Range of plasma brain natriuretic peptide (BNP) levels in hemodialysis patients at a high risk of 1-year mortality and their relationship with the nutritional status: a retrospective cohort study in one institute

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Abstract

Background: Brain natriuretic peptide (BNP) levels are used as a marker of heart failure, which is the leading cause of morbidity and mortality in dialysis patients. BNP levels increase as renal function declines. The range of BNP levels associated with satisfactory longevity in dialysis patients currently remains unknown.

Methods: In total, 660 patients receiving maintenance hemodialysis were enrolled. BNP levels were measured at the end of the year and in a follow-up to assess 1-year mortality between 2008 and 2012. Patients were divided into six groups according to BNP levels: < 50 (reference), 50 to < 100, 100 to < 300, 300 to < 500, 500 to < 1000, and ≥ 1000 pg/mL. One-year mortality at each BNP level was analyzed using Cox's proportional hazards model after adjustments for confounding factors.

Results: During the follow-up period, 78 (11.8%) deaths were recorded. After adjustments for confounding factors, such as gender, age, hemodialysis vintage, and primary disease, the risk of 1-year mortality was significantly high with BNP levels of 500 to < 1000 (hazard ratio [HR] 3.010; 95% confidence interval [CI] 1.065–10.729; P = 0.037) and more than 1000 pg/mL (HR 5.291; 95% CI 2.014–18.170; P = 0.0003). After adjustments for Kt/V, the risk of 1-year mortality was also significantly high with BNP levels of 500 to < 1000 (HR 3.045; 95% CI 1.065–10.929; P = 0.037) and more than 1000 pg/mL (HR 5.221; 95% CI 1.943–18.165; P = 0.0006). Following further adjustments for nutritional factors, such as albumin levels, total cholesterol levels, the normalized protein catabolic rate (nPCR), body mass index (BMI), and percent creatinine generation rate (%CGR), BNP levels of 500–1000 (HR 1.990; 95% CI 0.639–7.570; P = 0.244), and more than 1000 pg/mL (HR 2.100; 95% CI 0.663–8.105; P = 0.213) were no longer risk factors.

Continued on next page

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Background

Brain natriuretic peptide (BNP) levels are used as a marker of heart failure [1], which is the leading cause of morbidity and mortality in hemodialysis patients. BNP levels in these patients are crucial for diagnosing and assessing the severity of heart failure and predicting future cardiovascular morbidity and mortality [2]. Plasma BNP levels increase with declines in renal function, and BNP levels are elevated in hemodialysis patients, even in the absence of heart failure. However, the normal threshold of BNP levels in hemodialysis patients currently remains unknown.

The range of BNP levels in hemodialysis patients needs to be clarified in order to ensure satisfactory longevity. Therefore, the present study investigated the relationship between plasma BNP levels and 1-year mortality in hemodialysis patients and examined the range of BNP levels associated with an improved prognosis.

Methods

In total, 660 patients receiving maintenance hemodialysis were enrolled in the present study. BNP levels were measured at the end of the year and in a follow-up to assess 1-year mortality between 2008 and 2012. The hazard ratio (HR) for 1-year mortality was evaluated in six groups of patients divided according to BNP levels: BNP < 50 (control), BNP < 100, 100 ≤ BNP < 300, 300 ≤ BNP < 500, 500 ≤ BNP < 1000, and 1000 ≤ BNP. Analyses were performed in four steps. In the first step, we adjusted for basal confounding factors, such as gender, age, hemodialysis vintage, and primary disease. In the second step, we adjusted for Kt/V as a prescriptive factor. In the third step, we adjusted for nutritional factors, including serum albumin levels, total cholesterol levels, the normalized protein catabolic rate (nPCR), body mass index (BMI), and percent creatinine generation rate (%CGR). In the fourth step, we adjusted for transthyretin (also known as prealbumin) levels.

A blood sample was obtained before the first hemodialysis session of the week. BNP levels were measured using the automatic enzyme immunoassay device AIA-600II® (TOSO CORPORATION) with E-test TOSO II (BNP).

All statistical analyses were performed using JMP (ver.10). P values less than 0.05 were considered to be significant.

Conclusion: In dialysis patients, a BNP level ≥ 500 pg/mL is a risk factor for 1-year mortality. The risk associated with high BNP levels is reduced by nutritional factors, which suggests a relationship between high BNP levels and the nutritional status. In conclusion, efforts are needed to maintain BNP levels at lower than 500 pg/mL and improve the nutritional status.

Keywords: Brain natriuretic peptide, Hemodialysis, Mortality, Nutritional status

The present study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Research Ethics Committee of Kenwakai Hospital (No. 2019008).

Results

The baseline characteristics of study participants are shown in Table 1. Among 660 patients, 446 (67.6%) were male. As the primary disease, 318 (48.2%) had chronic glomerulonephritis (CGN), 255 (38.6%) diabetic nephropathy (DN), and 87 (13.2%) other diseases. Regarding patient characteristics related to heart disease, 578 (87.6%) out of 660 patients were prescribed antihypertensive agents, while 147 (22.3%) had a history of acute coronary syndrome, coronary intervention, or coronary surgery. Aortic stenosis and/or regurgitation of more than moderate severity according to the ACC/AHA practice guidelines were noted in 40 (6.2%) out of 645 patients examined by echocardiography. Mitral regurgitation of more than moderate severity and/or severe was detected in 26 (4.0%) out of 645 patients examined by echocardiography. Heart failure with a reduced ejection fraction (< 40%) was observed in 18 (2.80%) out of 641 patients examined by echocardiography. The most common hemodialysis vintage was 5–10 (29.7%). As a hemodialysis prescription factor, Kt/V values were the most frequently distributed between 1.4 and < 1.6 (30.6%). Nutritional factors were nPCR, serum albumin levels, total cholesterol levels, BMI, and %CGR. In the analysis of targeting factors, 147 patients had a BNP level of 100 to < 200 pg/mL (22.3%), and 143 had a transthyretin level of 20 to < 25 mg/dL (21.8%). As shown in Table 2, the mean age was 68.5 ± 12.9 years and mean vintage was 6.48 ± 5.09 years.

Table 3 shows the prognosis of study participants. During the observation period, there were 78 deaths (11.8%). Table 4 shows the causes of death: heart failure in 19, cerebrovascular disease in 13, infection in 11, cachexia/uremia in 10, sudden death in 6, malignant tumors in 5, gastrointestinal disease in 5, and myocardial infarction in 4. Table 5 shows HR for 1-year mortality after adjustments for confounding factors. DN as the primary disease was a significantly higher risk factor (HR 2.11; 95%CI 1.31–3.45; P = 0.0018) than CGN. Kt/V...
Table 1 Background characteristics of the study participants

| Basal factors                             | male   | female | total |
|-------------------------------------------|--------|--------|-------|
| Gender                                    | 446    | 214    | 660   |
| %                                         | 67.6   | 32.4   | 100   |
| Age (year)                                | 0~     | 30~    | 45~   | 60~   | 75~   | total |
| Number                                    | 6      | 24     | 115   | 285   | 230   | 660   |
| %                                         | 1      | 3.6    | 17.4  | 43.2  | 34.8  | 100   |
| Primary disease                           | CGN    | DM     | others | total |
| Number                                    | 318    | 255    | 87    | 660   |
| %                                         | 48.2   | 38.6   | 13.2  | 100   |
| Hemodialysis vintage                      | < 2    | 2~     | 5~    | 10~   | 15~   | 20~   | 25~   | ≥ 30 | total |
| Number                                    | 136    | 186    | 196   | 91    | 39    | 10    | 2     | 0    | 660 |
| %                                         | 20.6   | 28.2   | 29.7  | 13.8  | 5.9   | 1.5   | 0.3   | 0    | 100 |
| Hemodialysis prescription factor          | Kt/V   | <0.8   | 0.8~   | 1.0~   | 1.2~   | 1.4~   | 1.6~   | 1.8~   | ≥ 2.0 | total |
| Number                                    | 13     | 20     | 47    | 110   | 202   | 152   | 75    | 41    | 660 |
| %                                         | 2      | 3      | 7.1   | 16.7  | 30.6  | 23    | 11.4  | 6.2   | 100 |
| Nutrition factors                         | nPCR  (g/kg/day) | <0.5 | 0.5~   | 0.7~   | 0.9~   | 1.1~   | ≥ 1.3 | total |
| Number                                    | 21     | 175    | 320   | 124   | 17    | 2     | 660   |
| %                                         | 3.2    | 26.6   | 48.5  | 18.8  | 2.6   | 0.3   | 100   |
| Albumin (g/dl)                            | <3.0   | 3.0~   | 3.5~   | 4.0~   | ≥ 4.5 | total |
| Number                                    | 49     | 235    | 306   | 69    | 1     | 600   |
| %                                         | 7.4    | 35.6   | 46.4  | 10.5  | 0.1   | 100   |
| BMI (kg/m²)                               | <16    | 16~    | 18~    | 20~    | 22~   | 24~   | 26~   | ≥ 28 | total |
| Number                                    | 5      | 32     | 120   | 186   | 156   | 93    | 31    | 36    | 660 |
| %                                         | 0.7    | 4.9    | 18.2  | 28.2  | 23.7  | 14.1  | 4.7   | 5.5   | 100 |
| Total cholesterol (mg/dl)                 | <80    | 80~    | 120~   | 160~   | 200~   | ≤ 240 | total |
| Number                                    | 0      | 68     | 283   | 193   | 31    | 1     | 576   |
| %                                         | 0      | 11.8   | 49.1  | 33.5  | 5.4   | 0.2   | 100   |
| %CGR (%)                                  | <60    | 60~    | 70~    | 80~    | 90~   | 100~   | 110~   | 120~   | ≥ 130 | total |
| Number                                    | 66     | 48     | 78    | 95    | 110   | 115   | 71    | 38    | 35   | 656 |
| %                                         | 10.1   | 7.3    | 11.9  | 14.5  | 16.8  | 17.5  | 10.8  | 5.8   | 5.3  | 100 |

Analysis targeting factors

| BNP (pg/ml)                               | <50    | 50~    | 100~   | 200~   | 300~   | 500~   | ≥ 1000 | total |
| Number                                    | 97     | 99     | 147    | 62     | 79     | 92     | 84     | 660   |
| %                                         | 14.7   | 15     | 22.3   | 9.4    | 12     | 13.9   | 12.7   | 100   |
| Transthyretin (mg/dl)                      | <15    | 15-20  | 20-25  | 25-30  | 30-35  | 35-40  | ≥ 40   | total |
| Number                                    | 32     | 60     | 143    | 141    | 130    | 92     | 59     | 657   |
| %                                         | 4.9    | 9.1    | 21.8   | 21.4   | 19.8   | 14     | 9      | 100   |

values of 1.0 to < 1.2 were a significantly higher risk factor than 1.2 to < 1.4 (HR 2.42; 95%CI 1.12–5.18; p = 0.02). NPCR values of 0.5 to < 0.7 were a significantly higher risk factor than 0.7 to < 0.9 (HR 2.07; 95%CI 1.26–3.42; p = 0.0039). Serum albumin levels of 3.0 to < 3.5 g/dL were a significantly higher risk factor (HR 3.25; 95%CI 1.87–5.88; p < 0.0001) than 3.5 to < 4.0 g/dL. %CGR of 60–70% was a significantly higher risk factor than 90 to < 100% (HR 2.75; 95%CI 1.11–9.92; p < 0.030). Transthyretin levels of 15 to < 20 mg/dL were a significantly higher
risk factor than 20 to < 25 mg/dL (HR 3.86; 95%CI 1.92–8.00; P = 0.0002).

Figure 1 shows the results obtained in the Kaplan-Meier survival analysis of BNP levels. The 1-year survival rate was significantly low at a BNP level > 300 pg/mL. Figure 2 shows the estimated cubic spline transformation of the relationship between BNP levels and HR for 1-year mortality adjusted for age, gender, dialysis vintage, and primary diseases. BNP levels in hemodialysis patients correlated with 1-year mortality. Figure 3 shows a receiver operating characteristic (ROC) curve of the relationship between BNP levels and 1-year mortality. The area under the curve was 0.69, and the cut-off value was 299.2 pg/mL. Table 6 shows HR for 1-year mortality at each BNP level relative to that less than 50 pg/mL. After adjustments for basal confounding factors (gender, age, primary disease, and hemodialysis vintage) (model 1), comparisons with the reference group revealed that BNP levels of 500 to < 1000 pg/mL were a significantly high-risk factor (HR 3.01; 95%CI 1.07–10.73; P < 0.037), as were those higher than 1000 pg/mL (HR 5.29; 95%CI 2.01–18.17; P < 0.0003). After further adjustments for Kt/V values (model 2), similar results were obtained to those in model 1. A BNP level higher than 500 pg/mL was significantly high. After further adjustments for five nutritional factors (nPCR, serum albumin levels, BMI, total cholesterol levels, and %CGR) (model 3), BNP levels higher than 500 pg/mL were not significant. Table 7 also shows HR for 1-year mortality at each BNP level. Models 1 and 2 were the same as those in Table 6, whereas model 4 showed HR further adjusted for transthyretin. BNP levels higher than 500 pg/mL were also not significant.

Table 3 Prognosis of study participants

| Prognosis | Number | %    |
|-----------|--------|------|
| Survival  | 582    | 88.2 |
| Death     | 78     | 11.8 |
| Total     | 660    | 100  |

Table 4 Causes of death

| Cause of death          | Number | %    |
|-------------------------|--------|------|
| Heart failure           | 19     | 24.3 |
| Cerebrovascular disease | 13     | 16.7 |
| Infection               | 11     | 14.1 |
| Cachexia/uremia         | 10     | 12.8 |
| Sudden death            | 6      | 7.7  |
| Malignant tumor         | 5      | 6.4  |
| Gastrointestinal disease| 5      | 6.4  |
| Myocardial infarction   | 4      | 5.1  |
| Others                  | 5      | 6.4  |
| Total                   | 78     | 100  |

Table 8 shows correlation coefficients and P values for BNP and each parameter. BNP levels correlated with age, BMI, albumin levels, total cholesterol levels, Kt/V, nPCR, %CGR, and transthyretin levels. BNP levels showed the strongest correlation with transthyretin levels.

Discussion

The Japanese Society for Dialysis Treatment (JSDT) investigated several indices related to 1-year mortality in patients after adjustments for basal confounding factors, including gender, age, hemodialysis vintage, and primary disease; dialysis prescription factors, such as Kt/V; and nutritional factors, including nPCR, albumin levels, total cholesterol levels, BMI, and %CGR [3]. BNP levels were not included in these indices. In the present study, we used the JSDT method to analyze HR for 1-year mortality at different BNP levels. We concluded that a BNP level higher than 500 pg/mL is a significantly high-risk factor for 1-year mortality.

The present study confirmed previous findings showing that BNP levels are a predictor of mortality in hemodialysis patients [4–6]. Naganuma et al. reported that a BNP level less than 200 pg/mL was associated with a good prognosis after a 3-year follow-up [7], whereas Biasioli et al. showed that a BNP level less than 335 pg/mL was associated with a good prognosis after a 28-month follow-up [8]. Zoccali et al. identified a BNP level higher than 125 pg/mL as a significantly high-risk factor after a 26-month follow-up [9, 10]. Our follow-up period of 1 year was the shortest, while the number of factors used for adjustments was the largest. A shorter follow-up period is suitable for evaluating BNP levels as a tool for risk stratification and treatment guidance. BNP levels need to be maintained at lower than 500 pg/mL as a daily management goal.
The risk associated with a BNP level ≥ 500 pg/mL was canceled after adjustments for nutritional factors. Therefore, a relationship appears to exist between high BNP levels and the nutritional status. The presence of chronic heart failure with ongoing weight loss or a low BMI is a risk factor for death in hemodialysis patients. The results of the Cox proportional hazard regression analysis are summarized in Table 5.

### Table 5: Cox’s proportional hazard ratio of prognostic correcting factors (Continued)

| factor                  | Hazard ratio | 95%CI   | p value | lower | upper |
|-------------------------|--------------|---------|---------|-------|-------|
| **Total cholesterol (mg/dl)** |              |         |         |       |       |
| <80                     |              |         |         |       |       |
| 80 to <120              | 1.3127943    | 0.637005| 2.493205| 0.441 |
| 120 to <160 (reference) | 1            |         |         |       |       |
| 160 to <200             | 0.7676479    | 0.431736| 1.321843| 0.3451|
| 200 to <240             | 0.7481263    | 0.180457| 2.071826| 0.6148|
| 240 ≤                   | 7.12728      | 4.101126| 441.142 | 0.0104|
| **BMI (kg/m²)**         |              |         |         |       |       |
| <16                     | 2.6829842    | 0.593253| 12.33062| 0.1361|
| 16 to <18               | 1.4307039    | 0.532743| 3.250588| 0.4465|
| 18 to <20               | 0.764411     | 0.380715| 1.460268| 0.4227|
| 20 to <22 (reference)   | 1            |         |         |       |       |
| 22 to <24               | 0.7607745    | 0.405455| 1.390405| 0.3769|
| 24 to <26               | 0.6111911    | 0.258927| 1.292297| 0.206 |
| 26 to <28               | 0.2169053    | 0.012157| 1.389405| 0.2769|
| 28 ≤                    | 0.7508242    | 0.221565| 1.972202| 0.5806|
| **%CGR (%)**            |              |         |         |       |       |
| <60                     | 3.5766971    | 1.630619| 8.3974  | 0.0014|
| 60 to <70               | 2.7486736    | 1.107819| 6.919564| 0.0297|
| 70 to <80               | 1.4473888    | 0.56513 | 3.706997| 0.4341|
| 80 to <90               | 1.4485841    | 0.599571| 3.593324| 0.4081|
| 90 to <100 (reference)  | 1            |         |         |       |       |
| 100 to <110             | 1.166507     | 0.482823| 2.893589| 0.7313|
| 110 to <120             | 0.509893     | 0.112931| 2.205797| 0.287 |
| 120 to <130             | 0.6324356    | 0.094267| 2.454098| 0.5391|
| 130 ≤                   | 1.059352     | 0.230507| 3.550648| 0.9314|
| **Transthyretin (mg/dl)**|              |         |         |       |       |
| <15                     | 10.055064    | 4.997492| 20.87464| <.0001|
| 15 to <20               | 3.8640013    | 1.924016| 8.008218| 0.0002|
| 20 to <25 (reference)   | 1            |         |         |       |       |
| 25 to <30               | 1.089919     | 0.509545| 2.348036| 0.823 |
| 30 to <35               | 0.759041     | 0.312315| 1.705797| 0.287 |
| 35 to <40               | 0.350335     | 0.080339| 1.086298| 0.0712|
| 40 ≤                    | 5.23E-10     | 0.368802| 0.0002  |       |

BMI body mass index, CGN chronic glomerulonephritis, DN diabetic nephropathy, nPCR normalized protein catabolic rate, %CGR percent creatinine generation rate.

The risk associated with a BNP level ≥ 500 pg/mL was canceled after adjustments for nutritional factors. Therefore, a relationship appears to exist between high BNP levels and the nutritional status. The presence of chronic heart failure with ongoing weight loss or a low BMI is a...
predictor of muscle mass loss, a decline in exercise capacity, and a poor prognosis [11]. A syndrome involving weight loss, general fatigue, fat loss, and muscle wasting with chronic disease was recently recognized as cachexia. Cachexia is a prevalent and important pathological condition associated with chronic heart failure. It reduces survival independently of the heart failure function class and ejection [12, 13]. BNP levels play a major role in salt and water homeostasis, protecting the cardiovascular system from the effects of volume overload and cardiac comorbidities. In the bioimpedance method, BNP levels reflect individual variations in the hydration status of hemodialysis patients [14]. A value of 500 pg/mL has been used to differentiate between hemodialysis patients with or without volume overload [15, 16]. The extracellular water content to intracellular water content ratio increases as BMI decreases. A strong negative correlation was previously reported between excess fluid mass and BMI [17]. Patients with BNP levels higher than 500 pg/mL were overhydrated and weight loss from

Fig. 1 Kaplan-Meier survival analysis of BNP levels. One-year survival rates were 95.5% at BNP <50 pg/mL, 95.0% at 50-100 pg/mL, 90.0% at 100-200 pg/mL, 93.6% at 200-300 pg/mL, 87.3% at 300-500 pg/mL, 83.7% at 500-1000 pg/mL, and 70.2% at >1000 pg/mL. The 1-year survival rate was significantly low at BNP >300 pg/mL.

Fig. 2 Estimated cubic spline transformation of the relationship between BNP levels and the adjusted hazard ratio. The reference BNP for this plot (with HR fixed as 1.0) was <50 pg/mL. The hazard ratio of 1-year mortality was adjusted for age, gender, dialysis vintage, and primary diseases. Dotted lines are 95% confidence limits.
malnutrition resulted in additional fluid excess. On the other hand, even though BNP levels were high, good nutrition, and weight gain reduced volume overload. Chronic overhydration is an independent predictor of mortality in hemodialysis patients [18]. The risk associated with a high BNP level depends on the nutritional status. The combination of a high BNP level with a poor nutritional status needs to be treated not only by cardiological therapy, but also nutritional support. Despite the accepted importance of the influence of nutritional factors on the severity of cardiovascular disease, limited information is currently available on dietary intake and heart failure. Furthermore, existing nutritional interventions for heart failure were mostly pilot studies with small sample sizes and short follow-ups [19]. The findings of 17 randomized controlled trials indicated that education on nutritional interventions had positive effects on the clinical outcomes of patients; however, they

Fig. 3 Receiver operating characteristic (ROC) curve of the relationship between BNP levels and 1-year mortality. The area under the curve was 0.69 and the cut-off value was 299.2 pg/mL.

### Table 6 HR for 1-year mortality of BNP levels adjusted for basal factors, Kt/V and nutrition factors

| BNP (pg/ml) | Adjusted for basal factors (model 1) | Adjusted for basal factors and Kt/V (model 2) | Adjusted for basal factors, Kt/V and nutrition factors (model 3) |
|-------------|-------------------------------------|-----------------------------------------------|---------------------------------------------------------------|
|             | HR p value 95%CI                      | HR p value 95%CI                              | HR p value 95%CI                                              |
| <50 (reference) | 1 - - - | 1 - - - | 1 - - - |
| 50 to <100  | 0.997121 0.9966 0.262147 4.051568 | 0.964564 0.9574 0.253041 3.926629 | 0.838438 0.8047 0.205753 3.621547 |
| 100 to <200 | 1.907679 0.2326 0.678499 6.766743 | 1.840871 0.2619 0.652984 6.541653 | 0.9592779 0.9477 0.292026 3.725938 |
| 200 to <300 | 1.198396 0.28121 5.106865 | 1.165241 0.8354 0.260802 5.155792 | 0.8387627 0.8229 0.170045 4.04536 |
| 300 to <500 | 2.446838 0.1157 8.994658 | 2.5366 0.1026 0.835008 9.354117 | 2.5461197 0.133 0.758488 10.11498 |
| 500 to <1000 | 3.009917 0.0369 1.065084 10.72921 | 3.044996 0.037 1.065717 10.92917 | 1.9907521 0.2444 0.639274 7.570738 |
| ≥1000       | 5.291238 0.0003 2.013968 18.17073 | 5.221112 0.0006 1.943194 18.16484 | 2.0999726 0.2136 0.663497 8.104608 |

*HR* hazard ratio
all involved sodium and fluid restrictions [20]. After the administration of a high-caloric (600 kcal), high-protein (20 g), and oral nutritional supplement for 6 weeks to cachexic heart failure patients, significant improvements were observed in the quality of life, 6-m walking test, and tumor necrosis factor-α without the significant recovery of peak VO₂ or the left ventricular ejection fraction; BNP was not measured in that study [21]. After the administration of 500 mL/day of enteral nutrition for 3 months to elderly heart failure patients, marked improvements were noted in BNP, interleukin-6, tumor necrosis factor-α, and C-reactive protein levels [22].

After adjustments for transthyretin levels, the risk associated with BNP ≥500 pg/mL was no longer significant. Transthyretin is an important indicator of not only the nutritional status, but also the survival of hemodialysis patients after adjustments for age, gender, race, hemodialysis vintage, the diabetic state, and nutritional markers, including serum albumin levels [22, 23]. A recent study reported that serum transthyretin levels correlated with body fat mass [24]. The half-life of transthyretin is 2–3 days, which is shorter than that of serum albumin. A decline in serum transthyretin levels by 10 g/dL over 6 months is a robust predictor of increased mortality [25, 26]. The present results showed that a transthyretin level of less than 20 mg/dL was a high-risk factor. In hemodialysis patients, the combination of a BNP level ≥500 pg/mL and transthyretin level < 20 mg/dL, which is a decrease of more than 10 mg, warrants urgent treatment.

### Conclusions

In dialysis patients, a BNP level ≥500 pg/mL is a significantly high-risk factor for 1-year mortality. The risk associated with a high BNP level is canceled out after adjustments for nutritional factors. Therefore, a relationship appears to exist between high BNP levels and the nutritional status. Efforts are needed to maintain a BNP level of less than 500 pg/mL and improve nutritional factors. The risk associated with a BNP level ≥500 pg/mL also depends on transthyretin levels, which need to be maintained at > 20 mg/dL.

### Abbreviations

%CGR: Percent creatinine generation rate; BMI: Body mass index; BNP: Brain natriuretic peptide; CGN: Chronic glomerulonephritis; DN: Diabetic nephropathy; nPCR: Normalized protein catabolic rate

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### Authors’ contributions

EK wrote the manuscript and KH revised it. EK contributed to the research concept and study design. KF contributed to data acquisition, the risk of bias assessment, data analysis/interpretation, and statistical analyses. ST contributed to data interpretation. EK contributed to supervision and mentorship. The authors read and approved the final manuscript.

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### Availability of data and materials

All data generated or analyzed during this study are included in this manuscript.

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**Table 7** HR for 1-year mortality of BNP levels adjusted for basal correcting factors, Kt/V and transthyretin

| BNP (pg/ml) | Adjusted for basal factors (model 1) | Adjusted for basal factors and Kt/V (model 2) | Adjusted for basal factors, Kt/V and transthyretin (model 4) |
|-------------|-------------------------------------|---------------------------------------------|---------------------------------------------------------------|
|             | HR p value 95%CI | HR p value 95%CI | HR p value 95%CI |
| <50 (reference) | 1 - - | 1 - - | 1 - - |
| 50 to <100 | 0.997121 | 0.9966 | 0.262147 | 4.051568 | 0.964564 | 0.9574 | 0.253041 | 3.926629 | 0.8926794 | 0.8672 | 0.233334 | 3.644237 |
| 100 to <200 | 1.907679 | 0.2326 | 0.678499 | 6.766743 | 1.840871 | 0.2619 | 0.652984 | 6.541653 | 1.7642041 | 0.3025 | 0.619779 | 6.310716 |
| 200 to <300 | 1.198396 | 0.7993 | 0.282181 | 5.106865 | 1.165241 | 0.8354 | 0.260802 | 5.155792 | 0.8019716 | 0.7659 | 0.178553 | 3.594217 |
| 300 to <500 | 2.446838 | 0.1157 | 0.808727 | 8.994658 | 2.5366 | 0.1026 | 0.835008 | 9.354117 | 1.986255 | 0.2446 | 0.636523 | 7.46915 |
| 500 to <1000 | 3.009917 | 0.0369 | 1.065084 | 10.72921 | 3.044996 | 0.037 | 1.065717 | 10.92917 | 1.7769718 | 0.3121 | 0.602599 | 6.532927 |
| ≥1000 | 5.291238 | 0.0003 | 2.013968 | 18.17073 | 5.221112 | 0.0006 | 1.943194 | 18.16484 | 2.710241 | 0.0653 | 0.942719 | 9.854096 |

**Table 8** Correlation coefficients and p value for BNP and the studied parameter

| Parameter                        | Mean   | SD     | r       | p       |
|----------------------------------|--------|--------|---------|---------|
| Age                              | 68.5121 | 12.8628 | 0.222574 | <.0001  |
| Hemodialysis vintage (year)      | 6.476169 | 5.092643 | 0.017756 | 0.6489  |
| BMI (kg/m²)                      | 22.2116 | 3.056318 | -0.14469 | 0.0002  |
| Albumin (g/dl)                   | 3.490455 | 0.4122 | -0.29154 | <.0001  |
| Total cholesterol (mg/dl)        | 153.0382 | 29.14238 | -0.11052 | 0.0079  |
| Kt/V                             | 1.532889 | 0.342536 | -0.1803 | <.0001  |
| nPCR (g/kg/day)                  | 0.782168 | 0.15667 | -0.19454 | <.0001  |
| %CGR (%)                         | 92.01985 | 24.93402 | -0.21274 | <.0001  |
| Transthyretin (mg/dl)            | 28.45586 | 8.384788 | -0.39012 | <.0001  |

BMI body mass index, nPCR normalized protein catabolic rate, %CGR percent creatinine generation rate
Ethics approval and consent to participate
The present study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the research Ethics Committee of Kenwakai Hospital (No.2019008).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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