中文題目：血液透析病患N端腦鈉肽前體(NT-pro-BNP)與心衰竭及預後的關係

英文題目：The Relationships between NT-pro-BNP and Heart Failure or Prognosis in End-stage-renal-disease Patients with Maintenance Hemodialysis

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Background: N-terminal pro-brain natriuretic peptide (NT-pro-BNP) is one biomarker related to heart failure. Its range in the patients with maintenance hemodialysis is less studied. Is the diagnostic ability of NT-pro-BNP the same as or better than BNP or the parameters of cardiac echo for heart failure in the End-stage-renal-disease (ESRD) patients with maintenance hemodialysis? Whether NT-pro-BNP is related to the hard outcomes in ESRD patients with maintenance hemodialysis is unclear. Thus, we investigated the association of NT-pro-BNP, BNP, and other factors for the diagnosis of heart failure and the relationships between NT-pro-BNP and the prognosis of the ESRD patients with maintenance hemodialysis in this study.

Method: We did a retrospective cohort study since March 1st, 2021. 68 ESRD patients, who were all ≥18 year-old with maintenance hemodialysis in our hospital, were followed until Aug 15th, 2022. Three patients were excluded because the follow-up period was less than 3 months. We averaged all laboratory data within the first 3 months of each patient and used the averaged values for the analyses. The primary composite end-points include cardiovascular death, stroke, myocardial infarction, and

hospitalization for unstable angina and heart failure (5-point major acute cardiovascular events, 5P-MACE) and all-cause mortality. Heart failure in this study was defined as New York Heart Association Functional Classification III or IV.

Results: The 65 ESRD patients with maintenance hemodialysis were 67.2±12.2 years old. 35 patients (53.8%) were man. 50 patients (76.9%) had diabetes and 64 patients (98.5%) had hypertension. 16 patients (24.6%) took beta-blockers. 14 patients (21.5%) had 5P-MACE and 13 patients (20%) died during the follow-up period. NT-pro-BNPs were 5550 (2602-13845) and BNPs were 331 (158-865) in this study, shown in Table 1. Multivariate linear regression showed NT-pro-BNP was significantly related to pre-dialysis SBP, white blood cell count, ferritin, residual urine, triglyceride, ejection fraction, and parathyroid hormone. The r-squared of this multivariate lineal model was 0.674. The beta-coefficients were +0.44, +0.31, +0.22, -0.42, -0.38, -0.35, and -0.16. The ROC curve (Figure 1) showed the area under curve (AUC) of NT-pro-BNP and BNP for heart failure were 0.799 (*P value* < 0.001) and 0.799 (*P value* < 0.001). The best diagnostic cut-off were 15275 and 803 respectively. The AUC of ejection fraction (EF) of left ventricle for heart failure was 0.672 (*P value* = 0.024). Cox-regression showed hazard ratio (HR) (95% confidence internal) of 5P-MACE is 1.395 (1.065-1.825) per 1000 pg/ml increase of NT-pro-BNP in fully-adjusted model. The HR of the composite 5P-MACE and all-cause mortality is 1.186

(1.048-1.341) per 1000 pg/ml increase of NT-pro-BNP in these ESRD patients. (Table 2)

Conclusion: In ESRD patients with maintenance hemodialysis, we found the diagnostic ability of NT-pro-BNP for heart failure is as good as BNP and the best diagnostic cut-off were 15275 and 803. Pre-dialysis SBP and residual urine are two of the important factors to affect NT-pro-BNP. NT-pro-BNP, BNP, and EF all have significant diagnostic ability for heart failure. The HR of 5P-MACE significantly increased 39.5% and the HR of composite 5P-MACE and all-cause mortality significantly increased 18.6% when NT-pro-BNP increased 1000 pg/ml in these ESRD patients. Therefore, if the cardiac echo cannot be done regularly or in time in the certain region or country for these ESRD patients with maintenance hemodialysis, NT-pro-BNP can give a good guidance for the physicians to care these patients. More researches are warranted to evaluate if we lower NT-pro-BNP can improve the prognosis of these patients.

Table 1a. Baseline Characteristics of the Patients

No. of patients	65
Demographics data	
Age (year)	67.2±12.2
Male, n (%)	35 (53.8)
BMI (kg/m^2)	24.8±4.4
Diabetes, n (%)	50 (76.9)
HTN, n (%)	64 (98.5)
CAD, n (%)	22 (33.8)
Stroke, n (%)	18 (27.7)
PAOD, n (%)	17 (26.2)
Hemodialysis related parameters	
HD months	33.0 (12.0-69.5)
Darbepoetin equivalent (unit)	100.0 (60.0-100.0)
Residual urine (ml)	100 (0-300)
URR (%)	72.8±4.4
Pre-dialysis SBP (mmHg)	149.8±20.8
Pre-dialysis DBP (mmHg)	71.0±14.7
Laboratory data	
WBC (/ul)	6980 (5443-8598)
Hemoglobin (g/dl)	10.1±1.2
Sodium (mmol/l)	135.2±3.3
Potassium (mmol/l)	4.5±0.7
Glucose (mg/dl)	159 (125-193)
Phosphorus (mg/dl)	5.0±1.4
Uric acid (mg/dl)	6.3±1.7
GPT (mg/dl)	13.0±8.8
Cholesterol (mg/dl)	157.0±39.6
Triglyceride (mg/dl)	135.0 (99.5-184.0)
TIBC (ug/dl)	241.8±57.0
Ferritin (ng/ml)	337.1 (159.8-488.0)
NT-pro-BNP	5550 (2602-13845)
BNP	331 (158-865)
iPTH	218 (107-398)
Cardiothoracic ratio (%)	50.4±5.2
Medications	
Beta-blockers (%)	16 (24.6)
ACEI/ARBs (%)	22 (33.8)
Oral hypoglycemic agents (%)	27 (41.5)

Insulin (%)	15 (23.1)
Antiplatelet (%)	21 (32.3)

Abbreviations: ACEI, Angiotensin converting enzyme inhibitor; ARB, Angiotensin receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; CAD, coronary artery disease; DBP, diastolic blood pressure; HTN, hypertension; NT-pro-BNP, N terminal pro-brain natriuretic peptide; PAOD, peripheral artery occlusion disease; SBP, systolic blood pressure; TIBC, total iron binding capacity; URR, urea reduction rate

Table 1b. Baseline Electrocardiography and Echocardiography of the Patients

No. of patients	65
12-lead ECG results	
Af/AF, n (%)	3 (4.6)
Myocardial ischemia, n (%)	13 (20.0)
Echocardiography parameters	
LAD (mm)	39.0 (35.0-44.5)
EF (%)	65.0 (61.0-68.0)
FS (%)	36.0 (33.5-38.0)
LV mass index (g/m^2)	157.7±45.0

Abbreviations: Af, atrial fibrillation; AF, atrial flutter; ECG, electrocardiography; EF, ejection fraction; FS, fraction shortening; LAD, left atrium diameter; LV, left ventricle

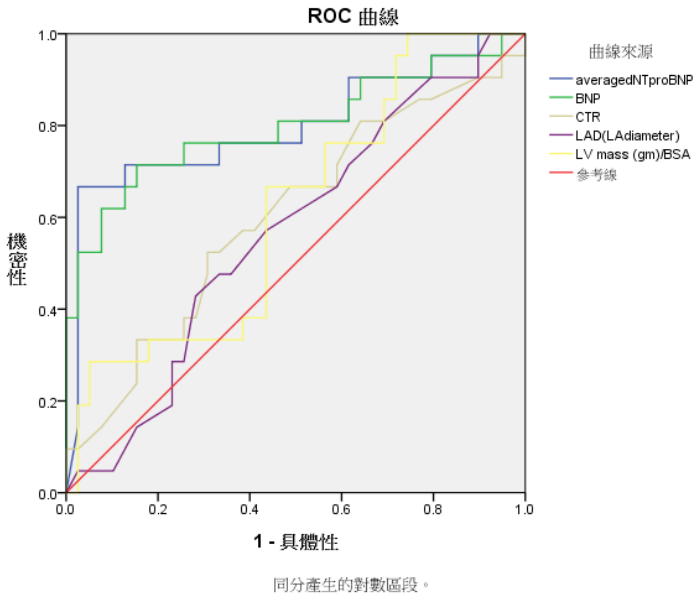
Table 2. Cox Regression for 5P-MACE and the Composite of 5P-MACE and All-cause Mortality by NT-pro-BNP per 1000 pg/ml. [a]

	5P-MACE			
	Unadjusted HR (95%CI)	**Model 1 (95%CI)**	**Model 2 (95%CI)**	**Fully-adjusted HR (95%CI)**
per 1000 NT-pro-BNP, pg/ml	1.049 (1.008-1.093)	1.059 (1.013-1.106)	1.068 (1.017-1.121)	1.395 (1.065-1.825)
	Composite of 5P-MACE and All-cause Mortality			
	Unadjusted HR (95%CI)	**Model 1 (95%CI)**	**Model 2 (95%CI)**	**Fully-Adjusted HR (95%CI)**
per 1000 NT-pro-BNP, pg/ml	1.050 (1.016-1.085)	1.060 (1.023-1.098)	1.078 (1.035-1.124)	1.186 (1.048-1.341)

Abbreviations: 5P-MACE, 5-point major adverse cardiovascular events; CI, confidence interval; HR, hazard ratio

a Models 1 is adjusted for age and gender. Model 2 is adjusted for age, gender, diabetes, hypertension, coronary artery disease, stroke, peripheral arterial occlusion disease and heart failure. Fully-adjusted model included variables from model 2 and white blood cell count, Hemoglobin, albumin, potassium, phosphorus, cholesterol, triglyceride, total iron binding capacity, parathyroid hormone, pre-dialysis systolic blood pressure, and residual daily urine amount.

a)



b)

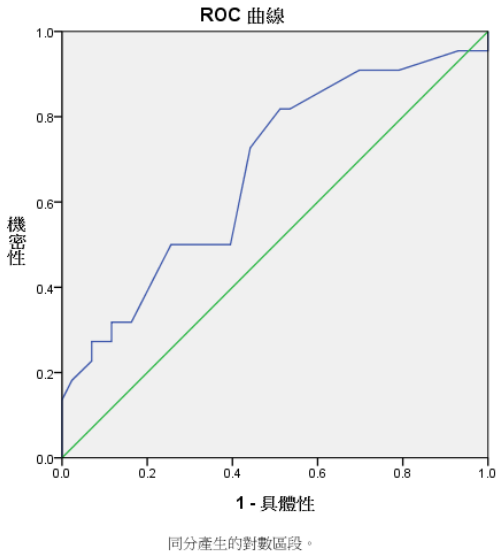


Figure 1. Receiver operating characteristic (ROC) curve for predicting heart failure. a) area under curve (AUC) of averaged NT-pro-BNP is 0.799 (*P value* < 0.001); AUC of BNP is 0.799 (*P value* < 0.001); AUC of CTR is 0.603 (*P value* = 0.193)AUC of left atrium diameter (LAD) is 0.568 (*P value* = 0.390); AUC of LV mass index = 0.615 (*P value* = 0.143); b) AUC of EF is 0.672 (*P value = 0.024*).