Association Between New Cardiac Biomarkers and Cardiovascular Abnormalities in Asymptomatic Hemodialysis Patients

Asemptomatik Hemodiyaliz Hastalarında Kardiyovasküler Biyobelirteçler ve Kardiyovasküler Anormallikler Arasındaki İlişki

Simge BARDAK[1]
Sibel SARI[1]
Mehmet HOROZ[2]
Kenan TURGUTALP[1]
Ebru GÖK OĞUZ[3]
Türkay ÖZCAN[4]
Arzu KANIK[5]
Serap DEMİR[1]
Ahmet KIYKIM[1]

1 Mersin University Faculty of Medicine, Department of Nephrology, Mersin, Turkey
2 Bahçeşehir University Faculty of Medicine, Department of Nephrology, İstanbul, Turkey
3 Dışkapı Yıldırım Beyazıt Education and Research Hospital, Department of Nephrology, Ankara, Turkey
4 Mersin University Faculty of Medicine, Department of Cardiology, Mersin, Turkey
5 Mersin University Faculty of Medicine, Department of Biostatistics, Mersin, Turkey

ABSTRACT

OBJECTIVE: Cardiovascular diseases are prevalent in asymptomatic chronic hemodialysis patients. New cardiac biomarkers are required for early diagnosis of cardiovascular diseases. In our study, we aimed to investigate associations of troponin-T (Tn-T), heart type fatty acid binding protein (H-FABP) and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels with clinical, echocardiographic and laboratory parameters of asymptomatic hemodialysis patients.

MATERIAL and METHODS: A total of 60 hemodialysis patients who were asymptomatic for cardiovascular diseases and 62 age- and sex-matched healthy subjects were enrolled. Demographic features were recorded, and Tn-T, H-FABP, and NT-proBNP were measured. Clinical, biochemical and echocardiographic evaluations were performed.

RESULTS: Tn-T, H-FABP, NT-proBNP levels were significantly higher in hemodialysis patients ($p<0.05$). There was no association between cardiac biomarkers and left ventricular hypertrophy or ejection fraction ($p>0.05$). However, NT-proBNP level >12914 pg/mL was associated with left ventricular hypertrophy. H-FABP was higher in the presence of pulmonary hypertension and tricuspid regurgitation ($p=0.025$). NT-proBNP was negatively correlated with C-reactive protein ($r=-41$, $p<0.01$) and albumin ($r=-0.29$, $p<0.05$). NT-proBNP was significantly higher in hypertensive hemodialysis patients ($p=0.038$).

CONCLUSION: Tn-T, H-FABP and NT-proBNP levels are higher in asymptomatic HD patients. Nonetheless, there are no strong correlations between the biomarkers and cardiac abnormalities and cut-off values for cardiac abnormalities should be determined in such these patients.

KEY WORDS: Cardiac biomarkers, Heart-type fatty acid binding protein, Hemodialysis, N-terminal pro-brain natriuretic peptide, Troponin-T

ÖZ

AMAÇ: Asemptomatik kronik hemodiyaliz hastalarında kardiyovasküler hastalıklar sık izlemektedir. Kardiyovasküler hastalıkların tanısı için yeni kardiyak biyomarkerlere ihtiyaç vardır. Çalışmamızda, asemptomatik hemodiyaliz hastalarında troponin-T (Tn-T), kalp tipi yağ asit bağlayıcı protein (H-FABP) ve N-terminal pro-brain natriuretik peptid (NT-proBNP) ile klinik, ekokardiyografik ve laboratuvar parametreleri ile ilişkileri araştırıldı.

GEREÇ ve YÖNTEMLER: Kardiyovasküler hastalıklar için asemptomatik olan toplam 60 hemodiyaliz hastası ve yaş ve cinsiyet açısından benzer 62 sağlıklı kontrol grubu çalışmaya alındı. Demografik özellikler kaydedildi ve Tn-T, H-FABP ve NT-proBNP ölçüldü. Klinik, biyokimyasal ve ekokardiyografik değerlendirme yapıldı.

BULGULAR: Tn-T, H-FABP, NT-proBNP düzeyleri hemodiyaliz hastalarında belirgin olarak daha yüksekti. Kardiyak biyomarkerler ve sol ventikül hipertrofisi veya ejeksiyon fraksiyonu arasında ilişki saptanmadı ($p>0.05$). Ancak, >12914 pg/ml üzerindeki NT-proBNP düzeyi ile sol ventrikül hipertrofisi ilişkili bulundu. H-FABP, pulmoner hipertansiyon ve triküspit yetmezliğinde daha yüksekti ($p=0.025$). NT-proBNP, C reaktif protein ($r=-41$, $p<0.01$) ve albumin ($r=-0.29$, $p<0.05$) ile ters ilişkili saptandı. NT-proBNP, hipertansif hemodiyaliz hastalarında daha yüksek saptandı ($p=0.038$).

SONUÇ: Tn-T, H-FABP ve NT-proBNP düzeyleri asemptomatik HD hastalarında daha yüksek bulundu. Ancak kardiyak biyomarkerler ve kardiyak anormallikler arasında güçlü ilişkiler yoktur ve bu hastalarda kardiyak sorunlar için eşik değerler belirlenmelidir.

ANAHTAR SÖZCÜKLER: Kardiyak biyomarkerler, Kalp tipi yağ asit bağlayıcı protein, N-terminal pro-brain natriüretik peptid, Troponin-T

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Correspondence Address:
Simge BARDAK
Mersin Üniversitesi Tıp Fakültesi, Nefroloji Bilim Dalı, Mersin, Turkey
Phone : + 90 324 241 00 00
E-mail : bardaksimge@gmail.com

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death in end stage renal disease (ESRD) (1). Most chronic hemodialysis (HD) patients have serious structural and functional cardiovascular abnormalities before the appearance of CVD symptoms (2). Early diagnosis of and intervention for CVD may improve the prognosis, morbidity and mortality (1). However, most of the cardiovascular risk scoring systems used for the general population may not be applied for HD patients equally (3). More accurate and reliable markers for early detection of cardiac injury are required for HD patients before the onset of cardiovascular symptoms (4,5).

Cardiac biomarkers that provide information about left ventricular mass and function are used in the diagnosis of CVD in the general population (6). Left ventricular hypertrophy (LVH) and left ventricular dysfunction are among the predictors of cardiovascular mortality in ESRD patients (7). Therefore, the use of cardiac biomarkers in CVD risk assessment of asymptomatic HD patients has attracted considerable interest.

In our study, we aimed to investigate the association of troponin-T (Tn-T), heart type fatty acid binding protein (H-FABP) and N-terminal pro-brain natriuretic peptid (NT-proBNP) levels with clinical, echocardiographic and laboratory parameters of asymptomatic HD patients. Furthermore, we tried to determine cut-off values that can be used for HD patients.

MATERIALS and METHODS

The study protocol was approved by the local ethics committee. A total of 60 HD patients and 62 healthy subjects were enrolled. HD was performed three times a week and four hours per session by using synthetic dialysers (polysulphone membranes for all) with a surface area of 1.5 m^2. All the patients whose target dry weight (normal blood pressure without symptomatic orthostatic hypotension and clinical fluid overload) had already been achieved were included in the study.

Interdialytic weight gain did not exceed 3% in the preceding month and no extra session for ultrafiltration and dialysis was required during this period.

Demographic features (age, sex, body mass index, blood pressure, smoking) for both groups were evaluated. Primary kidney diseases, dialysis duration, interdialytic weight gain, medications, residual renal function, predialysis systolic and diastolic blood pressure values were all recorded.

Patients with acute coronary syndrome, decompensated heart failure, and patients who had ischemic changes on the electrocardiogram and arrhythmia in the last 6 months were excluded. Patients with a history of recent cardiac catheterization, chronic obstructive lung disease, pulmonary thromboembolism, malignant disease, and an acute or chronic inflammatory process were also excluded. Patients who took cardiotoxic drugs, those who were treated for myocarditis in the last 6 months, and patients whose interdialytic weight gain was >3% were all excluded from the study. Patients who had arrhythmia affecting HD hemodynamics during HD sessions, and patients who had severe fluctuations in blood pressure or hypoxemia during HD sessions were also excluded.

Laboratory Studies

Biochemical Tests: All blood samples were collected at the beginning of the HD session in order to prevent possible influences of the dialysis process itself on the concentrations of the different parameters. Serum levels of urea, serum creatinine, albumin, uric acid, fasting blood glucose, and serum lipid parameters (total cholesterol, high density lipoprotein [HDL], and low density lipoprotein [LDL], triglyceride) were measured by the photometric method. Sodium, potassium, chloride ions were measured by the ion selective electrode (ISE) method, whereas C-reactive protein (CRP) was measured by the immunoturbidimetric method using an autoanalyzer (Cobas 501 Roche Mannheim, Germany).

Hemoglobin levels were measured with an autoanalyzer (Sysmex XT 2000i, Roche Mannheim, Germany). Serum parathyroid hormone (PTH) and serum ferritin levels were measured using an electrochemiluminescence method (Modular E170, Roche Mannheim, Germany). Tn-T was measured by an electrochemiluminescence method that depended on the sandwich principle, using an autoanalyzer (Modular Analytics E170, Roche, Mannheim Germany). H-FABP was analysed with a Sandwich ELISA method (Medcompare diagnostics, Triturus EIA Analyzer, Grifols, USA). NT-proBNP was measured with an electrochemiluminescence immunoassay method using the Cobas E immunoassay analyzer (Roche diagnostics, GmbH, Mannheim, Germany).

Electrocardiography: 12-lead electrocardiography was performed for all patients using the EDAN SE-12 device.

Echocardiography: Transthoracic echocardiography was performed for all patients by the same cardiologist (T.Ö.) who was unaware of the patients' clinical information. Echocardiography was performed with 2D and M-mode imaging in the parasternal and apical windows while the patients were in the left lateral decubitus position (PHILIPS HD11XE, Netherland). Associations between echocardiographic parameters and biochemical markers were evaluated.

Statistical Analysis

The MedCalc statistical program was used for data analysis. Power analysis was performed with 0.05 Type I and 0.20 Type II error (0.80 power), and it was revealed that at least 40 patients were required for the study. Mean, median, standard deviation and frequency values were obtained. The Shapiro-Wilk test was used for continuous measurements (HD duration etc.) to test the convenience of a normal distribution for permanent data. Differences between groups were evaluated with the t-test

or Mann-Whitney U test. Relationship between continuous measurements were analyzed by the Pearson correlation test or the Spearman rank correlation test. The association between categorical variables was evaluated with the chi square test. ROC curve analysis was applied in order to determine the power of continuous variables to discriminate patients and healthy subjects. Statistical significance was defined by a p value less than 0.05.

RESULTS

Demographic Findings

A total of 60 HD patients and 62 healthy subjects were enrolled. Both groups were similar for age, sex, smoking and alcohol use (p>0.05). Demographic features of the patient group and distribution of the patients by primary renal disease and drugs used are shown in Table I, whereas laboratory results and echocardiographic findings of HD patients are summarized in Table II.

Cardiovascular risk factors (smoking, dyslipidemia, hypertension, diabetes, obesity) were evaluated in HD patients. All of the patients (n=60) had at least one CVD risk factor in addition to chronic kidney disease (CKD), whereas 80% (n=48) had 2, 51.3% (n=31) had 3, 23.3% (n=14) had 4, and 13.3% (n=8) had 5 CVD risk factors.

Tn-T, H-FABP and NT-proBNP Levels

Serum levels of Tn-T, H-FABP, and NT-proBNP levels were higher in the patients than in the control group (Table III).

Table I: Demographic features of the patient group and distribution of patients due to primary renal diseases and drugs used.

Age (years) (mean+SD)	44.88±14.91
HD duration (month, mean+SD)	48.10±41.34
Primary Renal Diseases (n)	
Diabetes mellitus	15
Hypertension	14
Chronic pyelonephritis & nephrolithiasis	6
Chronic glomerulonephritis	5
Polycystic kidney disease	2
Amyloidosis	1
Unknown	17
Drugs used (n)	
Erythropoietin -beta (50-125 U/kg/week)	36
Amlodipine	12
Carvedilol	8
Ramipril	8
Doxazosin	4

SD: Standard deviation.

Table II. Laboratory and echocardiographic findings of hemodialysis patients.

Parameter	Mean ± standard deviation
Hemoglobin (gr/dl)	11.20±1.40
Albumin (gr/dl)	3.70±1.60
C-reactive protein (mg/L)	2.35±1.81
Parathyroid hormone (pg/ml)	231±163.5
End diastolic diameter (cm)	4.98±0.61
End systolic diameter (cm)	3.24±0.52
Diastolic septum thickness (cm)	1.15±0.25
Diastolic wall thickness (cm)	1.04±0.17
Ejection fraction (%)	60.40±6.93
Fractional shortening (%)	34.79±7.81
Aortic diameter (mm)	25.53±3.25
Aortic velocity (m/sn)	1.54±0.43
Pulmonary velocity (m/sn)	1.14±0.15
Pulmonary arterial pressure (mm/Hg)	38.52±10.46
Left atrial enlargement (cm)	3.90±0.59

Table III. Troponin T, H-FABP and NT-proBNP levels in hemodialysis patients and the control group.

Biomarkers	Control (n=62)	Patients (n=60)	p
Troponin-T (ng/ml)	<0.01	0.13±0.12	<0.001
H-FABP * (ng/ml) (Median)	1.23±1.47 (0.7)	2.22±2.32 (1)	0.006
NT-proBNP** (pg/ml) (Median)	36.18± 30.98 (21.69)	8722±10116.5 (5251)	<0.001

***H-FABP:** Heart-type fatty acid binding protein, ****NT-proBNP:** N-terminal pro-brain natriuretic peptide. Median values are shown in parentheses.

Association Between Tn-T, H-FABP, NT-proBNP and Demographic and Biochemical Parameters

There was no relationship between cardiac biomarkers and age, sex, HD duration, interdialytic weight gain, hemoglobin, and PTH levels. An inverse correlation existed between plasma albumin and NT-proBNP levels (r=-0.29, p<0.05). Besides, there was a negative correlation between CRP and NT-proBNP levels (r=-41, p<0.01).

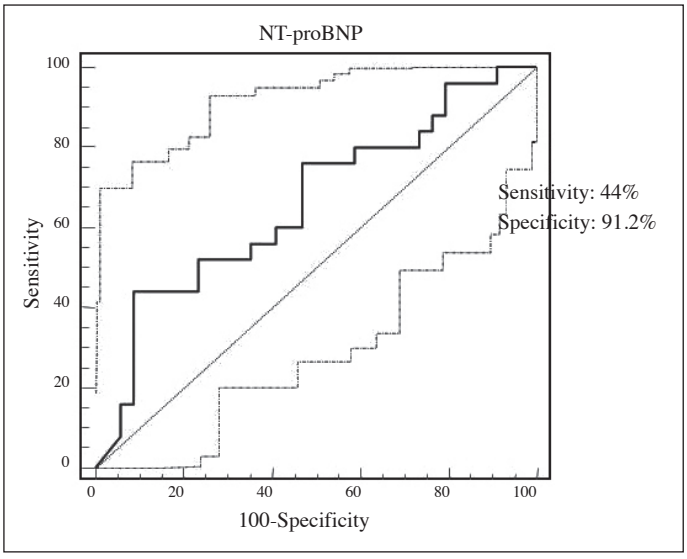

Figure 1: *Receiver operating characteristic (ROC) curves of serum NT-proBNP concentrations and presence of left ventricular hypertrophy. Cut off value of 12914 pg/ml for NT-proBNP was 91.2% specific (sensitivity 44%). Area under the curve (AUC): 0.663 (0.528-0.781) (p=0.022).*

Association Between Left Ventricular Hypertrophy and Tn-T, H-FABP, NT-proBNP

Tn-T and H-FABP levels did not reach statistical significance among the patients with and without LVH (p>0.05) (Table IV). However, LVH was more likely to be present when NT-proBNP was higher then 12914 pg/ml. Discriminating power of NT-proBNP for LVH (sensitivity) was 44% whereas it was 91.2% for a normal ventricle (specificity) (Receiver operating characteristic [ROC] curve analysis). Area under the curve was 0.663 (0.528 - 0.781) (p=0.022) (Figure 1).

Association Between Pericardial Fluid and Tn-T, NT-proBNP, H-FABP

Only 3 patients had pericardial effusion. There was no significant difference for the 3 biomarkers between the patients who had and who did not have pericardial fluid (p>0.05).

Association Between Pulmonary Artery Pressure and Tn-T, H-FABP, NT-proBNP

H-FABP was significantly higher in patients with higher pulmonary artery pressure (p=0.025) (Table V).

Association Between Heart Valve Disease and H-FABP, NT-proBNP, Tn-T

Pulmonary, aortic, tricuspid or mitral valve regurgitation was present in 11 (18.3%), 21 (35%), 21 (35%), and 31 (51.7%) patients respectively. No level of statistical significance was reached for NT-proBNP or Tn-T among patients with and without mitral, aortic or tricuspid valve regurgitation (p>0.05). H-FABP was significantly higher in tricuspid valve regurgitation (patients without tricuspid valve regurgitation: 0.69±0.678 ng/

Table IV. Association between LVH and Troponin-T, H-FABP, NT-proBNP levels.

Biomarkers	LVH***(-), n=35	LVH (+), n=25	p
Troponin-T (ng/ml) (Median)	0.08±0.05 (0.69)	0.17±0.15 (0.145)	0.232
H-FABP* (ng/ml) (Median)	1.46±1.74 (0.70)	0.91±0.91 (0.70)	0.334
NT-proBNP** (pg/ml) (Median)	6522.74±8724.75 (3005)	11714.12±11246.58 (6226)	0.370

***H-FABP:** Heart-type fatty acid binding protein, ****NT-proBNP:** N-terminal pro-brain natriuretic peptide, *****LVH:** Left ventricular hypertrophy. Median values are shown in parentheses.

Table V. Association between pulmonary artery pressure and Tn-T, H-FABP, NT-proBNP levels.

Biomarkers	PHT***(-), n=41	PHT (+), n=19	p
Troponin-T (ng/ml) (Median)	0.10±0.10 (0.063)	0.17±0.14 (0,15)	0.102
H-FABP* (ng/ml) (Median)	0.88±1.38 (0.6)	1.38±1.50 (0.8)	0.025
NT-proBNP** (pg/ml) (Median)	8937.22±10241.70 (4828.5)	8270.38±10108.83 (5251)	0.776

***H-FABP:** Heart-type fatty acid binding protein, ****NT-proBNP:** N-terminal pro-brain natriuretic peptide, *****PHT:** pulmonary hypertension

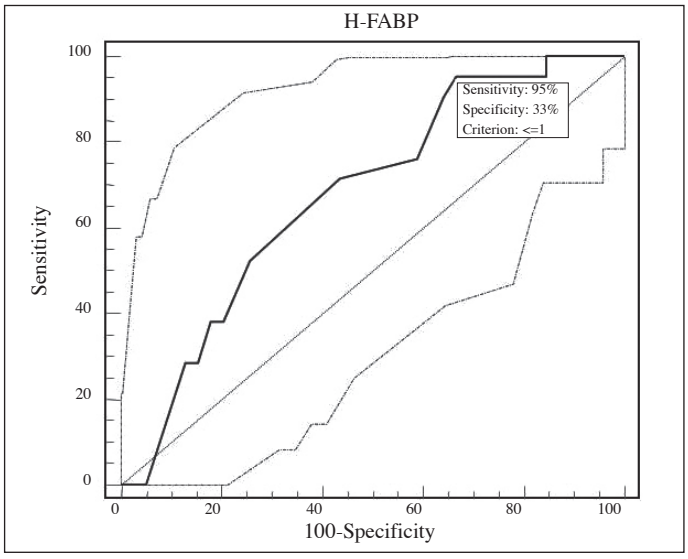

Figure 2: *Receiver operating characteristic (ROC) curves of H-FABP concentrations and presence of tricuspid valve regurgitation. Cut off value of 1 pg/dl for H-FABP had sensitivity of 95%, specificity of 33%. Area under the curve (AUC): 0.676 (0.543-0.791) (p=0.012).*

ml and patients with tricuspid valve regurgitation: 1.51±1.69 ng/ml) (p=0.025). Tricuspid valve regurgitation was more common when the H-FABP level was >1 pg/dl. However, sensitivity was 95% whereas specificity was 33% (ROC curve analysis). Area under the curve was 0.676 (0.543 - 0.791) (p=0.012) (Figure 2).

Other Results

Tn-T, H-FABP, NT-proBNP were not associated with echocardiographic parameters such as diastolic interventricular septum thickness, diastolic wall thickness, ejection fraction, fractional shortening, aortic diameter, aortic velocity, pulmonary velocity, pulmonary artery pressure and left atrial enlargement (p>0.05).

NT-proBNP was significantly higher in hypertensive patients (p=0.038), whereas there was no significant change in Tn-T and H-FABP levels (p=0.552). There was no difference in Tn-T, H-FABP and NT-proBNP levels between patients with and without diabetes mellitus (p>0.05).

Cardiac biomarkers used in this trial had no correlation with each other. No statistically significant relationship existed between the number of cardiovascular risk factors, type of antihypertensive drugs, use of erythropoietin, and Tn-T, H-FABP, NT-proBNP levels.

DISCUSSION

Cardiac biomarkers have attracted interest in screening CVD and predicting cardiovascular outcomes. These biomarkers may allow early intervention for CVD to improve outcomes. Asymptomatic chronic HD patients should be the target population for cardiovascular risk modification and intervention. However, decreased renal clearance needs to be considered as the plasma levels of these biomarkers may be affected. Therefore, the reference values that are used for general population cannot be used for ESRD patients (8). Different cutoff values need to be determined for them. Serum Tn-T, H-FABP and NT-proBNP levels (molecular weight of H-FABP: 15 kDa**,** Troponin T**:** 35 kDa, NT-Pro BNP: 8,400 Da) may be influenced by the dialysis process (9-11). For this reason, all blood samples were collected at the beginning of the HD session in our study.

Tn-T is one of the most common myocardial ischemia markers used today. In asymptomatic HD patients, elevated Tn-T is related to both cardiac and all cause mortality (12,13). As elevated Tn-T seems to be associated with a poor prognosis, Tn-T monitoring has become more popular in cardiovascular risk assessment and therefore in treatment planning (14). Tn-T can detect subclinical myocardial cell injury due to recurrent cardiac stress induced by HD sessions and relative ischemic stress related to cardiac remodelling due to heart failure and LVH (12). Although a relationship between elevated Tn-T and LVH has been reported (15), the association between Tn-T and mortality was found to be independent of the presence LVH (16). In our study, Tn-T levels were higher in asymptomatic HD patients than in control subjects. However, this finding did not correlate significantly with any clinical or laboratory parameters. Clinical significance of the elevation of Tn-T remains unclear.

H-FABP is another cardiac biomarker that can be used in myocardial injury detection (17). H-FABP is released from myocardial cells following an ischemic period. It is a biomarker for early diagnosis of acute myocardial infarction. However, as H-FABP is excreted by the kidneys, its diagnostic value is limited in CKD. High levels of H-FABP may present in HD patients even in the absence of myocardial injury (18). H-FABP can also predict outcome in patients with acute pulmonary embolism (19). Besides, recent studies have documented the association between elevated H-FABP levels and poor cardiac prognosis in chronic thromboembolic pulmonary hypertension (17). In our study H-FABP levels were significantly higher in the patients than the control subjects. In addition, H-FABP was significantly higher in the presence of higher pulmonary artery pressure and tricuspid regurgitation. We found that tricuspid valve regurgitation was more common when H-FABP level was >1 pg/dl (sensitivity: 95%, specificity: %33) (Figure 2). Pulmonary hypertension is an independent risk factor for mortality in HD patients (20). An elevated H-FABP level may therefore indicate a poor prognosis in HD patients.

The natriuretic peptide BNP and its inactive form NT-proBNP are secreted from cardiac myocytes as markers of myocardial wall stress (21). NT-proBNP has become increasingly important in the diagnosis of left ventricular dsyfunction and is excreted by the kidneys. The plasma level of NT-proBNP is higher in ESRD patients and only a small fraction is removed by HD (21). In CKD, an increase in NT-proBNP without left ventricular

dysfunction may be due to either decreased renal excretion (7,22) or chronic volume excess (23). Inflammation, nutritional status, comorbidities, and dialyser membranes are among the factors affecting NT-proBNP (9,24). For this reason, some trials have declared that NT-proBNP is not a useful biomarker for CVD in HD patients (7). In our study, we found higher NT-proBNP levels in HD patients, but there was no difference for NT-proBNP levels between the patients with and without LVH. This suggests that the increase in NT-proBNP level is not caused by myocardial pathology and elimination kinetics or variable volume status may be the underlying reasons instead. Although the absence of a relationship between left ventricular mass and NT-proBNP levels was parallel to some other trials (7,21), studies with opposing conclusions are also present in the literature (25,26).

The cutoff values of NT-proBNP for HD patients may help discriminate between left ventricular dysfunction and chronic volume excess (27). The optimal cutoff values of NT-proBNP are not well defined for HD patients (7,28). David S and al. documented that an NT-proBNP level ≥7200 ng/L could discriminate patients with left ventricular dysfunction with 80% sensitivity and 90% specificity. In the same study, a negative correlation was found between the NT-proBNP level and ejection fraction (27). In another study, the NT-proBNP level with a digit number of 5 or greater was found to be associated with cardiovascular diseases in ESRD patients. An NT-proBNP level of 10000 pg/mL was determined as the best cutoff level for left ventricular systolic dysfunction whereas a level of 6000 pg/mL was the best cutoff level for the diagnosis of coronary artery disease in ESRD patients (29). In our study, there was a statistically significant relationship between an NT-proBNP level >12914 pg/ml and LVH. However, no correlation was found between the NT-proBNP level and ejection fraction.

Malnutrition and inflammation may affect the NT-proBNP level (29). Therefore, interpretation of the NT-proBNP level is even more challenging in the coexistence of overhydration, malnutrition and inflammation in HD patients (30). In our study, there was an inverse correlation between plasma albumin, CRP and NT-proBNP levels. This association may have contributed to the absence of correlation between the ejection fraction and NT-proBNP levels.

In our study, NT-proBNP levels were higher in hypertensive patients than in normotensives. This can be expected as the hypertension in HD patients is mostly due to a positive water and sodium balance.

Despite the studies reporting higher NT-proBNP levels in HD patients with pulmonary hypertension (31), a similar association was not found in our study. This might be related to the small size of our study population.

The combined index of cardiovascular risk factors could supply additional information about cardiovascular mortality in HD patients (32). However, in our study there was no correlation between the cardiac biomarkers. Biomarkers that are popular for general population need to be defined better in HD patients.

Study Limitations

One of the limitations of this study is the small number of groups. The second is that the cardiac biomarkers were measured only once and no serial measurement had been performed.

CONCLUSIONS

Tn-T, H-FABP and NT-proBNP levels are higher in asymptomatic HD patients. Nonetheless there are not strong correlations between the biomarkers and cardiac abnormalities and cut-off values for cardiac abnormalities should be determined in such these patients.

Declaration of Interest

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Roberts MA, Hare DL, Ratnaike S, Ierino FL: Cardiovascular biomarkers in CKD: Pathophysiology and implications for clinical management of cardiac disease. Am J Kidney Dis 2006; 48:341-360
2. Hickman PE: Biomarkers and cardiac disease in patients with end-stage renal disease on dialysis. Clin Biochem Rev 2011; 32:115-119
3. Coll B, Betriu A, Martínez-Alonso M, Borràs M, Craver L, Amoedo ML, Marco MP, Sarró F, Junyent M, Valdivielso JM, Fernández E: Cardiovascular risk factors underestimate atherosclerotic burden in chronic kidney disease: Usefulness of non-invasive tests in cardiovascular assessment. Nephrol Dial Transplant 2010; 25:3017-3025
4. Hojs R, Bevc S, Ekart R: Biomarkers in hemodialysis patients. Adv Clin Chem 2012; 57:29-56
5. Hickman PE, McGill DA, Talaulikar G, Hiremagalur B, Bromley J, Rahman A, Koerbin G, Southcott E, Potter JM: Prognostic efficacy of cardiac biomarkers for mortality in dialysis patients. Intern Med J 2009; 39:812-818
6. Satyan S, Light RP, Agarwal R: Relationships of N-terminal pro-B-natriuretic peptide and cardiac troponin T to left ventricular mass and function and mortality in asymptomatic hemodialysis patients. Am J Kidney Dis 2007; 50:1009-1019
7. Helal I, Belhadj R, Mohseni A, Bazdeh L, Drissa H, Elyounsi F, Abdallah TB, Abdelmoula J, Kheder A: Clinical significance of N-terminal Pro-B-type natriuretic peptide (NT-proBNP) in hemodialysis patients. Saudi J Kidney Dis Transpl 2010; 21:262-268
8. Colbert G, Jain N, de Lemos JA, Hedayati SS: Utility of traditional circulating and imaging-based cardiac biomarkers in patients with predialysis CKD. Clin J Am Soc Nephrol 2015; 10:515-529

9. Locatelli F, Hannedouche T, Martin-Malo A, Jacobson SH, Vanholder R, Ronco C, La Milia V, Lopez Gomez JM, Stefoni S, Maheut H, Klinger M, Krummel T, Dhondt A, Berdud I, Gauly A: The relationship of NT-proBNP and dialysis parameters with outcome of incident haemodialysis patients: Results from the membrane permeability outcome study. Blood Purif 2013; 35:216-223
10. Tsukahara R, Haniu H, Matsuda Y, Tsukahara T: Heart-type fatty-acid-binding protein (FABP3) is a lysophosphatidic acid-binding protein in human coronary artery endothelial cells. FEBS Open Bio 2014; 4:947-951
11. TnT Human. [Cited: 20.08.2016]. Access: http://www.prospecbio.com/Troponin-T_Human_10_79/
12. Khan NA, Hemmelgarn BR, Tonelli M, Thompson CR, Levin A: Prognostic value of troponin T and I among asymptomatic patients with end-stage renal disease: A meta-analysis. Circulation 2005; 112:3088-3096
13. Needham DM, Shufelt KA, Tomlinson G, Scholey JW, Newton GE: Troponin I and T levels in renal failure patients without acute coronary syndrome: A systematic review of the literature. Can J Cardiol 2004; 20:1212-1218
14. Kalaji FR, Albitar S: Predictive value of cardiac troponin T and I in hemodialysis patients. Saudi J Kidney Dis Transpl 2012; 23:939-945
15. Löwbeer C, Gustafsson SA, Seeberger A, Bouvier F, Hulting J: Serum cardiac troponin T in patients hospitalized with heart failure is associated with left ventricular hypertrophy and systolic dysfunction. Scand J Clin Lab Invest 2004; 64:667-76
16. deFilippi C, Wasserman S, Rosanio S, Tiblier E, Sperger H, Tocchi M, Christenson R, Uretsky B, Smiley M, Gold J, Muniz H, Badalamenti J, Herzog C, Henrich W: Cardiac troponin T and C-reactive protein for predicting prognosis, coronary atherosclerosis and cardiomyopathy in patients undergoing long-term hemodialysis. JAMA 2003; 290:353-359
17. Lankeit M, Dellas C, Panzenböck A, Skoro-Sajer N, Bonderman D, Olschewski M, Schäfer K, Puls M, Konstantinides S, Lang IM: Heart-type fatty acid-binding protein for risk assessment of chronic thromboembolic pulmonary hypertension. Eur Respir J 2008; 31:1024-1029
18. Al-Hadi HA, William B, Fox KA: Serum level of heart-type fatty acid-binding protein in patients with chronic renal failure. SQU Medical Journal 2009;9:311-314
19. Liu M, Yuan X, Qiu X, Shan X, Lin D, Zhu L: Prognostic role of heart-type fatty acid binding protein in pulmonary embolism: A meta-analysis. Thromb Res 2015;135:20-25
20. Yigla M, Fruchter O, Aharonson D, Yanay N, Reisner SA, Lewin M, Nakhoul F: Pulmonary hypertension is an independent predictor of mortality in hemodialysis patients. Kidney Int 2009; 75:969-975
21. Rosner MH: Measuring risk in end-stage renal disease: Is N-terminal probrain natriuretic peptide a useful marker? Kidney Int 2007; 71:481-483
22. Takase H, Dohi Y: Kidney function crucially affects B-type natriuretic peptide (BNP), N-terminal proBNP and their relationship. Eur J Clin Invest 2014; 44:303-308
23. Fagugli RM, Palumbo B, Ricciardi D, Pasini P, Santirosi P, Vecchi L, Pasticci F, Palumbo R: Association between brain natriuretic peptide and extracellular water in hemodialysis patients. Nephron Clin Pract 2003; 95:c60-66
24. Snaedal S, Qureshi AR, Carrero JJ, Heimbürger O, Stenvinkel P, Bárány P: Determinants of N-terminal pro-brain natriuretic peptide variation in hemodialysis patients and prediction of survival. Blood Purif 2014; 37:138-145
25. Trapé J, Pérez A, Naval I, Escudero J, Comerma I, Sans A, Franquesa J, Vidal C: Nt-proBNP in haemodialysis patients: A preliminary study. Scand J Clin Lab Invest 2008; 68:415-420
26. Choi SY, Lee JE, Jang EH, Kim MO, Baek H, Ki CS, Park SW, Kim DJ, Huh WS, Oh HY, Kim YG: Association between changes in N-terminal pro-brain natriuretic peptide levels and changes in left ventricular mass index in stable hemodialysis patients. Nephron Clin Pract. 2008; 110:c93-100
27. David S, Kümpers P, Seidler V, Biertz F, Haller H, Fliser D: Diagnostic value of N-terminal pro-B-type natriuretic peptide (NT-proBNP) for left ventricular dysfunction in patients with chronic kidney disease stage 5 on haemodialysis. Nephrol Dial Transplant 2008; 23:1370-1377
28. Sato Y: Diagnostic and prognostic property of NT-proBNP in patients with renal dysfunction. J Cardiol 2013; 61:446-447
29. Iwasaki M, Joki N, Tanaka Y, Ikeda N, Hayashi T, Kubo S, Asakawa T, Takahashi Y, Hirahata K, Imamura Y, Hase H: Efficacy of N-terminal pro-brain natriuretic peptide digit number for screening of cardiac disease in new haemodialysis patients. Nephrology (Carlton) 2013; 18:497-504
30. Jacobs LH, van de Kerkhof JJ, Mingels AM, Passos VL, Kleijnen VW, Mazairac AH, van der Sande FM, Wodzig WK, Konings CJ, Leunissen KM, van Dieijen-Visser MP, Kooman JP: Inflammation, overhydration and cardiac biomarkers in haemodialysis patients: A longitudinal study. Nephrol Dial Transplant 2010; 25:243-248
31. Abdelwhab S, Elshinnawy S: Pulmonary hypertension in chronic renal failure patients. Am J Nephrol 2008; 28:990-997
32. Bargnoux AS, Morena M, Jaussent I, Maurice F, Chalabi L, Leray-Moragues H, Terrier N, Dupuy AM, Badiou S, Canaud B, Cristol JP: A combined index of cardiac biomarkers as a risk factor for early cardiovascular mortality in hemodialysis patients. Clin Chem Lab Med 2013; 51:1865-1874