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NT-proBNP as a biomarker for fluid management in hemodialysis patients: Insights from CHF and Non-CHF subgroups

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Abstract

The secrection of N-terminal probrain natriuretic peptide (NT-proBNP) is triggered by elevated myocardial strain and excess volume in the left ventricle (LV). The association between NT-proBNP and volume status in hemodialysis (HD) patients with congestive heart failure (CHF) is not fully understood. We aimed to elucidate this relationship. HD patients undergoing treatment for more than three months were included. Volume overload was defined using interdialytic weight gain (IDWG) between HD sessions. CHF was diagnosed with left ventricle ejection fraction (LVEF) below 60%. The predictive capacity of NT-proBNP for volume overload in patients, both with and without CHF, was retrospectively analyzed. The cohort was composed of 144 HD patients, 85 males and 59 females, with a median age of 62 years (IQR: 52-74). The median level of NT-proBNP was 4936 pg/ml (IQR: 2430–21217 pg/ml). The average IDWG was 5.3±2.0%, with a median dialysis duration of 48 (IQR: 26.9–93.4) months. Elevated NT-proBNP levels were significantly associated with a higher risk of volume overload (OR = 1.9; 95% CI: 1.304–2.630 p=0.002), independent of age, gender, serum potassium, serum uric acid, and CHF status. The area under the curve (AUC) for predicting volume overload using NT-proBNP was 0.865 [95% CI: 0.791–0.940 p <0.001] in patients without CHF and 0.832 [95% CI: 0.682–0.981 p = 0.001] in those with CHF. The NT-proBNP cutoff was 3512 pg/ml for patients without CHF and 4936 pg/ml for those with CHF. Increased NT-proBNP levels are linked to a higher risk of fluid overload in HD patients regardless of CHF status, highlighting NT-proBNP as a valuable tool for managing fluid balance in this population.

Keywords: volume overload, hemodialysis, congestive heart failure, fluid balance, N-terminal pro-brain natriuretic peptide

1. Introduction

Volume overload is one of the primary indicators of mortality for HD patients (1,2). It has been associated with systemic hypertension, inflammation, malnourishment, left ventricular hypertrophy and left atrial dilatation before the onset of heart failure (3).

Accurate and objective techniques for determining volume status are necessary to control volume in hemodialysis patients. Most volume assessments are done by clinical examination, although this method is erroneous and unreliable. Other approaches include echocardiography, radioactive dilution techniques, and using ultrasonography to estimate the inferior vena cava diameter. All of these procedures take time and require specialized knowledge to perform (4,5).

Alternatively, both NT-proBNP and BNP have been linked to volume overload and cardiac dysfunction. However, serum creatinine levels, cardiac conditions and dialysis treatment may influence BNP levels, potentially limiting its effectiveness as a marker of fluid overload in dialysis patients (6,7).

The goal of this investigation was to examine the relationship between NT-proBNP levels and volume overload in HD patients, both with and without congestive heart failure, using interdialytic weight gain (IDWG) as a metric.

2. Materials and Methods

2.1. Study Population

In this study, 144 HD patients from a tertiary care hospital in Turkey who had been receiving care for longer than three months were included.

Excluded were patients under 18 years of age or those with the acute myocardial infarction or acute cerberovascular event within the last three months.

Based on NT-proBNP quartiles, patients were categorized into four groups: ≤2430 pg/ml, 2430 <NT-proBNP ≤ 4936 pg/ml, 4936 <NT-proBNP ≤ 21217 pg/ml, and >21217 pg/ml. Those with NT-proBNP values ≤2430 pg/ml were classified as the lowest quartile group, while those with values >21217 pg/ml were classified as the highest quartile group.

Volume overload was defined as IDWG exceeding 4.5% (8). IDWG is the variation between a patient's weight before

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dialysis and their weight at the end of the preceding HD session. CHF was defined as an LVEF measured below 60% on transthoracic echocardiography (5).

The patients underwent three sessions of low-flux hemodialysis per week, each lasting four hours, using dialyzers with synthetic membranes (The BLS514SD Polyflux 14L, manufactured by Gambro Dialysatoren GmbH, Hechingen, Germany). At a rate of 200–240 mL/min was the blood flow, with the dialysate flow set at 400 mL/min.

The study was approved by the Institutional Review Board of Nevşehir Hacı Bektaş Veli University with approval number 2400087905/2024.05.01.Because of the study's retrospective design, informed consent was not required.

2.2. Data Collection

The following demographic and clinical variables were collected: age, sex, comorbidities including diabetes mellitus, hypertension, and CHF, hospital length of stay (HLOS), as well as mortality.

Following a 15-minute rest in a semi-upright position, blood was drawn in the morning before the dialysis session. Measurements of NT-proBNP, sodium (Na), potassium (K), serum albumin (Alb), calcium (Ca), phosphate (P), blood urea nitrogen (BUN) serum creatinine (SCr), magnesium (Mg), low-density lipoprotein (LDL), hemoglobin (Hb), C-reactive protein (CRP), uric acid (UA), parathyroid hormone (PTH), thyroid stimulating hormone (TSH), ferritin, pH, and bicarbonate (HCO3) were made using a standard protocol.

Removed volume during dialysis was noted. Weight measurements were taken before and after dialysis to determine the interdialytic weight gain. Prior to the dialysis session, the sistolic and diastolic blood pressures (SBP and DBP) were also recorded.

2.3. Outcomes

The mortality data refer to all-cause mortality within the 12 months prior to data collection. This information was obtained retrospectively from electronic hospital records, including dialysis unit follow-up notes and death certificates, where applicable.

2.4. Statistical Analysis

Statistical analyses were performed using SPSS software version 22.0. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed data. Comparisons between NT-proBNP quartile groups were made using the chi-square test for categorical variables, ANOVA for normally distributed continuous variables, and the Mann–Whitney U test for non-parametric data.

Pearson correlation analysis was conducted to evaluate the relationships between NT-proBNP levels and other variables. Simple linear regression and stepwise multiple linear regression analyses were used to identify predictors of volume overload. In addition, receiver operating characteristic (ROC) curve analysis was performed to assess the predictive ability of NT-proBNP levels for volume overload in patients with and without congestive heart failure. A p-value <0.05 was considered statistically significant.

3. Results

The median age of the 144 hemodialysis patients who were enrolled was 62 (52–74) years old. The cohort consisted of 85 males and 59 females. The median (IQR) dialysis duration was 48 (26.9–93.4) months.

The median level of NT-proBNP was 4936 pg/ml (IQR: 2430–21217), and IDWG's mean ±SD percentage was 5.32±2.0%. The absolute value of IDWG was a mean of 3.4±1.2 kg. The most common comorbid diseases of the patients were hypertension (75%) and diabetes mellitus (47%). The median SBP value measured before dialysis was 124 mmHg (IQR: 110-132), while the DBP value was 72 mmHg (IQR: 64-82). Within the cohort, 31% of patients had CHF, and 46% of cases involved volume overload.

Table 1 lists the main clinical characteristics of the patients throughout the NT-proBNP quartiles. In contrast to the NT-proBNP group in the lowest quartile, the highest quartile NT-proBNP group had higher age (66 vs 55 years; p=0.004), a higher male proportion (61% vs 33%; p=0.019), higher serum K levels (5.3 ±0.8 vs 5.1±0.4 mmol/l; p=0.016), greater ferritin levels (666 vs 455 ng/ml; p=0.037), higher TnI levels (86.1 vs 30.7 ng/l; p=0.004), higher CRP levels (8.8 vs 3.9 mg/l; p=0.023), a higher proportion of CHF (33% vs 8.1%; p=0.006), with a greater mortality rate (34.3% vs 8.3%; p=0.049). However, patients in the highest quartile NT-proBNP group had lower SCr (7±2.2 vs 8.6 ±2.6 g/dl; p=0.018), lower UA levels (5.9±1.3 vs 6.7±1.0 mg/dl; p=0.009), and lower Alb levels (37.3 ±4.4 vs 41.0±7.8 g/l; p=0.031) (Table 1).

There was a correlation observed between serum NT-proBNP levels and hypervolemia ($r = 0.808$, $p<0.001$) by simple linear regression analysis (Table 2). There was also a positive correlation between age and hypervolemia ($r = 0.252$, $p = 0.002$), CHF ($r = 0.395$, $p<0.001$), and serum potassium levels ($r = 0.289$, $p < 0.001$) but negatively correlated with sex ($r = -0.183$, $p = 0.028$) and serum uric acid levels ($r = -0.244$, $p = 0.003$). An investigation of stepwise multiple linear regression revealed that hypervolemia was positively related to NT-proBNP levels ($\beta = 0.582$, $p<0.001$), CHF ($\beta = 0.277$, $p<0.001$), and serum potassium levels ($\beta = 0.191$, $p = 0.001$).

Serum NT-proBNP levels were found to be independently correlated with hypervolemia in all patients (OR = 1.9; 95% CI: 1.304–2.630, p=0.002), even after controlling for covariates such age, sex, serum K, serum UA, and the existence of CHF. NT-proBNP levels were observed to be linked to a higher risk of volume overload in the subgroup of CHF patients

(OR=2.9; 95% CI: 1.224–6.635, p=0.015). The NT-proBNP level was associated with a 2.4-fold risk of volume overload in individuals without CHF (OR=2.431; 95% CI: 1.450–4.077, p=0.001).

We developed a ROC curve using the cutoff value to determine the potential utility of NT-proBNP in evaluating volume overload among patients with and without CHF. For the subgroup of patients without CHF, the sensitivity was 83.3%, specificity was 83.8%, and the AUC was 3512 pg/ml, with a 95% confidence interval (CI) of 0.791–0.940 and p < 0.001 (Fig. 1). Conversely, in the CHF group, the sensitivity was 82.6%, specificity was 75.0%, the NT-proBNP cutoff value was 4936 pg/ml, and the AUC was 0.832 (95% CI: 0.682–0.981, p = 0.001) (Fig. 2).

Table 1. Baseline characteristics of hemodialysis patients according to NT-proBNP quartiles

Variable	Total (n=144)	Q1 ≤ 2430	Q2 2430–4936	Q3 4936–21217	Q4 > 21217	p-value*
Age (years)	62 (52–74)	55 (44–65)	63 (54–74)	70 (56–75)	66 (56–76)	0.004
Male (%)	59%	33%	33%	64%	61%	0.019
IDWG (% body weight)	5.3 ± 2.0	4.8 ± 1.8	4.6 ± 1.8	5.4 ± 1.9	6.1 ± 2.3	0.070
Volume overload (%)	46%	25%	36%	53%	69%	0.023
CHF prevalence (%)	31%	14%	22%	22%	31%	0.007
Mortality (%)	19.4%	8.3%	17.0%	19.4%	34.3%	0.049
Serum creatinine (mg/dL)	7.9 ± 2.6	8.7 ± 2.9	7.6 ± 2.6	8.4 ± 2.3	7.0 ± 2.4	0.018
Uric acid (mg/dL)	6.4 ± 1.2	6.8 ± 1.0	6.6 ± 1.2	6.3 ± 1.1	5.9 ± 1.3	0.009
Albumin (g/L)	38.4 ± 4.7	41.0 ± 7.8	37.9 ± 5.9	38.3 ± 4.2	37.3 ± 4.4	0.031
Potassium (mmol/L)	5.2 ± 0.7	5.0 ± 0.6	5.1 ± 0.6	5.6 ± 0.8	5.3 ± 0.9	0.016
CRP (mg/L)	4.9 (2.0–12.0)	3.7 (1.8–9.9)	5.6 (2.3–11.8)	3.0 (1.2–7.0)	8.9 (4.0–25.1)	0.023
Ferritin (ng/mL)	543 (319–797)	455	431.5	520	666	0.037

*Only variables with statistically significant or clinically relevant differences across NT-proBNP quartiles are presented. Abbreviations: IDWG = Interdialytic weight gain, CHF = Congestive heart failure, CRP = C-reactive protein.

Table 2. Factors associated with the volume overload in patients on hemodialysis

Factors	Simple linear regression analysis correlation coefficient	*p*-value	Stepwise multiple linear regression analysis standardized coefficient	*p*-value
NT-proBNP	0.808	<0.001	0.582	<0.001
Gender	-183	0.028		
Age (years)	0.252	0.002		
CHF	0.395	<0.001	0.277	<0.001
Uric acid	-0.244	0.003		
Potassium	0.289	<0.001	0.191	0.001

Abbreviations: NT-proBNP, N-Terminal pro-Brain Natriuretic Peptide; CHF, congestive heart failure

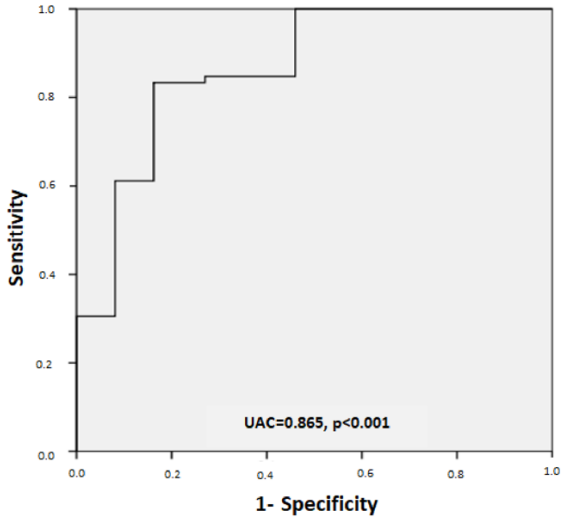

Fig.1. ROC curve for prediction of volume overload based on the serum NT-proBNP level in hemodialysis patients without CHF. Optimal cut-off value for NT-proBNP is 3512 pg/mL. AUC for NT-proBNP = 0.865 [95% CI (0.791–0.940)], p < 0.001. ROC, receiver operating characteristic curve; AUC, area under the curve.

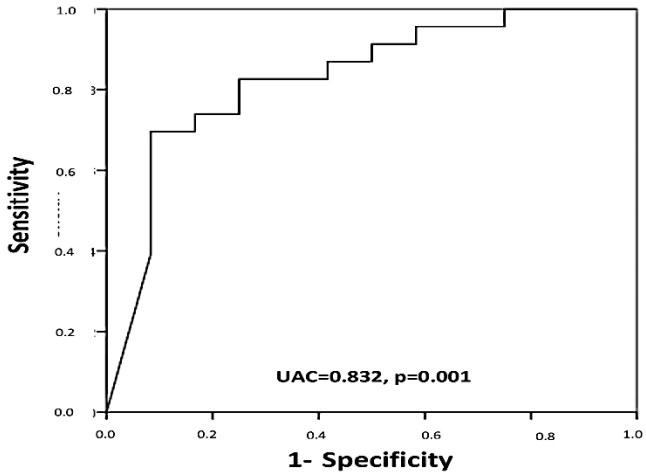

Fig.2. ROC curve for prediction of volume overload based on the serum NT-proBNP level in hemodialysis patients with CHF. Optimal cut-off value for NT-proBNP is 4936 pg/mL. AUC for NT-proBNP = 0.832 [95% CI (0.682–0.981)], p = 0.001. ROC, receiver operating characteristic curve; AUC, area under the curve.

4. Discussion

According to our research, NT-proBNP may be a useful tool to predict volume overload in hemodialysis patients, regardless of CHF status. In patients with CHF, elevated NT-proBNP levels were linked to a 2.9-fold greater risk of volume overload, while in patients without CHF, the risk was 2.4-fold increased. Our findings align with recent international studies investigating NT-proBNP as a biomarker for volume status in hemodialysis patients, both with and without heart failure. Previous studies have shown that NT-proBNP levels are significantly correlated with fluid overload assessed by objective methods such as bioimpedance spectroscopy, supporting its role as a non-invasive marker of volume status in hemodialysis patients (5). In more recent work, volume status has also been linked to structural cardiac alterations, including increased left ventricular mass and diastolic dysfunction, with elevated NT-proBNP levels serving as a predictive marker in this context (9). These findings are consistent with the results of our study, which highlight the utility of NT-proBNP in identifying volume overload, particularly in both CHF and non-CHF patient populations. The finding that NT-proBNP predicts volume overload even in patients without clinically diagnosed congestive heart failure is supported by prior research indicating that NT-proBNP levels can reflect fluid burden independently of overt cardiac dysfunction (10).

Improving the quality of life for individuals with volume overload requires early diagnosis and treatment. Traditional clinical methods such as assessing blood pressure, lung rales, peripheral edema, and jugular venous distention are often used to evaluate a patient's hydration status. However, because these methods do not precisely reflect the volume status of patients, they are subjective and have limited diagnostic accuracy. As a result, a lot of work has gone into creating accurate and impartial techniques for determining volume status in recent years. Among these, NT-proBNP levels have emerged as the least invasive alternative method (9,11). However, it is important to note that the interpretation of NT-proBNP levels in dialysis patients may be complicated by reduced renal clearance and peptide accumulation in end-stage renal disease (6).

We noted that the patients in the higher quartile of NT-proBNP levels had increased rates of CHF and mortality. Similar associations have been reported for high NT-proBNP levels in both hemodialysis and peritoneal dialysis patients (11-13). These findings suggest that elevated volume load leads to ventricular hypertrophy, which subsequently promotes CHF and increases the mortality rate associated with hemodialysis and chronic kidney disease. Research has demonstrated a strong correlation between natriuretic peptides and cardiovascular disorders as well as other markers of cardiac anatomy and functionality (14,15).

Serum NT-proBNP levels rise in response to declining kidney function since the kidney health is principally responsible for clearing NT-proBNP (16–18). As a result, it has been determined that NT-proBNP serves as a biomarker for heart failure in both hemodialysis patients and the general population (19,20). However a meta-analysis found that NT-proBNP could not be utilized as a marker of improvement in heart failure among HD patient, (21). Furthermore, not much is known regarding its usefulness as a volume status indicator in the presence of both volume overload and CHF.

Previous data have demonstrated a positive correlation between the concentration of NT-proBNP in multivariate regression analysis and female sex and age, as well as a negative correlation between the concentration and BMI and Hb (22–24).

The age-related increase in natriuretic peptide levels may be attributed to reductions in glomerular filtration rate and left ventricular compliance (25,26). It has been demonstrated that estrogen increases the expression and release of the cardiac natriuretic peptide gene, which may account for women's higher levels of these proteins compared to men (27,28). Lower hemoglobin levels may adversely affect cardiac function by reducing cardiac work efficiency and oxygen transport to the myocardium (29,30). Since natriuretic peptide clearance receptors (NPR-C) are known to be abundantly expressed in adipocytes, some have hypothesized that this may be the cause of the low serum NT-proBNP levels linked to obesity (31,32). Many theories have been proposed to try to explain the connection between these variables and levels of circulating NT-proBNP, but as of yet, no single theory has been supported by solid evidence.

This study has several important limitations. First, due to its retrospective design, there is a risk of selection bias, and causal relationships cannot be firmly established. Second, the study was conducted in a single center, which may limit the generalizability of the findings to broader populations. Third, we were unable to control for all potential confounding factors that could affect NT-proBNP levels, such as comorbidities or medication use. Fourth, variations in kidney function among patients may have influenced NT-proBNP levels, but this was not adjusted for in our analysis. Additionally, volume overload was assessed solely using interdialytic weight gain (IDWG), which, while practical, may not fully reflect the complexity of fluid status in hemodialysis patients. We also lacked longitudinal data to assess changes in NT-proBNP over time, which could have provided greater insight into its prognostic value. Furthermore, all patients received low-flux hemodialysis with relatively low blood flow rates (200–240 mL/min), reflecting local clinical practices; this may differ from standard protocols elsewhere and thus limit external applicability. Finally, objective imaging-based methods such as inferior vena cava diameter measurement, chest radiography, or lung ultrasound were not used to evaluate fluid status, which could have enhanced the accuracy of volume assessment. These limitations should be taken into account

when interpreting our findings and highlight the need for further prospective, multi-center studies.

Compared to prior studies, our research adds value by stratifying NT-proBNP performance across CHF and non-CHF subgroups and determining distinct cutoff values for volume overload prediction in each. Taken together, these comparisons reinforce the growing evidence supporting NT-proBNP as a clinically valuable biomarker for fluid status monitoring in hemodialysis, while also highlighting the need for patient-specific interpretation.

Volume overload in HD patients, is reliably predicted by NT-proBNP irrespective of CHF status, Incorporating NT-proBNP measurements into routine clinical practice may enhance the early detection and management of volume overload, ultimately improving patient outcomes.

Conflict of interest

All authors state that there is no potential conflict of interest.

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None to declare.

Authors' contributions

Concept: M.P., Design: M.P., Data Collection or Processing: M.P., Analysis or Interpretation: M.P., Ö.K., Literature Search: M.P., Ö.K., Writing: M.P., Ö.K.

Ethical Statement

The study was conducted with the approval of the Institutional Review Board of Nevsehir Hacı Bektaş Veli University with approval number 2400087905/2024.05.01. Because of the study's retrospective design, informed consent was not required.

References

1. Siriopol D, Siriopol M, Stuard S, et al. An analysis of the impact of fluid overload and fluid depletion for all-cause and cardiovascular mortality. *Nephrol Dial Transplant*. 2019;34(8):1385-1393. doi:10.1093/ndt/gfy396
2. Dekker MJE, Kooman JP. Fluid status assessment in hemodialysis patients and the association with outcome: review of recent literature. *Curr Opin Nephrol Hypertens*. 2018;27(3):188-193. doi:10.1097/MNH.0000000000000409
3. Dekker MJ, Marcelli D, Canaud BJ, et al. Impact of fluid status and inflammation and their interaction on survival: a study in an international hemodialysis patient cohort. *Kidney Int*. 2017;91(5):1214-1223. doi:10.1016/j.kint.2016.12.008
4. Loutradis C, Sarafidis PA, Ferro CJ, Zoccali C. Volume overload in hemodialysis: diagnosis, cardiovascular consequences, and management. *Nephrol Dial Transplant*. 2021;36(12):2182-2193. doi:10.1093/ndt/gfaa182
5. Wang Y, Cao X, Yu J, et al. Association of N-Terminal Pro-brain Natriuretic Peptide With Volume Status and Cardiac Function in Hemodialysis Patients. *Front Cardiovasc Med*. 2021;8:646402. Published 2021 Feb 22. doi:10.3389/fcvm.2021.646402
6. Chaikijurajai T, Choles HR, Tang WHW. Do Natriuretic Peptide Measurements Provide Insights into Management of End-Stage Renal Disease Patients Undergoing Dialysis? *Curr Heart Fail Rep*. 2020;17(6):449-456. doi:10.1007/s11897-020-00488-6
7. Akkus G, Seyithanoglu M, Akkus H, Ulu S, Ciftcioglu M, Erken E, Altunoren O, Gungor O. Serum NT-proBNP levels are associated with cognitive functions in hemodialysis patients. *Semin Dial*. 2021 Mar;34(2):170-175. doi:10.1111/sdi.12948. Epub 2021 Jan 10. PMID: 33423325.
8. Fouque D, Vennegoor M, ter Wee P, et al. EBPG guideline on nutrition. *Nephrol Dial Transplant*. 2007;22 Suppl 2
9. Han BG, Lee JY, Kim JS, Yang JW, Park SW. The mediating role of the left ventricular mass index on the relationship between the fluid balance and left ventricular diastolic function in patients with chronic kidney disease. *Kidney Res Clin Pract*. 2024;43(1):101-110. doi:10.23876/j.krcp.22.246
10. Park WY, Park S, Kim YW, Jin K. Clinical efficacy of biomarkers for evaluation of volume status in dialysis patients. *Medicine (Baltimore)*. 2020;99(31).
11. Alexandrou ME, Balafa O, Sarafidis P. Assessment of Hydration Status in Peritoneal Dialysis Patients: Validity, Prognostic Value, Strengths, and Limitations of Available Techniques. *Am J Nephrol*. 2020;51(8):589-612. doi:10.1159/000509115
12. Liu T, Zhao D, Huang J, et al. Research hotspots and development trends in volume management of peritoneal dialysis patients: a bibliometrics and visual analysis up to 2022. *Int Urol Nephrol*. Published online November 22, 2023. doi:10.1007/s11255-023-03869-7
13. Canaud B, Kooman J, Maierhofer A, Raimann J, Titze J, Kotanko P. Sodium First Approach to Reset Our Mind for Improving Management of Sodium, Water, Volume, and Pressure in Hemodialysis Patients and to Reduce Cardiovascular Burden and Improve Outcomes. *Front Nephrol*. 2022;2:935388. Published 2022 Jul 7. doi:10.3389/fneph.2022.935388
14. Zoair AM, Abdel-Hafez MA, Mawlana W, Sweylam MA. Serum levels of N-terminal-pro B-type natriuretic peptide as a diagnostic marker for left ventricular dysfunction in children with end-stage renal disease on hemodialysis. *Saudi J Kidney Dis Transpl*. 2016;27(6):1114-1122. doi:10.4103/1319-2442.
15. Ishigami J, Iimori S, Kuwahara M, Sasaki S, Tsukamoto Y. Diagnostic value of B-type natriuretic peptide for estimating left atrial size and its usefulness for predicting all-cause mortality and cardiovascular events among chronic haemodialysis patients. *Nephrology (Carlton)*. 2014;19(12):777-783. doi:10.1111/nep.12329
16. Palmer SC, Yandle TG, Nicholls MG, Frampton CM, Richards AM. Regional clearance of amino-terminal pro-brain natriuretic peptide from human plasma. *Eur J Heart Fail*. 2009;11(9):832-839. doi:10.1093/eurjhf/hfp099
17. Potter JM, Simpson AJ, Kerrigan J, et al. The relationship of plasma creatinine (as eGFR) and high-sensitivity cardiac troponin and NT-proBNP concentrations in a hospital and community outpatient population. *Clin Biochem*. 2017;50(15):813-815. doi:10.1016/j.clinbiochem.2017.04.003
18. Bruch C, Fischer C, Sindermann J, Stypmann J, Breithardt G, Gradaus R. Comparison of the prognostic usefulness of N-terminal pro-brain natriuretic Peptide in patients with heart failure with versus without chronic kidney disease. *Am J Cardiol*. 2008;102(4):469-474. doi:10.1016/j.amjcard.2008.03.082
19. Masson S, Latini R. Amino-terminal pro-B-type natriuretic peptides and prognosis in chronic heart failure. *Am J Cardiol*. 2008;101(3A):56-60. doi:10.1016/j.amjcard.2007.11.024
20. Kristensen SL, Jhund PS, Køber L, et al. Relative Importance of

History of Heart Failure Hospitalization and N-Terminal Pro-B-Type Natriuretic Peptide Level as Predictors of Outcomes in Patients With Heart Failure and Preserved Ejection Fraction. *JACC Heart Fail*. 2015;3(6):478-486. doi:10.1016/j.jchf.2015.01.014

21. Yin L, Han Z, Zhang Q, Xie J, Wang C, Zhao L. The effect of hemodialysis on N-terminal pro-brain natriuretic peptide: A systematic review and meta-analysis. *Am J Emerg Med*. 2021;44:244-249. doi:10.1016/j.ajem.2020.03.056

22. Olsen MH, Hansen TW, Christensen MK, et al. N-terminal pro brain natriuretic peptide is inversely related to metabolic cardiovascular risk factors and the metabolic syndrome. *Hypertension*. 2005;46(4):660-666. doi:10.1161/01.HYP.0000179575.13739.72

23. Wang TJ, Larson MG, Levy D, et al. Impact of obesity on plasma natriuretic peptide levels. *Circulation*. 2004;109(5):594-600. doi:10.1161/01.CIR.0000112582.16683.EA

24. Lainscak M, von Haehling S, Anker SD. Natriuretic peptides and other biomarkers in chronic heart failure: from BNP, NT-proBNP and MR-proANP to routine biochemical markers. *Int J Cardiol*. 2009;132(3):303-311. doi:10.1016/j.ijcard.2008.11.149

25. Arbab-Zadeh A, Dijk E, Prasad A, et al. Effect of aging and physical activity on left ventricular compliance. *Circulation*. 2004;110(13):1799-1805. doi:10.1161/01.CIR.0000142863.71285.74

26. McCullough PA, Duc P, Omland T, et al. B-type natriuretic peptide and renal function in the diagnosis of heart failure: an analysis from the Breathing Not Properly Multinational Study. *Am J Kidney Dis*. 2003;41(3):571-579. doi:10.1053/ajkd.2003.50118

27. Huang J, Guan H, Booze RM, Eckman CB, Hersh LB. Estrogen regulates neprilysin activity in rat brain. *Neurosci Lett*. 2004;367(1):85-87. doi:10.1016/j.neulet.2004.05.085

28. Guo Q, Zhang Q, He Y, Shi J, Li H, Peng H. Gender difference of association between plasma N-terminal pro-atrial natriuretic peptide and metabolic syndrome. *Hormones (Athens)*. 2020;19(4):541-548. doi:10.1007/s42000-020-00222-w

29. Hamada M, Shigematsu Y, Takezaki M, Ikeda S, Ogimoto A. Plasma levels of atrial and brain natriuretic peptides in apparently healthy subjects: Effects of sex, age and hemoglobin concentration. *Int J Cardiol*. 2017;228:599-604. doi:10.1016/j.ijcard.2016.11.197

30. Otaki Y, Watanabe T, Sato N, et al. Brain Natriuretic Peptide (BNP) and N-Terminal-proBNP in Cardio-Renal Anemia Syndrome - Difference in Prognostic Ability. *Circ Rep*. 2019;1(2):71-77. Published 2019 Jan 22. doi:10.1253/circrep.CJ-18-0004

31. Sengenès C, Berlan M, De Glisezinski I, Lafontan M, Galitzky J. Natriuretic peptides: a new lipolytic pathway in human adipocytes. *FASEB J*. 2000;14(10):1345-1351.

32. Kalra PR, Tigas S. Regulation of lipolysis: natriuretic peptides and the development of cachexia. *Int J Cardiol*. 2002;85(1):125-132. doi:10.1016/s0167-5273(02)00241-3.