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ORIGINAL ARTICLE

Neutrophil to Lymphocyte Ratio as a Predictor of Left Ventricular Hypertrophy in Patients with Newly Diagnosed Hypertension

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Abstract

Objective: Concentric or eccentric left ventricular hypertrophy (LVH) is an independent prognostic factor of major cardiovascular events in hypertension (HT). A high neutrophil to lymphocyte ratio (NLR) is correlated with high mortality and poor prognosis in cardiovascular disease. This study was performed to investigate the associations between NLR and different left ventricular (LV) geometric patterns in patients with newly diagnosed HT.

Methods: The study population consisted of 222 patients with newly diagnosed HT (mean age: 53.2 ± 10.0 years). Echocardiographic examination was performed in all patients. Four different geometric patterns were determined in hypertensive patients according to the left ventricular mass index (LVMI) and relative wall thickness (RWT).

Results: The baseline demographic characteristics were similar in all groups. The NLR and platelet to lymphocyte ratio (PLR) were higher in the eccentric hypertrophy and concentric hypertrophy groups compared to the normal geometry and concentric remodeling groups ($p < 0.05$, for all). NLR was positively and significantly correlated with LVMI ($r = 0.508$, $p < 0.001$). Linear regression analysis showed that LVMI was independently correlated with NLR ($\beta = 5.440$, $p < 0.001$), systolic blood pressure ($\beta = 0.284$, $p < 0.001$), ejection fraction ($\beta = -0.201$, $p < 0.001$), E/A ($\beta = -2.270$, $p = 0.24$), and high-density lipoprotein cholesterol ($\beta = -0.245$, $p < 0.001$).

Conclusions: We demonstrated that patients with newly diagnosed HT with LVH had significantly higher NLR and PLR compared to those without LVH. In addition, NLR predicted LVH in hypertensive patients. The results of this study suggested that inflammation plays a role in the pathogenesis of LVH in hypertensive subjects.

Introduction

The prevalence of hypertension (HT) is increasing across the world irrespective of income status [1]. HT persists as a major public health problem that the global prevalence of hypertension was estimated to be 1.13 billion in 2015, with a prevalence of over 150 million in central and Eastern Europe [2]. It also affects more than one third of the adult population in USA [3].

There are four different geometric patterns of left ventricle (LV) in HT. These geometric patterns include normal LV geometry (NG), concentric remodeling (CR), eccentric hypertrophy (EH) and concentric hypertrophy (CH). Left ventricular hypertrophy (LVH) is traditionally classified as concentric or eccentric, which is one of the substantial HT-mediated organ damage. It is a fundamental process of adaptation to an increased hemodynamic overload [4]. LVH is an independent prognostic factor for major cardiovascular events including sudden cardiac death, acute myocardial infarction, stroke, and congestive heart failure in hypertensive subjects [5]. For this reason, hypertensive patients with LVH have an increased risk of cardiovascular events compared to hypertensive patients without LVH [6].

It is well known that low-grade inflammation plays a significant pathophysiological role in HT and cardiovascular disease [7,8]. Several study have been demonstrated that LVH is a low-grade inflammatory state, which is predominantly managed by various inflamma-

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tory cascades [9,10]. Animal studies demonstrated that inflammatory markers in fibrotic process are the main component in ventricular remodeling [11,12].

The neutrophil to lymphocyte ratio (NLR) is mostly used as are liable biomarker of systemic inflammatory status [13]. NLR is a simple and readily available marker for chronic low-grade inflammation that can be easily obtained from differential counts of white blood cell (WBC) subtypes [14]. Based on aforementioned results, the present study aimed to investigate whether NLR are associated with LV remodeling in newly diagnosed hypertensive patients.

Methods

Study population

Between January 2018 and February 2019, consecutive subjects who admitted our outpatient clinic and having newly diagnosed essential HT were enrolled to the study. HT was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or a diastolic blood pressure (DBP) ≥ 90 mmHg (blood pressure taken from three seperate measurements in office in seated position) and SBP ≥ 130 mmHg and/or DBP ≥ 80 mmHg based on the mean 24-h circadian ambulatory blood pressure monitoring [15].

The exclusion criteria were defined as any condition that has a capability to alter cardiac structures and functions: patients with a history of anti-hypertensive drug therapy, secondary HT, history of coronary artery disease, cardiomyopathy, a body mass index (BMI) over 30 kg/m^2, diabetes mellitus, renal failure, chronic inflammatory disease, gestational HT, congenital heart disease, LV systolic dysfunction (ejection fraction < 50%), atrial fibrillation, liver disease, obstructive sleep apnea, valvular heart disease, patients with active infection, and WBC count of > 12 × 10^3/μl or < 4 × 10^3/μl.

Study protocol

All patients underwent a complete medical assessment, physical examination, blood analyze, electrocardiography (ECG), and transthoracic echocardiography (TTE). The institutional ethics committee approved the study protocol.

All echocardiographic examinations were performed using a Vivid 5 Pro device (General Electric, Horten, Norway) with a 2.5 MHz transducer. The measurements were performed in the left lateral decubitus position as recommended by current guideline American Society of Echocardiography [16], and three consecutive cycles were avaraged for each parameter. Standard echocardiographic analysis included two dimensional, M-mode, Doppler flow, and tissue Doppler flow measurements. Diastolic interventricular septum thickness (IVS), diastolic posterior wall thickness (PWT), left atrial (LA) diameter, left ventricle end systolic (LVESD) and end diastolic dimensions (LVEDD) were measured from parasternal long-axis view. Ejection fraction (EF) was calculated by using modified Simpson method. Mitral early diastolic velocity (E), mitral late diastolic velocity (A) were recorded from the apical transducer position of the sample volume situated between the mitral leaflet tips, and the ratio of E to A (E/A ratio) was calculated. Myocardial early diastolic velocity (Em) and myocardial late diastolic velocity (Am) wave velocities were measured with the sample volume using PWD from the mitral lateral and septal annulus.

LV mass (LVM) was calculated from M-mode echocardiograpy using the American Society of Echocardiography recommended Cube formula as following [16]:

$$LVM\ (g) = 0.8 \times 1.04\ [(IVS + PWT + LVEDD)^3 - LVEDD^3] + 0.6$$

LVM was divided by body surface area to obtain the LVM index (LVMI, g/m^2), which cut-off values of 115 g/m^2 and 95 g/m^2 for men and women respectively. Body surface area (m^2) was calculated using the Du Bois formula [weight (kg)$^{0.425}$ × height (cm)$^{0.725}$ × 0.007184]. Relative wall thickness (RWT = 2 × PWT in end diastole/LV diastolic diameter in end diastole) was calculated. Normal RWT was defined as values ≤ 0.42 and increased RWT as > 0.42 [16]. Patients with increased LVMI and increased RWT were considered to have CH, and those with increased LVMI and normal RWT were considered to have EH. Those with normal LVMI and increased or normal RWT were considered to have concentric remodeling CR or NG, respectively.

Diastolic dysfunction was classified by mitral inflow pattern according to recent guidelines [17]. Grade I diastolic dysfunction was defined as E/A ratio of less than 0.8 along with a peak velocity of ≤ 50 cm/sec and normal left atrial pressure (LAP); grade II diastolic dysfunction was characterized by an E/A ratio > 0.8 but < 2 and increased LAP; and grade III diastolic dysfunction was defined as an E/A ratio of greater than 2 and increased LAP.

After a 12-h fasting period, bloods samples were obtained from the cephalic vein using a traumatic venipuncture and mixed with EDTA. Complete WBC counts, including neutrophil and lymphocyte counts, were measured using an automated hematology analyzer CELL-DYN Ruby (Abbott Diagnostics, Abbott Park, IL, USA) and expressed as × 1.000 cells/mm^3. Hemoglobin and platelet count were also calculated. NLR was calculated by dividing the neutrophil count by the lymphocyte count, and platelet to lymphocyte ratio (PLR) was calculated as the number platelets divided by the lymphocyte count, both of which were obtained from the same blood samples. Plasma triglyceride, low-density lipoprotein, high-density lipoprotein, glucose, creatinine, uric acid and C-reactive protein (CRP) were analyzed on the Architect c8000 Chemistry System (Abbott Diagnostics, USA) using commercial kits (Abbott).

Statistical analysis

All analyses were performed using SPSS 17.0 (SPSS for Windows 17.0, Chiacago, IL). Continuous variables were presented as the mean ± standard deviation. Categorical variables were presented as frequencies and percentages. Kolmogorov Smirnov test was used to determine whether the continuous variables were distributed normally. Comparisons of categorical variables between the groups were conducted using the chi-square test. Analysis of variance (ANOVA) was used in the analysis of continuous variables. Pearson's correlation test was used for the variables with a linear correlation and Spearman's correlation test was used for those without a linear correlation. Lineer regression analysis was used to determine which variables affects LVMI. 95.0% confidence intervals (95.0% CI) were determined. A two-tailed p-value of 0.05 was considered statistically significant.

Results

A total of 383 consecutive subjects with newly diagnosed essential HT were initially enrolled to the study. Forty-five patients were excluded owing to diabetes mellitus, 20 patients due to chronic renal insufficiency, 60 patients due to ischemic heart disease, 25 patients due to moderate or severe valvular heart disease, and 11 patients due to secondary HT. Consequently, measurements were obtained from 222 patients with newly diagnosed essential HT in this study (mean age: 53.2 ± 10.0 years, male: 112 patients). In the present study, four different LV geometric patterns were determined according to LVMI and RWT: (i) 58 patients with NG group, (ii) 60 patients with CR group, (iii) 50 patients with EH group, and (iv) 54 patients with CH group.

Table 1: Clinical and echocardiographic characteristics of different left ventricular geometry.

Variables	NG group n = 58	CR group n = 60	EH group n = 50	CH group n = 54	p-value
Age (years)	53.2 ± 10	54.1 ± 9.5	50.6 ± 12.1	54.6 ± 7.9	0.181
Sex (male), n(%)	31 (%53.4)	33 (%55)	24 (%48)	24 (%44.4)	0.658
Smoking, n (%)	17 (%29.3)	19 (%31.7)	21 (%42.6)	22 (%40)	0.404
BMI (kg/m^2)	27.3 ± 2.3	27.1 ± 2.3	26.8 ± 2.1	27.1 ± 2.4	0.560
DBP (mmHg)	83.6 ± 8.5^{a}	86.1 ± 10.5^{aa}	90.0 ± 9.1	91.4 ± 9.8	< 0.001
SBP (mmHg)	142.3 ± 9.6^{b}	147.2 ± 14.0^{bb}	154.0 ± 11.3	157.5 ± 16.4	< 0.001
EF (%)	60.8 ± 4.8^{c}	61.1 ± 3.9^{cc}	58.5 ± 5.2	57.9 ± 4.6	< 0.001
LVEDD (cm)	4.6 ± 0.3^{d}	4.4 ± 0.3^{dd}	5.1 ± 0.3^{ddd}	4.8 ± 0.2	< 0.001
LVESD (cm)	3.1 ± 0.2^{e}	3.0 ± 0.2^{ee}	3.3 ± 0.3	3.2 ± 0.3	< 0.001
IVS (cm)	1.00 ± 0.10^{f}	1.11 ± 0.12^{ff}	1.17 ± 0.7^{fff}	1.23 ± 0.13	< 0.001
PW (cm)	0.90 ± 0.10^{f}	1.04 ± 0.11^{g}	1.05 ± 0.50^{ddd}	1.17 ± 0.14	< 0.001
LAD (cm)	3.3 ± 0.3^{h}	3.4 ± 0.3^{hh}	3.7 ± 0.3	3.6 ± 0.4	< 0.001
RWT (g/m^2)	0.38 ± 0.02^{i}	0.47 ± 0.05^{hh}	0.40 ± 0.02^{ddd}	0.49 ± 0.06	< 0.001
LV mass (g)	152.8 ± 38.1^{b}	166.8 ± 34.8^{k}	225.5 ± 32.5	223.2 ± 43.3	< 0.001
LVMI (g/m^2)	79.9 ± 18.2^{b}	85.9 ± 16.1^{k}	121.5 ± 17.1	126.7 ± 29.7	< 0.001
E/A	1.1 ± 0.5^{m}	0.8 ± 0.3	0.9 ± 0.4	0.9 ± 04	0.002
E/Em	8.0 ± 2.1^{n}	8.6 ± 3.0	9.2 ± 2.2	10.3 ± 3.9	0.001

^{a}p = 0.004 between NG and EH groups, p < 0.001 between NG and CH groups; ^{aa}p = 0.020 between CR and CH groups; ^{b}p < 0.001 between NG, EH and CH groups; ^{bb}p = 0.030 between CR and EH groups, p = 0.003 between CR and EH groups; ^{c}p = 0.007 between NG and CH groups; ^{cc}p = 0.019 between CR and EH groups, p = 0.002 between CR and CH groups; ^{d}p = 0.002 between NG and CR groups, p < 0.001 between NG and EH groups, p = 0.021 between NG and CH groups; ^{dd}p = 0.002 between NG and CR groups, p < 0.001 between CR, EH and CH groups;

^{ddd}p < 0.001 between EH and CH groups; ^{e}p = 0.012 between NG and EH groups; ^{ee}p < 0.001 between CR and EH goups, p = 0.005 between CR and CH groups; ^{f}p < 0.001 between NG, CR, EH and CH groups; ^{ff}p = 0.009 between CR and EH groups, p < 0.001 between CR and CH goups; ^{fff}p = 0.068 between EH and CH groups; ^{g}p < 0.001 between CR and CH groups; ^{h}p < 0.001 between NG and EH groups, p = 0.014 between NG and CH groups; ^{hh}p < 0.001 between CR and EH groups; ^{i}p < 0.001 between NG, CR and CH groups, p = 0.004 between NG and EH goups; ^{k}p < 0.001 between CR, EH and CH groups; ^{m}p = 0.003 between NG and CR groups, p = 0.008 between NG and CH groups; ^{n}p = 0.044 between NG and EH groups, p = 0.002 between NG and CH groups.

NG: Normal Geometry; CR: Concentric Remodelling; EH: Eccentric Hypertrophy; CH: Concentric Hypertrophy; BMI: Body Mass İndex; DBP: Diastolic Blood Pressure; SBP: Systolic Blood Pressure; EF: Ejection Fraction; LVEDD: Left Ventricular End-Diastolic Dimension; LVESD: Left Ventricular End-Systolic Dimension ; IVS: İnterventricular Septal Thickness; PW: Posterior Wall Thickness; LAD: Left Atrial Diameter; RWT: Relative Wall Thickness; LV: Left Ventricular; LVMI: Left Ventricular Mass İndex; E/A: Peak Velocity of Early Diastolic Flow/Peak Velocity of Late Diastolic Flow; E/Em: Peak Velocity Of Early Diastolic Flow Across Mitral Valve/Myocardial Peak Velocity of Early Diastole.

Comparison of baseline and echocardiographic characteristics of the groups were presented in Table 1. There was no statistically difference in terms of age, sex, smoking, and BMI among the groups (p > 0.05, for all). SBP, DBP, EF, LVEDD, LVESD, IVS, PWT, LA diameter, RWT, LV mass, E/A, and E/Em values were different among the groups (p < 0.05, for all). The measurements of SBP, DBP, LVMI and the ratio E/Em were increasing, while the ratio of E/A was decreasing from NG group to the CH group.

Comparison of laboratory characteristics of the groups were demonstrated in Table 2. No significant dif-

Table 2: Comparison of laboratory parameters in the study groups.

Variables	NG group n = 58	CR group n = 60	EH group n = 50	CH group n = 54	p-value
Hemoglobin (g/dL)	13.7 ± 1.3	13.9 ± 1.6	13.7 ± 1.5	13.6 ± 1.4	0.737
WBC (10^3/μL)	8.7 ± 2.0	8.9 ± 1.7	8.9 ± 1.6	9.1 ± 1.8	0.737
Platelet (10^3/μL)	256.3 ± 82.0	254.1 ± 75.5	268.2 ± 85.3	265.0 ± 61.5	0.733
Neutrophils (10^3/μL)	4.8 ± 1.2[a]	4.9 ± 1.1[aa]	5.4 ± 1.1	5.8 ± 1.2	< 0.001
Lymphocytes (10^3/μL)	2.7 ± 0.7[b]	2.6 ± 0.7[bb]	2.1 ± 0.6	2.3 ± 0.5	< 0.001
NLR	1.89 ± 0.44[c]	1.93 ± 0.47[cc]	2.69 ± 0.59	2.63 ± 0.53	< 0.001
PLR	103.2 ± 46.2[d]	100.9 ± 35.5[dd]	135.9 ± 53.9	120.6 ± 29.0	< 0.001
Blood glucose (mg/dL)	95.7 ± 5.6	95.6 ± 8.0	95.3 ± 6.6	97.3 ± 6.9	0.436
Creatinine (mg/dL)	0.87 ± 0.19	0.92 ± 0.18	0.90 ± 0.16	0.92 ± 0.20	0.550
Total cholesterol (mg/dL)	189.5 ± 25.2[e]	190.0 ± 29.8	190.6 ± 33.3	204.6 ± 34.7	0.030
LDL-cholesterol (mg/dL)	114.3 ± 23.7	113.4 ± 28.7	118.7 ± 26.7	126.0 ± 28.7	0.057
HDL-cholesterol (mg/dL)	24.2 ± 7.7[f]	43.7 ± 8.5	40.7 ± 6.9	39.1 ± 5.7	0.006
Triglyceride (mg/dL)	193.9 ± 102.4	203.3 ± 95.9	170.0 ± 64.31	181.1 ± 85.0	0.224
Uric acid (mg/dL)	4.5 ± 0.9[g]	4.6 ± 0.7[gg]	4.9 ± 0.9	5.1 ± 0.9	0.003
C-reactive protein (mg/dL)	0.43 ± 0.11	0.39 ± 0.13	0.40 ± 0.10	0.40 ± 0.12	0.342

[a]p < 0.001 between NG and CH groups; [aa]p < 0.001 between CR and CH groups; [b]p < 0.001 between NG and EH groups, p = 0.002 between NG and CH groups; [bb]p < 0.001 between CR and EH groups, p = 0.003 between CR and CH groups; [c]p < 0.001 between NG, EH and CH groups; [cc]p < 0.001 between CR, EH and CH groups; [d]p = 0.006 between NG and EH groups; [dd]p = 0.001 between CR and EH groups, p = 0.008 between CR and CH groups; [e]p = 0.049 between NG and CH groups; [f]p = 0.004 between NG and CH groups; [g]p = 0.003 between NG and CH groups; [gg]p = 0.028 between CR and CH groups.

NG: Normal Geometry; CR: Concentric Remodelling; EH: Eccentric Hypertrophy; CH: Concentric Hypertrophy; WBC: White Blood Cell Count; NLR: Neutrophil Lymphocyte Ratio; PLR: Platelet to Lymphocyte Ratio; LDL: Low Density Lipoprotein Cholesterol; HDL: High Density Lipoprotein Cholesterol.

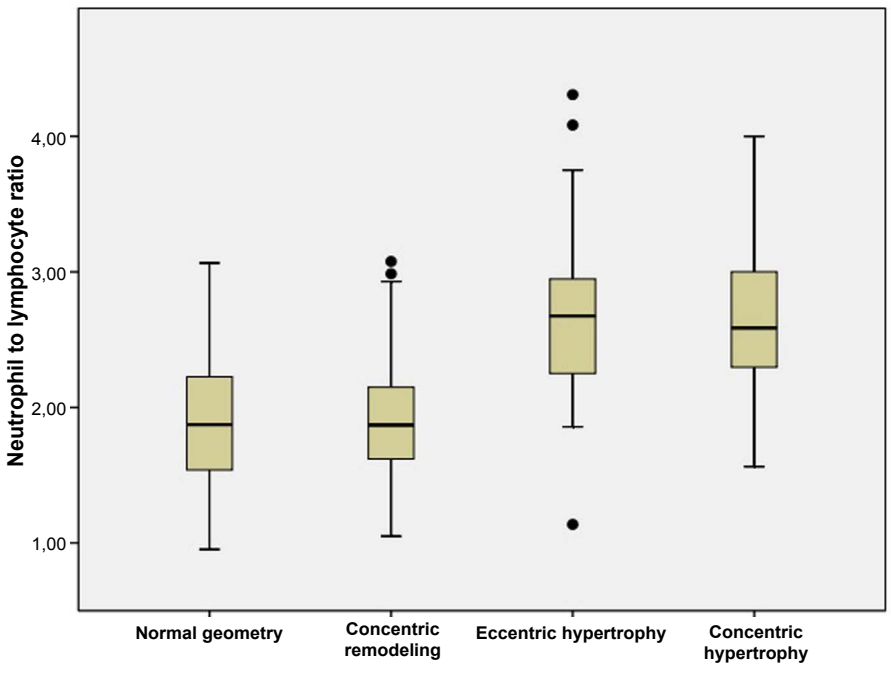

Figure 1: The relationship between neutrophil to lymphocyte ratio and different left ventricle geometry patterns.

ference was found among the groups regarding hemoglobin, WBC counts, platelet, fasting glucose, creatinine, low-density lipoprotein cholesterol, triglyceride, CRP levels. Neutrophils, lymphocytes, NLR, PLR, total cholesterol, high-density lipoprotein cholesterol, and uric acid levels were different among the groups ($p < 0.05$, for all). The highest NLR and PLR levels were observed in the EH and CH groups compared with other groups ($p < 0.05$, for all). Also, NLR and PLR levels of the NG and CR groups were similar ($p < 0.05$, for all). Comparison of NLR levels is shown in Figure 1.

Pearson correlation analyses showed that LVMI was correlated positively and moderately with NLR ($r = 0.508$, $p < 0.001$) and weakly with PLR ($r = 0.229$, $p = 0.001$) (Figure 2). In addition, Sperman's correlation analyses demonstrated that SBP and DBP were correlated positively and weakly with NLR ($r = 0.293$, $p < 0.001$ and $r = 0.227$, $p = 0.001$, respectively) (Figure 3 and Figure 4).

Linear regression analysis show that LVMI was independently correlated with NLR (β = 5.440, 95% CI:

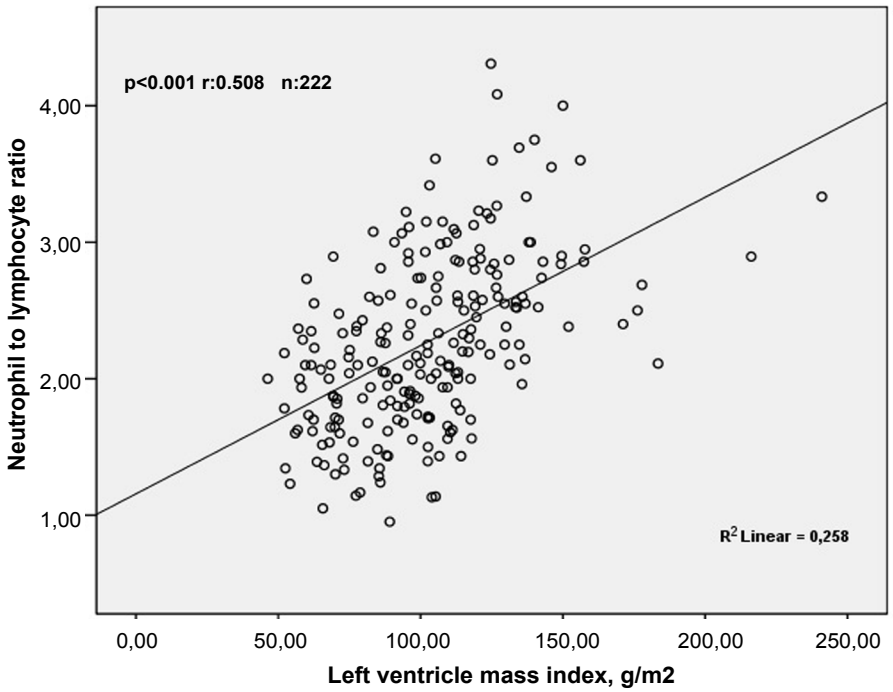

Figure 2: The relationship between neutrophil to lymphocyte ratio and left ventricle mass index.

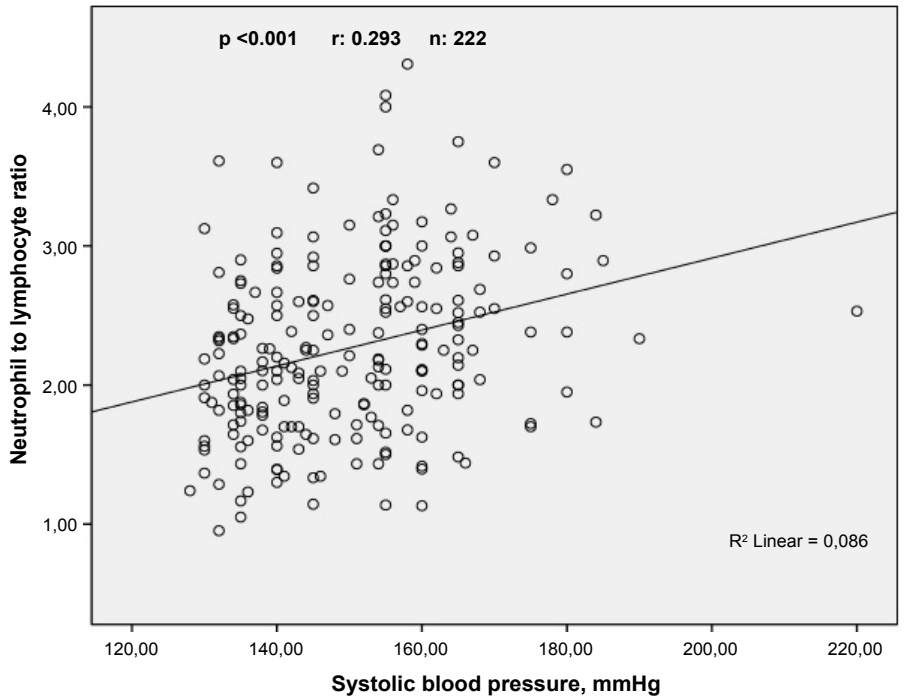

Figure 3: The relationship between neutrophil to lymphocyte ratio and systolic blood pressure.

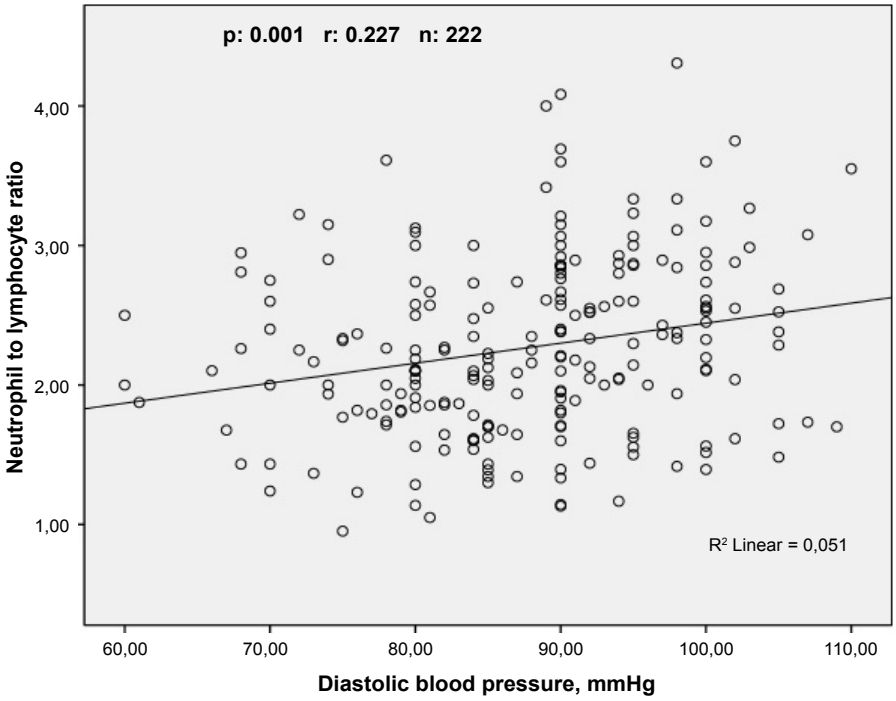

Figure 4: The relationship between neutrophil to lymphocyte ratio and diastolic blood pressure.

Table 3: Linear regression analysis for predictors of left ventricular mass index in patients newly diagnosed essential hypertension.

Parameters	B coefficient	95.0% CI	p
SBP (mmHg)	0.284	0.313 – 0.883	< 0.001
EF (%)	-0.201	-1.862 –-0.470	< 0.001
E/A	-2.270	-168.55 – -0.967	0.024
NLR	5.440	9.259 – 21.715	< 0.001
HDL (mg/dL)	-0.245	-1.376 – -0.553	< 0.001

SBP: Systolic Blood Pressure; EF: Ejection Fraction; E/A: Peak Velocity of Early Diastolic Flow/Peak Velocity of Late Diastolic Flow; NLR: Neutrophil Lymphocyte Ratio; HDL: High Density Lipoprotein Cholesterol.

9.259 - 21.715; p < 0.001), SBP (β = 0.284, 95% CI: 0.313 - 0.883; p < 0.001), EF (β = -0.201, 95% CI: -168.55 - -0.967; p < 0.001), E/A (β = -2.270, 95% CI: -168.55 - -0.967; p = 0.24), and high-density lipoprotein cholesterol (β = -0.245, 95% CI: -1.376–0.553; p < 0.001) (Table 3).

Discussion

This is the first study which investigated the relationship between NLR and different LV geometry patterns in newly diagnosed hypertensive patients. In the present study, the major finding is that in patients with newly diagnosed HT, the NLR and PLR that were measured on admission were both significantly higher in patients with EH and CH. There was a positive and significant correlation between NLR and LVMI, SBP, and DBP. Moreover, we found that NLR is an independent predictor of LVH in newly diagnosed hypertensive patients.

In clinical studies, LVH is generally indentified as LVMI and it develops in response to chronic pressure and volume overload, which are responsible for cardiomyocyte hypertrophy and cardiac fibrosis. In addition, non-hemodynamic factors such as age, sex, obesity, body size, insulin, and the renin-angiotensin system contribute to LVH development [18]. Also, non-hemodynamic factors, including transforming growth factor β1, tumor necrosis factor-alpha (TNF-a), and cytokines plays an important role in LV remodelling [19,20].

The physiological response of leukocytes to systemic inflammatory conditions is an increase in the number of neutrophils and a corresponding decrease in the relative lymphocyte count. WBC counts and its subtypes, such as neutrophil and lymphocyte, have an important role in modulating the inflammatory respose in the atherosclerotic process [21], heart failure [22], aortic stenosis [23], HT [24] and LVH [25]. For this reason, the NLR is used as a biomarker of subclinical inflammation. In many studies, a higher NLR is generally correlated with high mortality and poor prognosis in cardiovascular disease [21,22]. Hypertrophic geometric patterns (EH, CH) are associated with poor prognosis in hypertensive patients [26]. In the present study, we found that NLR was higher in eccentric and concentric LV geometric patterns.

Rosello Lleti, et al. was assessed the 251 hypertensive patients in a study, and demonstrated that hypertensive patients with LVH had a higher inflammatory cytokine levels than the hypertensive patients without hypertrophy [24]. In addition, the authors of this study showed that TNF-receptor was an independent predictor of LVH. Cai, et al. [27] demonstrated that pro-inflammatory factors (TNF-a and IL-6) promote left ventricular remodelling in different stage of HT. At the same time, it should be noted that the literature data in terms of pro-inflammatory cytokine is unclear. But, Leibowitz, et al. [28] demonstrated that hypertensive patients with higher LVM were inconsistent with cytokine levels when compared to those with normal LVM. A recent study demonstrated that there was no association between TNF-α levels and LVH in hypertensive patients. In the same study, the authors emphasized that the lack of an increase in TNF-α levels does not exclude the presence of an active level of this cytokine in the plasma, because of its soluble receptors, which change during HT [29]. In an experimental research, macrophage activation and accumulation in myocardium is a critical step in acute cardiac inflammatory response to high blood pressure [30].

In recent years, many studies have investigated the relationship between NLR, HT, and LVMI. Shi, et al. [20] demonstrated that a strong correlation between WBC counts (particularly neutrophil counts) and LVMI in hypertensive patients currently taking anti-hypertensive medication. Our findings are consistent with this study results, and we showed that NLR was positively correlated whit LVH in CH and EH groups. In another study [31], it has been demonstrated that NLR and monocyte levels were significantly higher in the non-dipper hypertensive patients compared with the dipper hypertensive patients. This study enrolled patients who have chronic HT and receiving appropriate antihypertensive medications, as well. A recent study indicated that higher NLR levels in hypertensive patients over 80 years of age admitted to the hospital are good predictors for all-cause mortality 90 days after admission [32].

Several studies indicated that increased platelet activity was associated with the severity of inflammation [33,34]. PLR, which is an another marker, can play an importante role in the inflammatory processes. It has been proposed that PLR was a predictive and prognostic marker for coronary artery disease [35]. In addition, PLR was significantly higher in the non-dipper hypertensive patients than in the dipper hypertensive patients [36]. Sunbul, et al. [37] demonstrated that patients with non-dipper hypertension had significantly higher NLR and PLR compared with patients with dipper hypertension. To the best of our knowledge, no information is available from previous studies about association between these inflammatory markers and different LV geometric patterns. We demonstrated that the NLR and PLR were associated with LVH in patients with newly diagnosed HT. Our results support the relationship between the immune system activation and the presence of LVH in patients with HT. But, this relationship has generally been shown in the literature by more specific inflammation markers such as, cytokines and adhesion molecules in both experimental and clinical studies [38,39]. Moreover, NLR and PLR from peripheral venous blood are less accurate than *in vitro* studies [40] suggesting that cytokines are associated with cardiac myocyte hypertrophy in predicting LVH. Therefore, we can say that the power of our study is lower.

As LVH effectively and independently predicts morbidity and mortality in cardiovascular disease, it is important to diagnose LVH both for clinical practice and research. In clinical practice, the diagnosis of LVH usually includes ECG and TTE. ECG is widely used and routine test in all patients with HT. However, a normal ECG doesn't excluded the presence of LVH due to its low sensitivity [41]. M-mode echocardiography is currently the standard clinical diagnosis method for LVH [26]. Data from real-time three dimensional (3D) echocardiography with regarding to LVM were performed few studies [42]. Even so, 3D echocardiographic LVM data available in normal subjects are not sufficient and its use in clinical practice is not recommended [16]. Cardiac magnetic resonance imaging is a very accurate method for LVH detection. It is recommended for clinical trials investigating LVM regression [41]. Nonetheless, its use in clinical practice is quite difficult and expensive. The present study showed that NLR measured on admission might be usefull marker to predict the LVMI. It is convenient marker and can be easily measured blood samples.

Study Limitations

The limitations of the present study are as follows. (i) The current study included a relatively small number of patents, and didn't include control group. (ii) Only one measurement of admission full blood count and calculation of PLR and NLR were included in the analysis. (iii) Although, many studies have demonstrated relationships between cytokines and LVH, we didn't evaluate cytokines in the present study. (iv) These type of studies do not establish causality.

Conclusions

Our study suggested that NLR and PLR are related with different LV geometry patterns in hypertensive patients, which has not been reported previously. Also, NLR was an independent predictor of LVH in hypertensive patients. The present study demonstrated that NLR might be a useful and cost-effective marker to evaluate LVH in newly diagnosed hypertensive patients. However, larger scale studies are needed to support these results.

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References

1. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, et al. (2013) Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA 310: 959-968.
2. Zhou B, Bentham J, Di Cesare M, Bixby H, Danaei G, et al. (2017) Worldwide trends in blood pressure from 1975 to 2015: A pooled analysis of 1479 population-based measurement studies with 19.1 million participants. Lancet 389: 37-55.
3. Egan BM, Zhao Y, Axon RN (2010) US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. JAMA 303: 2043-2050.
4. Lavie CJ, Milani RV, Shah SB, Gilliland YE, Bernal JA, et al. (2008) Impact of left ventricular geometry on prognosis-a review of ochsner studies. Ochsner J 8: 11-17.
5. Verdecchia P, Angeli F, Achilli P, Castellani C, Broccatelli A, et al. (2007) Echocardiographic left ventricular hypertrophy in hypertension: Marker for future events or mediator of events? Curr Opin Cardiol 22: 329-334.
6. Bluemke DA, Kronmal RA, Lima JA, Liu K, Olson J, et al. (2008) The relationship of left ventricular mass and geometry to incident cardiovascular events. the MESA (Multi-Ethnic Study of Atherosclerosis) Study. J Am Coll Cardiol 52: 2148-2155.
7. Virdis A, Dell'Agnello U, Taddei S (2014) Impact of inflammation on vascular disease in hypertension. Maturitas 78: 179-183.
8. Miguel CD, Rudemiller NP, Abais JM, Mattson DL (2015) Inflammation and hypertension: New understandings and potential therapeutic targets. Curr Hypertens Rep 17: 507.
9. Marvar PJ, Thabet SR, Guzik TJ, Lob HE, McCann LA, et al. (2010) Central and peripheral mechanisms of T-lymphocyte activation and vascular inflammation produced by angiotensin II-induced hypertension. Circ Res 107: 263-270.
10. Carreño JE, Apablaza F, Ocaranza MP, Jalil JE (2006) Cardiac hypertrophy: Molecular and cellular events. Rev Esp Cardiol 59: 473-486.
11. Kuwahara F, Kai H, Tokuda K, Kai M, Takeshita A, et al. (2002) Transforming growth factor-beta function blocking prevents myocardial fibrosis and diastolic dysfunction in pressure-overloaded rats. Circulation 106: 130-135.
12. Kuwahara K, Kai H, Tokuda K, Niiyama H, Tahara N, et al. (2003) Roles of intercellular adhesion molecule-1 in hypertensive cardiac remodeling. Hypertension 41: 819-823.
13. Imtiaz F, Shafique K, Mirza SS, Ayoob Z, Vart P, et al. (2012) Neutrophil lymphocyte ratio as a measure of systemic inflammation in prevalent chronic disease in Asian population. Int Arch Med 5: 2.
14. Pereira IA, Borba EF (2008) The role of inflammation, humoral and cell mediated autoimmunity in the pathogenesis of atherosclerosis. Swiss Med Wkly 138: 534-539.
15. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, et al. (2013) 2013 ESH/ESC guidelines for the management of arterial hypertension: the task force for the management of arterial hypertension of the European society of hypertension (ESH) and of the European society of cardiology (ESC). J Hypertens 31: 1281-1357.
16. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, et al. (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American society of echocardiography and the european association of cardiovascular imaging. J Am Soc Echocardiogr 28: 1-39.
17. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, et al. (2016) Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An Update from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr 29: 277-314.
18. Kahan T, Bergfeldt L (2005) Left ventricular hypertrophy in hypertension: Its arrhythmogenic potential. Heart 91: 250-256.
19. de Simone G, Pasanisi F, Contaldo F (2001) Link of nonhemodynamic factors to hemodynamic determinants of left ventricular hypertrophy. Hypertension 38: 13-18.
20. Shi H, Chu H, LV Z, Qi G, Guo J, et al. (2017) Association of white blood cell counts with left ventricular mass index in hypertensive patients undergoing anti-hypertensive drug therapy. Exp Ther Med 13: 1566-1571.
21. Wang X, Zhang G, Jiang X, Zhu H, Lu Z, et al. (2014) Neutrophil to lymphocyte ratio in relation to risk of all-cause mortality and cardiovascular events among patients undergoing angiography or cardiac revascularization: A meta-analysis of observational studies. Atherosclerosis 234: 206-213.
22. Uthamalingam S, Patvardhan EA, Subramanian S, Ahmed W, Martin W, et al. (2011) Utility of the neutrophil to lymphocyte ratio in predicting long-term outcomes in acute decompensated heart failure. Am J Cardiol 107: 433-438.
23. Avci A, Elnur A, Göksel A, Serdar F, Servet I, et al. (2014) The relationship between neutrophil/lymphocyte ratio and calcific aortic stenosis. Echocardiography 31: 1031-1035.
24. Roselló-Lletí E, Rivera M, Martínez-Dolz L, González Juanatey JR, Cortés R, et al. (2009) Inflammatory activation and left ventricular mass in essential hypertension. Am J Hypertens 22: 444-450.
25. Salles GF, Fiszman R, Cardoso CR, Muxfeldt ES (2007) Relation of left ventricular hypertrophy with systemic inflammation and endothelial damage in resistant hypertension. Hypertension 50: 723-728.
26. Ruilope LM, Schmieder RE (2008) Left ventricular hypertrophy and clinical outcome in hypertensive patients. Am J Hypertens 21: 500-508.
27. Cai JY, Zhai GL, Gao W, Zhu L, Li Y (2008) A study of the relationship between remodeling of left ventricle and endothelial injury and pro-inflammatory mediators in different stages of essential hypertension. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue 20: 743-745.
28. Leibowitz D, Planer D, Ben-Ivgi F, Weiss AT, Bursztyn M (2005) Tumor necrosis factor and interleukin-6 levels in hypertensive patients with and without left ventricular hypertrophy. Blood Press 14: 21-24.
29. Tsoy LG, Polupanov AG, Sabirov IS, Zalova TB, Rysmatova FT (2018) Predictors of left ventricular hypertrophy development in patients with essential hypertension: role of pro- and anti-inflammatory cytokines. Heart, Vessels and Transplantation 2: 97-105.
30. Ma F, Feng J, Zhang C, Li Y, Qi G, et al. (2014) The requirement of CD8+ T Cells to initiate and augment acute cardiac inflammatory response to high blood pressure. J Immunol 192: 3365-3373.

31. Demir M (2013) The relationship between neutrophil lymphocyte ratio and non-dipper hypertension. Clinical and Experimental Hypertension 35: 570-573.

32. Sun x, Luo L, Zhao X, Ye P, Du R (2017) The neutrophil-to-lymphocyte ratio on admission is a good predictor for all-cause mortality in hypertensive patients over 80 years of age. BMC Cardiovascular Disorders 17: 167.

33. Massberg S, Grahl L, von Bruehl ML, Manukyan D, Pfeiler S, et al. (2010) Reciprocal coupling of coagulation and innate immunity via neutrophil serine proteases. Nat Med 16: 887-896.

34. Projahn D, Koenen RR (2012) Platelets: Key players in vascular inflammation. J Leukoc Biol 92: 1167-1175.

35. Nording HM, Seizer P, Langer HF (2015) Platelets in inflammation and atherogenesis. Front Immunol 6: 98.

36. N Bayrakci, N Ozkayar, F Akyel, I Ates, S Akyel, et al. (2015) The platelet-to-lymphocyte ratio as an inflammation marker in non-dipper hypertensive patients. Hippokratia 19: 114-118.

37. Sunbul M, Gerin F, Durmus E, Kivrak T, Sari I, et al. (2014) Neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with dipper versus non-dipper hypertension. Clin EXP Hypertens 36: 217-221.

38. Malmqvist K, Walle´n HN, Held C, Kahan T (2002) Soluble cell adhesion molecules in hypertensive concentric left ventricular hypertrophy. J Hypertens 20: 1563-1569.

39. López B, González A, Lasarte JJ, Sarobe P, Borrás F, et al. (2005) Is plasma cardiotrophin-1 a marker of hypertensive heart disease? J Hypertens 23: 625-632.

40. Yokoyama T, Nakano M, Bednarczyk JL, McIntyre BW, Entman M, et al. (1997) Tumor necrosis factor-α provokes a hypertrophic growth response in adult cardiac myocytes. Circulation 95: 1247-1252.

41. Alfakih K, Reid S, Hall A, Sivananthan MU (2006) The assessment of left ventricular hypertrophy in hypertension. J Hypertens 4: 1223-1230.

42. Lang RM, Badano LP, Tsang W, Adams DH, Agricola E, et al. (2012) EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr 25: 3-46.