences in natriuretic peptide level or prevalence of adverse outcome were noted between the two groups.

Concordance rate

Figure 1 depicts the concordance rate of group classification between actual BNP concentration and estimated BNP concentration using Equations 1 and 2. Using Equation 1, complete concordance of group classification was observed in 70% (258/375). Using Equation 2, the corresponding concordance rate was 72% (269/375).
Table 1. Characteristics of the Study Population

| Variable                          | Derivation cohort (n=374) | Validation cohort (n=375) | P     |
|-----------------------------------|---------------------------|--------------------------|-------|
| Mean age (year)                   | 71 ± 12                   | 69 ± 13                  | 0.21  |
| Men/women                         | 252/122                   | 239/136                  | 0.29  |
| Body surface area (/m²)           | 1.60 (IQR; 1.48 to 1.73)  | 1.61 (1.47 to 1.73)      | 0.68  |
| Body mass index (kg/m²)           | 22.2 (20.2 to 24.7)       | 22.2 (20.3 to 25.0)      | 0.97  |
| SBP (mmHg)                        | 134 (114 to 150)          | 131 (115 to 149)         | 0.59  |
| DBP (mmHg)                        | 73 (64 to 83)             | 73 (64 to 83)            | 0.48  |
| NYHA class I/II/III/IV             | 209/102/36/27             | 191/119/42/23            | 0.41  |
| Hypertension (%)                  | 265 (71%)                 | 241 (64%)                | 0.05  |
| Diabetes (%)                      | 130 (35%)                 | 136 (36%)                | 0.54  |
| Hypercholesterolemia (%)          | 158 (42%)                 | 128 (34%)                | 0.02  |
| Ischemic heart disease (%)        | 152 (41%)                 | 142 (38%)                | 0.44  |
| Valvular heart disease (%)        | 39 (10%)                  | 47 (13%)                 | 0.37  |
| Dilated cardiomyopathy (%)        | 20 (5%)                   | 18 (5%)                  | 0.73  |
| Secondary cardiomyopathy (%)      | 29 (8%)                   | 27 (7%)                  | 0.77  |
| Hypertrophic cardiomyopathy (%)   | 9 (2%)                    | 11 (3%)                  | 0.65  |
| Atrial fibrillation (%)           | 72 (19%)                  | 78 (21%)                 | 0.60  |
| BNP (pg/ml)                       | 154 (47 to 417)           | 141 (46 to 337)          | 0.20  |
| NT-proBNP (pg/ml)                 | 1,230 (187 to 5,291)      | 948 (168 to 3,796)       | 0.13  |
| eGFR (ml/min/1.73m²)              | 49.7 (21.1 to 67.3)       | 51.9 (23.8 to 68.2)      | 0.60  |
| Hb (g/dl)                         | 12.2 ± 2.1                | 12.2 ± 2.1               | 0.82  |
| CRP (mg/dl)                       | 0.17 (0.05 to 1.08)       | 0.14 (0.04 to 0.53)      | 0.07  |
| Uric acid (mg/dl)                 | 5.8 (4.8 to 7.0)          | 5.8 (4.7 to 7.1)         | 0.80  |
| Blood urea nitrogen (mg/dl)       | 21 (15 to 33)             | 19 (15 to 32)            | 0.15  |
| Creatinine (mg/dl)                | 1.07 (0.80 to 2.27)       | 1.01 (0.79 to 2.03)      | 0.43  |
| Sodium (mmol/dl)                  | 140 (138 to 141)          | 140 (138 to 141)         | 0.91  |
| Potassium (mmol/dl)               | 4.2 (3.9 to 4.5)          | 4.2 (3.9 to 4.5)         | 0.23  |
| Chloride (mmol/dl)                | 104 (102 to 106)          | 104 (102 to 106)         | 0.97  |
| LVEDVI (ml/m²)                    | 63 (49 to 83)             | 64 (55 to 81)            | 0.37  |
| LVESVI (ml/m²)                    | 31 (24 to 53)             | 32 (24 to 46)            | 0.92  |
| LVEF (%)                          | 45 (32 to 54)             | 47 (35 to 56)            | 0.09  |
| LAVImax (ml/m²)                   | 35 (26 to 48)             | 36 (25 to 50)            | 0.58  |
| E/A                               | 0.76 (0.60 to 1.05)       | 0.78 (0.64 to 1.08)      | 0.33  |
| e’ (cm/sec)                       | 5.6 (4.3 to 7.3)          | 5.8 (4.3 to 7.2)         | 0.73  |
| E/e’                              | 12.4 (9.4 to 17.8)        | 12.6 (9.1 to 17.8)       | 0.78  |
| SPAP (mmHg)                       | 33 (29 to 38)             | 32 (28 to 38)            | 0.49  |
| Follow up period (month)          | 12.3 (7.1 to 17.9)        | 12.1 (7.1 to 16.9)       | 0.49  |
| Cardiac death (%)                 | 16 (4%)                   | 23 (6%)                  | 0.08  |
| MACEs (%)                         | 46 (12%)                  | 49 (14%)                 | 0.72  |

Continuous data are expressed as mean ± standard deviation or median and interquartile range (IQR). Categorical data are presented as absolute value and percentage. BNP: brain natriuretic peptide, CRP: C reactive protein, DBP: diastolic blood pressure, Hb: hemoglobin, E/A: early diastolic left ventricular filling velocity/peak atrial filling velocity, e’: early diastolic mitral annulus velocity, LVEDVI: left ventricular end-diastolic volume index, LVESVI: left ventricular end-systolic volume index, LVEF: left ventricular ejection fraction, LAVImax: maximum left atrial volume index, MACE: major adverse cardiac event, NT-proBNP: N-terminal proBNP, NYHA: New York Heart Association, SBP: systolic blood pressure, SPAP: systolic pulmonary arterial pressure.
Outcome

Of the 375 subjects in the validation cohort, follow-up data could not be obtained from 8 patients (2%) due to contact failure. During a median follow-up of 12.1 months (IQR: 7.1 to 16.9 months), 23 patients reached the primary end point, while the secondary end points were evident in 49 patients: 23 cases of cardiac death, 25 cases of HF requiring hospitalization, and 1 case of non-fatal myocardial infarction. Figure 2 shows the primary end point (cardiac death) free rate among the 4 groups specifically stratified according to actual BNP and NT-proBNP concentrations (Fig. 2A and 2B) or estimated BNP concentrations (Fig. 2C and 2D).

Table 2. Linear regression analysis for the association of BNP and NT-proBNP in the derivation group

|       | Log BNP   | Log NT-proBNP |
|-------|-----------|---------------|
|       | t-value   | P             | t-value   | P             |
| age   | 3.34      | 0.001         | 2.58      | 0.010         |
| sex   | 0.45      | 0.653         | -0.20     | 0.841         |
| BMI   | -2.03     | 0.043         | -1.80     | 0.072         |
| BSA   | -3.06     | 0.002         | -3.01     | 0.003         |
| eGFR  | -9.38     | <0.001        | -15.67    | <0.001        |
| Log BNP |          |               | 39.14     | <0.001        |
| Log NT-proBNP |        |               | 39.14     | <0.001        |

BMI: body mass index, BSA: body surface area, eGFR: estimated glomerular filtration rate, BNP: brain natriuretic peptide, NT-proBNP: N-terminal proBNP.

Fig. 1. Concordance rate of group classification between actual brain natriuretic peptide (BNP) level and estimated BNP level by equation 1 (A) and equation 2 (B) in the validation cohort and their Bland-Altman analysis. In the linear regression graph, the X-axis denotes log-transformed estimated BNP concentration calculated using the equation, while the Y-axis shows log-transformed actual BNP concentration. The orange, red and brown dotted lines represent BNP concentrations of 100 pg/ml, 200 pg/ml and 600 pg/ml, respectively. In the Bland-Altman plot, the X-axis denotes the average of the actual and estimated BNP. The Y-axis shows the difference between the actual and estimated BNP. The orange and blue solid lines indicate the mean difference, and the dotted lines represent the range of 95% limits of agreement.
Group stratification by actual measurements of natriuretic peptide concentrations, as well as estimated BNP concentrations derived from the two equations, could be used to identify a group of patients at high-risk of future cardiac death. Univariate Cox proportional hazard analysis revealed that the actual natriuretic peptide level [BNP: HR; 1.87 (95%CI: 1.35 to 2.62, \(P < 0.001\)), NT-proBNP: 1.53 (1.23 to 1.92, \(P < 0.001\))] and the estimated BNP level by two equations [estimated BNP using equation 1: 1.97 (1.40 to 2.83, \(P < 0.001\)), BNP using equation 2: 2.03 (1.44 to 2.93, \(P < 0.001\))] was a significant predictor of cardiac death. Figure 3 shows the MACE free rate among the 4 groups stratified according to actual or estimated natriuretic peptide concentrations. All modalities provided significant prognostic power for predicting MACE. Univariate Cox proportional hazard analysis revealed that the actual natriuretic peptide level [BNP: HR; 2.23 (95%CI: 1.78 to 2.81, \(P < 0.001\)), NT-proBNP: 1.68 (1.43 to 1.98, \(P < 0.001\))] and the estimated BNP level derived from equations [estimated BNP using equation 1: 2.33 (1.81 to 3.02, \(P < 0.001\)), estimated BNP using equation 2: 2.41 (1.87 to 3.14, \(P < 0.001\))] were a significant predictor of MACE.

**Reliability of NT-pro BNP concentration**

Although NT-proBNP concentration is reported to be stable for two years after plasma samples have been stored at \(-20^\circ C\) [15, 16], the concentration might change during storage. In 188 patients, NT-proBNP
was also measured on the same day that BNP was measured, thus allowing us to compare NT-proBNP concentration at the time when fresh plasma was obtained with that at a median of 513 days (IQR; 292 to 552 days) after storage as a frozen sample. Although the values from the fresh sample (median; 1,817 pg/ml, IQR; 469 to 5,148 pg/ml) were significantly higher than those derived from the stored samples (median; 1,779 pg/ml, IQR; 439 to 4,999 pg/ml, \( P = 0.001 \)), there was a good correlation between the two measurements (\( r = 0.93 \)). If we excluded 5 cases in which the NT-proBNP concentration in the fresh plasma sample was more than 35,000 pg/ml, the correlation was improved even further (\( r = 0.99 \)) (Fig. 4).

### Discussion

The major findings of this study can be summarized as follows. 1) There was a good correlation between log-transformed BNP and log-transformed NT-proBNP. 2) Two equations provided by multivariate regression showed highly corrected r values. 3) Although the complete concordance rate for group classification according to actual and estimated BNP concentration was modest, estimated BNP had a similar prognostic value compared with actual BNP and NT-proBNP for predicting future cardiac death and MACEs.

Natriuretic peptides are potent cardiac biomarkers for determining the cause of dyspnea in the emergency department, evaluating the efficacy of HF therapy, and
predicting future outcome for several cardiac patholo-
gies [1–9]. Several previous studies have shown that,
overall, both peptides have an equivalent potency for
diagnosing left ventricular (LV) dysfunction and pre-
dicting future cardiovascular outcome with a slightly
better predictive power for NT-proBNP over BNP [11,
13, 17–20]. Despite the selection of either BNP or NT-
proBNP being solely reliant upon the preference of the
attending physician and the local availability of assay
equipment, NT-proBNP may become more popular
than BNP, considering some evidence [11, 20]. How-
ever, many physicians who are currently using BNP
testing as a guide for HF therapy may not intuitively
be able to convert the observed NT-proBNP level to a
predicted BNP level.

We verified that there was a strong correlation be-
tween BNP concentration and NT-proBNP concentra-
tion when using actual measured values (r = 0.77) and
when using log-transformed values (r = 0.90); this was
in agreement with previous studies [11–13]. In addi-
tion, univariate analysis revealed that both natriuretic
peptides correlated well with age, BSA and eGFR;
these observations were also in line with previous pub-
llications [18, 21]. In order to predict log-transformed
BNP concentrations, we created two equations. Equa-
tion 1 consisted of three independent variables (age,
eGFR and log-transformed NT-proBNP), while the
other consisted of two variables (eGFR and log-trans-
formed NT-proBNP); the latter was simpler and thus
more clinically relevant. When we divided patients
into 4 groups according to known cut-off values for
BNP concentration, the rate of complete group agree-
ment was modest between actual BNP concentration
and BNP concentration estimated by our equations.
However, their prognostic strength was equivalent to
actual BNP or NT-proBNP. Our results also clearly
showed that estimation of BNP using the simpler equa-
tion (Equation 2) was not inferior to the estimation of
BNP using the formula determined by multivariate
analysis (Equation 1). Thus, in routine clinical prac-
tice, it might be better to use the simpler equation for
the estimation of BNP concentration from actual NT-
proBNP concentrations.

In Table 3 we present a nomogram which can be used
to estimate BNP concentration according to the vari-
ous NT-proBNP and eGFR concentrations obtained in
this study. This conversion sheet could be very useful
for clinical practice, especially when physicians who
are very familiar with BNP testing begin to use NT-
proBNP instead of BNP for HF management.

There were several limitations to this study, which
should be considered when interpreting our conclu-
sions. First, the study subjects were not a consecutive
series of patients whose attending physician ordered
BNP measurements. However, the sample size was
large enough to create equations in the derivation co-

Fig. 4. Correlation of N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration from the same patient in
fresh plasma (1st) and after storage (2nd). A: The entire population (n = 188), B: After the exclusion of 5 cases whose NT-
proBNP level at 1st examination was > 35,000 pg/ml (n = 183)
hort, and to compare prognostic strength in the validation cohort. Furthermore, immunoassays rely on antibodies that measure an epitope within the target molecule, and thus not necessarily the actual peptide [22]. Cross-reactivity is another problem for accurate measurement. Our results could not be extrapolated when using different antibodies from different manufactures for natriuretic peptide analysis. BNP and NT-proBNP were not measured on the same day. We found that after storage there was a slight but statistically significant reduction in NT-proBNP level, which was more pronounced at higher levels of NT-proBNP. However, these differences were reduced, and the correlation slope reached 1.0, when we excluded 5 cases in which the NT-proBNP level in the fresh sample was > 35,000 pg/ml. Thus, the observed differences might have been caused primarily by the sample dilution technique. Another limitation is that our results in this study may be useful only for the BNP immunoassay method used in this study, not for other BNP immunoassay methods. It is known that BNP levels vary widely according to the immunoassay method used for the assay of BNP [21]. Therefore, using immunoassay should be taken into consideration when using our nomogram.

**Conclusion**

Brain natriuretic peptide (BNP) concentrations were reliably estimated from an equation featuring NT-proBNP and eGFR. Estimated BNP concentrations were closely associated with future cardiovascular outcome, and its prognostic ability was almost equivalent to the original BNP level. The nomogram provided herein will be very useful when physicians need to infer BNP concentrations from actual NT-proBNP concentrations.

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**Conflict of Interest**

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**Table 3. Nomogram for the estimation of BNP level according to NT-proBNP and eGFR level**

| NT-proBNP (pg/ml) | eGFR (ml/min/1.73m²) |
|-------------------|----------------------|
| 5                 | 10                   | 20     | 30     | 40     | 50     | 60     | 70     | 80     | 90     | 100    |
| 50                | <100                 | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   |
| 100               | <100                 | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   |
| 200               | <100                 | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   |
| 400               | <100                 | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   | <100   |
| 900               | <100                 | <100   | <100   | 100–200| 100–200| 100–200| 100–200| 100–200| 100–200| 100–200|
| 2,000             | 100–200              | 100–200| 100–200| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600|
| 4,000             | 200–600              | 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600|
| 6,000             | 200–600              | 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| >600   |
| 8,000             | 200–600              | 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| >600   | >600   |
| 10,000            | 200–600              | 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| 200–600| >600   | >600   |

Estimated BNP concentration is calculated by the following equation.

\[
\text{Log BNP} = (0.72 \times \text{log NT-proBNP}) + (0.01 \times \text{eGFR}) - 0.53
\]

BNP: brain natriuretic peptide, NT-proBNP: N-terminal proBNP, eGFR: estimated glomerular filtration rate.
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NT-proBNP値によるBNP値の推算

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要 旨：脳性ナトリウム利尿ペプチド（BNP）とBNP前駆体N末端フラグメント（NT-proBNP）は、心不全患者の診断と治療指標として不可欠なバイオマーカーである。しかしながら、古くからBNPに慣れ親しんだ臨床医にとっては、NT-proBNP値からBNP値を推測することはしばしば困難である。我々は、NT-proBNP値からBNP値を推算する式を作成し、推算されたBNP値が実際のBNP値と同等の予後予測能を有するかを検討した。我々は、心不全あるいは心不全疑い患者374例（導出群）のデータから、多変量解析を用いてBNP値推算式を作成した。検証群375例において、推定BNPレベルが実際のBNPおよびNT-proBNPレベルと比較して同等の予後予測能を有するかを検証した。導出群において、logBNPとlogNT-proBNPとの間には強い相関があった（r = 0.90）。検証群では49例で主要有害心臓事象が発生した。Cox比例解析により、実際のBNPレベルと推定BNPレベルが将来の心血管転帰に対する同等かつ有意な予測因子であることが明らかとなった。したがって、この推算式は、特にNT-proBNP検査に慣れていない医師にとって有用である可能性が示唆された。

キーワード：ナトリウム利尿ペプチド、予後、心不全。

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