EJONS International Journal on Mathematic, Engineering and Natural Sciences ISSN 2602 - 4136

Article Arrival Date 17.05.2020 | Article Type Research Article | Article Published Date 12.06.2020

Doi Number: http://dx.doi.org/10.38063/ejons.249

NT-PROBNP DETERMINES RENAL DYSFUNCTION IN ELDERLY AND MIDDLE-AGED PATIENTS WITH HEART FAILURE

Ünsal GÜNDOĞDU

University of Health Sciences Izmir Bozyaka Education and Research Hospital, Medical Biochemistry, Izmir, Turkey

ORCİD: 0000 0002 6442 6671

Öznur ASİL

University of Health Sciences Izmir Bozyaka Education and Research Hospital, Medical Biochemistry, Izmir, Turkey

ORCİD: 0000 0001 9450 0046

ABSTRACT

Objectives: The aim of this study was to investigate the hypothesis that increased NT pro-BNP levels may be associated with impaired cardiac and renal function in elderly and middle-aged patients. Therefore, we have examined possible relationships between NT-PROBNP levels and other tests in every aspect.

Methods: The data of NT-proBNP, Urea, Creatinine, GFR, CK-MB, Trop I and CRP tests of 374 patients admitted to our hospital between September 2019 and November 2019 were evaluated retrospectively. In order to determine the effect of renal dysfunction on NT-proBNP test levels, four study groups, one control group, were formed according to age and NT-proBNP test levels.

Results:

NT-proBNP levels below <125 pg / ml and within the normal reference value range of the control group were 80.7 ± 14.6 pg / ml. The average age. 59.1 ± 13.5. Significant correlations were found between NT-proBNP levels and Age, Urea, GFR, CK-MB and Trop I levels in this group. (respectively, r: 0.45, P <0.001; r: 0.23, P <0.01; r: -0.17, P <: 0.05; r: 0.18, P <0.05 0.36, P <0.001). Significant correlations were found between NT-proBNP levels and Urea, krea, GFR and Trop I levels in the group of patients aged> 81-102 years with NT-proBNP levels> 10000 pg / ml. (respectively, r: 0.25, P <0.05; r: 0.32, P <0.01; r: -0.25, P <: 0.05; r: 0.33, P <0 , 01).

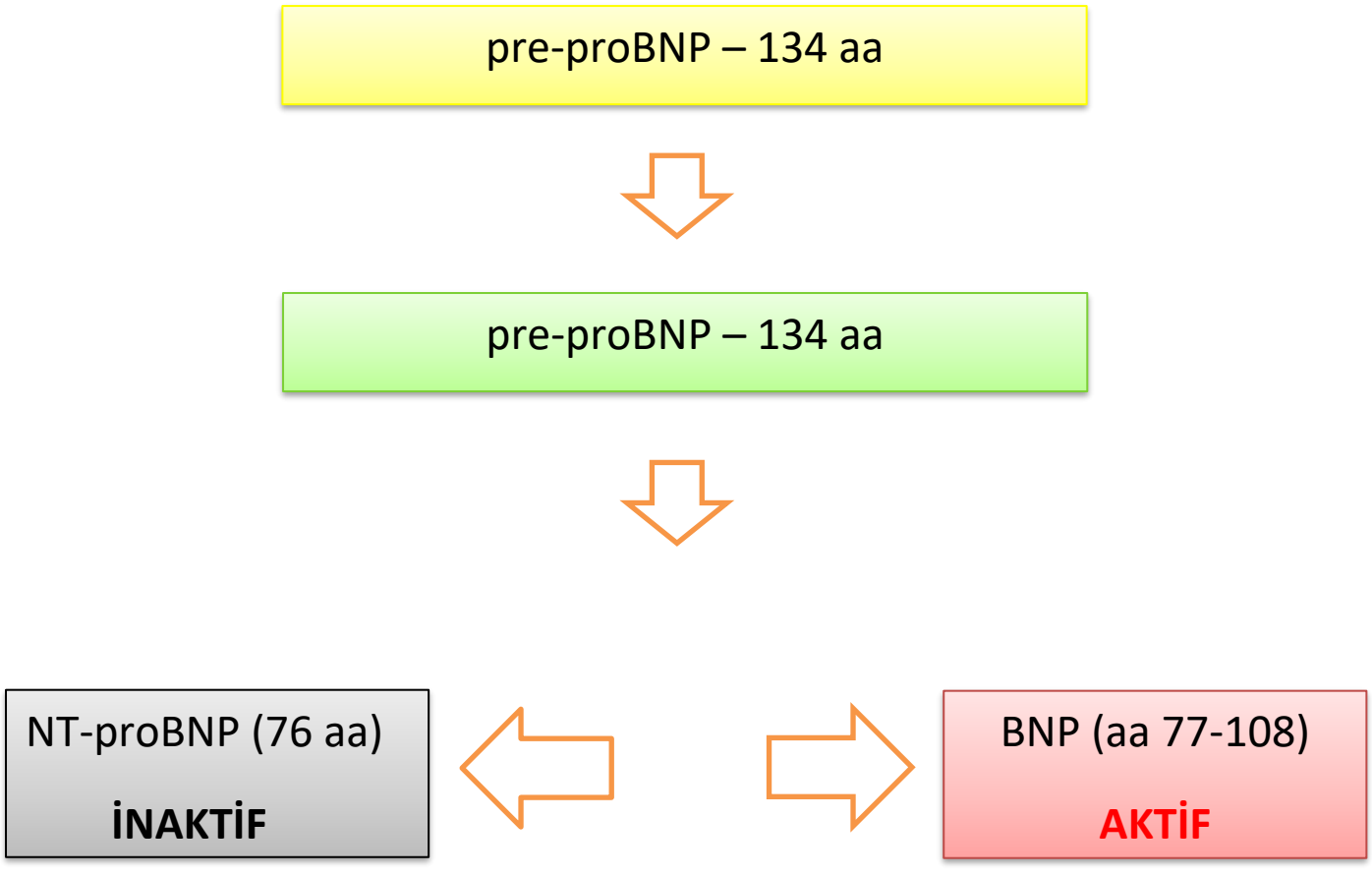
Conclusion: This study showed that NT pro-BNP levels in elderly patients with heart failure and renal dysfunction should be evaluated by considering the patient's renal impairment as well as the age group.

Keywords: Natriuretic peptides, NT-proBNP, cardiovascular diseases

1. INTRODUCTION

Coexistence of heart and kidney diseases is a common condition. A comorbidity that is frequently seen in heart failure patients and is very closely related to mortality in renal failure. Cardiovascular diseases due to accelerated atherosclerosis in all stages of chronic renal failure are an important cause of morbidity and mortality(1,2). Briefly, cardiorenal syndrome, which can be defined as the coexistence of these two diseases, is an area where studies have been intensified in recent years. Although the importance of natriuretics in prognosis and mortality in acute heart failure and acute coronary syndrome is known from previous studies, there is no definite information about the role of natriuretics in chronic renal failure(3). NT-proBNP, a prognostic biomarker for heart failure (HF), is secreted through the coronary sinuses, from myocytes, and possibly directly from the fibroblasts in the perimyocardial region, with the stimulation of ventricular tension and various neurohormonal factors. NT-proBNP is first synthesized as prepro-BNP containing 132 amino acids. The prepro-BNP is then converted to proBNP containing 108 amino acids. ProBNP is separated by proteolysis into active BNP and inactive N-terminal proBNP (NT-proBNP) containing 76 amino acids. Its half-life is about 90-120 minutes. It is passively cleared from the body by organs with high blood flow (kidneys, liver, muscles). Renal extraction rate for NT-proBNP is approximately 15% to 20% (4,5,6). It stimulates natriuresis, increases glomerular filtration rate, and causes peripheral arterial dilatation and reduces cardiac filling pressures. It also antagonizes the effects of angiotensin 2, aldosterone and arginine-vasopressin via the central nervous system. In this way, it compensates for the negative effects of heart failure (7).

Figure 1. Secretion mechanism of NT-proBNP



NP levels are higher in patients with significant renal failure and lower in obese patients (8).Therefore, it is necessary to investigate its usability in chronic renal failure patients with asymptomatic cardiovascular disease. In order to predict prognosis in acute, HF patients, it is important to evaluate NT-proBNP results and renal functions together (9). The aim of this study is to investigate the hypothesis that increased NT pro-BNP levels may be associated with impaired cardiac and renal function in elderly and middle-aged patients.

2. MATERİALS AND METHODS

The data of NT-proBNP, Urea, Creatinine, GFR, CK-MB, Trop I and CRP tests of 374 patients admitted to our hospital between September 2019 and November2019 were evaluated retrospectively. In order to determine the effect of renal dysfunction on NT-proBNP test levels, four study groups, one control group, were formed according to age and NT-proBNP test levels. Group A (mean age, 86.8 ± 4.1, age range 81-102, 58% female) had 82 patients with NT-proBNP levels> 10.000 pg / ml. Group B (mean age 85.9 ± 4.9, age range 80-95, 62% female) consisted of 60 patients with NT-proBNP levels between 2500 to 10,000 pg / ml. Group C (mean age 75.2 ± 11.0, age range 41-93, 54% female) had 121 patients. Finally, 111 subjects (mean age 59.1 ± 13.2, mean age 23-91, 47% female) with NT-proBNP test levels within the normal (<125 pg / ml) reference range formed the control group. Urea, creatinine, CRP levels were analyzed in our emergency biochemistry laboratory, AU680 (Beckman Coulter Diagnostics, USA) autoanalyser. The NT-proBNP tests was analyzed on the AQT 90 FLEX Immunoassay (Radiometer Copenhagen, Denmark) instrument. UniCel DxI 800 (Beckman Coulter Diagnostics, USA) immunoassay device was used to analyze cardiac tests (CK-MB, Trop I). Statistical analyzes were performed in IBM SPPP 25 statistical program. Since our data did not show normal distribution, it was decided to use nonparametric tests. Since we had four study groups, Kruskal-Wallis variance analysis test was used to compare urea, creatinine and GFR tests between the control group and other groups. Nonparametric Spearman correlation test was used to calculate the correlations between NT-proBNP and other tests in the control and study groups.

3. RESULTS

In our study, there were total 374 patients (45% male and 55% female) in four groups. According to the test results, the distribution between the groups was different (P <0.000) and this distribution was statistically significant (P <0.001).

Table 1. Demographic data and biochemical parameters of the patient and control groups are given in the tables below

Variables	Study GroupA n=(82)	Study Group B n=(60)	Study Group C n=(121)	Control Group n=(111)
Age(Years)	86.8±4.1	85.9±4.8	75.2±11.0	59.1±13.5
Sex Male(%) Female(%)	 35(43) 47(57)	 23(38) 37(62)	 55(45) 66(55)	 59(53) 52(47)
NT-proBNP(ng/L)	20042.8±8410	5313.0±2209.1	12774.1±9311.5	80.7±14.6
Urea(mg/dl)	89.8±45.9	58.3±30.6	81.6±40.9	34.9±13.1
Creatinine(mg/dl)	1.9±1.2	1.3±0.4	2.0±1.6	1.0±0.2
GFR	34.5±14.2	47.2±18.5	39.8±20.1	72.9±18.5
CK-MB(ng/ml)	6.2±9.7	4.0±4.2	6.0±20.0	2.3±2.0
Trop I(pg/ml)	167.3±306.9	35.7±32.1	393.4±2685.6	5.2±2.9
CRP(mg/L)	64.0±75.7	44.1±51.7	48.6±62.8	14.4±41.7

Table 2. Correlations and significance levels in Group A.

NT-proBNP	r	P
Yaş	-0,08	0,23
Üre	0,25	0,01
Kreatinin	0,32	0,002
GFR	-0,25	0,01
CK-MB	0,13	0,10
Trop I	0,33	0,001
CRP	0,11	0,14

In Group A, significant correlations were found between NT-pro-BNP and urea, creatinine, GFR and Trop I levels. (respectively, r: 0.25, P <0.05; r: 0.32, P <0.01; r: -0.25, P <: 0.05; r: 0.33, P <0 , 01).

Table 3. Correlations and significance levels in Group B.

NT-proBNP	r	P
Yaş	-0.10	0.20
Üre	0.20	0.05
Kreatinin	0.24	0.003
GFR	-0.20	0.05
CK-MB	-0.11	0.19
Trop I	0.15	0.11
CRP	0.03	0.40

In Group B, significant correlations were found between NT-pro-BNP and urea, creatinine,GFR (respectively, r: 0.20, P :0.05; r: 0.24, P <0.01; r: -020, P : 0.05).

Table 4.Correlations and significance levels in Group C.

NT-proBNP	r	P
Yaş	-0.03	0.33
Üre	0.38	0.000
Kreatinin	0.36	0.000
GFR	-0.33	0.000
CK-MB	0.25	0.004
Trop I	0.53	0.000
CRP	0.20	0.01

In Group C, Significant correlations were found between NT-proBNP levels and Urea, creatinine, GFR, CK-MB, Trop I and CRP levels. (respectively, r: 0.38, P <0.001; r: 0.36, P <0.001; r: - 0.33, P <0.001; r: 25, P <0.01; r: 0.53, P <0.001; r: 0.20, P <0.05).

Table 4.Correlations and significance levels inControl Group.

NT-proBNP	r	P
Age	-0.45	0.000
Urea (mg/dl)	0.23	0.006
Creatinine(mg/dl)	0.03	0.34
GFR	-0,17	0.03
CK-MB	0.18	0.02
Trop I	0.36	0.000
CRP	0.03	0.34

Significant correlations were found between NT-proBNP levels and Age, Urea, GFR, CK-MB and Trop I levels in Control group. (respectively, r=0.45; P =0.000, r:=0.23; P =0.006; r= -0.17;P= 0.03, r= 0.18; P =0.02 r=0.36; P=0.000).

4. DİSCUSSİON

Natriuretic peptides are widely used prognostic markers in the diagnosis and treatment of cardiovascular diseases such as hypertension, heart failure and acute coronary syndrome, which are involved in cardiac, vascular and renal adaptation mechanisms against hemodynamic changes in heart failure (10). Goetze stated that proBNP derivatives are highly sensitive and specific in demonstrating ventricular dysfunction, which is directly proportional to the severity of the cardiac condition (11). Both BNP and NT-proBNP measurements are useful in the diagnosis of heart failure, but there are some differences between them. NT-proBNP is less affected by sodium consumption and glomerular filtration rate than BNP. Today, NT-proBNP measurements are more widely used than BNP measurements (12,13).

The available data show that the reason for the increase in BNP levels in renal insufficiency is not only due to the simple reduction of passive renal clearance, but is multifactorial as part of the regulatory response from the heart to the kidney (14-15). BNP levels have been shown to increase in patients with renal insufficiency, even without heart failure ([16,17). The Working Group of the European Society of Cardiology (2012) reported that NT-proBNP test measurement levels should be interpreted together with renal disease, and higher results can be seen in patients with renal failure (16,17). We found that the correlations between age and NT-proBNP levels differed according to age groups. In Group A (age range 81-102) and Group B (age range 81-95) patients with a mean age of> 80, the correlations between NT-proBNp levels and age were insignificant (r=- 0.08; p=0.23, r=- 0.10; p=0.20)(Table 5, Table 6). In Group C(age range 43-91) correlations between NT-proBNp levels and age were insignificant(r=-0.03 ; p=0.33)(Table 7). The mean age in this group is 75.1±11.0 (Table 3).

However, in our control group (age range 23-91) with the lowest mean age (59.1±13.5)), a significant positive correlation was found between NT-proBNP and age(r=0.45; p=0.000)(Table 8). There was a significant correlation between NT-proBNp levels with urea, creatinine and GFR at Group C, which had the lowest mean age (r=0.38; p=0.000, r=0.36; p=0.000, r=-0.33; p=0.000)(Table 3).

Hua Cui (18) and colleagues in their study, in patients older than 80 when years, NT pro-BNP level greater than ≥ 3000 pg / ml are reported that the results is determined by impaired renal function in these patients. They studied a patient group with an NT pro-BNP test level of around 3000 -10000 pg / ml and another group of patients with an NT pro-BNP test level of 10000pg / ml. Correlations between NT-proBNP levels and renal function tests (urea, creatinine and GFR) were more significant in the group whose NT-proBNP level was above 10000pg / ml (p<0.001). (r=0.25; p=0.01,r=0.32;p=0.002, r=-0.25;p=0.01)(Table1). In our study, Correlations between NT-proBNP levels and renal function tests (urea, creatinine and GFR) were more significant in the Group A with NT-proBNP levels> 10000pg / ml compared to Group B (r=0.25; p=0.01,r=0.32;p=0.002, r=-0.25;p=0.01)(Table1). When we examined the correlations between renal function tests such as urea, creatinine and GFR and NT-proBNP levels, the highest significance level (P <0.001) was seen in the Group C have patients. As the mean age increased in the patient groups, the correlation between NT-proBNP with renal function tests (urea, creatinine and GFR) decreased. NT pro-BNP level (80.7 ± 14.6 pg / ml) was found in the control group and the correlations between NT pro-BNP and Age and Trop I tests were significant(r=0.23; p=0.006, r=0.36; p=0.000)(Table 8).

In the control group, the correlations between NT-proBNP and urea, creatinine and GFR tests were not significant for creatinine(r=0.03; p=0.34), significant for urea(r=0.23;p=0.006), and significant for GFR (r=-0.17;P= 0.03)(Table 8).

5. CONCLUSİON

There is a significant relationship between NT pro-BNP level and renal function tests. In patients aged 75 years and older with NT pro-BNP test level between 12500-20000 pg / ml NT pro-BNP test results determine by renal function. However, this relationship begins to decrease in patients over 85 years of age. Therefore, when is determining renal threshold for NT pro-BNP test in patients with renal insufficiency, not only according to patient GFR levels, but also the age groups of the patients should be taken into consideration.

REFERENCES

1. Foley RN, Parfrey PS. Cardiovascular disease and mortality in ESRD. J Nephrol. 1998; 11: 239-245
2. Raine AE, Margreiter R, Brunner FP, Ehrich JH, Geerlings W, Landais P, et al. Report on management of renal failure in Europe, XXII, 1991. Nephrol Dial Transplant. 1992; 7: 7-35
3. Nishikimi T, Futoo Y, Tamano K. Plasma brain natriuretic peptide levels in chronic hemodialysis patients: Influence of coronary artery disease. Am J Kidney Dis 2001; 37: 1201-1208.

4. Thygesen, K. et al. (2012). Euro Heart J, 33, 2001-2006.
5. Schou, M. et al. (2005). J Appl Physiol, 99, 1676-1680
6. DeFilippi, C. et al. (2008). Clin Chem, 55(7), 1271-1273.
7. Felker, M. et al. (2006). CMAJ, 175, 611-617.
8. van Kimmenade, R.L. et al. (2006). J Am Coll Cardiol, 48: 1621-1627. Cardiovasc J Afr. 2013 Aug;24(7):286-9. doi: 10.5830/CVJA-2013-055. Review. BMC Cardiovasc Disord. 2012 Jul 26;12:57. doi: 10.1186/1471-2261-12-57
9. Hunt PJ, Richards AM, Nicholls MG, Yandle TG, Doughty RN, Espiner EA. Immunoreactive amino-terminal pro-brain natriuretic peptide (NT-PROBNP): A new marker of cardiac impairment. Clin Endocrinol (Oxf) 1997; 47: 287-296.
10. Duygu H, Türk U, Zoghi M, Nalbantgil S. The importance of plasma B-type natriuretic peptide levels in cardiovascular diseases. Anadolu Kardiyol Derg 2005;5:305-11.
11. Swedberg K, Cleland J, Dargie H, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005). Eur Heart J 2005; 26: 1115-1140.
12. Maisel AS, McCord J, Nowak RM, et al. Bedside B-type natriuretic peptide in the emergency diagnosis of heart failure with reduced or preserved ejection fraction. Results from the Breathing Not Properly Multinational Study. J Am Coll Cardiol 2003; 41: 2010-2017.
13. Januzzi JL Jr, Camargo CA, Anwaruddin S, et al. The N-terminal Pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) study. Am J Cardiol 2005; 95: 948-954.
14. Palazzuoli A, Gallotta M, Quatrini I, Nuti R. Natriuretic peptides (BNP and NT-proBNP): measurement and relevance in heart failure. Vasc Health Risk Manag 2010;6:411-8. [CrossRef]
15. Fonarow GC; ADHERE Scientific Advisory Committee. The Acute Decompensated Heart Failure National Registry (ADHERE): opportunities to improve care of patients hospitalized with acute decompensated heart failure. Rev Cardiovasc Med 2003;4 Suppl 7:21-30.
16. Palazzuoli A, Gallotta M, Quatrini I, Nuti R. Natriuretic peptides (BNP and NT-proBNP): measurement and relevance in heart failure. Vasc Health Risk Manag 2010;6:411-8. [CrossRef]
17. Noppert SJ, Mayer G. In search for the troponin of the kidney. Curr Med Chem 2009;16:4219-29. [CrossRef]
18. Association of Cardiac and Renal Function With Extreme N-terminal Fragment pro-B-type Natriuretic Peptide Levels in Elderly Patients DOI: 10.1186/1471-2261-12-57