N-terminal pro brain natriuretic peptide as a cardiac biomarker in Japanese hemodialysis patients

Short title: N-terminal pro brain natriuretic peptide in Japanese hemodialysis patients

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Abstract

Purpose: This study examined the clinical significance of NT-proBNP level as a cardiac marker in Japanese hemodialysis (HD) patients.

Methods: This was a multicenter cross-sectional study involving 1,428 Japanese HD patients. Ultrasonic cardiography (UCG) data at post-HD were obtained from 395 patients. We examined whether serum NT-proBNP levels were associated with cardiac parameters and assessed cut-off values, and investigated factors associated with a reduced ratio of NT-proBNP levels pre- and post-HD.

Results: Multivariate logistic regression analysis showed that pre- and post-HD NT-proBNP levels were associated with left ventricular hypertrophy (LVH) on electrocardiogram (ECG) (odds ratio (OR): 3.10; P<0.001 at pre-HD and OR: 2.70; P<0.001 at post-HD) and LVH on UCG (OR: 3.06; P<0.001 at pre-HD and OR: 3.15; P<0.001 at post-HD). Post-NT-proBNP levels were also significantly associated with ejection fraction (EF) on UCG (OR: 35.83; P<0.001). Receiver operating characteristic curves for predicting the presence of LVH on ECG and UCG showed similar sensitivity (57.7%, 57.3% at pre-HD and 63.9%, 48.2% at post-HD) and specificity (66.5%, 72.9% at pre-HD and 59.2%, 81.9% at post-HD). Decreased EF on UCG showed better sensitivity (78.6%) and specificity (88.7%). The NT-proBNP reduction ratio during a HD session correlated with Kt/V, membrane area, membrane type, modality, body weight gain ratio, treatment time, and ultrafiltration rate (UFR) with multiple linear regression (R: 0.53; P<0.001 except for UFR P=0.003).

Conclusion: Both pre- and post-HD NT-proBNP are associated with the presence of LVH in this population. The post-HD NT-proBNP level is a useful marker for systolic dysfunction.

Keywords: biomarker, cardiac dysfunction, hemodialysis, left ventricular hypertrophy, N-terminal pro brain natriuretic peptide

Introduction

The annual mortality for hemodialysis (HD) patients is much higher than the general population, with cardiovascular disease (CVD) accounting for 34% of deaths (1, 2). HD patients are therefore recognized as a group at high risk for CVD. Many dialysis clinicians periodically check chest X-rays and electrocardiograms (ECG) to help prevent CVD in routine clinical practice; however, many patients still die from CVD (1) and more effective management is required to reduce the incidence of CVD.

N-terminal pro brain natriuretic peptide (NT-proBNP) and brain natriuretic peptide (BNP) are released from the heart in response to cardiac strain (3, 4), with both being markers of heart failure (5). Compared with BNP, NT-proBNP has several advantages in clinical settings, including that samples can be kept at room temperature because of their greater stability (6, 7) and that NT-proBNP can be measured from a serum sample without the need to obtain an additional plasma sample. However, NT-proBNP is a 76-amino acid polypeptide and is excreted from the kidneys, and it therefore accumulates with a decline in renal function. Although the clinical usefulness of NT-proBNP has been reported for the detection of cardiac dysfunction in the general population (8), its usefulness among HD patients remains to be validated.

It is reported that HD patients in Japan undergo slightly different treatment methods than HD patients in other countries, such as increased use of an arteriovenous fistula compared with a vascular catheter or arteriovenous graft, longer duration of HD because of a slower transition to transplantation, higher use of a high-flux membrane, slightly lower blood flow, slightly longer treatment time, and have better mortality (9-12). These differences suggest that the clinical significance of NT-proBNP in Japanese HD patients should be determined in large clinical studies.

The current study was a multicenter cross-sectional study to evaluate the clinical usefulness of NT-proBNP in 1,428 Japanese HD patients. We examined whether NT-proBNP is associated with left ventricular hypertrophy (LVH) using ECG, and also examined the association between serum NT-proBNP levels and ultrasonic cardiography (UCG) findings in 395 patients in whom it was possible to successfully carry out UCG after a HD session. Finally, the influence of a HD session on the NT-proBNP level was examined.

Methods

Study population

Fourteen facilities in Hiroshima participated in the study. There were 1,430 outpatients who were treated at HD facilities three times per week and were initially enrolled in the study. Exclusion criteria were patients under 20 years old, had undergone combined therapy with peritoneal dialysis, had received HD on a conventional schedule except three sessions per week, had a poor prognosis, advanced cancer, or active infection, showed symptoms of heart failure during rest (New York Heart Association classification IV), or mentally or otherwise unfit to give informed consent. Patients were registered from 1 December 2011 to 30 November 2012. One patient refused to participate in the study. After registration, one patient withdrew. Analyses were eventually performed using data from 1,428 patients.

The Ethics Committees of all participating hospitals approved the study protocol (H480) and written informed consent was obtained from each patient. This study was conducted in accordance with the principles contained within the Declaration of Helsinki.

Data collection

Blood samples for measurement of NT-proBNP were collected at pre- and post-HD at the first dialysis session of the week and were stored at room temperature. An ECLusys reagent NT-proBNP II kit (Roche Diagnostics, Tokyo, Japan) was used to measure NT-proBNP. An ECG was taken for all patients and UCG was performed at post-HD within 1 week before or after measurement for NT-proBNP. LVH was defined as a composite amplitude of SV1 or V2 + RV5 or V6 ≥35 mm on ECG according to the Sokolow-Lyon standard (LVH on ECG), the method commonly used to diagnose LVH on ECG in the clinical setting, and as left ventricular mass index >50 g/$m^{2.7}$ for males and >47 g/$m^{2.7}$ for females on UCG (LVH on UCG). Systolic ventricular dysfunction was defined as an ejection fraction (EF) <40% on UCG (decreased EF on UCG) using the Teichholz method, in which measurement is made from the long axis of the left ventricle using M-mode echocardiography. Clinical data, including cause of end-stage kidney disease, smoking status, previous history of CVD, dialysis prescriptions, hematological findings, clinical findings, and medications were checked using medical records. Urine volume was determined from a patient questionnaire survey. History of cardiovascular disease was defined as a combined history of heart failure, angina pectoris, myocardial infarction, stroke, and peripheral arterial disease.

Statistical analysis

Continuous variables are expressed as mean ± SD or median (interquartile range) and categorical variables as percentages. Variables that did not show normal distribution underwent logarithmic transformation before analysis. To assess variables that were associated with LVH on ECG, LVH on UCG, and decreased EF

on UCG, multivariate logistic regression analysis was performed. Except for age and gender, stepwise multiple regression analysis was performed to find independent predictors of cardiac dysfunction among potential confounders with $P<0.1$ in the univariate analysis. Age, gender, and the selected variables were used for the multiple logistic analysis. Receiver operating characteristic (ROC) curves were used to investigate cut-off values for pre- and post-HD NT-proBNP levels to detect LVH on ECG and UCG, and for post-HD NT-proBNP levels to detect decreased EF on UCG. Multiple linear regression analysis was performed among variables selected by stepwise regression analysis. In multivariate regression, a *P*-value <0.05 was considered statistically significant. All analyses were performed using SPSS statistical software (ver. 22.0; IBM, Armonk, NY).

Results

The main clinical and laboratory characteristics of the 1,428 HD patients are shown in Table 1. Data were similar to those for general Japanese HD patients (1). The median pre-HD NT-proBNP level was 3,633 pg/mL and post-HD NT-proBNP was 2,144 pg/mL. Because both pre- and post-NT-proBNP did not show a normal distribution, logarithmic transformation was performed. There were 635 (44.5%) patients with a history of CVD. In addition, UCG was performed for 397 (27.8%) patients; two patients were unable to be evaluated because of poor-quality images. Clinical characteristics did not differ between the entire population and the group that underwent UCG except for an increased heart failure ratio (263 (18.4%) for the entire population and 91 (23.0%) for the UCG group). For cardiac dysfunction, there were 242 (16.9%) patients with LVH on ECG in total, 60 (15.2%) with LVH on ECG in the UCG group, 251 (63.5%) with LVH on UCG, and 14 (3.5%) with decreased EF in the

UCG group.

To evaluate the clinical usefulness of NT-proBNP as a marker of cardiac dysfunction, we examined the association between NT-proBNP level and LVH on ECG. The predictors of LVH on ECG using multivariate logistic regression analysis are shown in Table 2. Univariate analysis was performed using the clinical parameters except for age and gender, and pre- and post-HD NT-proBNP levels, history of CVD, body weight gain ratio, cardiothoracic ratio (CTR), mean blood pressure (MBP), and serum albumin showed a correlation (P<0.1). Stepwise multiple regression analysis was performed with the potential confounders (P<0.1) in univariate analysis. Multivariate logistic analysis was performed using age, gender, and the selected variables, and pre-HD NT-proBNP level, age, body weight gain ratio, serum albumin, and MBP were identified independent predictors of LVH on ECG (odds ratio (OR): 3.10, 0.98, 1.14, 1.61, and 1.02; P<0.001, 0.012, 0.008, 0.040, and 0.002, respectively). Post-HD NT-proBNP level, age, body weight gain ratio, and MBP showed significant associations with LVH on ECG (OR: 2.70, 0.98, 1.13, and 1.02; P<0.001, 0.001, 0.015, and 0.001, respectively) (Table 2).

The predictors of LVH on UCG using multivariate logistic regression analysis are shown in Table 3. Similarly, except for age and gender, stepwise regression analysis was performed to determine candidate predictors of LVH on UCG among the variables with P<0.1 in univariate analysis. After adding age and gender to the selected variables, multivariate logistic analysis identified pre-HD NT-proBNP level, gender, duration of dialysis treatment, and CTR as independent predictors of LVH on UCG (OR: 3.06, 1.62, 1.00, and 1.12; P<0.001, 0.049, 0.011, and 0.001, respectively) and post-HD NT-proBNP level, gender, duration of dialysis treatment, and CTR correlated with LVH on UCG (OR: 3.15, 1.66, 1.00, and 1.12; P<0.001,

0.039, 0.019 and 0.001, respectively) (Table 3).

Given that decreased EF is the most representative indicator of heart failure, we assessed whether post-HD NT-proBNP was independently associated with decreased EF in patients who underwent UCG. From multivariate logistic analysis among age, gender, and selected variables in univariate analysis with $P<0.1$, and following stepwise regression analysis, post-HD NT-proBNP level and MBP (OR: 35.83 and 0.95; $P<0.001$ and 0.009, respectively) showed significant associations with decreased EF on UCG (Table 4).

ROC for pre- and post-HD NT-proBNP levels to detect LVH on ECG, LVH on UCG, and ROC for post-HD level to detect decreased EF had the following areas under the curve: 0.652 and 0.645 in LVH on ECG (Fig. 1A and B); 0.683 and 0.693 in LVH on UCG (Fig. 1D and E); and 0.859 in decreased EF on UCG (Fig. 1G). The sensitivity and specificity for LVH were similar between pre- (57.7%, 57.3% and 66.5%, 72.9%) and post-HD (63.9%, 48.2% and 59.2%, 81.9%) (Fig. 1C and F). The sensitivity and specificity for decreased EF on UCG (78.6% and 88.7%) were better than those for LVH, and the cut-off value for detecting decreased EF was 10,407 pg/mL at post-HD (Fig. 1H).

Because the molecular weight of NT-proBNP is 8,460 Da, the HD setting may influence the NT-proBNP level during a session. To identify those factors that contribute to changing NT-proBNP levels, we performed regression analysis between the percent reduction ratio (%reduction ratio) of NT-proBNP and parameters of dialysis efficacy. The %reduction ratio of NT-proBNP was calculated as: (pre-HD NT-proBNP level − post-HD NT-proBNP level) / pre-HD NT-proBNP level × 100. The %reduction ratio of NT-proBNP was close to having a normal distribution and mean ± standard deviation was 42 ± 15%. As shown in Table 5, after selecting

variables by stepwise regression analysis, multiple linear regression analysis identified Kt/V, membrane area, membrane type, modality, body weight gain ratio, treatment time, and ultrafiltration rate (UFR) as correlating with %reduction ratio of NT-proBNP (R: 0.53; $P<0.001$, except for UFR which was $P=0.003$).

Discussion

NT-proBNP level significantly correlated with LVH on ECG in this study. Among patients in whom UCG was successfully performed after a dialysis session, logistic regression analysis identified that NT-proBNP was not only associated with LVH on UCG but also was a marker of decreased EF. The sensitivity and specificity for LVH were similar between pre- and post-HD. Because of the low sensitivity and specificity results, the cut-off value for LVH was not able to be confirmed, whereas that for decreased EF was determined as 10,407 pg/mL at post-HD. The NT-proBNP level decreased during a HD session and the change correlated with parameters of the HD setting, such as Kt/V, membrane area, membrane type, modality, body weight gain ratio, treatment time, and UFR. These findings suggest that, although NT-proBNP increase in HD patients, NT-proBNP level reflects cardiac morphological and functional abnormalities.

In this study, we found that the NT-proBNP level was associated with LVH on both ECG and UCG in this population of Japanese HD patients. The Copenhagen City Heart Study reported that increased NT-proBNP correlates with LVH in people who do not have chronic kidney disease (16). The Chronic Renal Insufficiency Cohort has also reported that NT-proBNP exhibits strong associations with prevalent LVH in non-dialysis chronic kidney disease patients (17). In HD patients, the NT-proBNP level shows a significant correlation with LVH on UCG, even though the NT-

proBNP level increases with a decline in renal function (18). LVH is the most frequent cardiovascular manifestation in HD patients and is associated with a poor prognosis (19). Because LVH screening is important for the daily management of HD patients, measurement of NT-proBNP could be a simple and useful tool regardless of renal function. These findings suggest that the NT-proBNP level may assist in evaluating the presence of LVH among HD patients at clinics that do not have a UCG unit.

Previous studies have reported that the NT-proBNP level is associated with EF in not only the general population but also in HD patients in Western countries (20). In this study, we found that the NT-proBNP level was associated with a decreased EF in this population of Japanese HD patients, suggesting that increased NT-proBNP indicates left ventricular systolic dysfunction in HD patients as well as LVH. It is well-recognized that many heart failure therapies decrease the concentrations of natriuretic peptides. For example, the Valsartan Heart Failure Trial and the Randomized Aldactone Evaluation Study reported that therapies with valsartan and spironolactone can reduce brain natriuretic peptide levels (21, 22). The Anglo-Scandinavian Cardiac Outcomes Trial also reported that amlodipine-based treatment reduced the NT-proBNP level (23). Therefore, NT-proBNP may not only be a complementary factor for the diagnosis of cardiac dysfunction but also a therapeutic monitoring tool.

In HD patients, both diet and fluid intake result in increased fluid volume, affecting the NT-proBNP level at pre-HD. A previous study reported that a higher systolic blood pressure is associated with a 2% higher baseline NT-proBNP level using multivariable regression analysis (23). Even though the post-HD NT-proBNP level is not when considering the impact of increased fluid volume, the level is likely underestimated because of removal through the high-flux dialyzer, which is a popular

treatment instrument for Japanese HD patients. We found that the NT-proBNP level decreased during the HD session in almost all patients, and that the %reduction ratio correlated with markers of dialysis efficacy. Given the significant correlation with LVH and decreased EF, the NT-proBNP level is a possible clinical screening tool for cardiac abnormalities.

Although no studies have evaluated the optimal cut-off value for NT-proBNP in the diagnosis of LVH in HD patients, our data suggest cut-off values for the pre-HD NT-proBNP level to detect LVH on ECG and UCG of 5,342 pg/mL and 4,175 pg/mL, respectively, and for post-HD levels of 2,433 pg/mL and 3,202 pg/m, respectively. However, because of the low sensitivity and specificity, the cut-off value for LVH was not able to be confirmed. Additionally, we found that 10,407 pg/mL for post-HD NT-proBNP was the cut-off value that indicated an EF <40%. A previous study reported that the best post-HD NT-proBNP cut-off value is ≥7,200 pg/mL for the diagnosis of left ventricular systolic dysfunction defined as EF <45% (20). Therefore, the optimal cut-off value in the current study was determined to be different from other countries. As there are differences in HD settings among Japan and other countries, such as arteriovenous fistula as the common type of vascular access, greater use of a high-flux membrane, slightly lower blood flow, slightly longer treatment time, and blood sampling at the first HD session of the week, these may be the reasons for the differences in the suggested cut-off values.

The strengths of the study include the relatively large number of Japanese HD patients, measurement of NT-proBNP levels at both pre- and post-HD, and that the characteristics of the study population are similar to general Japanese HD patients. This study has some limitations. UCG could only be performed in patients who had undergone HD at those facilities that have a UCG unit. Because UCG was

performed only at the post-HD session, we could not compare the sensitivity and specificity for reduced EF between pre- and post-HD. Past history was mainly based on self-reported patient histories. We did not independently measure volume status using bioelectrical impedance analysis, though volume overload likely influenced NT-proBNP level to some extent. Blood pressure data were obtained from measurement at the beginning of the HD session. As numerous kinds of dialyzers were used, we analyzed the membrane type as binary data regardless of whether polysulfone was used. Modality also showed several variations, such as pre-dilution hemodiafiltration or post-dilution hemodiafiltration with varying amounts of fluid replacement. These were also analyzed as binary data regardless of HD or hemodiafiltration.

Conclusions

This multicenter cross-sectional study investigated the clinical usefulness of NT-proBNP level as a cardiac biomarker in Japanese HD patients. NT-proBNP levels at both pre- and post-HD significantly correlated with LVH on ECG and UCG. Similarly, there was a close association between NT-proBNP level at post-HD and decreased EF. The post-HD NT-proBNP level was influenced by Kt/V, membrane area, membrane type, modality, body weight gain ratio, treatment time, and UFR. Although the timing of sampling did not affect the sensitivity and specificity for LVH, the values were not able to be used to confirm cut-off values. Cut-off values for decreased EF are likely suitable to detect systolic dysfunction. These findings suggest that the NT-proBNP level is a simple and useful biomarker in maintenance HD patients.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Table 1 Baseline characteristics of the total population and ultrasonic cardiography (UCG) patients

	Total	UCG
Sample number, n	1428	395
Age, years[a]	66 ± 12	67 ± 12
Gender, male, n (%)	877 (61.4)	240 (60.8)
Body mass index, kg/m^{2}[a]	22 ± 4	22 ± 4
Smoking, n (%)	Never 716 (50.1)	Never 217 (54.9)
	Ever 502 (35.2)	Ever 132 (33.4)
	Current 206 (14.4)	Current 46 (11.6)
	Unknown 4 (0.2)	
Cause of ESKD, n (%)	CGN 522 (36.6)	CGN 144 (36.5)
	DM 518 (36.3)	DM 133 (33.7)
	NS 149 (10.4)	NS 60 (15.2)
	PKD 54 (3.8)	PKD 16 (4.0)
	others 185 (13.0)	others 42 (10.6)
History of heart failure, n (%)	263 (18.4)	91 (23.0)
History of angina pectoris, n (%)	243 (17.0)	70 (17.7)
History of myocardial infarction, n (%)	146 (10.2)	45 (11.4)
History of stroke, n (%)	253 (17.7)	52 (13.2)
History of PAD, n (%)	170 (11.9)	43 (10.9)
Atrial fibrillation, n (%)	81 (5.7)	20 (5.1)
Duration of dialysis treatment, month[b]	70 (29–137)	68 (26–137)
Modality, n (%)	HD 1 306 (91.5)	HD 375 (94.9)
	HDF 122 (8.5)	HDF 20 (5.1)
Treatment time, h/week[b]	12.0 (10.5–12.0)	12.0

Type of dialyzer, n (%)	PS 907 (63.5)	PS 268 (67.8)
	PES 246 (17.2)	PES 62 (15.7)
	CTA 171 (12.0)	CTA 44 (11.1)
	PEPA 104 (7.3)	PEPA 21 (5.3)
UFR, mL/mmHg/h[a]	60.1 ± 12.5	60.1 ± 12.6
Vascular access, n (%)	AVF 1332 (93.3)	AVF 359 (90.9)
	AVG 79 (5.5)	AVG 25 (6.3)
	others 17 (1.2)	others 11 (2.8)
Urine volume, mL, n (%)	Anuria: 968 (67.8)	Anuria: 245 (62.0)
	<500: 321 (22.5)	<500: 106 (26.8)
	500–1000: 108 (7.6)	500–1000: 35 (8.9)
	≥1000: 30 (2.1)	≥1000: 9 (2.3)
	Unknown 1	
Fluid removal, kg[a]	2.4 ± 0.9	2.4 ± 0.9
Body weight gain ratio, %[a]	4.4 ± 1.6	4.5 ± 1.6
Kt/V single-pool[a]	1.46 ± 0.28	1.45 ± 0.27
Systolic BP, mmHg[a]	150 ± 24	149 ± 25
Diastolic BP, mmHg[a]	79 ± 15	78 ± 16
CTR, %[a]	49.9 ± 5.1	50.9 ± 4.6
Hemoglobin, g/dL	10.8 ± 1.1	10.6 ± 1.0
Serum albumin, mg/dL	3.7 ± 0.4	3.7 ± 0.4
Serum C-reactive protein, mg/dL[b]	0.1 (0.05–0.30)	0.1 (0.05–0.36)
Serum phosphate, mg/dL[a]	2.4 ± 0.9	2.4 ± 0.9
Adjusted serum calcium, mg/dL[a]	9.3 ± 0.7	9.2 ± 0.7
Serum intact PTH, pg/mL[b]	118 (64–183)	125 (76–180)
Antihypertensive drug user, n (%)	960 (67.2)	252 (63.8)
RAS inhibitor, n (%)	725 (50.8)	175 (44.3)

ARB, n (%)	700 (49.0)	167 (42.3)
ACE-I, n (%)	104 (7.3)	33 (8.4)
DRI, n (%)	35 (2.5)	6 (1.5)
CCB, n (%)	661 (46.3)	176 (44.6)
α-blocker, n (%)	216 (15.1)	57 (14.4)
αβ-blocker, n (%)	249 (17.4)	76 (19.2)
β-blocker, n (%)	65 (4.6)	19 (4.8)
Diuretics user, n (%)	363 (25.4)	136 (34.4)
ESA user, n (%)	1300 (91.0)	361 (91.4)
Statin user, n (%)	280 (19.6)	86 (21.8)
Phosphate binder user, n (%)	1153 (80.7)	303 (76.7)
Vitamin D user, n (%)	868 (60.8)	230 (58.2)
Cinacalcet user, n (%)	278 (19.5)	73 (18.5)

[a] Values are mean ± standard deviation. [b] Values are median (interquartile range). ESKD, end-stage kidney disease; CGN, chronic glomerulonephritis; DM, diabetes mellitus; NS, nephrosclerosis; PKD, polycystic kidney disease; PAD, peripheral arterial disease; HD, hemodialysis; HDF, hemodiafiltration; UFR, ultrafiltration rate; AVF, arteriovenous fistula; AVG, arteriovenous graft; Kt/V: K = dialyzer clearance, t = time, V = volume of water a patient's body contains; BP, blood pressure; CTR, cardiothoracic ratio; ARB, angiotensin II receptor blocker; ACE-I, angiotensin-converting enzyme inhibitor; DRI, direct renin inhibitor; CCB, calcium channel blocker; ESA, erythropoiesis-stimulating agent.

Table 2 Multivariate logistic regression analysis showing predictors of left ventricular hypertrophy (LVH) on electrocardiogram (ECG)

	OR	95%CI	*P*	R
Pre-HD			<0.001	0.35
Log_{10}(NT-proBNP), 1	3.10	2.30-4.18	<0.001	
Age, 1 year	0.98	0.97-1.00	0.012	
Body weight gain ratio, 1%	1.14	1.03-1.25	0.008	
Serum albumin, 1%	1.61	1.02-2.54	0.040	
MBP, 10 mmHg	1.02	1.01-1.03	0.002	
Post-HD			<0.001	0.33
Log_{10}(NT-proBNP), 1	2.70	2.04-3.58	<0.001	
Age, 1 year	0.98	0.97-1.00	0.001	
Body weight gain ratio, 1%	1.13	1.02-1.24	0.015	
MBP, 10 mmHg	1.02	1.01-1.03	0.001	

The study was of 242 (16.9%) patients with LVH on ECG in total and 60 (15.2%) with LVH on ECG in the group that underwent UCG. Stepwise multiple regression analysis was performed to find independent predictors of LVH among potential confounders (P<0.1) in the univariate analysis except for age and gender. Final logistic regression analysis was performed using age, gender, and variables associated with LVH on ECG in the stepwise multiple regression analysis. OR, odds ratio; CI, confidence interval; CVD, cardiovascular disease; CTR, cardiothoracic ratio; MBP, mean blood pressure.

Table 3 Multivariate logistic regression analysis showing predictors of left ventricular hypertrophy (LVH) on ultrasonic cardiography (UCG)

	OR	95%CI	*P*	R
Pre-HD			<0.001	0.46
Log_{10}(NT-proBNP), 1	3.06	1.83-5.11	<0.001	
Gender, male	1.62	1.00-2.62	0.049	
Duration of dialysis treatment, 1	1.00	0.99-1.00	0.011	
CTR, 1%	1.12	1.06-1.19	<0.001	
Post-HD			<0.001	0.47
Log_{10}(NT-proBNP), 1	3.15	1.90-5.22	<0.001	
Gender, male	1.66	1.03-2.69	0.039	
Duration of dialysis treatment, 1	1.00	0.99-1.00	0.019	
CTR, 1%	1.12	1.06-1.20	<0.001	

The study was of 251 (63.5%) patients with LVH on UCG in the group that underwent UCG. Stepwise multiple regression analysis was performed to find independent predictors of LVH among potential confounders (P<0.1) in the univariate analysis except for age and gender. Final logistic regression analysis was performed using age, gender, and variables associated with LVH on UCG in the stepwise multiple regression analysis. OR, odds ratio; CI, confidence interval; CVD, cardiovascular disease; CTR, cardiothoracic ratio; MBP, mean blood pressure.

Table 4 Multivariate logistic regression analysis showing independent predictors of decreased ejection fraction (EF) on ultrasonic cardiography (UCG)

	OR	95%CI	*P*	R
Post-HD			<0.001	0.59
Log_{10}(NT-proBNP), 1	35.83	8.30-154.64	<0.001	
MBP, 10 mmHg	0.95	0.92-0.99	0.009	

The study was of 14 (3.5%) with decreased EF in the group that underwent UCG. Stepwise multiple regression analysis was performed to find independent predictors of decreased EF on UCG among potential confounders (P<0.1) in the univariate analysis except for age and gender. Final logistic regression analysis was performed using age, gender, and variables associated with decreased EF on UCG in the stepwise multiple regression analysis. OR, odds ratio; CI, confidence interval; MBP, mean blood pressure.

Table 5 Multiple regression analysis of the pre- and post-HD NT-proBNP ratio

	Partial	β	*P*	95%CI
Kt/V	16.01	0.30	<0.001	13.35–18.66
Membrane area	1.26	0.25	<0.001	0.97–1.55
Membrane type	1.97	0.21	<0.001	1.52–2.42
Modality	10.8	0.20	<0.001	8.35–13.25
Body weight gain ratio	−1.74	−0.18	<0.001	−2.18–1.30
Treatment time	0.93	0.09	<0.001	0.43–1.43
UFR	0.11	0.08	0.003	0.04–0.18
Constant	−16.94			−23.77–10

R: 0.53. Variables were determined using stepwise regression analysis. CI, confidence interval; Kt/V: K = dialyzer clearance, t = time, V = volume of water a patient's body contains; UFR, ultrafiltration coefficient.

Figure legends

Fig1. Receiver operating characteristic (ROC) curve of N-terminal pro brain natriuretic peptide (NT-proBNP) levels for the prediction of left ventricular hypertrophy (LVH) and decreased ejection fraction (EF).

(A) Graph showing ROC curve of serum pre-HD NT-proBNP level for the prediction of LVH on ECG. **(B)** Graph showing ROC curve of serum post-HD NT-proBNP level for the prediction of LVH on ECG. **(C)** Obtained cut-off values and their sensitivity and specificity from ROC curves of pre- and post-HD NT-proBNP levels for the prediction of LVH on ECG are summarized. **(D)** Graph showing ROC curve of serum pre-HD NT-proBNP level for the prediction of LVH on UCG. **(E)** Graph showing ROC curve of serum post-HD NT-proBNP level for the prediction of LVH on UCG. **(F)** Obtained cut-off values and their sensitivity and specificity from ROC curves of pre- and post-HD NT-proBNP levels for the prediction of LVH on UCG are summarized. **(G)** Graph showing ROC curve of serum post-HD NT-proBNP level for the prediction of decreased EF on UCG. **(H)** Obtained cut-off value and their sensitivity and specificity from ROC curve of post-HD NT-proBNP level for the prediction of decreased EF on UCG are summarized.