Neutrophil to lymphocyte ratio predicts poor functional capacity in patients with heart failure

Nötrofil/lenfosit oranı kalp yetersizliği bulunan hastalarda fonksiyonel kapasite düşüklüğünü öngörmektedir

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ABSTRACT

Objectives: We aimed to assess the relationship between neutrophil to lymphocyte ratio (N/L ratio) and functional capacity (FC) of patients with compensated heart failure (CHF).

Study design: A total of 94 consecutive CHF patients and age-gender matched 70 subjects with normal echocardiographic examination were enrolled. Peripheral venous blood samples were drawn before echocardiography examination and treadmill test in all study population. The treadmill test based on modified Bruce protocol was used to determine the functional status of CHF patients. Poor FC was defined as <5 metabolic equivalant (MET) in the exercise test. Afterwards, patients with CHF were divided into two groups with respect to the top and bottom 3 of the N/L ratio.

Results: FC (3.2±2.05 MET *vs.* 6.1±2.04 MET, p<0.001), ejection fraction (%31.5±7.64 *vs.* %34.8±6.82, p=0.028) were found to be lower and N-terminal pro-brain natriuretic peptide (NT-proBNP) level (3360±2742 pg/dl *vs.* 1613±1334 pg/dl, p<0.001) pulmonary artery pressure (46.3±11.50 mmHg *vs.* 41.5±9.45 mmHg, p=0.049), left atrial diameters (4.6±0.52 cm vs. 4.3±0.43 cm, p=0.005), E/Ea ratio (12.2±4.37 vs. 9.2±3.20, p<0.001) were found to be higher in CHF patients with an N/L ratio >3 than with an N/L ratio <3. The N/L ratio, and log-NT-proBNP level were determined to be a predictive factor of poor FC (odds ratio [OR]=3.085, 95% confidence interval [CI] = 1.520-6.260, p=0.002 and OR=1.585, 95% CI=1.201-2.091, p=0.001, respectively). A cut-off point of 2.74 for the N/L ratio had 79.4% sensitivity and 80% specificity in predicting poor FC.

Conclusion: N/L ratio can be used to predict poor FC in patients with CHF.

ÖZET

Amaç: Kompanse kalp yetersizliği (KKY) bulunan hastaların fonksiyonel kapasiteleri (FK) ve nötrofil/lenfosit oranı (N/L oranı) arasındaki ilişkiyi değerlendirmeyi amaçladık.

Çalışma planı: Kompanse kalp yetersizliği tanısı konan ardışık 94 hasta ve yaş-cinsiyet eşleştirilmiş ekokardiyografi değerlendirmesi normal olan 70 birey çalışmaya alındı. Efor testi ve ekokardiyografik muayene öncesi tüm çalışma popülasyonundan periferik venöz kan örnekleri alındı. KKY'li hastaların FK'lerinin belirlenmesi için modifiye Bruce yöntemiyle uygulanan egzersiz testi kullanıldı. Düşük FK, egzersiz testine göre <5 metabolik eşdeğeri (MEK) olarak belirlendi. Daha sonra, KKY'li hastalar N/L oranı 3'ün altı ve üstü olmak üzere iki guruba ayrıldı.

Bulgular: Nötrofil lenfosit oranları >3 olan KKY'li hastalarda FK (3.2±2.05 MEK ve 6.1±2.04 MEK, p<0.001), ejeksiyon fraksiyonu (%31.5±7.64 ve %34.8±6.82, p=0.028) daha düşük olarak bulundu. N-terminal pro-beyin natriuretik peptid (NT-proBNP) seviyesi (3360±2742 pg/dl ve 1613±1334 pg/dl, p<0.001), pulmoner arter basıncı (46.3±11.50 mmHg ve 41.5±9.45 mmHg, p=0.049), sol atriyum çapları (4.6±0.52 cm ve 4.3±0.43 cm, p=0.005), E/Ea oranı (12.2±4.37 ve 9.2±3.20, p<0.001) N/L oranı >3 KKY'li hastalarda N/L oranı <3 olanlardan daha yüksek olarak bulundu. N/L oranı ve NT-proBNP düzeyi (sırasıyla, odds oranı [OO]=3.085, %95 GA=1.520-6.260, p=0.002, ve OO=1.585, %95 GA=1.201-2.091, p=0.001) düşük FK için öngördürücü faktörler olarak saptandı. N/L oranı için 2.74 kestirim değeri düşük FK'yi öngörmede %79.4 duyarlılık ve %80 özgüllüğe sahipti.

Sonuç: N/L oranı KKY'li hastalarda düşük FK'yi öngörmek için kullanılabilir.

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Heart failure (HF) is an inflammatory neuroendocrine syndrome with negative effects on functional capacity (FC) and quality-of-life, and which causes increased morbidity and mortality.[1,2] Immunological and inflammatory responses appear to be involved in the development and advancement of chronic HF.[3]

The neutrophil/lymphocyte ratio (N/L ratio) is one of several inflammatory parameters that have been proposed as prognostic markers to determine the systemic inflammatory response. The N/L ratio, which is calculated from a complete blood count with differential, is an inexpensive and easy to obtain a marker of inflammation that can aid in the risk stratification of patients with various cardiovascular diseases alongside traditionally used markers.[4] A high N/L ratio is said to be associated with an increased risk of morbidity and mortality in patients with acute decompensated HF.[5] However, its role in the risk stratification of patients with compensated heart failure (CHF) has not been described. In addition, no data exist regarding the association between N/L ratio and FC.

In the present study, we investigated the relationship between N/L ratio and markers of a poor prognosis for patients with HF, including the FC, N-terminal pro-brain natriuretic peptide (NT-proBNP) level, pulmonary artery pressure (PAP), ratio of the early to late ventricular filling velocities (E/Ea ratio), and left atrial (LA) diameter in CHF patients exhibiting left ventricular (LV) systolic dysfunction (LVSD).

Abbreviations:

CHF	*Compensated heart failure*
CI	*Confidence interval*
EF	*Ejection fraction*
FC	*Functional capacity*
HF	*Heart failure*
LA	*Left atrial*
LV	*Left ventricular*
LVSD	*Left ventricular systolic dysfunction*
MET	*Metabolic equivalent*
MPV	*Mean platelet volume*
NLR	*Neutrophil/lymphocyte ratio*
NT-proBNP	*N-terminal pro-brain natriuretic peptide*
OR	*Odds ratio*
PAP	*Pulmonary artery pressure*
ROC	*Receiver operating characteristics curve*
STEMI	*ST-segment elevation myocardial infarction*

PATIENTS AND METHODS

Study population

Patients with chronic HF referred to our department for echocardiographic examination between February and July 2013 and who met the entry criteria for the study were invited to participate. We prospectively studied 94 consecutive HF patients with diagnosed at least 2 years with LVSD secondary to ischemic (n=55) or idiopathic dilated cardiomyopathy (n=39). Age- and gender-matched 70 healthy subjects who had normal echocardiographic findings with using acetylsalicylic acid for the primary prevention of cardiovascular events were enrolled to the study as a control group. On the same day, peripheral venous blood samples were drawn before echocardiography examination and treadmill test in all study population. All patients were screened; the study cohort consisted of patients who fulfilled the following criteria: (1) symptomatic HF associated with systolic dysfunction on echocardiographic examination (ejection fraction [EF] <45%). (2) Optimized oral therapy for the treatment of HF, including the use of acetylsalicylic acid (100-300 mg), angiotensin-converting enzyme-inhibitors or angiotensin receptor antagonists, beta-blockers. Exclusion criteria were as follows: hypoalbuminemia, malignancy, rheumatic valve disease, constrictive pericarditis, hypothyroidism, renal dysfunction (serum creatinine >1.5 mg/dl with or without hemodialysis treatment), cirrhotic liver disease; immunologic or inflammatory disease, hematological diseases, sepsis, active local or systemic infections, a history of recent infection and/or fever on the last month, anemia, history of blood transfusion on the last 3 months and use of steroidal or non-steroidal anti-inflammatory drugs on the last a month. In addition, patients with decompensated HF who had one of the following criteria were excluded from the study: LVSD with bilateral inspiratory rales, edema, findings on the chest X-ray including pulmonary venous congestion and/or pleural effusions. The investigation conforms with the principles outlined in the declaration of Helsinki. This study was approved by the institutional committee, and informed consent was obtained from all patients before participation.

Transthoracic echocardiography

A comprehensive echocardiographic examination was performed in all subjects by using a Vivid E9 echocardiography machine (GE Vingmed Ultrasound AS, Horten, Norway). The LV and LA diameters were measured from the-apical four chamber view. LV EF was estimated from apical four- and two-chamber views using Simpson's biplane method.[6,7] Mitral inflow was evaluated at pulsed Doppler analysis. Pulsed-wave Tissue Doppler imaging were used to assess early myocardial relaxation velocity (Ea), plac-

ing the sample volume in the ventricular myocardium immediately adjacent to the lateral mitral annulus. Mitral inflow E-wave and Ea were then used to calculate E/Ea ratio, which was used as an indicator of LV filling pressure.[8]

Functional capacity (FC)

Various methods have been proposed to determine the functional status of HF patients. NYHA classification is the most widely used method.[9] In our study, the treadmill exercise test was used because of the subjective nature of the NYHA classification. The best objective method to determine FC is the peak O_2 consumption measured by cardiopulmonary exercise test.[10] However, the cardiopulmonary exercise test is not always available and requires expertise. Instead of it, exercise capacity is usually measured indirectly and expressed as metabolic equivalent (MET).[11] FC status of CHF patients was assessed undergoing symptom-limited treadmill test based on modified Bruce protocol by physicians blinded to the patients' echocardiographic results. Poor FC was defined as achievement of <5 MET in the exercise test.

Laboratory measurements

Peripheral venous blood samples were drawn before echocardiography examination and treadmill test in all study population. Venous blood samples were collected in a tube containing K3 EDTA for measurement of hematologic indices in all patients. Hematologic indices were evaluated from complete blood count analysis performed using the XT-2000i (Sysmex Corporation of America, Long Grove, Illinois, USA) analyzer. NT-proBNP measurement was performed using an electrochemiluminescence sandwich immunoassay (ECLIA, Roche Diagnostics) on a Modular analytics Hitachi Cobas 6000. The N/L ratio was calculated by dividing neutrophil count to lymphocyte count. Afterwards, patients with CHF were divided into two groups with respect to the top and bottom 3 of the N/L ratio.

Table 1. Echocardiographic characteristics, functional capacity and NT-proBNP level of patients with heart failure (n=94)

	n	%	Mean±SD
Ischemic cardiomyopathy	55	58.5	
Idiopathic dilated cardiomypopathy	39	41.5	
Atrial fibrillation	12	12.7	
Sinus rhythm	82	87.3	
Functional capacity (Metabolic equivalent)	5.0 (1.0-10.0)		4.8±2.49
NT-proBNP level (pg/ml)	1680.0 (90.0-8900.0)		2375.5±2233.9
Ejection fraction (%)	33.0 (20.0-45.0)		33.4±7.34
Systolic pulmonary artery pressure (mmHg)	40.0 (30.0-70.0)		43.6±10.61
Left ventricle end-diastolic diameter (cm)			5.9±0.46
Left ventricle end-systolic diameter (cm)			5.0±0.62
Mitral inflow E-wave (cm/sn)			0.94±0.79
Mitral inflow A-wave (cm/sn)			0.75±0.24
Ea (cm/sn)			9.0±2.89
Aa (cm/sn)			7.0±2.60
E/Ea ratio			10.4±4.00
Interventicular septum end-diastolic diameter (cm)	1.0 (0.80-1.70)		
Left atrium maxdiameter (cm)			4.4±0.49
Mitral regurgitation (mild/moderate/severe)	53/24/17		
Tricuspid regurgitation (mild/moderate/severe)	72/16/5		

Continious variables were expressed as mean±standard deviation or median (minimum-maximum), and categorical variables as number of cases and percentage (%). Aa: Atrial contraction velocity using Doppler tissue imaging; Ea: Early diastolic filling using Doppler tissue imaging; NT-proBNP: N-terminal pro-brain natriuretic peptide.

Statistical analysis

Statistical analysis was performed with the use of SPSS 15.0 for Windows (SPSS Inc.). The one sample Kolmogorov-Smirnov test was used to determine whether the data was distributed normally. Continuous variables with the normal distribution were reported mean±standard deviation, and compared using Student's t-test, and those without normal distribution were reported as median (min-max), and compared using Mann–Whitney's U-test. Categorical variables were defined as percentages and assessed by chi-square test. If one of the cells had an expected count of among 5-10, we used continuity correction test instead of the chi-square test. Correlation analysis was performed using Spearman's or Pearson test. In consideration of the wide range and of the not skewed distribution of NT-proBNP levels was logaritmic transformed to reduce the effects of extreme values and to obtain a normal distribution for statistical tests. The association of different variables in HF patients with poor FC (<5 MET) were calculated in the univariate analysis. The variables for which p value was <0.25 in the univariate analysis were identified as potential risk factors for poor FC and included in the full multivariate model as covariates. Backward elimination multivariate logistic regression analysis using likelihood ratio test was utilized to eliminate variables. Patients with CHF (n=94) were categorized into two groups with respect to the top and bottom 5 MET of their FC and these groups were identified as the state variable in the receiver operating characteristics curve (ROC) analysis. The state variable values of CHF patients with poor FC <5 MET and with FC >5 MET were defined to be "1" and "0" respectively. Continuous form of N/L ratio was included as a test variable in this analysis. The value at which sensitivity and specificity of N/L ratio are closest was accepted as the cut-off point for CHF patients with poor FC. P<0.05 was considered as statistically significant.

RESULTS

The baseline characteristics, NT-proBNP levels, and functional capacities of the patients with CHF are presented in Table 1; a comparison of this group with

Table 2. Comparison of patients with heart failure and control individuals in terms of clinical, biochemical and hematological characteristics

	Control (n=70)			Heart failure (n=94)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			53.3±12.35			56.7±10.90	0.445*
Male gender	35	50.0		59	62.8		0.102‡
Body mass index (kg/m^2)			26.5±3.62			26.6±3.10	0.912*
Diabetes mellitus	13	18.6		14	14.9		0.530‡
Hypertension	16	22.9		33	35.1		0.090‡
Smoking	18	25.7		34	36.2		0.155‡
LDL-cholesterol (mg/dl)			107.8±30.73			111.0±28.89	0.502*
Plasma creatinine (mg/dl)			0.69±0.13			0.77±0.13	**<0.001***
White blood cell (10^3/mm^3)			7.9±1.62			7.6±1.54	0.141*
Neutrophil (10^3/mm^3)			4.5±1.27			4.8±1.30	0.295*
Lymphocyte (10^3/mm^3)			2.5±0.60			1.8±0.63	**<0.001***
Neutrophil lynphocyte ratio	1.8 (1.0-3.8)			2.6 (1.1-6.3)			**<0.001†**
Hemoglobin (g/dl)			14.2±1.13			13.8±0.98	0.014*
Platelet (10^3/mm^3)			263.8±65.55			215.8±61.15	**<0.001***
Mean platelet volume (fl)	9.1 (6.0-10.9)			10.3 (6.2-13.0)			**<0.001†**
Use of statin	15	21.4		22	23.4		0.765‡

Continuous variables were expressed as mean±standard deviation or median (minimum-maximum), and nominal variables as number of cases and percentage (%). *Student's t-test, †Mann-Whitney U-test, ‡Pearson Chi-square test was used for nominal variables. LDL: Low-density lipoprotein.

the control group is provided in Table 2. There was no significant difference between the groups in terms of age, sex, body mass index, hypertension, diabetes mellitus, smoking history, low-density lipoprotein cholesterol level, white blood cell count, and neutrophil count (>0.05). The lymphocyte counts (1.8±0.63 × 10^3 *vs.* 2.5±0.60 × 10^3; p<0.001) were lower in the CHF group than in the control group. Moreover, the N/L ratios (2.9±1.30 *vs.* 1.8±0.55; p<0.001) were higher in the CHF group. Additionally, in a subgroup analysis, the N/L ratio tertile was found to be similar between patients with idiopathic dilated cardiomyopathy and ischemic cardiomyopathy (2.7±1.29 × 10^3 *vs.* 3.0±1.30 × 10^3; p=0.245). Therefore, the N/L ratio tertile was found to be significantly higher in patients with atrial fibrillation than in those with a normal sinus rhythm (3.67±1.12 × 10^3 *vs.* 2.79±1.29 × 10^3; p=0.029). The patients with CHF were divided into two groups with respect to the top and bottom three N/L ratios. A comparison of patients with an N/L ratio >3 with those having an N/L ratio <3 in terms of poor prognostic markers of HF is shown in Table 3. The FC levels (3.2±2.05 MET *vs.* 6.1±2.04 MET; p<0.001) were lower in those CHF patients with an N/L ratio ≥3 than in those with an N/L ratio <3 (Fig. 1). A correlation analysis between the FC levels and several variables of the CHF patients revealed a significant relationship between FC and N/L ratio (r=−0.612, p<0.001) (Table 4). Afterwards, the CHF patients were divided into two groups; low (<5 MET, n = 39) and high (>5 MET, n=55) FC, according to their functional status in an exercise test. Among the variables for which the p<0.25 in the univariate analysis including the smoking, atrial fibrillation, mitral and tricuspid regurgitation, log-NT-proBNP, N/L ratio, LV end-systolic diameter, mean platelet volume (MPV), LV EF, systolic PAP, LA diameter, E/Ea ratio, body mass index, hemoglobin values were included multivariate regression analysis and the N/L ratio and log-NT-proBNP were identified to be predictors of patients

Table 3. Association of neutrophil lymphocyte ratio with heart failure patients' characteristics

	N/L ratio <3 (n=53)			N/L ratio >3 (n=41)			*p*
	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			57.6±9.33			55.6±12.68	0.400*
Gender (female)	20	37.7		15	36.6		0.909‡
Body mass index (kg/m^2)			26.7±3.27			26.3±2.89	0.516*
Diabetes mellitus	7	13.2		7	17.1		0.818§
Hypertension	17	32.1		16	39.0		0.484‡
Smoking	18	34.0		16	39.0		0.612‡
LDL-C (mg/dl)			111.1±32.89			110.8±23.12	0.952*
Plasma creatinine (mg/dl)			0.6±0.14			0.6±0.13	0.721*
Log-NT-proBNP level (pg/ml)			3.0±0.46			3.3±0.38	**<0.001***
Functional capacity (MET)	6.0 (1.0-10.0)			2.0 (1.0-9.0)			**<0.001†**
Ejection fraction (%)	35.0 (20.0-45.0)			30.0 (20.0-45.0)			0.028†
Systolic PAP (mmHg)	38.0 (30.0-70.0)			45.0 (30.0-70.0)			0.049†
E/Ea ratio			9.2±3.20			12.2±4.37	**<0.001***
Atrial fibrilation	2	3.8		10	24.4		0.008§
LAmax diameter (cm)			4.3±0.43			4.6±0.52	**0.005***
MPV (fl)	10.3 (6.5-13.0)			10.5 (6.2-12.2)			0.052†
Use of statin	12	22.6		10	24.4		0.843‡

Continious variables were expressed as mean±standard deviation or median (minimum-maximum), and nominal variables as number of cases and percentage (%). *Student's t-test; †Mann-Whitney U-test; ‡Pearson Chi-square; §Continuity Correction test were used for nominal variables whichever is appropriate. E/Ea ratio: Mitral velocity of early diastolic filling from transmitral flow/early diastolic filling using Doppler tissue imaging; LDL: Low-density lipoprotein cholesterol; LA: Left atrium; MPV: Mean platelet volume; MET: Metabolic equivalent; NLR: Neutrophil lymphocyte ratio; PAP: Pulmonary artery pressure; NT-proBNP: N-terminal pro-brain natriuretic peptide.

Table 4. Correlation between functional capacity (metabolic equivalent) and clinical, echocardiographic, biochemical parameters by using correlation analysis

	r	p
Neutrophil to lymphocyte ratio	-0.612	**<0.001**†
N-terminal pro-brain natriuretic peptide (pg/ml)	-0.586	**<0.001**†
E/Ea ratio	-0.555	**<0.001***
Aa (cm/sn)	0.300	**0.007***
Systolic pulmonary artery pressure (mmHg)	-0.456	**<0.001**†
Ejection fraction (%)	0.413	**<0.001**†
Left atrium max diameter (mm)	-0.355	**0.001***
Left ventricul end-systolic diameter (mm)	-0.400	**<0.001***
Left ventricul end-diastolic diameter (mm)	-0.302	**0.004***
Mitral regurgitation	-0.308	**0.002**†
Tricuspid regurgitation	-0.472	**<0.001**†
Hemoglobin (g/dl)	0.263	**0.010***

*Pearson test, †Spearman's rho. Aa: Atrial contraction velocity using Doppler tissue imaging, E/Ea ratio: Mitral velocity of early diastolic filling from transmitral flow/early diastolic filling using Doppler tissue imaging.

with a poor FC (≤5 MET) (respectively: odds ratio [OR]=3.085, 95% confidence interval [CI]=1.520-6.260, p=0.002 and OR=1.585, 95% CI=1.201-2.091, p=0.001). The cut-off value of N/L ratio for prediction of poor FC was >2.74 with a sensitivity of 79.4% and a specificity of 80% (+LR: 3.97, −LR: 0.26, +PV: 73.8, −PV: 84.6) in the ROC curve analysis (AUC: 0.819; 95% CI: 0.731-0.908; p<0.001) (Fig. 2).

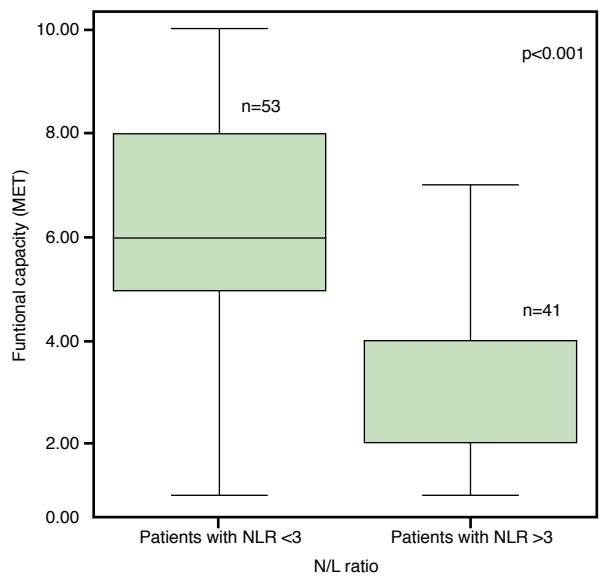

Figure 1. Functional capacity of patients with heart failure according to N/L ratio.

DISCUSSION

In the current study, the lymphocyte count was found to be significantly lower despite a normal neutrophil count, and the N/L ratio was found to be significant-

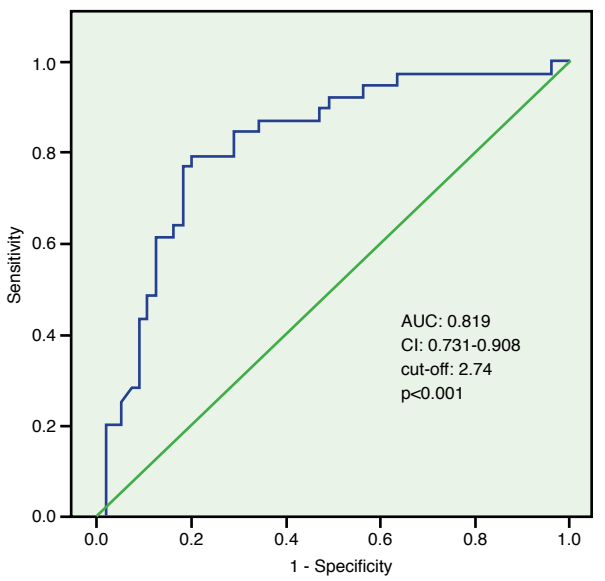

Figure 2. The cut-off value of N/L ratio for prediction of poor functional capacity in patients with heart failure was >2.74 with a sensitivity of 79.4% and a specificity of 80% in the receiver operating characteristics curve analysis (AUC: 0.819; 95% confidence interval: 0.731-0.908; p<0.001).

ly higher in patients with CHF than in normal subjects. Lymphocytopenia and increased mortality are independently associated in patients with acute and chronic HF.[12] Reduced lymphocyte proliferation and differentiation, neurohumoral activation, and lymphocyte apoptosis are possible mechanisms of lymphocytopaenia.[12] Relative lymphopenia is evidence of the cortisol-induced stress response in patients with cardiovascular disease.[13]

The N/L ratio has been proposed as a prognostic marker of the systemic inflammatory response. It is a new addition to the long list of such inflammatory markers. A high N/L ratio is associated with a poor clinical outcome in various cardiac diseases, including acute coronary syndrome, non-ST-segment elevation myocardial infarction (STEMI), and STEMI.[13-15] Tamhane et al.[13] reported that patients with non-STEMI or STEMI in tertile 3 had higher in-hospital and 6 months mortality rates. Additionally, a search of the literature revealed only one study of the association between N/L ratio and a poor prognosis in patients with decompensated HF. In that study, Uthamalingam et al.[5] reported that an increase in N/L ratio was associated with increased mortality and morbidity in these patients. Additionally, they found that patients with decompensated HF in tertile 4 had higher morbidity and mortality rates. However, to date, the N/L ratio has not been investigated in patients with CHF. In our study, markers of a poor prognosis in CHF, including FC, NT-proBNP level, E/Ea ratio, PAP, LA diameter, and a EF were found to be significantly higher in those patients with an N/L ratio >3. According to these results, the N/L ratio may be used as an inexpensive marker to aid in the risk stratification of patients with CHF.

Exercise performance is an important parameter since a lower FC translates into independence in daily activities and an improved quality-of-life. Besides, it is an independent predictor of morbidity and mortality in HF patients. Immunological and inflammatory responses are major pathophysiological features in the exercise performance of HF patients.[16] Leukocyte activation and the migration of these cells from the blood to sites of inflammation may play a significant role in reduced exercise capacity.[16,17] Therefore, recent investigations have suggested that proinflammatory cytokines (e.g., tumor necrosis factor-alpha and interleukin-1 [IL-1]) are capable of modulating cardiac function, peripheral vascular function, and exercise performance via a number of mechanisms, including the production of oxygen free radicals and apoptosis.[16-19] Previous studies have demonstrated the lack of a relationship between exercise capacity and conventional echocardiographic parameters such as LV function, and LV diameter.[20-25] Similarly, we found that FC was poorly correlated with echocardiographic parameters. In contrast, a strong correlation was found between N/L ratio and FC; moreover, N/L ratio was identified as an independent determinant of exercise capacity. We also found that the cut-off value of 2.74 for N/L ratio was a predictor of a poor FC in HF patients (≤5 MET). According these findings, we conclude that the N/L ratio is an inexpensive and easy to obtain a marker that can be used to procure preliminary information about exercise performance in CHF patients.

In the current study, the MPV was increased significantly in the HF group. The MPV, a marker of platelet activity, is increased in patients with acute myocardial infarction and stroke, and it has been shown to be a predictive marker for future adverse coronary events following myocardial infarction.[26,27] A poorly contracting ventricle allows blood stasis, which can lead to thrombus formation. Previously, Tekin et al.[28] reported that the MPV was significantly greater in patients with DCMP than in normal subjects and that it was strongly associated with LV thrombus formation in these patients. In our study, the MPV was significantly higher in HF patients with an N/L ratio >3 than in those with an N/L ratio <3 and in the control subjects. These results indicate that the thrombogenicity may be increased in patients with an N/L ratio >3. However, further study is needed to determine whether the N/L ratio contributes to LV thrombus formation.

Study limitations

The major limitation of the present study was the relatively small number of patients; subjects were only selected from patients with CHF. Furthermore, the cross-sectional design limited our ability to determine the significance of changes in the N/L ratio for the long-term prognosis and mortality of patients with LVSD. Therefore, other inflammatory parameters such as IL-6, tumor necrosis factor-α and high sensitive C-reactive protein were not measured simultaneously because they are mostly not available in daily practice.

The current study shows that[1] the N/L ratio was increased in CHF patients;[2] the N/L ratio was strongly related to markers of a poor prognosis, including the NT-proBNP level, a low EF, exercise capacity, LA diameter, E/Ea ratio, and PAP;[3] the aforementioned parameters were significantly higher in patients with an N/L ratio>3 than in those with an N/L ratio<3 and in the controls; and[4] a cut-off point of 2.74 for the N/L ratio can be used to predict a poor FC, and it may be used as a new biomarker for poor outcome in patients with HF. However, further study is needed to determine whether the N/L ratio contributes to the estimated poor outcome in CHF patients.

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