EJMI

DOI: 10.14744/ejmi.2021.79007
EJMI 2021;5(2):172–179

Research Article

Relationship of Serum Copper and Zinc Levels with Plasma NT-proBNP Level in Men with Ischemic Origin Chronic Heart Failure

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Abstract

Objectives: Heart failure (HF) is one of the main causes of cardiovascular mortality and mobidity today. Despite all the advances in the diagnosis and treatment of HF, mortality and morbidity rates could not be reduced to the desired levels. Therefore, it is important to identify new prognostic factors in these patients. Recent studies show that micronutrient dyshomeostasis may play a role in the pathophysiology of HF. In this study, it was aimed to investigate the relationship between copper (Cu), zinc (Zn) and Cu / Zn ratio and N-terminal pro-B type natriuretic peptide (NT-proBNP) levels in male patients followed with ischemic HF.

Methods: 57 male patients who were followed up in the cardiology outpatient clinic with a diagnosis of compensated chronic HF of ischemic origin were divided into two groups as high and low according to the NT-proBNP level, whose prognostic limit value was reported as 1000 ng / L. The control group was composed of 24 patients with similar demographic characteristics, except for the presence of HF.

Results: In the high nt-proBNP group, the serum Cu mean level was low compared to the nt-proBNP group ($p < 0.001$) and the control group ($p < 0.001$). Serum Zn mean level was statistically significantly lower in the high NT-proBNP group than in the low nt-proBNP group ($p < 0.001$) and control groups ($p = 0.005$). In addition, nt-proBNP group with high median Cu / Zn ratio was statistically significantly higher than low NT-proBNP ($p = 0.004$) and control groups ($p < 0.001$) ($p < 0.001$). However, there was no statistically significant difference between the low NT-proBNP group and the control group in terms of serum mean Cu level (p = 1,000), serum mean Zn level ($p = 0.343$) and median Cu / Zn ratio ($p = 0.636$).

Conclusion: There is a statistically significant relationship between NT-proBNP level, whose elevated levels are considered to be associated with poor prognosis in patients with ischemic origin, increased serum Cu level and Cu / Zn ratio and negative in serum Zn level. In these patients, large-volume prospective studies are needed to investigate the relationship between Cu chelation and Zn supportive therapy with nt-proBNP level and mortality rates.

Keywords: Copper, Zinc, Ischemic heart failure, NT-proBNP, Mortality

Cite This Article: *Aksu E, Avci D, Kilinc M, Celik E, Sahin AR, Onus AE. Relationship of Serum Copper and Zinc Levels with Plasma NT-proBNP Level in Men with Ischemic Origin Chronic Heart Failure. EJMI 2021;5(2):172–179.*

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Submitted Date: April 07, 2021 **Accepted Date:** May 18, 2021 **Available Online Date:** May 25, 2021

Heart failure (HF) is among the most frequent causes of increased cardiovascular mortality and morbidity in the present day. Two-third of the causes of HF consists of the ischemia developed owing to coronary artery disease.[1] Arrhythmia and cardiac remodeling arising from neurohormonal activation, oxidative stress, and increased inflammation are the primary factors responsible for the increase in cardiovascular mortality and morbidity. Despite all diagnostic and treatment-related developments targeting these mechanisms and clinical cases, the mortality and morbidity rates have not been reduced to the desired levels. Therefore, it is critical to determine the new prognostic factors and indicators for these patients.

The latest studies show that the trace element levels in HF cases may have a role in the pathophysiology of HF;[2] two of the most important trace elements are copper (Cu) and zinc (Zn) that have important roles in oxidant/anti-oxidant mechanisms. Many studies have been conducted to examine the relationship between these elements and heart failure etiopathogenesis.[3,4] N-terminal pro-B type natriuretic peptide (NT-proBNP) is among the laboratory methods frequently used in diagnosing HF, monitoring the treatment, and determining the prognosis. High plasma NT-proBNP level in HF cases has been shown to be related to increased mortality and morbidity.[5–7] Nevertheless, relevant studies from the literature have yielded contradictory results; one of the reasons for these results may be related to the probability that the etiology of HF and its reflection on the clinical picture differs, which was a determinant factor in setting the design of this study. A homogeneous group formation with HF patients who were male was targeted. Coronary ischemia was a determinant factor in the etiology of the condition among the participants.

This study aimed to examine the relationship between Cu, Zn, and Cu/Zn ratio and plasma NT-proBNP levels among male patients monitored owing to ischemic HF diagnosis.

Methods

Patient Selection

This study is a prospective observational study. Fifty-seven male patients who were monitored upon the diagnosis of ischemic compensated chronic HF in a tertiary cardiology out patient clinic and who met the inclusion criteria were divided into two groups as those with high plasma NT-proBNP level (n=34) and low plasma NT-proBNP level (n=21). NT-proBNP level higher than 1000 ng/dl has been reported as the indicator of poor prognosis regarding HF.[8] Accordingly, the NT-proBNP threshold level was set as 1000 ng/L. Left ventricular ejection fraction lower than 40% was defined as HF. The control group was set particularly to consist of 24 patients who had HF, coronary artery disease, and similar demographic characteristics to eliminate the complicated role of ischemic heart disease. The exclusion criteria included morbid obesity, renal failure (Glomerular filtration rate <60 ml/dk/1.73m^2), liver function disorder (ALT and AST values being two times higher than the upper threshold), systemic inflammatory disease, history of hematologic disease, thyroid function disorder, history of using products containing trace element and vitamin, insufficient nutrition, and grade 3 and 4 exertional dyspnea (based on New York Heart Association). The routine transthoracic echocardiography and electrocardiography (EKG) screenings were recorded.

Laboratory Investigation

After patients stayed hungry for 12 hours, routinely-processed blood biochemistry (blood sugar, lipid profile, blood urea nitrogen (BUN), creatinine, potassium, sodium, alanine aminotransferase (ALT), aspartate aminotransferase (AST), NT-proBNP) and complete blood count values were recorded. The serum, obtained from all participants, to determine the serum Cu and Zn levels were stored at -80°C. The Cu and Zn levels were determined through the flame spectrometry method on the Perkin Elmer Analyst model 800 atomic absorption spectrometer after serum samples were diluted at ½ and ¼ by 10% and 5% glycerol consecutively. Absorbance values were determined through standard graphics and results were presented as µg/dl.

Ethical Consideration

The study protocol that was in conformity with the Helsinki Declaration was approved by the Ethics Committee. (Approval Date: 05.02.2020; Protocol No:2020/03/06).

Statistical Analysis

The goodness of fit was assessed through the Shapiro-Wilk test and visuals. In the case of the normal distribution, mean ± standard deviation figures were used for continuous variables; if the distribution was not normal, mean (minimum-maximum) figures were used. In cases of a normal distribution for the paired comparisons of continuous variables, Student's t-test was preferred, and the Mann-Whitney U test was used if normality was not present in the distribution. One-way ANOVA or Kruskal-Wallis tests were used in the comparisons between the continuous variables of more than two independent groups. In posthoc calculations, Bonferroni and Tamphane's T2 tests were used. Moreover, for categorical comparisons, the chi-square test was used. To show the predictive characteristics of trace elements in regard to HF, receiver operating characteristic (ROC) curves and areas under the curve (AUC) were used. The significance level was determined at p<0.050. During the statistical analyses, Statistical Package for the Social Sciences (SPSS) version 21.0 (SPSS Inc., Chicago, IL, US) was used.

Results

Patients were examined in two groups as "those who had heart failure" and "those who did not have heart failure", and serum Cu level was 112.1±28.0 µg/dl in the group with heart failure, and 94.3±20.4 µg/dl in the control group (p=0.007). Serum Zn level was 87.1±30.3 µg/dl in the group with heart failure, and 95.9±21.9 µg/dl in the control group (p=0.204). Cu/Zn ratio was 1.57 (0.44-9.32) in the patient group and 1.04 (0.57-1.84) in the group that did not have heart failure (p=0.013) (Table 1).

We divided heart failure patients group into two group according to NT-pro BNP level as high (n=34, NT-pro BNP level>1000) and low (n=21, NT-pro BNP level<1000 ng/L). Serum Cu level was significantly higher in high NT-proBNP group than low NT-proBNP group (p<0.001) and control group (p<0.001). Additionally, serum Zn level was significantly lower in the high NT-proBNP group than low NT-proBNP group (p<0.001) and control group (p=0.005). Cu/Zn ratio was significantly higher in the high NT-proBNP group than the low NT-proBNP group (p=0.004) and control group (p<0.001). Furthermore, the serum Cu level (p=1.000), serum Zn level (p=0.334), and Cu/Zn ratio (p=0.636) were similar between the low NT-proBNP group and control group (Table 2).

The relationship between the medications used in the heart failure group, NT-proBNP level, and trace elements was examined. The copper level was higher among the users of spironolactone compared to those who did not use (p=0.014), and lower among the users of statin compared to those who did not use (p=0.007). Moreover, the Zn level was lower among the users of furosemide (p=0.012). Other than these results, no significant relationship was found between the medications used in HF treatment, NT-proBNP and trace elements (Table 3).

The correlation between Cu, Zn, and Cu/Zn ratio and other variables among HF patients were analyzed (Table 4). A positive, advanced, and statistically significant correlation was found between Cu and NT-proBNP (p<0.001). A positive,

Table 1. Comparison of some characteristics and trace elements according to the presence of heart failure in patients

	Control (n=24)	Heart Failure (n=55)	p
Age (years)	63.1±9.9	66.2±11.4	0.257
Cu (µg/dl)	94.3±20.4	112.1±28.0	**0.007***
Zn (µg/dl)	95.9±21.9	87.1±30.3	0.204
Cu/Zn ratio	1.04 (0.57-1.84)	1.57 (0.44-9.32)	**0.013***
BMI (kg/m^2)	29.1±4.8	27.1±2.9	0.073
DM	%33.3 (8/24)	%29.1 (39/55)	0.706
HT	%70.9 (16/24)	%66.7 (39/55)	0.706
HL	%70.8 (17/24)	%72.7 (40/55)	0.863

Cu: Copper; Zn: Zinc; BMI: Body mass index; DM: Diabetes mellitus; HT: Hypertension; HL: Hyperlipidemia; *: The difference is statistically significant.

Table 2. Comparison of serum trace elements of heart failure patients and control group classified according to serum NT-proBNP levels

	High NT-proBNP HF group (n=34)	Low NT-proBNP HF group (n=21)	Control group (n=24)	p
Cu, µg/dl	124.5±26.5^{a,b}	91.9±16.4^{a,c}	94.3±20.4^{b,c}	**<0.001**^{a,*} **<0.001**^{b,*} 1.000^{c}
Zn, µg/dl	74.3±19.2^{d,e}	107.7±33.9^{d,f}	95.9±21.9^{e,f}	**<0.001**^{d,*} **0.005**^{e,*} 0.334^{f}
Cu/Zn ratio	1.60 (0.92-9.32)^{g,h}	0.93 (0.44-1.59)^{g,i}	0.87 (0.57-1.84)^{h,i}	**0.001**^{g,*} **0.004**^{h,*} 0.636^{i}
NT-proBNP	2755 (1000-35000)^{j,k}	320 (109-911)^{j,l}	105.5 (44-268)^{k,l}	**<0.001**^{j,k,l}

NT-proBNP: N-terminal pro-B type natriuretic peptide; HF: Heart failure; Cu: Copper; Zn: Zinc; *: The difference is statistically significant. The letters used as superscripts indicate which two values the p value is between.

Table 3. The relationship of drugs used by patients with heart failure with serum NT-proBNP and trace element levels

	Use of ACE inhibitor/ARB (-) (n=7)	Use of ACE inhibitor/ARB (+) (n=48)	p		Use of beta blockers (-) (n=3)	Use of beta blockers (+) (n=52)	p
NT-proBNP (ng/L)	1570 (143-7760	1800 (109-35000)	0.181	NT-proBNP (ng/L)	1450 (109-7660)	1735 (143-35000)	0.713
Copper	99.7±16.9	113.9±29.0	0.213	Copper	110.1±103.6	112.7±28.8	0.903
Zinc	107.9±45.7	84.0±26.7	0.051	Zinc	99.9±43.6	86.3±29.8	0.457
Cu/Zn ratio	1.07 (0.54-1.73)	1.26 (0.44-9.32)	0.129	Cu/Zn ratio	1.26 (0.73-1.73)	1.26 (0.44-9.32)	0.793
Age (years)	59.7±14.2	67.1±10.8	0.108	Age (years)	72.3±12.1	65.8±11.4	0.340
	Use of spironolactone (-) (n=31)	**Use of spironolactone (+) (n=24)**	**p**		**Use of hydrochlorothiazide (-) (n=34)**	**Use of hydrochlorothiazide (+) (n=21)**	**p**
NT-proBNP (ng/L)	1450 (109-16100)	2005 (190-35000)	0.338	NT-proBNP (ng/L)	1735 (143-14600)	1650 (109-35000)	0.391
Copper	104.0±23.6	122.5±30.3	**0.014***	Copper	114.0±29.9	108.9±25.0	0.934
Zinc	87.8±30.6	86.1±30.6	0.842	Zinc	86.8±33.9	87.5±24.1	0.517
Cu/Zn ratio	1.19 (0.44-3.23)	1.49 (0.61-9.32)	0.248	Cu/Zn ratio	1.26(0.54-9.32)	1.26 (0.44-2.60)	0.890
Age (years)	67.7±11.9	64.3±10.6	0.544	Age (years)	63.9±12.3	69.8±8.8	0.062
	Use of furosemide (-) (n=13)	**Use of furosemide (+) (n=42)**	**p**		**Use of CCB (-) (n=36)**	**Use of CCB (+) (n=19)**	**p**
NT-proBNP (ng/L)	1280 (109-7660)	1885 (176-35000)	0.109	NT-proBNP (ng/L)	1735 (109-35000)	1450 (170-16100)	0.750
Copper	106.3±26.6	105.5±28.5	0.404	Copper	114.4±31.5	107.5±19.7	0.390
Zinc	105.2±35.4	81.1±26.6	**0.012***	Zinc	83.5±32.5	93.7±25.2	0.238
Cu/Zn ratio	1.10 (0.44-1.73)	1.41 (0.54-9.32)	0.060	Cu/Zn ratio	1.19 (0.44-9.32)	1.11 (0.61-2.60)	0.196
Age (years)	66.4±11.5	66.2±11.5	0.942	Age (years)	65.0±10.6	65.8±11.8	0.596
	Use of statin (-) (n=16)	**Use of statin (+) (n=39)**	**p**		**Total grup (n=55)**		
NT-proBNP (ng/L)	2522 (109-35000)	1650 (143-14600)	0.243	NT-proBNP (ng/L)	1650 (109-35000)		
Copper	127.7±32.1	105.6±23.7	**0.007***	Copper	112.1±28.0		
Zinc	79.7±35.6	90.1±27.8	0.255	Zinc	87.1±30.3		
Cu/Zn ratio	1.58 (0.61-9.58)	1.19 (0.44-2.60)	0.072	Cu/Zn ratio	1.27 (21.2-196.4)		
Age (years)	67.1±14.2	65.8±10.2	0.365	Age (years)	59.7±14.2		

NT-proBNP: N-terminal pro-B type natriuretic peptide; ACE: Angiotensin converting enzyme; ARB: Angiotensin receptor blocker; CCB: Calcium channel blocker; Cu: Copper; Zn: Zinc; *: The difference is statistically significant.

Table 4. Correlational relationships between serum trace elements and some cardiac parameters

	Cu		Zn		Cu/Zn	
	r	p	r	p	r	p
NT-proBNP (ng/L)	0.704	**<0.001***	-0.712	**<0.001***	0.836	**<0.001***
LA (mm)	0.381	**0.004***	-0.350	**0.010***	0.421	**0.002***
EF (%)	-0.390	**0.004***	0.173	0.212	-0.346	**0.010***
LVEDD (mm)	0.428	**<0.001***	-0.366	**0.006***	0.468	**<0.001***
IVST (mm)	-0.139	0.316	0.173	0.212	-0.159	0.252
sPAB (mmHg)	0.467	**<0.001***	0.433	**0.001***	0.553	**<0.001***
BMI (kg/m^2)	0.099	0.472	0.105	0.447	-0.099	0.471

Cu: Copper; Zn: Zinc; NT-proBNP: N-terminal pro-B type natriuretic peptide; LA: Left atrium; EF: Ejection fraction; LVEDD: Left ventricular end-diastolic diameter; IVST: Interventricular septum thickness; sPAP: Systolic pulmonary artery pressure; BMI: Body mass index; *: The difference is statistically significant.

weak and statistically significant correlation was present between Cu, left atrium (LA) (p=0.004), and systolic pulmonary artery pressure (sPAB) (p<0.001). A negative and statistically significant relationship was present between Serum Cu level and left ventricular ejection fraction (EF) (p=0.004), and a positive, weak, and statistically significant relationship was found between left ventricular end-diastolic diameter (p<0.001) and sPAB (p<0.001). A negative and statistically significant correlation was present between serum Zn level and NT-proBNP (p<0.001), LA (p=0.001), LVEDD (p=0.006) and sPAB (p=0.001). The relationship between Zn and NT-proBNP was advanced, compared to other parameters. An advanced and statistically significant relationship was found between the Cu/Zn ratio and NT-proBNP (p<0.001), and a weak and statistically significant correlation was present between Cu/Zn ratio and LA (p=0.002). Moreover, the relationship between Cu/Zn ratio and EF was negative, weak, and statistically significant (p=0.001) (Table 4).

The ROC calculations performed to examine the predictive capabilities of serum trace elements regarding the high BNP group indicated that serum copper (AUC:0.844, 95% CI: 0.759-0.929, p<0.001) and serum Cu/Zn ratio (AUC:0.871, 95% CI: 0.797-0.945, p<0.001) predicted the high BNP group well (Table 5 and Fig. 1). Moreover, the predictive capabilities of trace elements in regard to HF is presented in Table 6 and Figure 2.

Discussion

This study aimed to reflect the relationship between serum trace elements and plasma NT-proBNP KY that is known to be related to increased mortality among HF patients. Both groups consisted of male patients who had stable coronary artery disease but the participants in the study group were also diagnosed with HF. Previous studies found serum Cu level higher among HF patients compared to the control group, and the Zn level was significantly lower among the former.[9–10] However, the control groups in these studies consisted of healthy voluntary people. The control group in the present study had similar demographic characteristics with the patient group, except the HF. A significant and positive correlation was found between high NT-proBNP levels and serum copper level among HF patients, and a negative and significant correlation was present between high NT-proBNP levels and serum zinc level.

Table 5. Examination of areas under the curve (AUC) defining the ability of trace elements to predict heart failure patients with elevated NT-proBNP

	AUC	95% confidence intervals	p
Cu (µg/dl)	0.844	0.759-0.929	**<0.001***
Zn (µg/dl)	0.211	0.111-0.312	**<0.001***
Cu/Zn ratio	0.871	0.797-0.945	**<0.001***

NT-proBNP: N-terminal pro-B type natriuretic peptide; AUC: Areas under the curve; Cu: Copper; Zn: Zinc; *: The difference is statistically significant.

Table 6. Examination of blood areas (AUC) under the curve regarding the predictability of NT-proBNP and trace elements

	AUC	95% confidence intervals	p
NT-proBNP (ng/L)	0.971	0.942-1.001	**<0.001***
Cu (µg/dl)	0.695	0.572-0.817	**0.006***
Zn (µg/dl)	0.373	0.246-0.500	0.073
Cu/Zn ratio	0.677	0.553-0.800	**0.013***

NT-proBNP: N-terminal pro-B type natriuretic peptide; AUC: Areas under the curve; Cu: Copper; Zn: Zinc; *The difference is statistically significant.

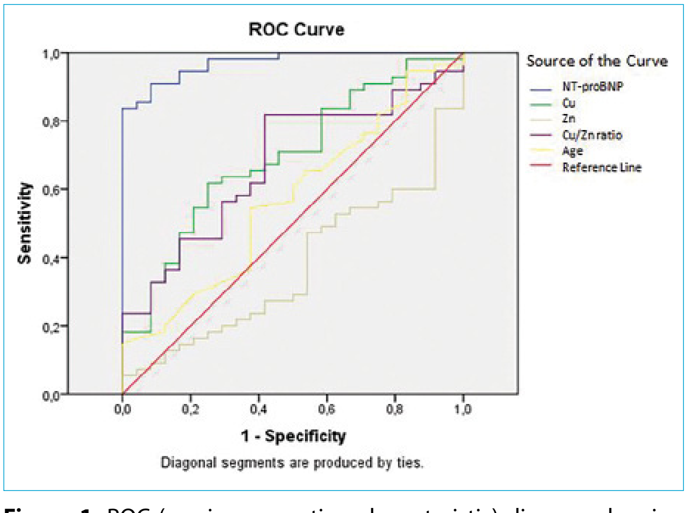

Figure 1. ROC (receiver operating characteristic) diagram showing the power of trace elements to predict heart failure.

NT-proBNP: N-terminal pro-B type natriuretic peptide; Cu: Copper; Zn: Zinc.

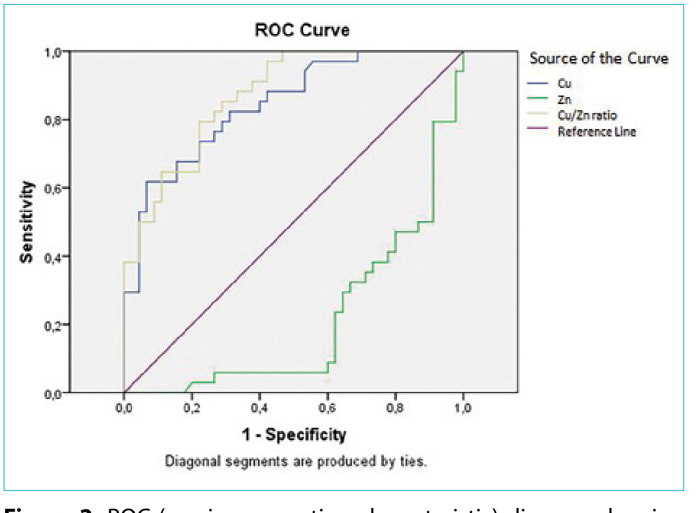

Figure 2. ROC (receiver operating characteristic) diagram showing the power of trace elements to predict NT-proBNP.

NT-proBNP: N-terminal pro-B type natriuretic peptide; Cu: Copper; Zn: Zinc.

HF is regarded as a public issue due to high mortality and morbidity levels. The annual mortality level of HF under control is 7.2%, and this rate is 13.5% among the people with advanced HF. The five-year mortality level reaches 50%.[11] Despite the developments in interventional and pharmacological treatment methods for HF in recent years, mortality and morbidity rates are still high, which was encouraging for the studies examining the mechanisms that might be responsible in the etiopathogenesis.

Recent studies have reported that high trace element count or deficiency of these elements might have an impact on the mortality and morbidity of cardiovascular diseases.[2-4] Trace elements are under 100 mg/kg in the human body, and they are defined as the important components that play a key role in the metabolic pathways required for the maintenance of organs' functions including the cardiac functions. Studies have indicated that changing the bodily content of trace elements might play a role in the formation of myocardial metabolic disorder and dilated cardiomyopathy.[12] The contribution of trace elements to this process could occur as cardiac oxidative stress, remodeling, and increased inflammation.[2] Zn and Cu are two of the essential trace elements that play key roles in many signal pathways.

The patient group was divided into two as those with and without a negative prognosis to examine the importance of trace elements in the prognosis, which was performed using the NT-proBNP that could also be used to determine the HF-related prognosis as a practical, easily accessible, and inexpensive test. Many studies have reported that plasma NT-proBNP levels determined as prognostic indicators are related to the severity of heart failure and that these levels are independent predictive components for mortality, cardiovascular mortality, and hospitalization owing to any reasons.[13–15] In addition, the effort capacity that is closely associated with the prognosis in HF and structural changes in the myocardium were also examined in this study. Effort capacity was assessed based on the classification of the New York Heart Association. The structural state of the myocardium was assessed through the transthoracic echocardiography method.

Many relevant studies have indicated that the formation of some cardiovascular diseases could be related to the high Cu levels.[9,16,17] Cu is a molecule that has an important role of increasing free radical damage as the co-factor of the oxidant system increasing hydroxyl (OH) levels.[18] The serum level of Cu has been noted as an inflammatory indicator.[19] Moreover, high Cu serum level has been reported to be related to the high mortality level in ischemic HF cases.[20] A significant correlation was present between high NT-proBNP level, one of the poor prognostic indicators, and high Cu level in this study. Moreover, increased left atrium and left ventricular diameter, two of transthoracic echocardiography results, high systolic pulmonary artery pressure, and suppressed left ventricular ejection fraction were found to be correlated.

There are results indicating that Zn has strong anti-oxidative and anti-inflammatory characteristics.[21] Many studies performed with HF patients indicated that the Zn level among these patients was low compared to the healthy people.[10,22] Insufficient nutrition, absorption disorders that may arise from the edema in intestines and neurohormonal activation, and increased urination owing to using diuretic medications and neurohormonal activation may suggest the low Zn level among HF cases.[23,24] Low Zn level has been reported to increase inflammation and oxidative stress and cause myocardial damage.[25,26] The number of studies reviewing the relationship between serum Zn level and prognosis in HF cases was quite limited, but the study conducted by Yoshihisa et al.[27] found that decreased serum Zn levels were related to distorted exercising capacity and increased mortality rate. However, the sub-group analyses of these studies indicated no relationship between serum Zn levels and age, gender, co-morbidities, medications, other micro-nutrient levels, and other important variables such as NT-proBNP and EF. The present study showed that a negative and significant relationship was present between increased left atrial and left ventricular diameter, mortality indicators of heart failure such as high systolic pulmonary artery pressure, and Zn.

The relationship between the medications used by heart failure patients and serum Cu and Zn levels has been examined in many studies. Contradictory results regarding the impacts of medications targeting the renin-angiotensin aldosterone system activation on serum Cu and Zn levels have been found.[4,28] The present study found that serum Zn level was solely low in furosemide users and that it had no impacts on angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, beta-blocker, spironolactone, calcium channel blocker, and statin use. Moreover, serum copper level was higher among the users of spironolactone compared to those who did not use, and lower among the users of statin. Owing to the anti-inflammatory impact, statin treatment was found to be related to the low serum copper level.[29] Based on the high serum Cu level among the users of spironolactone, more severe clinical cases might occur among the patients. Other renin-angiotensin system blockers and diuretics used by patients had no significant effect on the serum copper level.

Certain studies from the literature have claimed that the prognostic value of the imbalance in the Cu/Zn ratio could be a lot higher than the Zn or Cu levels.[30] Malavolta et al.[31] suggested that increased Cu/Zn ratio could be the indicator of all-cause mortality among the people aged 70 years and older. The present study particularly assessed the relationship between NT-proBNP level and Cu/Zn ratio among HF cases. The significant relationship between Cu and Zn continued with the high NT-proBNP levels displayed by Cu and Zn. In addition, the Cu/Zn ratio was correlated with increased left atrium and left ventricular diameter, high systolic pulmonary artery pressure, and suppressed left ventricular ejection fraction, some of transthoracic echocardiographic mortality indicators of HF.

Cu, Zn, and Cu/Zn values were found to be similar in low NT-proBNP group in the comparisons made with the control group following the division performed based on the prognostic state of the ischemic HF patients. The distinct differentiation found in the NT-proBNP group in relation to the poor prognosis could be the indicator of HF-related increased mortality. Moreover, high serum copper, copper/zinc ratio, or low zinc levels could predict HF or high NT-proBNP level although the importance of this probability in clinical practice has yet to be known.

Study Limitations

The limited scope of the study and its single-center structure was the main limitation of the study. Results did not cover women and people with heart failure that had an etiology other than ischemic heart failure, which was another limitation.

Conclusion

The primary results of this study were that a positive correlation was present between the Cu and Cu/Zn ratio among the male patients with a plasma NT-proBNP level over 1000 ng/L compared to HF patients with NT-proBNP level lower than 1000 ng/L and control group without HF; and a negative, advanced and statistically significant correlation was present with Zn; the secondary result was that the plasma NT-proBNP levels in terms of serum trace elements among the patients with a plasma NT-proBNP level higher than 1000 ng/L were significantly different compared to those whose plasma NT-proBNP level was lower than 1000 ng/L.

A few studies have shown that the supportive treatment performed with trace elements and multi-vitamins had positive effects on myocardial remodeling and raised the left ventricular ejection fraction, but the impact on the prognosis has yet to be revealed.[32,33] This study suggests that changes in Cu, Zn, and Cu/Zn ratios are important in terms of monitoring the HF-related prognosis.

Disclosures

Ethics Committee Approval: The study protocol that was in conformity with the Helsinki Declaration was approved by the Ethics Committee with 05/02/2020 and 2020/03/06 number.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – E.A., D.A., M.K.; Design – E.A.,D.A.; Supervision – E.A., M.K., A.R.S.; Materials – E.A., E.C., A.E.O. M.K.; Data collection &/or processing – E.A., D.A., M.K.; Analysis and/or interpretation – E.A., D.A.; Literature search – E.A., D.A., E.C.; Writing – E.A.,D.A.; Critical review – E.A, D.A., A.R.S.

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