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Original Article

Stratifying the Optimal Thresholds of Point-Of-Care Testing NT-proBNP as Acute Heart Failure Marker in Elder Patients with Impaired Kidney Function

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SUMMARY

Background: Ageing is characterized by progressive renal dysfunction to varying degrees, but its effect on N-terminal pro-brain natriuretic peptide (NT-proBNP) is vague. We hypothesized that the thresholds of NT-proBNP for heart failure are stratified in elders with different stages of chronic kidney disease (CKD).
Methods: In this cross-sectional study, elders aged > 65 with an estimated glomerular filtration rate (eGFR) < 60 ml/min for ≥ 3 months were included. Heart failure with reduced ejection fraction (HFrEF) is defined as a left ventricular ejection fraction (LVEF) is 40% or less and is accompanied by progressive left ventricular dilatation and adverse cardiac remodeling. The receiver operating characteristic (ROC) curves were used to assess the optimal thresholds of NT-proBNP for diagnosing HFrEF.
Results: This study analyzed a cohort comprising 1009 patients with CKD (222 cases of stage 3, 257 cases of stage 4, and 530 cases of stage 5). Of the subjects, 475 were with HFrEF and 534 without HFrEF. Mean NT-proBNP levels are 3060 pg/ml, 4360 pg/ml, and 16030 pg/ml for CKD stage 3, stage 4, and stage 5 patient groups, respectively. Mean NT-proBNP levels in the HFrEF group were about 4-fold higher compared to the non-HFrEF group. Optimal NT-proBNP cut-offs of HFrEF diagnosis for CKD stage 3, stage 4, and stage 5 were 1420 pg/ml, 2540 pg/ml, and 19800 pg/ml, respectively.
Conclusions: NT-proBNP was elevated in advance staged CKD even in the absence of HFrEF, and the magnitude of increase in NT-proBNP was significant in the elderly population. Using higher thresholds according to CKD stages, NT-proBNP can help diagnose HFrEF.

1. Introduction

Brain natriuretic peptide (BNP) is first extracted from the porcine brain and was found mainly released by cardiomyocytes in response to cardiac stretch due to ventricle expansion.[1,2] BNP is a pre-hormone that can cleave to active 32-amino acid polypeptide BNP and inactive N-terminal proBNP (NT-proBNP).[3] BNP has multiple physiological effects. In the renal aspect, it can promote endothelin secretion and inhibit the renin-aldosterone angiotensin (RAA) system, facilitating the natriuretic effect, inhibiting sodium reuptake, and lowering blood pressure.[4,5] In the cardiac aspect, it has antifibrotic and anti-hypertrophic effects, which inhibit maladaptive cardiac hypertrophy.[6] In heart failure, natriuretic peptides include BNP release due to myocardial stretch to counteract RAA and Sympatho-Adrenergic systems.[7] The level of BNP and NT-proBNP were both relevant to diagnosing Heart failure with reduced ejection fraction (HFrEF) or heart failure with preserved ejection fraction (HFpEF) and prognosis.[8]

Multiple factors, such as patient profiles and clinical conditions, can influence BNP and NT-proBNP levels. Age and gender can affect the reference range of BNP and NT-proBNP.[9] The mean and upper limit values are increased with age in both BNP and NT-proBNP. The possible explanation might be decreased renal clearance, reduced platelet-associated clearance receptors, and decreased left ventricular compliance.[9] Obesity and medication (angiotensin receptor-neprilysin inhibitor) also can influence the diagnostic range of natriuretic peptides.[10,11]

Clinical underlying conditions may influence BNP and NT-proBNP interpretation, including valvular heart disease, cardiomyopathy, atrial fibrillation/flutter, renal dysfunction, anemia, stroke, pulmonary disease, and sepsis.[12] Specifying respect to renal dysfunction, BNP and NT-proBNP were found both to be elevated by chronic kidney disease (CKD) in heart failure, even not heart failure.[13] BNP was partly cleared by pre-renal fashion and was found to be adjusted to a cutoff value of 200 pg/ml in CKD stages 3–5. There was no need to adjust the value in CKD stages 1–2.[14,15] The kidney

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mainly excreted NT-proBNP, and the Impact was even more in renal dysfunction. The cut-off value in advanced CKD (stage 3–5) was higher (1200–6000 pg/ml) than in stage 1–2 CKD. However, the sensitivity and specificity were low.[16]

Although BNP and NT-proBNP results are interchangeable in the diagnosis and prognosis of heart failure (HF), NT-proBNP has the advantage of detecting asymptomatic left ventricle (LV) dysfunction and early mild systolic or diastolic HF. Besides, it can be used in HF, which uses angiotensin receptor-neprilysin inhibitor (ARNI). BNP is subject to degradation by neprilysin but not NT-proBNP.[11] It is essential to clarify the cut-off value of advanced renal failure in each stage, especially NT-proBNP. In this study, we hypothesized and tried to stratify the NT-proBNP cut-off value of heart failure in different renal failure staging in geriatric patients.

2. Methods

2.1. Study design and participants

The Institutional Review Board of MacKay Memorial Hospital approved this study: 20MMHIS275e. The study is a cross-sectional retrospective medical record database research of the interested population. Recruitment of consecutive elder subjects with CKD was carried out from the emergency department. The inclusion criteria were older than 65 years and a history of CKD. Patient information, including demographics and clinical history, was collected.

The assessment of CKD was taken as an estimated glomerular filtration rate (eGFR) of $\leq$ 60 ml/min. The Modification of Diet in Renal Disease (MDRD) Study equation [eGFR (mL/min/1.73 m^2) = 175 (Serum CRE) – 1.154 $\times$ (Age) – 0.203 $\times$ 0.742 (if female) $\times$ 1.21 (if African American)] was used for calculating the eGFR of the study subjects from plasma creatinine (Cr), age, and body weight of the subjects.[17] The CKD staging was carried out into CKD stage 3 (eGFR 30–60 ml/minute), stage 4 (eGFR 15–29 ml/minute), and stage 5 (eGFR < 15 ml/minute).[18] Patients were classified as having HFrEF based on the International Classification of Diseases (ICD) diagnosis code issued by the cardiologist after hospitalization or outpatient clinic.[19]

2.2. Measurement of NT-proBNP data

We do the point-of-care biomarker testing of the blood samples via the "RADIOMETER" AQT90 FLEX Analyzer, which results in 10 minutes. The detection unit is pg/mL. Limit of detection: $\leq$ 20 (ng/L). Reportable range: 70–35,000 ng/L. Correlation vs. Roche Modular: y = 1.008x – 8.196, R^2 = 0.99, n = 104. This novel detection method did not sacrifice low-concentration reproducibility.

2.3. Statistical analyses

The statistical analysis was performed with MedCalc 18.9.1 (MedCalc Software, Ostend, Belgium). The data were reported as the mean $\pm$ standard deviation (range, if data were nonnormally distributed). The sensitivity and specificity were analyzed by ROC curves to assess the diagnostic performance of NT-proBNP, and the area under the curve (AUC) was calculated.[20] The optimal cut-off values for the ROC curves were determined using a maximized Youden's index.[21] In all analyses, $p < 0.05$ indicates statistical significance.

3. Results

3.1. Clinical characteristics and NT-proBNP data

The study cohort included 1009 consecutive participants, including 475 patients (47.1%) with HFrEF and 534 patients (52.9%) without HFrEF. The mean age of the participants was 78.6 years, and there were fewer males (472 patients, 46.8%) than females (537 patients, 53.2%) in this study population. There were statistically significant differences between the HFrEF and non-HFrEF groups in the comorbidities, including CKD, myocardial infarction, liver cirrhosis, and atrial fibrillation ($p < 0.05$). The prevalence of HFrEF in CKD stage 3, stage 4, and stage 5 groups are 33.3%, 38.9%, and 56.8%, respectively. Mean NT-proBNP levels in the HFrEF group were about 4-fold higher compared to the non-HFrEF group ($p < 0.01$). Demographic descriptors of these cohorts are provided in Table 1.

Table 1
Clinical descriptors of the derivation and validation cohorts at the baseline.

	Heart failure		*p* value
	No (n = 534)	Yes (n = 475)	
Demographics			
Sex, N (%)			< 0.01
Male	272 (57.63)	200 (42.37)	
Female	262 (48.79)	275 (51.21)	
Age (y), mean (95% of CI)	78.06 (8.04)	79.13 (9.72)	0.058
Comorbidities, N (%)			
COPD	55 (48.25)	59 (51.75)	0.288
DM	87 (46.52)	100 (53.48)	0.052
MI	19 (38.78)	30 (61.22)	< 0.05
CVA	64 (48.48)	68 (51.52)	0.273
Cirrhosis	10 (26.32)	28 (73.68)	< 0.01
HTN	281 (55.64)	224 (44.36)	0.083
AF	68 (36.36)	119 (63.64)	< 0.01
CKD stage, N (%)			
3	148 (66.67)	74 (33.33)	< 0.01
4	157 (61.09)	100 (38.91)	< 0.01
5	229 (43.21)	301 (56.79)	< 0.01
Biomarker			
NT-proBNPPOCT (mg/dl), medium (IQR)	1,460 (4,743)	15,200 (32,430)	< 0.01

AF, atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebral vascular accident; DM, diabetes mellitus; HTN: hypertention; MI, myocardial infarction.
The values are given as the mean (confidence interval), n (%) or medium (interquartile-range).

Figure 1 shows the proportion of different CKD stage groups in various levels of NT-proBNP. Among the cohort, the distribution of baseline CKD stage was as follows: 222 with stage 3 (22.00%), 257 with stage 4 (25.47%), and 530 with stage 5 (52.53%). Mean NT-proBNP levels are 3060 pg/ml, 4360 pg/ml, and 16030 pg/ml for CKD stage 3, stage 4, and stage 5 patient groups, respectively. Figure 2 shows the proportion of HFrEF patients in various levels of NT-proBNP.

3.2. ROC-AUC analysis

Stratifying with the CKD stages, NT-proBNP showed varying discriminative ability for diagnosing heart failure in the cohort. Optimal NT-proBNP cut-offs of HFrEF diagnosis for CKD stage 3, stage 4, and stage 5 were 1420 pg/ml, 2540 pg/ml, and 19800 pg/ml, respectively. Table 2 presents the sensitivity, specificity, AUCs, and cut-offs for NT-proBNP in different CKD stages.

For the CKD stage 3 group (Figure 3), a sensitivity of 67.6% (95% CI: 55.7 to 78.0%) and specificity of 75.0% (95% CI: 67.2 to 81.7%) were calculated at the cut-off of 1420 pg/ml. The AUC is 0.737 (95% CI: 0.674 to 0.794, $p < 0.0001$).

For the CKD stage 4 group (Figure 4), a sensitivity of 56.0% (95% CI: 45.7 to 65.9%) and specificity of 73.9% (95% CI: 66.3 to 80.6%) were calculated at the cut-off of 2540 pg/ml. The AUC is 0.682 (95% CI: 0.621 to 0.738, $p < 0.0001$).

For the CKD stage 5 group (Figure 5), a sensitivity of 66.5% (95% CI: 60.8 to 71.8%) and specificity of 100.0% (95% CI: 98.4 to 100.0%) were calculated at the cut-off of 19800 pg/ml. The AUC is 0.841 (95% CI: 0.807 to 0.871, $p < 0.0001$).

4. Discussion

To our knowledge, this may be the first report to stratify the threshold of each cut-off value in heart failure in advanced CKD combined, specifically in geriatric patients. In a meta-analysis of nine studies in 2015, CKD stage 3–5 had twice higher cut-off values (ranging from 1200–6000 pg/ml) in acute heart failure compared to CKD stage 1–2.[16] In the 2019 Heart Failure Association of European Society of Cardiology, practical guidance on natriuretic peptide concentrations revealed that the diagnostic value of HF should be adjusted to renal function while eGFR < 60 ml/min.[22] Charmetant X et al. analyzed 3699 acute dyspnea patients at the Emergency Unit of St. Joseph St. Luc Hospital, Lyon, France. The cut-off values in CKD stages 3–5 were 2,283, 4,108, and 7,288 ng/L.[23] Compared to previous studies, our studies delineated that the cut-off value of heart failure might be separate in geriatric patients. It is important to clarify each level in different advanced CKD.

In Figure 5, we can observe that the cut-off value was much higher in CKD stage 5 (19800 pg/ml). In end-stage renal disease patients, many factors can influence NT-proBNP level, including with or without dialysis (including different dialysis methods, high or low flux device), volume status, and medication.[24–26] In a previous 2021 meta-analysis conducted by Lin Y et al., the NT-proBNP level was not influenced by hemodialysis (HD). However, NT-proBNP can be affected by many other factors.[25] Ludka O et al. studied 99 patients of HD and 18 patients of peritoneal dialysis (PD) with similar duration of dialysis, left ventricular function, and cardiothoracic ratio. The number of elevated NT-proBNP was higher in HD than in PD (97% vs. 44%, $p < 0.0001$).[26] Park WL et al. enrolled 80 Korean patients and compared the volume status and dialysis marker and found significant associations between relative hydration status and higher NT-proBNP in both HD and PD patients (Relative hydration status (ΔHS, %) was defined in terms of the hydration status-to-extracellular water ratio with a cut-off of 15%).[24] In several reports, the NT-proBNP level decreased HD in a high-flux membrane but increased in a low-flux membrane.[27] Besides, blood pressure, hemoglobin, dialysis duration, and intensive catabolism were frequent changes in a dialysis patient, which make NT-proBNP much more variable than the resting stage of CKD.[28] Even in the same patients with regular dialysis, MA Fahim et al. found that coefficients of variation were 27% for weekly measurement and 35% for monthly measurement unaffected by dialysis modality, hydration status, inflammation, or cardiac comorbidity.[29] In our study, the cut-off value may be attributed to the high percentage of HD and acute decompensated heart failure with hypervolemia patients in the emergency department.

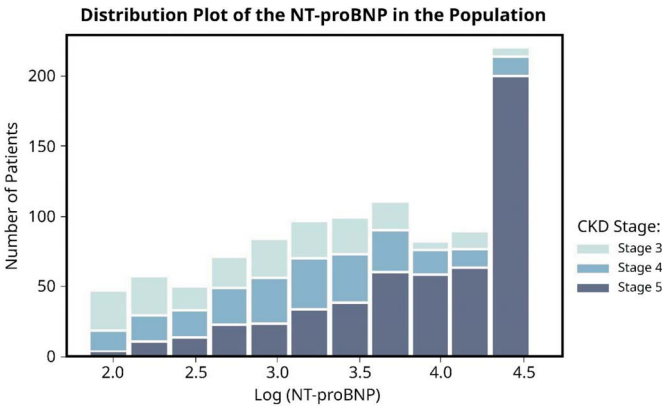

Figure 1. The histogram shows the proportion of different chronic kidney disease (CKD) stage groups in various levels of NT-proBNP.

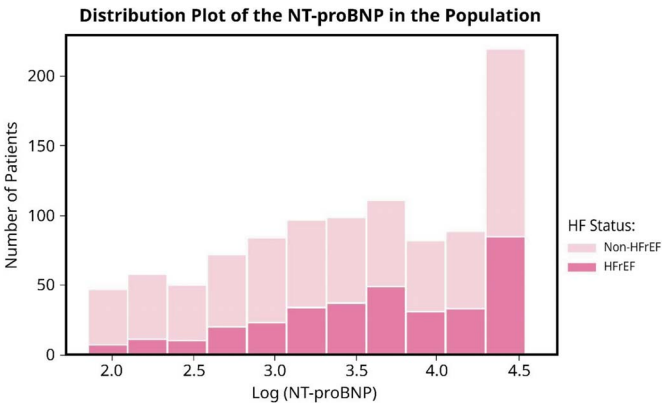

Figure 2. The histogram shows the proportion of heart failure patients with reduced ejection fraction (HFrEF) in various levels of NT-proBNP.

Table 2
ROC analysis for NT-proBNP in different CKD stages.

CKD stage/metrcs	Cut-off	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
3	1,420 pg/mL	0.737 (0.674, 0.794)	67.6 (55.7, 78.0)	75.0 (67.2, 81.7)
4	2,540 pg/mL	0.682 (0.621, 0.738)	56.0 (45.7, 65.9)	73.9 (66.3, 80.6)
5	19,800 pg/mL	0.841 (0.807, 0.871)	66.5 (60.8, 71.8)	100 (98.4, 100.0)

AUC, the area under the curve; CI, confidence interval; CKD, chronic kidney disease.

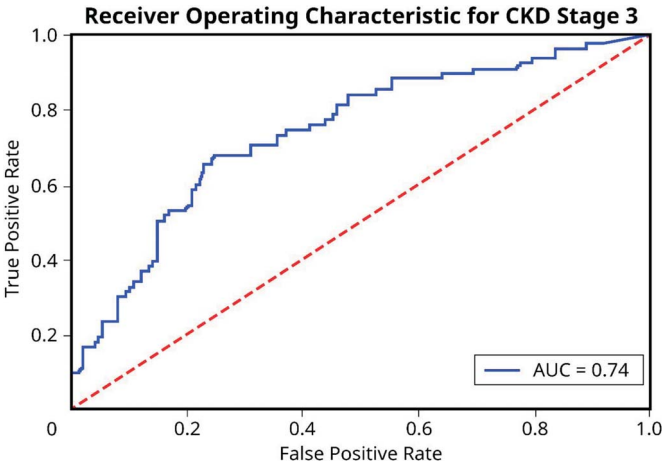

Figure 3. The receiver-operating characteristic (ROC) curve for assessing the diagnostic performance of NT-proBNP in chronic kidney disease (CKD) stage 3.

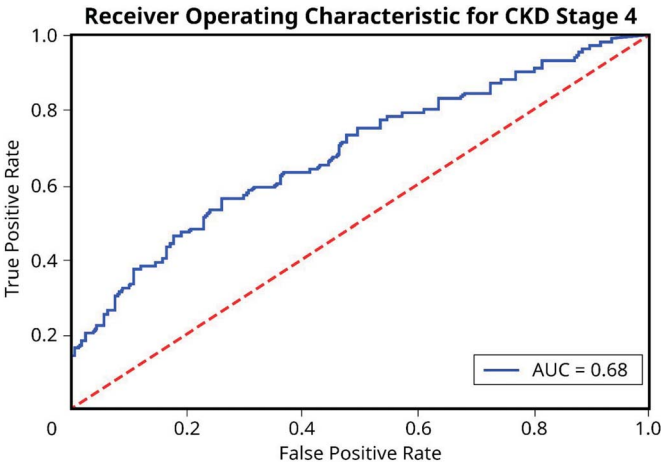

Figure 4. The receiver-operating characteristic (ROC) curve for assessing the diagnostic performance of NT-proBNP in chronic kidney disease (CKD) stage 4.

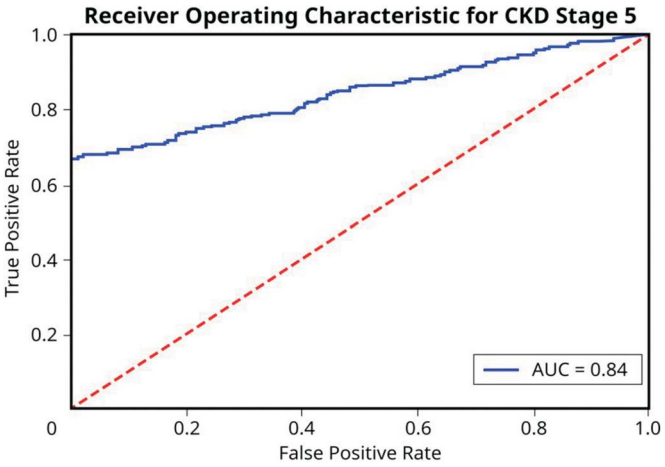

Figure 5. The receiver-operating characteristic (ROC) curve for assessing the diagnostic performance of NT-proBNP in chronic kidney disease (CKD) stage 5.

In our study, we used point-of-care testing (POCT). POCT was gradually adopted in the emergency department, the intensive care unit, the inpatient setting, and even the outpatient setting. POCT turns the original examination time which takes hours to days in the central laboratory, into minutes at the bedside. It really can facilitate rapid diagnosis and treatment, especially in emergency settings. Protera C. et al. compared 88 patients' BNP levels in capillary blood with a POCT method and those measured in a traditional venous blood sample in Unicell DxI 800 platform. The data revealed a close correlation between the two methods.[30] In a previous study, BNP and NT-proBNP in the POCT method showed similar diagnostic accuracy in HF.[31] Taylor KS et al. conducted a meta-analysis in 2018 focused on primary care setting revealed NT-proBNP got slightly higher accuracy than BNP (Pooled sensitivity: 0.99 (0.56 to 1.00) vs. 0.95 (0.91 to 0.97), Pooled specificity: 0.60 (0.44 to 0.74) vs. 0.53 (0.43 to 0.70)).[32] Kosowosky JM et al. conducted a small sample (88 patients) study of POCT BNP level in the emergency department; in patients' initial not diagnosis of HF, elevated BNP levels did influence medical decision-making. POCT helps physicians in these challenging cases and facilitates treatment and disposition in emergency settings.[33]

Our studies have some limitations: First, it is a single-center, cross-sectional observational study. The sample size was relatively small. The cut-off value may need further validation. Second, we didn't exclude the confounding effect of liver cirrhosis and previous myocardial infarction on the level of NT-proBNP (Table 1). Mihailovici AR et al. compare 82 liver cirrhosis patients with 120 healthy patients who exclude renal function impairment and found a significant elevation of NT-proBNP level in the liver cirrhosis group.[34] Wei BQ et al. divided previous myocardial infarction patients into non-heart failure (New York Heart Association Functional Classification (NYHAFc) class I) and heart failure (NYHAFc II-IV) groups and found significant differences within both groups.[35] The influence of each factor in the cut-off value in heart failure with CKD may need further research to clarify. Finally, we cannot define whether the heart failure was acute decompensated heart failure or chronic systolic failure. The NT-pro BNP level decreased after hemodynamic improvements, such as cardiac index and pulmonary capillary pressure.[36] The data was collected at ED, representing the acute decompensated phase mostly.

5. Conclusion

Age and renal dysfunction can influence the NT-proBNP cut-off value in HFrEF. The synergic effect of both factors may increase the cut-off value. Our studies delineated the different cut-off values in each advanced CKD staging. It may be helpful for physicians' daily practice, which should be validated in the future.

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References

1. Sudoh T, Kangawa K, Minamino N, et al. A new natriuretic peptide in porcine brain. *Nature.* 1988;332:78–81.

2. Maalouf R, Bailey S. A review on B-type natriuretic peptide monitoring: assays and biosensors. *Heart Fail Rev.* 2016;21:567–578.
3. Schellenberger U, O'Rear J, Guzzetta A, et al. The precursor to B-type natriuretic peptide is an O-linked glycoprotein. *Arch Biochem Biophys.* 2006;451:160–166.
4. Wilkins MR, Unwin RJ, Kenny AJ. Endopeptidase-24.11 and its inhibitors: potential therapeutic agents for edematous disorders and hypertension. *Kidney Int.* 1993;43:273–285.
5. Kohan DE, Barton M. Endothelin and endothelin antagonists in chronic kidney disease. *Kidney Int.* 2014;86:896–904.
6. Nishikimi T, Maeda N, Matsuoka H. The role of natriuretic peptides in cardioprotection. *Cardiovasc Res.* 2006;69:318–328.
7. Richards AM. The renin-angiotensin-aldosterone system and the cardiac natriuretic peptides. *Heart.* 1996;76:36–44.
8. Krishnaswamy P, Lubien E, Clopton P, et al. Utility of B-natriuretic peptide levels in identifying patients with left ventricular systolic or diastolic dysfunction. *Am J Med.* 2001;111:274–279.
9. Wang TJ, Larson MG, Levy D, et al. Impact of age and sex on plasma natriuretic peptide levels in healthy adults. *Am J Cardiol.* 2002;90:254–258.
10. Madamanchi C, Alhosaini H, Sumida A, et al. Obesity and natriuretic peptides, BNP and NT-proBNP: mechanisms and diagnostic implications for heart failure. *Int J Cardiol.* 2014;176:611–617.
11. Sbolli M, deFilippi C. BNP and NT-proBNP interpretation in the neprilysin inhibitor era. *Curr Cardiol Rep.* 2020;22:150.
12. Gaggin HK, Januzzi JL Jr. Biomarkers and diagnostics in heart failure. *Biochim Biophys Acta.* 2013;1832:2442–2450.
13. Anwaruddin S, Lloyd-Jones DM, Baggish A, et al. Renal function, congestive heart failure, and amino-terminal pro-brain natriuretic peptide measurement: results from the ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study. *J Am Coll Cardiol.* 2006;47:91–97.
14. Sato Y. Diagnostic and prognostic property of NT-proBNP in patients with renal dysfunction. *J Cardiol.* 2013;61:446–447.
15. 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;41:571–579.
16. Schaub JA, Coca SG, Moledina DG, et al. Amino-terminal pro-B-type natriuretic peptide for diagnosis and prognosis in patients with renal dysfunction: a systematic review and meta-analysis. *JACC Heart Fail.* 2015;3:977–989.
17. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976;16:31–41.
18. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis.* 2002;39:S1–S266.
19. Ponikowski E, Voor A, Anker S. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129–2200.
20. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics.* 1988;44:837–845.
21. Youden WJ. Index for rating diagnostic tests. *Cancer.* 1950;3:32–35.
22. Mueller C, McDonald K, de Boer RA, et al. Heart Failure Association of the European Society of Cardiology practical guidance on the use of natriuretic peptide concentrations. *Eur J Heart Fail.* 2019;21:715–731.
23. Charmetant X, Pecquet M, Poirié P, et al. Impact of age and renal function on usefulness of NT-proBNP to diagnose heart failure. *Clin Nephrol.* 2019;92:65–72.
24. Park WY, Park S, Kim YW, et al. Clinical efficacy of biomarkers for evaluation of volume status in dialysis patients. *Medicine.* 2020;99:e21460.
25. Yin L, Han Z, Zhang Q, et al. 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.
26. Ludka O, Spinar J, Tomandl J, et al. Comparison of NT-proBNP levels in hemodialysis versus peritoneal dialysis patients. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2013;157:325–330.
27. Laveborn E, Lindmark K, Skagerlind M, et al. NT-proBNP and troponin T levels differ after haemodialysis with a low versus high flux membrane. *Int J Artif Organs.* 2015;38:69–75.
28. Bednarek-Skublewska A, Zaluska W, Ksiazek A. The relationship between serum level of N-terminal pro-B-type natriuretic peptide and nutritional status, and inflammation in chronic hemodialysis patients. *Clin Nephrol.* 2010;73:14–20.
29. Fahim MA, Hayen A, Horvath AR, et al. N-terminal pro-B-type natriuretic peptide variability in stable dialysis patients. *Clin J Am Soc Nephrol*. 2015;10:620–629.
30. Prontera C, Masotti S, Franzini M, et al. Comparison between BNP values measured in capillary blood samples with a POCT method and those measured in plasma venous samples with an automated platform. *Clin Chem Lab Med*. 2015;53:e125–e127.
31. Jungbauer CG, Kaess B, Buchner S, et al. Equal performance of novel N-terminal proBNP (Cardiac proBNP®) and established BNP (Triage BNP®) point-of-care tests. *Biomark Med.* 2012;6:789–796.
32. Taylor KS, Verbakel JY, Feakins BG, et al. Diagnostic accuracy of point-of-care natriuretic peptide testing for chronic heart failure in ambulatory care: systematic review and meta-analysis. *BMJ.* 2018;361:k1450.
33. Kosowsky JM, Weiner C, Aronson AA, et al. Impact of point-of-care B-type natriuretic peptide (BNP) measurement on medical decision-making for older emergency department patients with dyspnea. *J Emerg Med.* 2006;31:147–150.
34. Mihailovici AR, Donoiu I, Gheonea DI, et al. NT-proBNP and echocardiographic parameters in liver cirrhosis: Correlations with disease severity. *Med Princ Pract.* 2019;28:432–441.
35. Wei BQ, Zhang J, Yang YJ, et al. Value of plasma NT-proBNP for diagnosing heart failure in patients with previous myocardial infarction. *Zhonghua Xin Xue Guan Bing Za Zhi.* 2012;40:34–38.
36. Zhang X, Yang S, Xu Z. The relationship between angiotensin–neprilysin treatment, echocardiographic parameters, and NT-proBNP levels in HFpEF patients with acute decompensated heart failure. *Comput Math Methods Med*. 2022;2022:4298644.