According to their NT-pro-BNP levels, patients were divided into two groups: group A (18 patients with levels of NT-pro-BNP between 0 and 14.75 pmol/L) and group B (44 patients with levels of NT-pro-BNP higher than 14.75 pmol/L). Reduced systolic function of the left ventricle (SFLV) was found in 90.9% of patients in group B and 5.6% of patients in group A. Diastolic function of the left ventricle (DFLV) was diminished in 83.3% of patients in group A and 100% of patients in group B.

A strong correlation was found between levels of NT-pro-BNP and systolic and diastolic functions of the left ventricle: ejection fraction (EF) \( r = -0.459, p < 0.01 \); fraction shortening (FS) \( r = -0.367, p < 0.05 \); relation of maximal early (PE) and late (PA) diastolic speed of loading (PE/PA) \( r = -0.469, p < 0.01 \); deceleration time of early diastolic flow (DT) \( r = 0.582, p < 0.01 \); and isovolumetric relaxation time of the left ventricle (IVRT) \( r = 0.545, p < 0.01 \). In group A, a correlation was found only for IVRT \( r = 0.545, p < 0.01 \). In group B, a correlation was found only for the level of NT-pro-BNP and systolic and diastolic functions of the left ventricle.

In patients with ACS, there is a high correlation between increased levels of NT-pro-BNP and systolic and diastolic functions of the left ventricle. NT-pro-BNP is very specific sensitive to changes in systolic and diastolic function of the left ventricle.
Brain natriuretic peptide (BNP) was first isolated in brain tissue, but it has since been found in myocardial cells. BNP acts in vasodilation, intensifies natriuresis and decreases aldosterone secretion. Pro BNP (108 amino acids) is synthesised in cardiomyocytes and is split into N-terminal pro BNP (76 amino acids) and C-terminal BNP (32 amino acids) (1). Many studies have shown that patients with hypertension, acute coronary syndrome (ACS), cardiac deficiency (inborn and earned), and fibrillation of atria have increased levels of these peptides (2-7).

Some studies show that variations of peptide concentration in a patient’s serum can be found before chemodynamic and echocardiographic changes (8). It was also shown that NT-pro-BNP level in serum is proportional to left ventricle load (9, 10).

Acute coronary syndrome (ACS) is an acute phase of ischaemic heart disease, and it includes several clinical forms such as unstable angina pectoris, acute infarct of the myocardium without ST elevation, acute infarct of the myocardium with ST elevation and sudden heart death. Most of these begin with angina pain. Increased pressure on ventricular walls and ischaemic myocardium increases synthesis of natriuretic peptides in cardiomyocytes, which explains the higher levels of natriuretic peptides in ACS patients’ serum. Consequently, vasodilation of veins and arteries and a reduction in blood influx to the heart occur. Tonus of vagues is increased, but noradrenaline release and tonus of sympathicus are reduced. There is increased diuresis, and renin angiotensin is inhibited.

Considering the above data, we focused our investigation on a potential diagnostic role of NT-pro-BNP in the evaluation of left ventricle function in patients with ACS.

METHODS

The subjects for the study included 62 ACS patients (13 females and 49 males), ranging in age from 43 to 75 years (average= 60±13 years of age).

Patients for this study met the following criteria:
1) diagnosis of ACS established by WHO (minimum 2 of 3 criteria): existence of chest pain, evolutive electrocardiographic changes (ST elevation or depression ≥ 1 mm, or negative T wave), evolutive changes of serum cardiac markers (CK, CK-Mb, TnT).
2) patients under 75 years of age (because increased levels of NT-pro-BNP were found in patients over 75 years of age without cardiovascular disease).
3) patients do not suffer from other disease that can cause an elevation of NT-pro-BNP levels (such as artery hypertension, heart weakness, indigenous or gain heart failure, vestibule fibrillation, hypertension of the lungs, chronic lung diseases, acute and chronic insufficiency of kidneys, ascites, hyperthyreosis, hypothyreosis, Cushing’s syndrome, and diabetes).

Concentration of NT-pro-BNP in serum was determined 24 hours after the admission of the patients, when maximal values are expected. The NT-pro-BNP determination kit was manufactured by Hoffman La Roch, Ltd. Normal levels of NT-pro-BNP range from 0 to 14.75 pmol/L. NT-pro-BNP concentration in the serum was determined by electrochemiluminiscent immunoassay application on an Elecsys 2010 analyser (Roche Diagnostics).

Based on these results, we divided patients into two groups. Group A consisted of 18 ACS patients with NT-pro-BNP levels ranging from 0-14.75 pmol/L. Group B included 44 ACS patients with NT-pro-BNP levels higher than 14.75 pmol/L. The levels of serum cardiac pointers (CK, CK-Mb and troponin) were measured. Systolic and diastolic functions of the left ventricle were measured by heart echocardiography using the Aisent Sonos 5500 ultrasound device.

To evaluate systolic function, we determined ejection fraction (EF), left ventricle diastolic dimension (LVEDD), left ventricle systolic dimension (LVESD), left ventricle posterior wall thickness (PWT), septum thickness (ST) and fraction shortening (FS). To evaluate diastolic function, we determined maximal early (PE) late (PA) diastolic load speed, their relation (PE/PA), deceleration time of early diastolic flow (DT), left isovolumetric ventricle relaxation time (IVRT) and peak systolic wall stress (PSWS). Criteria for normal systolic function were EF>50% and FS in interval of 28-42%. Normal diastolic function measurements should satisfy the following: PE/PA≥1 and <2; DT>150 and <220 ms; IVRT>60 and <100 ms.

A basic statistical program, Student’s T test and Pearson’s correlation coefficient were used. Group A had 18.2~16 degrees of freedom, so its linear correlation coefficient was 0.468 (for the probability of the null hypothesis = 0.05) and 0.590 (for the probability of the null hypothesis = 0.01). However, group B had 44.2~42 degrees of freedom, and its linear correlation coefficient was 0.304 (for the probability of the null hypothesis = 0.05) and 0.393 (for the probability of the null hypothesis = 0.01).

The probabilities of p<0.05 and p<0.01 were considered significant and highly significant, respectively.

Sensitivity and specificity levels of NT-pro-BNP measurements and echocardiographic parameters of systolic and diastolic function of the left ventricle were determined.

RESULTS

Table 1 shows the demographic parameters of both groups with ACS. Group A consisted of patients with ACS and normal NT-pro-BNP levels and included 14 males and 4 females aged 43 to 75 years with an average of 60±6.6 years. Their NT-pro-BNP levels ranged from 2.5 to 13.4 pmol/L, with an average of 5.9±3.2 pmol/L.

Group B consisted of 44 patients with ACS and increased NT-pro-BNP levels. There were 35 males and 9 females, aged 54 to 75 years with an average of 62±7.3 years. Their NT-pro-BNP levels ranged from 18.7 to 731 pmol/L, with an average of 157±178 pmol/L.

Table 2 shows the echocardiographic parameters of systolic and diastolic function of left ventricle in both groups. Minimum, average, maximum and standard deviation are shown. Regards of parameters of systolic function of the left ventricle, group B had considerably lower EF values (p<0.01) than group A. The difference between the groups in FS values (p>0.05) was minor. As far as parameters of diastolic function
of the left ventricle, PE/PA, DT and IVRT values differ considerably (p<0.05) between groups A and B.

Figures 1 and 2 present the degree of correlation between peptide levels and parameters of left ventricle systolic and diastolic function for ACS patients.

In group A, as the NT-pro-BNP level increased, EF value decreased with a statistically minor correlation of -0.398 (p>0.05). Also, as the NT-pro-BNP level increased, FS values increased as well, with a positive correlation of 0.14, which was not statistically significant (p>0.05). As for diastolic function of the left ventricle, parameters for NT-pro-BNP and PE/PA showed no considerable correlation (r=-0.278 and p>0.05), which is distinct from the high positive correlation found between increasing NT-pro-BNP levels and DT values (r=0.676 and p<0.01) as well as IVRT values.

In group B, there is a high correlation between all parameters of systolic and diastolic function of the left ventricle and NT-pro-BNP levels (p<0.05, p<0.01). Increase of NT-pro-BNP levels is followed by DT and IVRT increase and EF, FS, and PE/PA decrease (fig. 2).

As shown in Table 3, sensitivity and specificity were calculated. NT-pro-BNP sensitivity for SFLV was 97.56% (40/41) and 74.57% for DFLV. On the other hand, specificity for SFLV was 80.95% (40/41) but 100% for DFLV (Figure 3). Seventeen patients in group A (94.4% of patients in this group) had normal SFLV, but only 4 patients (9.1%) in group B had normal SFLV (table 3). Compromised SFLV was recorded in 1 patient (5.6%) of group A and 40 patients (90.09%) of group B. Three (16.7%) patients in group A and 0 patients in group B had normal DFLV, whereas compromised DFLV was found in 15 (83.3%) group A patients and 44 (100%) group B patients.

Derived NT-pro-BNP sensitivity for SFLV was 40 / 41 = 97.56% and 44 / 59 = 74.57% for DFLV (Figure 3).

NT-pro-BNP specificity for SFLV was 17 / 21 = 80.95% and 3 / 3 = 100% for DFLV.

![Figure 1](image1.png)

** Figure 1. Correlation among levels of NT-pro-BNP and echocardiographic parameters of systolic and diastolic function of left ventricle in group A

** p<0.01 * p<0.05

![Figure 2](image2.png)

** Figure 2. Correlation among NT-pro-BNP levels and echocardiographic parameters of systolic and diastolic function of the left ventricle in group B

** p<0.01 * p<0.05

![Figure 3](image3.png)

** Figure 3. Sensitivity and specificity levels NT-pro-BNP and echocardiographic parameters of systolic and diastolic function of the left ventricle, ACS patients.
DISCUSSION

According to the demographic data presented in table 1, both groups consisted of more males than females because the research was done in a military facility where the percentage of males is higher. Groups were formed according to NT-pro-BNP levels. Group B (71% of all examinees) demonstrated higher NT-pro-BNP levels and was larger than group A, which was composed of patients with normal peptide levels. This was expected because most of the literature indicate that NT-pro-BNP levels are elevated in 47 to 96% of patients with ACS (11-13).

NT-pro-BNP levels of patients in group B (157±178 pmol/L) were significantly higher (p<0.01) than those of patients in group A (5.9±3.2 pmol/L). A study that included 7800 patients with ACS showed that NT-pro-BNP levels varied from 2.3 to 4320 pmol/L (14). Other research showed that patients with ACS can have normal as well as extremely high levels of this peptide in serum (10, 12).

According to the parameters of SFLV, patients with increased NT-pro-BNP levels had much lower EF (p<0.01) than patients with normal peptide levels (table 2). Since ischaemia is a basic cause of increased NT-pro-BNP levels, it was expected that patients with normal peptide levels would have larger EF values. Only 5.6% of patients in group A had reduced systolic function of the left ventricle, whereas 90.09% of group B patients demonstrated reduced systolic function of the left ventricle. Several studies (15, 16, 17) have shown significant influence of myocardial ischaemia on NT-pro-BNP levels in ACS patients. In addition, there is a major difference in diastolic function parameters between the two groups (table 2). We concluded that reduced diastolic function was characteristic of both groups, but in group B, this function was more severely compromised. There are a high percentage of patients (83.3%) with reduced diastolic function but with average NT-pro-BNP levels, which shows that diastolic function disorder is not necessarily followed by NT-pro-BNP level increase. Changes in NT-pro-BNP concentration are directly related to systolic function disorder, but no relation with diastolic function of the left ventricle was found. Our results are compatible with other research that found that decreased diastolic function of the left ventricle was usually followed by high levels of peptides. However, this was not always the case; sometimes, normal NT-pro-BNP values were found.

Jernberg and associates compared the results of a few clinical trials regarding NT-pro-BNP and discovered that increasing NT-pro-BNP was followed by a decrease in systolic and diastolic heart functions, but the correlation between NT-pro-BNP values and SFLV parameters was higher than the correlation of NT-pro-BNP and echocardiographic parameters of diastolic function (17).

By using linear correlating, we tried to determine if there is a connection between NT-pro-BNP levels and parameters of systolic and diastolic function of the left ventricle in ACS patients. In patients with normal NT-pro-BNP levels, we concluded with a high probability that the systolic function of the left ventricle is not compromised, which is not the case in diastolic function. In addition, we found that normal NT-pro-BNP levels are not correlated with left ventricle systolic and diastolic function.

Linear test correlation of the parameters of systolic and diastolic function shows major differences between the two groups (fig. 2). These results demonstrate a high correlation between NT-pro-BNP levels and SFLV and DFLV levels (p<0.01). This shows that increased NT-pro-BNP levels are directly related to parameters of left ventricle systolic and diastolic function, which is not the case for normal peptide levels.

Pfister and Schlötz study (10) of 150 patients shows this negative linear correlation between NT-pro-BNP level and left ventricle systolic function (10). Khan and associates studied 356 patients with ACS and discovered a high correlation between NT-pro-BNP levels and systolic function of the left ventricle (LV) (p<0.0001) in patients with ACS (diastolic function in LV was not considered) (18, 19).

In fig. 3, we show NT-pro-BNP sensitivity and its specific role in systolic and diastolic LV function. NT-pro-BNP sensitivity for SFLV was 97.56%, whereas its specificity was 80.95%. NT-pro-BNP sensitivity for DFLV was 74.57%, whereas its specificity was 100%.

Emad and associates found high sensitivity of NT-pro-BNP for SFLV (98%), and the specificity of NT-pro-BNP for SFLV reached 86% (20). Lubien and colleagues studied 294 patients with ACS and found high specificity (83%) and sensitivity (85%) of NT-pro-BNP for DFLV (21). Footea and associates also found high sensitivity of NT-pro-BNP (90%) as a predictor of compromised systolic function of the LV (22).

According to our results, we conclude that ACS patients with normal NT-pro-BNP levels have considerably less compromised systolic and diastolic LV function than patients with increased levels of this peptide. However, peptide levels do not correlate with SFLV values, whereas diastolic function correlation was found in two out of three parameters of DFLV. High degrees of correlation between increased NT-pro-BNP values and systolic and diastolic functions of the LV were found in ACS patients. NT-pro-BNP shows high sensitivity and specificity to systolic and diastolic LV function. Considering our results, which are supported by similar clinical investigations, we suggest that serum NT-pro-BNP levels are of great clinical importance in the evaluation of left ventricular function.

REFERENCES


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