Ann Med Res 2020;27(4):1241-5

Annals of Medical Research

DOI: 10.5455/annalsmedres.2019.11.770

Original Article

Efficacy of ProBNP and CRP/ Albumin ratio in patients with acute heart failure in the Emergency Department

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Abstract

Aim: Heart failure (HF) is one of the most common diseases in patients over 65 years of age.It is a clinical condition which is often mortal and requires intensive care follow-up. Therefore, some tests are used to predict the diagnosis, treatment and prognosis. In this study, we aimed to compare the effect of natriuretic peptides (ProBNP) and CRP/albumin ratio on mortality and prognosis in patients who referred to the emergency department (ED) with HF.

Material and Methods: The patients with ICD codes of I50 and J81 in two different hospital ED between 2018 and 2019 were analyzed retrospectively. Demographic data of the patients and the parameters planned to be studied were recorded in a Microsoft Excel 2010 file. NCSS (Number Cruncher Statistical System) 2007 software was used for the statistical analysis.

Results: Our study consisted of 301 patients. A very weak positive (CRP/albumin ratio increased as the ProBNP value increased) correlation of 0.193 between ProBNP measurements and CRP/albuminratios of the participants was found to be statistically significant($r=0.193$; $p=0.001$; $p<0.01$).

Conclusion: According to our study, no significant correlation was found between ProBNP and CRP/albumin ratio. The CRP/albumin ratio is not appropriate to be used alone to determine the definitive diagnosis and mortality in cases with acute HF. However, since there are not enough studies regarding this subject, more studies need to be done in a more extended period and with more patients.

Keywords: Acute heart failure; CRP/Albumin ratio; emergency department; ProBNP

INTRODUCTION

Heart failure (HF) is one of the most common diseases seen in patients over 65 years of age (1). Acute HF is defined as a clinical syndrome, whereas the typical signs and symptoms of HF occur suddenly or gradually and require immediate treatment. The pathophysiological trial of decompensated HF (pulmonary edema) includes congestion, myocardial injury and cardiorenal syndrome (2). This clinical condition is often mortal and requires intensive care follow-up, and patients usually apply the emergency departments (EDs) of hospitals. Therefore, some tests are used to predict the diagnosis, treatment, and prognosis. Some biomarkers that are used in patients presenting with dyspnea guide us on whether the cause is cardiac or not, and natriuretic peptides (BNP, NT-ProBNP) are the most commonly used markers among (BNP, NT-ProBNP).

BNP is a neurohormone consisting of 32 amino acids. It is primarily synthesized, stored in the left ventricle, and secreted from the left ventricle as well. BNP and NT-ProBNP are secreted into the circulatory system based on pulsation through coronary sinuses from the myocytes by the stimulation of neurohormonal factors and increased ventricular tension and some directly from the peri-myocardial fibroblasts (3). Due to its high negative predictive value, ProBNP at normal concentration reduces the likelihood of acute HF (4).

Serum C-reactive protein (CRP) is a positive acute-phase reactant. It is synthesized from the liver, and the level of CRP increases in the blood within hours under inflammatory and infectious conditions (4). The half-life of CRP is short, and CRP is easily measurable and closely related to prognosis. Prognosis is used to monitor the effectiveness of treatment and to determine mortality (5). Albumin is a negative acute phase reactant and decreased albumin level is associated with inflammation, poor prognosis, and mortality in cases of infection. Albumin is used for monitoring inflammation and malnutrition (5,6). CRP and albumin have often been used as an acute phase reactant separately for many years in cases of inflammation. However, recent studies have shown that CRP/albumin

Received: 25.11.2019 **Accepted:** 12.02.2020 **Available online:** 16.04.2020
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ratio is a reliable parameter that could be used to determine mortality in inflammation, infection, ischemia, and several diseases. CRP/ albumin ratio was found to be significant in cardiac origin studies such as myocardial infarction with ST-elevation and its complications, and it was shown to be useful in determining prognosis. (7,8).

We aimed to determine whether there was a correlation between ProBNP and CRP/albumin ratio in patients with pulmonary edema who referred to the ED with dyspnea and whether this rate could be used to evaluate prognosis and mortality in patients with pulmonary edema (PE).

MATERIAL and METHODS

The files of patients with ICD codes of I50 and J81 in two different education and research hospital EDs between January 2018 and January 2019 were analyzed retrospectively, and 301 patients with acute PE were included in the study. Patients with malignancy, anemia, acute or chronic infection(s) and acute or chronic renal failure presence on the file examinations were not included in the study. Serum albumin and CRP levels were measured by using Siemens Dimension RxL Max Chemistry Analyzer (USA). CRP levels were measured according to the immunoturbidimetric method, and serum albumin levels were analyzed by the bromocresol purple method. The CAR was defined as the serum CRP level divided by the serum albumin level. Normal ranges were 0-5 mg/dl for CRP, 3.4-5 g/l for albumin, and 0-300 pg/ml for ProBNP. Demographic data such as age and gender of the patients and the parameters planned to be studied were recorded in a Microsoft Excel 2010 file.

Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software was used for the statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum and maximum) were used when evaluating the study data. Mann-Whitney U test was used for the comparison of non-normative quantitative variables between two groups. Kruskal-Wallis test and Dunn-Bonferroni test were used for the comparison of quantitative variables with abnormal distribution between more than two groups. Fisher-Freeman-Halton Exact Test was used to compare the qualitative data. Spearman correlation analysis was used to evaluate the correlations between the quantitative variables. Diagnostic screening tests (sensitivity, specificity, PPV, NPV) and ROC analysis were used to determine the predictive value for the parameters. Statistical significance was determined as $p < 0.05$.

RESULTS

The study consisted of 301 patients, 46.2% (n = 139) were males, and 53.8% (n = 162) were females who were referred to the ED of two education and research hospitals between January 2018- January 2019. The age range of the cases included in the study varied between 27 years and101 years, with a mean age of 70.54 ± 13.19 years. Age, gender, duration of stay in the ED, and outcome of the patients are shown in Table 1.

Table 1. Age, gender, duration of stay in the ED and outcome of the patients

Age	Min-Max (Median)	27-101 (71)
	Mean±SD	70.54±13.19
Gender	Male	139 (%46.2)
	Female	162 (%53.8)
Duration of Stay in Emergeny Department	1 Day	264 (%87.7)
	2 Days	29 (%9.6)
	≥ 3 Days	8 (2.7)
	Transfer	68 (%22.6)
Outcome	Hospitalization	11 (%3.7)
	Discharge	219 (%72.8)
	Death	3 (%1.0)

ProBNP measurements of the cases ranged from 111 to 35,000, with an average of 7,935.56 ± 10,064.16. CRP measurements varied between 10 and 536, with an average of 72.83 ± 80.54, while CRP/Albumin ratio was between 0.23 and 18.58, with an average of 2.24 ± 2.71. No statistically significant difference was found between the ages and genders and outcomes according to the test results of the patients in the ED ($p>0.05$) (Table 2).

Table 2. Evaluation of Outcomes According to Demographic Characteristics

		Outcome				Test Value
		Transfer (n=68)	Hospitalization (n=11)	Discharge (n=219)	Death (n=3)	P
Age	Min-Max (Median)	33-97 (73)	56-92 (71)	27-101 (71)	56-91 (86)	χ^2:2.009
	Mean±SD	71.97±12.00	71.82±12.14	69.93±13.54	77.67±18.93	[a] **0.571**
Gender	**Female**	33 (23.7)	4 (2.9)	101 (72.7)	1 (0.7)	χ^2:0.858
	Male	35 (21.6)	7 (4.3)	118 (72.8)	2 (1.2)	[b] **0.870**

[a] Kruskal Wallis Test [b] Fisher Freeman Halton Test

Table 3. Evaluation of ProBNP and CRP/Albumin Measurements According to Results

		Pro BNP		CRP/Albumin	
		Min-Max (Median)	Mean±SD	Min-Max (Median)	Mean±SD
Outcome	Transfer (n=68)	262-35000 (8877)	14545.75±13292.00	0.23-18.58 (1.6)	2.70±3.44
	Hospitalization (n=11)	329-14269 (3720)	5216.55±3948.10	0.25-4.4 (1.36)	1.69±1.31
	Discharge (n=219)	111-35000 (2763)	5909.56±7916.60	0.24-15.05 (1.43)	2.13±2.51
	Death (n=3)	1878-35000 (11041)	15973.00±17102.93	0.26-3.08 (2.87)	2.07±1.57
Test Value	p	χ^2:31.207	[a] **0.001****	χ^2:1.107	[a] **0.775**

[a] Kruskal Wallis Test ** p<0,01

Considering the outcomes, a statistically significant difference was found between ProBNP measurements of patients (p=0,001; p<0.01). According to Dunn-Bonferroni test results, which were performed to determine the difference, the ProBNP value of the transferred patients was significantly higher than the patients who were discharged (p=0.001; p<0.01).There was no statistically significant difference between the CRP/Albumin ratios of the cases (p>0.05) (Table 3).

According to the relationship between ProBNP and CRP/Alb measurements; A very weak positive (CRP/Albumin ratio increased as the ProBNP value increased) correlation of 0.193 between ProBNP measurements and CRP/Albumin ratios of the participants was found to be statistically significant (r=0.193; p=0,001; p<0.01). ProBNP values of patients with hospitalization indication were significantly high than the patients who were discharged from the ED (p=0.001; p<0.01). However, there was no statistically significant difference between the CRP/Albumin measurements (p>0.05) (Table 4).

As a result of the evaluations, the cut-off point determined for ProBNP was found to be ≥7,789. For the ProBNP, cut-off value of 7,789 and above, sensitivity was 52.44%, specificity was 79.45%, positive predictive value was 48.9%, and the negative predictive value was 81.7% (Table 5). The area under the ROC curve determined for ProBNP was found to be 70%, and the standard error was 3.5% (Figure 1).

Table 4. Evaluation of ProBNP and CRP/Albumin Measures According to Hospitalization and Discharge Status

		Prognosis		Test Value
		Discharge (n=219)	Hospitalization and Death (n=82)	p
ProBNP	Min-Max (Median)	111-35000 (2763)	262-35000 (7993.5)	Z:-5.345
	Mean±SD	5909.56±7916.60	13346.49±12873.47	[c] **0.001****
CRP/Albumin	Min-Max (Median)	0.24-15.05 (1.43)	0.23-18.58 (1.6)	Z:-0.867
	Mean±SD	2.13±2.51	2.54±3.19	[c] **0.386**

[c] Mann Whitney U Test ** p<0,01

Table 5. Diagnostic Screening Tests and ROC Curve Results for ProBNP According to the Outcome

	Diagnostic Scan					ROC Curve		
	Cut off	Sensitivity	Specifity	Positive Predictive Value	NegativePredictive Value	Area	95% Confidence Interval	p
ProBNP	≥7789	52.44	79.45	48.9	81.7	**0.700**	0.632-0.768	**0.001****

* p<0,05 ** p<0,01

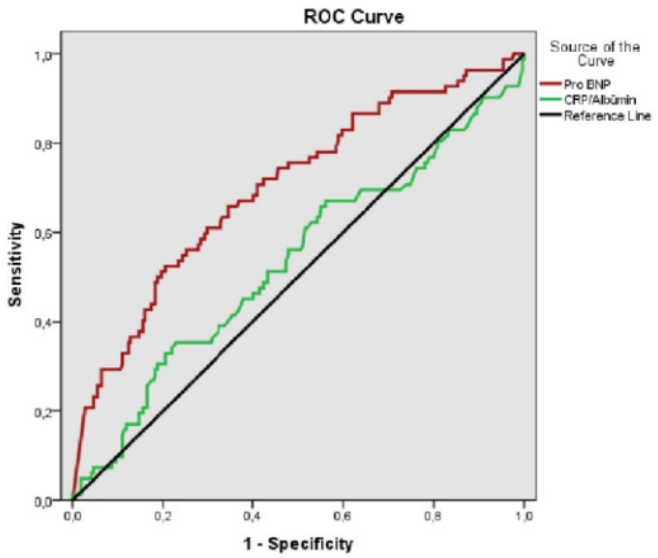

Figure 1. ROC Curve of ProBNP and CRP/Albumin Measurements According to the Outcome

DISCUSSION

Since the number of elderly patients and survival rates of elders due to treatment methods are increasing, the number of elderly patients with heart failure is increasing worldwide (10). Similar to the literature, in our study, the mean age of our cases was 70.54 ± 13.19. The advanced age is a common risk factor for both male and female genders in most of the chronic diseases, and there was no statistically significant difference between the genders, according to our study.

Diagnosis of acute HF should be supported not only by symptoms but also by clinical (peripheral edema, pulmonary rates, tachycardia) and objective findings (echocardiographic findings and elevation of natriuretic peptides) (11). In a meta-analysis of 31 studies consisting of a total of 17,893 patients, the cut-off value of NT-ProBNP was determined to be 50 pg/ml, but the results were interpreted as manifestation and prognosis would be worse as the ProBNP value increased, not as there was HF or not (12). In our study, NT-ProBNP values varied between 111 and 35000, and our cut-off value was found to be ≥7789 pg/ml. Similar to the literature, NT-ProBNP levels were found to be significantly higher in the hospitalized (intensive care and ward) group than the values of the discharged group, and its value in supporting the clinical diagnosis and predicting mortality was similar to other studies.

The diagnosis of acute HF (or PE) does not always require hospitalization. Hemodynamic instability, presence of concomitant acute coronary syndrome, presence of SaO2 <90 despite O2 treatment, lack of improvement in clinical condition, and need for further examination are considered among the hospitalization indications. In our study, we found that patients had an extended stay in the ED, and most of them (72.8%) were discharged from the ED. The reason for this result was thought to be the fact that one of the study hospitals was among the hardest working and highest number of referrals accepting hospitals in Turkey. Patients with an indication for hospitalization are followed-up in the ED and discharged from there due to the lack of space in the wards (13).

CRP and albumin are known to be acute phase reactants and are used to identify and follow-up the inflammatory process and predict prognosis in many diseases. Many studies conducted in recent years have shown that CRP/Albumin ratio is an independent predictor in diagnosis and mortality. In our study, NT-ProBNP and CRP/Albumin ratio were compared, and a very weak positive correlation of 0.193 was found between these parameters (CRP/Albumin ratio increased as the ProBNP value increased). In contrast to other studies on this subject, our study showed that CRP/Albumin ratio did not have a reliable value in predicting diagnosis and mortality in acute HF.

As in the review of Pasqualinave et al., the predictive value of NT-ProBnp in predicting mortality in acute HF was found to be statistically significant also in our study, while the value of CRP/Albumin ratio was not statistically significant (14).

CONCLUSION

While most of the studies on the ratio of CRP/Albumin are related to diseases in which infection and inflammation are at the forefront, there are no studies on acute HF. According to our study, no significant correlation was determined between ProBNP and CRP/Albumin ratio. The CRP/Albumin ratio is not appropriate to be used alone to determine the definitive diagnosis and mortality in cases with acute HF. However, since there are not enough studies regarding this subject, more studies are needed to be planned in a more extended period and with more patients.

Competing interests: The authors declare that they have no competing interest.
Financial Disclosure: There are no financial supports.
Ethical approval: Ethics Committee of Maltepe University Medical Faculty Clinical Researches 2019/900/28.

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