THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Neutrophil Gelatinase-Associated Lipocalin Level Can Predict Early Organ Damage in Primary Hypertensive Patients: A Pilot Study

ABSTRACT

Background: Early detection and treatment of complicated arterial hypertension will prevent its effect on the target organs. In line with this purpose, we aimed to reveal the prediction capability of neutrophil gelatinase-associated lipocalin to complicated hypertension.

Methods: In total, 46 patients with hypertension and 21 healthy volunteers were included in the study. Left ventricle morphology and geometry, as systolic and diastolic functions, were analyzed. Global longitudinal strain was measured from recorded apical 3-chamber views. An ophthalmic examination was performed to investigate the presence of retinopathy in individuals with hypertension. In addition, plasma neutrophil gelatinase-associated lipocalin values were evaluated via the method of the enzyme-linked immunosorbent assay.

Results: Both neutrophil gelatinase-associated lipocalin levels and global longitudinal strain percentages were statistically significant between the groups with diastolic dysfunction and the groups without diastolic dysfunction. Complicated hypertension was detected in 42 patients. Here, it was found that the neutrophil gelatinase-associated lipocalin level of 144.3 ng/mL predicted complicated hypertension with 0.872 sensitivity and 0.65 specificity values.

Conclusion: Analyzing neutrophil gelatinase-associated lipocalin levels in patients with hypertension in routine practice can easily and practically detect complicated hypertension patients earlier.

Keywords: Hypertension, early organ damage, diastolic dysfunction, neutrophil gelatinase-associated lipocalin, global longitudinal strain

ORIGINAL INVESTIGATION

INTRODUCTION

Arterial hypertension (HT) is considered the most widespread chronic condition seen among cardiovascular diseases. The presence of early organ damage in HT cases indicates a poor prognosis. It has been shown that early organ damage can be prevented with early diagnosis and treatment.[1] In addition, high blood pressure (BP) levels lead to complex findings in the cardiovascular system, such as left ventricular (LV) hypertrophy, ischemic heart disease, conduction abnormalities, and systolic or diastolic heart failure.[2] Since LV function and dynamics can be evaluated by measuring global longitudinal strain (GLS) via speckle tracking echocardiography, it has been shown that GLS is very useful for subclinical changes in the myocardium by being a more robust parameter than LV ejection fraction.[3,4] Uncontrolled and longstanding high BP affects ocular system circulation and retinal microvascular pathologies.[5,6] In addition, systemic HT causes progressive renal damage.[7] Hypertensive renal injury is defined as a renal impairment that originates or accelerates with the effect of systemic BP increase.[7]

Neutrophil gelatinase-associated lipocalin (NGAL) is a 25 kDa glycoprotein containing 178 amino acids and found in neutrophil granules. Neutrophil gelatinase-associated lipocalin is an essential mediator in vascular remodeling and atherosclerotic plaque instability.[8] Moreover, NGAL has been determined to be a

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Received: January 28, 2023
Accepted: April 18, 2023
Available Online Date: May 25, 2023

Cite this article as: Nurkoç SG, Ünlü S, Şen B, Tefon Arıbaş B, Reisoğlu MH, Şahinarslan A. Neutrophil gelatinase-associated lipocalin level can predict early organ damage in primary hypertensive patients: A pilot study. *Anatol J Cardiol.* 2023;27(9):513-518.

DOI:10.14744/AnatolJCardiol.2023.2991

precise indicator of renal impairment as it rapidly increases after renal damage.

Vascular remodeling and atherosclerosis are the initial forms of early organ damage caused by HT before cardiac, renal, and ocular symptoms occur.

A practical and feasible evaluation strategy that can early reveal the effects of HT on the target organs in the initial period is not yet available. For this purpose, we examined to what extent NGAL, as a practical and applicable biomarker, can predict asymptomatic organ damage in patients with HT.

METHODS

Selection Criteria for Patients

This pilot study encompassed patients aged 18-70 years with high BP values and newly diagnosed stage two or two antihypertensive treatment healthy volunteers aged 18-70 years with normal ejection fraction. Patients with a record of diabetes mellitus, cerebrovascular disease, cardiac insufficiency, functional abnormality of myocardium segments, obesity body mass index (BMI > 30), secondary HT, history of coronary artery disease, arrhythmia or conduction abnormality, chronic renal failure, pregnancy, liver disease, chronic inflammatory diseases, moderate-to-severe valve disease, and patients with lousy image quality were excluded from the study. In total, 46 patients with HT (19 men, 27 women) and 21 healthy volunteers (10 men, 11 women) were included. After resting for at least 10 minutes, they underwent a test of BP calculated in the supine position by the same person with the appropriate sleeve thickness and manual device from both arms based on Korotkoff phase I and phase V sounds. The mean BP values of the patients were recorded by measuring the BP at three separate visits. Hypertension diagnosis was confirmed by ambulatory BP monitoring and excluding white coat HT in newly diagnosed patients.

Biochemical and Laboratory Analysis

Subsequent to receiving blood samples from each patient, they were subjected to the process of centrifuge at 5000 rpm for 5 minutes, while plasma samples were taken into Eppendorf tubes with the help of a micropipette and stored in a -80 °C cooler until the test day. Plasma sample NGAL kits were studied with Micro Enzyme-Linked Immunosorbent Assay (ELISA; Sunredbio Brand Shanghai, China). The plasma level was measured as ng/mL using ELISA. The formula of modification of diet in renal disease was used so as to measure the glomerular filtration rate (GFR) by applying plasma creatinine. Patients with low GFR values were excluded from the study.

HIGHLIGHTS

- Early diagnosis of organ damage and taking early measures for the causes can prevent complications that may occur.
- Can neutrophil gelatinase-associated lipocalin (NGAL) detect organ damage early?
- Can NGAL change treatment strategy in patients with early organ damage?

Echocardiographic and Electrocardiographic Evaluation

Patients diagnosed with HT underwent 12 lead electrocardiography (ECG) before transthoracic echocardiography. Those with LV hypertrophy findings according to Sokolow-Lyon or Cornell criteria were noted. The patients were examined with Philips Affinity 70 (Philips Medical Systems) brand echocardiography device by lying on the left supine position in the standard echocardiography examination. Echocardiographic examinations were conducted by the same expert during midday in order to eliminate the effect of circadian variations on diastolic abnormality. All echocardiographic images were recorded. Measurements and echocardiographic evaluations were performed and interpreted based on the guidelines declared by the American Society of Echocardiography (ASE). Left ventricle mass index (LVMI) was calculated according to the formula suggested by ASE. Left ventricle mass index $\geq$ 95 g/m^2 in women and $\geq$115 g/m^2 in men was considered LV hypertrophy.[9]

Evaluation of Diastolic Functions

Mitral valve velocity traces were measured by obtaining the apical 4-chamber view with a 1-3 mm sample volume placed on the mitral leaf ends with pulsed wave (PW) Doppler, along with recording were recording findings regarding peak early filling (E wave), late diastolic filling (A wave) velocities, E/A ratio, and early filling deceleration time (DT). Isovolumic relaxation time was recorded with continuous wave Doppler placed on the LV outflow tract. Tissue velocities of the mitral annulus were identified in apical 4-chamber images by placing a sample volume of 2-5 mm in the septal and lateral parts of the mitral annulus. Attention was given to minimal angulation (<20°) between the cardiac movement plan and the ultrasound beam. Records were taken in at least 3 cardiac cycles at a rate of 50-100 mm/s and with the appropriate frame rate. The mean tissue Doppler measurements were taken from the lateral and septal sides of the mitral annulus to evaluate the global LV diastolic function of systolic (S), early diastolic (e'), and late diastolic (a') velocities. American Society of Echocardiography guidelines were used for the classification of diastolic functions.

Global Longitudinal Strain Analysis

Global longitudinal strain measurements of apical 4-, 3-, and 2-chamber views were analyzed on QLAB software (version 9.0, Philips, Netherlands). Left ventricle-focused images with at least 3 cycles and optimal frame rate (40-80 Hz) were used for the GLS analysis. Global longitudinal strain analysis was performed offline with QLAB (version 9.0, Philips, Netherlands) program. Patients who were not eligible for GLS measurement were excluded from the study.

Ophthalmological Examination

Each patient underwent an ophthalmological examination. A 45° non-mydriatic digital camera was used in order to take the retinal photographs centered on the macula and showing the optic disc, the macula, and substantial portions of the temporal vascular arcades subsequent to the dilatation of the pupil using tropicamide phenylephrine eye drops. The severity and staging of hypertensive retinopathy were performed.

Statistical Analysis

Statistical analyses were conducted through SPSS (Statistical Package for Social Sciences, 2014, USA) 23.0 program, as numerical variables were determined as mean ± standard deviation and median [interquartile range]. However, categorical factors were demonstrated by percentage and number. Before analyzing the correlation of continuous numerical variables, we performed a normality analysis for the groups through the Kolmogorov–Smirnov test. We also analyzed the variables related to numerical values via the Student *t*-test for 2 independent groups so as to determine whether parametric test assumptions were met, while the Mann–Whitney *U* test was applied in cases when parametric test assumptions were not met. In addition, we used the chi-squared test in order to assess the differences between the categorical variables, as well as examine the difference between the groups by one-way analysis of variance so as to detect whether parametric test assumptions were met. While Bonferroni correction was performed for post hoc tests, we applied the Kruskal–Wallis test when parametric test assumptions could not be met. The Pearson correlation test was used to examine the connection between the variables. Receiver operating characteristics analysis and area under the curve were used to evaluate the predictive power of NGAL levels to complicated HT diagnosis. The significance level has been determined as $P < .05$.

RESULTS

Demographic characteristics and laboratory values of groups are provided in Table 1. No significant difference was detected with regard to gender distribution, age, and smoking in both groups ($P1 = .620$; $P2 = .360$; $P3 = .080$, respectively). Body mass index was statistically significant between the groups ($P = .010$) (Table 1).

Apart from the use of alpha-blockers, statistically significant differences were obtained regarding the use of drugs between the groups. The use of angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker, and Hydrochlorothiazide was found to be significant between both groups ($P < .001$). In addition, beta blocker use was found to be significant between both groups ($P = .010$). Statistically higher NGAL values were obtained in the hypertensive group ($P = .020$). Retinopathy was not detected in any of the healthy patients, and retinopathy was detected in 4 (8.7%) patients in the hypertensive group ($P = .160$).

Basic Echocardiographic Results of the Patient and Control Groups

The echocardiographic data of the groups are presented in Table 2. Diastolic indices were shown to be significantly different between study groups (Table 2). Global longitudinal strain value was calculated as -18.2 ± 4.8% in the hypertensive group and -23.7 ± 3.2% in the healthy group ($P < .001$). In the hypertensive group, the absolute value of GLS was statistically significantly decreased with regard to the control group ($P < .001$). In addition, GLS and NGAL demonstrated a high correlation ($r = 0.753$, $P < .001$).

Table 1. Demographic Characteristics and Laboratory Values of Groups

Variables	Healthy Group (n = 21)	Hypertensive Group (n = 46)	*P*
Age (year)	50.7 ± 8.9	52.8 ± 7.2	.36
Men (%)	10 (47.6%)	19 (41.3%)	.62
Women (%)	11 (52.4%)	27 (%58.7)	.62
Smoking (%)	3 (14.3%)	16 (%34.8)	.08
BMI (kg/m^2)	25.3 ± 2.6	27.1 ± 2.1	**.01**
Retinopathy (%)	0 (0%)	4 (8.7%)	.16
FBG (fasting blood glucose) (mg/dL)	92.4 ± 12.2	92.9 ± 10.0	.87
HB (g/dL)	14.0 ± 1.6	13.8 ± 1.7	.56
PLT (K/mm^3)	279.5 ± 116.3	285.2 ± 58.4	.83
WBC (K/mm^3)	7.5 ± 1.6	7.3 ± 2.0	.61
Total cholesterol (mg/dL)	184.1 ± 38.8	201.7 ± 35.6	.08
LDL cholesterol (LDL) (mg/dL)	110.9 ± 27.0	124.4 ± 30.8	.07
Triglyceride (mg/dL)	123.5 ± 72.1	154.2 ± 63.9	.10
HDL cholesterol (LDL) (mg/dL)	49.2 ± 13.6	47.6 ± 9.8	.63
NGAL (ng/mL)	148.4 ± 18.5	160.3 ± 19.3	**.02**
GFR (ml/min/m^2)	107.8 ± 11.3	102.3 ± 18.1	.20
ECG hypertrophy finding	0 (0.0%)	5 (10.9)	.11
Systolic BP (mm Hg)	120.2 ± 7.8	146.9 ± 17.2	**< .001**
Diastolic BP (mm Hg)	77.1 ± 4.6	92.1 ± 10.5	**.008**
Women (%)	11 (52.4%)	27 (58.7%)	.62
Men (%)	10 (47.6%)	19 (41.3%)	.62
Smoker (%)	3 (14.3%)	16 (34.8%)	.08
Using ACEI (%)	0 (0.0) %)	25 (54.3)	**< .001**
ARB user (%)	0 (0.0%)	20 (43.5#)	**< .001**
BB user (%)	0 (0.0%)	12 (26.1%)	**.01**
KKB user (%)	0 (0.0)	22 (47.8%)	**< .001**
HCT user (%)	0 (0.0)	37 (80.4%)	**< .001**
Alpha blocker user (%)	0 (0.0%)	1 (2.2%)	.496

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta blocker; BMI, body mass index; BP, blood pressure; CCB, calcium channel blocker; FBG, fasting blood sugar; GFR, glomerular filtration rate; HCT, hydrochlorothiazide; HDL, high density lipoprotein; LDL, low-density lipoprotein; NGAL, neutrophil gelatinase-associated lipocalin; PLT, platelet; WBC, white blood cell.

Change of Parameters According to Diastolic Dysfunction Stage

Global longitudinal strain and NGAL values in the stages of diastolic dysfunction (DDF) are given in Table 3. There was an increase in NGAL value and a decrease in GLS percentage in a corollary manner with the stage of DDF and statistical significance was obtained. The increase in age and systolic BP numerical values increased in correlation with the DDF stage and statistically significant findings were obtained ($P1 < .001$, $P2 = .010$, respectively). Statistically significant results were obtained between DDF stages, GLS, and tissue Doppler parameters. In addition, when relative wall thickness (RWT) and LVMI were evaluated according to the DDF stage, the

Table 2. Echocardiographic Data of Groups

Variables	Healthy Group (n = 21)	Hypertensive Group (n = 46)	*P*
IVS thickness (mm)	9.5 ± 1.5	11.8 ± 1.8	**< .001**
PW thickness (mm)	8.5 ± 1.2	10.6 ± 1.1	**< .001**
LVEDD (mm)	46.0 ± 3.9	46.9 ± 2.9	.37
LVESD (mm)	28.2 ± 3.1	29.5 ± 2.5	.11
DEV (ml)	98.3 ± 20.8	100.3 ± 20.8	.72
SEV (ml)	30.9 ± 6.8	35.9 ± 10.7	**.026**
LV EF (%)	67.3 ± 3.6	65.5 ± 3.2	.06
LV KI (g/m^2)	77.0 ± 16.6	105.6 ± 21.8	**< .001**
E wave velocity (cm/sn)	80.8 ± 21.8	73.5 ± 17.8	.18
A wave velocity (cm/sn)	69.2 ± 20.3	82.9 ± 17.9	**.01**
E/A	1.1 ± 0.2	0.9 ± 0.2	**.002**
e' wave velocity (cm/sn)	10.5 ± 1.7	8.1 ± 1.7	**< .001**
E/e'	8.1 ± 2.5	9.1 ± 1.8	.12
DT (msn)	224.5 ± 38.2	234.1 ± 53.5	.40
IVRT (msn)	85.2 ± 8.8	88.0 ± 11.3	.32
GLS (%)	-23.7 ± 3.2	-18.2 ± 4.8	**< .001**

DEV, diastolic end volume; DT, deceleration time; GLS, global longitudinal strain; IVRT, isovolumic relaxation time; IVS, interventricular septum; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; MI, mass index; PW, posterior wall; SEV, systole end volume.

values obtained from the groups were observed to be significant ($P < .001$, $P < .001$, respectively).

Relationship Between Neutrophil Gelatinase-Associated Lipocalin and End-Organ Damage

Complicated HT was detected in 42 patients in the hypertensive group, including renal end-organ damage in 13 patients and cardiac end-organ damage in 42 patients. It was found that the NGAL level of 144.3 ng/mL predicted complicated HT with 0.872 sensitivity and 0.65 specificity values (Figure 1).

DISCUSSION

This pilot study aims to find an applicable method to show early organ damage in hypertensive patients and be used in our daily practice.

Many functional and morphological changes of LV can be observed in hypertensive patients. In our study, we found significantly lower absolute GLS measurements in hypertensive patients in comparison to healthy individuals. The relationship between different patterns of LV geometry and prognosis has been shown in previous studies. In a survey of the morphological changes in LV and deformation parameters, GLS was found to be lower in patients with LV concentric remodeling and concentric hypertrophy in comparison to patients with typical geometry.[10] We observed a significant difference between the groups in terms of LV geometry.

We observed no statistically significant difference in terms of the presence of retinopathy between the groups. The main reasons for this situation are the assumption that the patients encompassed in the research are newly diagnosed with HT and that their BP values may be well controlled in patients using medication. Another reason is that the time required for the development of retinopathy has not passed in newly diagnosed patients. The lack of a sufficient number of retinopathy patients in this study can account for the lack of statistically significant values. As applied in previous studies, tissue Doppler-based strain and strain rate imaging method was used to investigate early organ damage in patients with HT, and a significant relationship was found between retinopathy and strain values.[11]

Table 3. Variability of Parameters According to the Stage of Diastolic Dysfunction

	Stage 0 DDF	Stage 1 DDF	Stage 2 DDF	*P*
GLS (%)	-24.0 ± 2.7$^{(‡*)}$	-19.4 ± 5.4$^{(*)}$	-16.6 ± 3.5$^{(‡)}$	**< .001**
NGAL (ng/mL)	144.1 ± 16.2$^{(‡*)}$	159.8 ± 17.8$^{(*)}$	163.7 ± 18.6$^{(‡)}$	**.001**
Age (year)	47.4 ± 5.3$^{(*)}$	56.7 ± 8.1$^{(*)}$	51.7 ± 6.7	**< .001**
Diastolic BP (mm Hg)	79.0 ± 5.3	80.6 ± 11.8	82.0 ± 2.0	.58
Systolic BP (mm Hg)	123.1 ± 10.1$^{(‡)}$	134.5 ± 16.9	131.7 ± 16.7$^{(‡)}$	**.01**
EF (%)	67.5 ± 3.4$^{(*)}$	64.6 ± 3.5$^{(*)}$	66.1 ± 3.4	**.01**
IVST (mm)	9.5 ± 1.4$^{(‡*)}$	12.0 ± 1.8$^{(*)}$	11.7 ± 1.8$^{(‡)}$	**< .001**
PW thickness (mm)	8.6 ± 1.2$^{(‡*)}$	10.4 ± 1.1$^{(*)}$	10.7 ± 1.3$^{(‡)}$	**< .001**
E wave velocity, (cm/sn)	89.2 ± 19.8$^{(*)}$	60.6 ± 10.3$^{(‡*)}$	79.5 ± 15.0$^{(‡)}$	**< .001**
e' wave velocity (cm/sn)	11.4 ± 1.2$^{(*)}$	8.2 ± 0.9$^{(*)}$	7.2 ± 1.1$^{(*)}$	**< .001**
A wave velocity (cm/sn)	70.4 ± 21.3$^{(*)}$	88.5 ± 13.8$^{(*)}$	75.8 ± 19.4	**.004**
E/A	1.2 ± 0.1$^{(*)}$	0.69 ± 0.02$^{(*)}$	0.98 ± 0.2$^{(*)}$	**< .001**
E/e'	8.2 ± 2.3$^{(*)}$	7.3 ± 0.9$^{(‡)}$	10.9 ± 0.8$^{(‡*)}$	**< .001**
Deceleration speed (ms)	208.2 ± 27.1$^{(*)}$	280.7 ± 39.2$^{(‡*)}$	198.9 ± 27.7$^{(‡)}$	**< .001**
IVRT (ms)	81.3 ± 4.3$^{(*)}$	99.9±3.7$^{(‡*)}$	78.8 ± 5.7$^{(‡)}$	**< .001**
RWT	0.37 ± 0.05$^{(‡*)}$	0.44±0.05$^{(*)}$	0.42 ± 0.06$^{(‡)}$	**< .001**
LV mass index (g/m^2)	78.6 ± 19.4$^{(‡*)}$	105.3±22.3$^{(*)}$	104.3 ± 21.6$^{(‡)}$	**< .001**

‡, *Shows subgroup analysis. BP, blood pressure; DDF, diastolic dysfunction; EF, ejection fraction; GLS, global longitudinal strain; IVRT, isovolumic relaxation time; IVST, interventricular septum thickness; LV, left ventricular; NGAL, neutrophil gelatinase-associated lipocalin; PW, posterior wall; RWT, relative wall thickness.

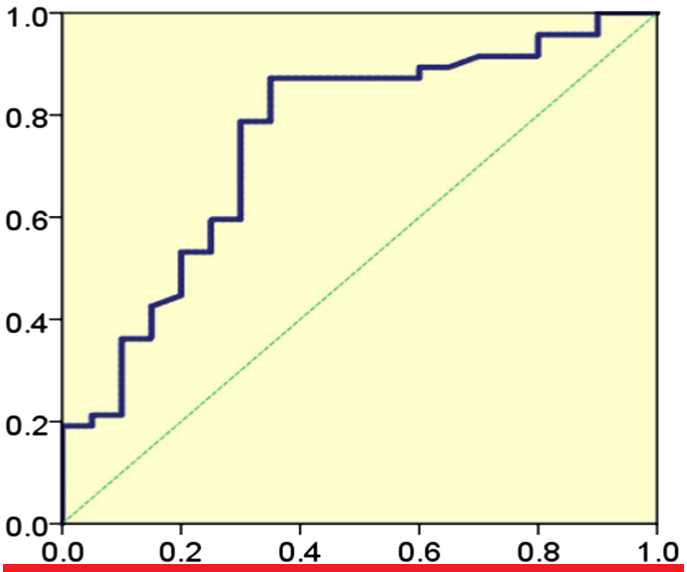

Figure 1. Curve of predicting complications of neutrophil gelatinase-associated lipocalin in hypertensive patients.

One of the early organ damage markers of HT is NGAL. Neutrophil gelatinase-associated lipocalin is a small stable protein synthesized from various epithelial cells, neutrophils, and proximal tubules of the kidney. Initially, it was suggested to be used for diagnostic purposes for infection and some types of adenocarcinoma, while the dramatic increase in urine after kidney injury has made NGAL a biomarker used for kidney damage today.[12] In a study that includes analysis of serum and urine NGAL levels, information about the progression of chronic kidney injury independent of GFR was obtained.[13,14]

In a study investigating the relationship between kidney damage and plasma NGAL, IL18, and urinary retinol-binding protein levels in pediatric patients with HT, serum NGAL levels were detected to be high in patients.[15] A study conducted on pregnant women with HT found a positive relationship between NGAL and serum urea, creatinine values, BP, and proteinuria.[16] In another study, serum NGAL levels were increased in patients with non-dipper HT compared to patients with dipper HT.[17] Increased NGAL values have been determined in patients with LV hypertrophy.[18] In this research, NGAL level was detected to be increased in patients with complicated HT and it was statistically significant. There is a high correlation between NGAL and GLS levels in hypertensive patients. The fact that these 2 parameters were detected to be statistically significant in patients with geometric cardiac dysfunction means that NGAL levels may be effective and adequate in showing early organ damage. Neutrophil gelatinase-associated lipocalin can be a biomarker that can be included in our clinical practice with more comprehensive studies. The results obtained in our study support the relationship between NGAL, GLS levels and DDF. As the stage of DDF increased, an increase in NGAL level and a decrease in the absolute value of GLS were observed. When the groups with normal diastolic functions were checked in terms of DDF, there was a significant difference in NGAL and GLS values. But there was no significant difference between the stage 1 DDF group and the stage 2 DDF group in terms of NGAL and GLS values, which must be caused by the limited number of patients involved in the research. The GLS value suggests a more precise evaluation of LV functions than the wall motion score index and ejection fraction. Many authors argue that the GLS value may be the most appropriate method for the evaluation of global LV systolic function.[19] In addition, although there is not enough study on cardiac dysfunction performed with NGAL, the fact that NGAL values are significantly correlated with GLS absolute values between the groups in this study suggests that it may be a sensitive and early-rising biomarker in showing cardiac dysfunction.

Even if plasma creatinine and GFR values are within normal limits in patients with HT, this does not mean that renal damage does not develop. This is because renal vascular resistance and filtration fraction increase due to arterial HT. Thus, renal blood flow remains normal. Due to this change, glomerular hyperperfusion occurs, and progressive renal function loss may occur as a result of glomerular structural damage.[20] In cases where afferent vasodilation and standard protective renal autoregulatory mechanisms are impaired (such as diabetes and chronic renal failure), the transfer of BP to the microvascular structure and renal damage is more pronounced. In the presence of HT, which is at the limit of autoregulation, vasoconstriction develops in afferent vascular systems, and renal blood flow (glomerular capillary pressure) remains stable. Therefore, the effect of a particular BP (fixed or fluctuating) on the renal microvascular system is related to the amount of increase in BP and renal autoregulation capacity. In general, renal autoregulation range enlargement in HT is a chronically protective mechanism. However, if the upper limit is exceeded, hypertensive damage develops. This damage is more distinctive in the vascular system, especially in the glomerulus. In today's conditions, there is no practical and applicable method to detect asymptomatic organ damage in the early period in patients with HT. In these studies, high NGAL values were obtained in the presence of asymptomatic organ damage in patients with HT. This is because HT triggers inflammatory events such as vascular remodeling and atherosclerosis. Studies are showing that NGAL level increases in parallel with atherosclerosis in remodeling. This suggests that NGAL can demonstrate early organ damage more efficiently and practically in our clinical practice. Our study showed that the NGAL level had high sensitivity (0.872) and specificity (0.65) in detecting complicated HT.

Study Limitations

The low number of single-center and recruited patients in our study can be shown as the main limiting factor. In addition, the insufficient number of complicated hypertensive patients can be considered another limiting reason. However, our patient selection and evaluation methods significantly increased the accuracy of our study.

CONCLUSION

Neutrophil gelatinase-associated lipocalin can be a practical and valuable biomarker that increases early and shows early

organ damage in hypertensive individuals with asymptomatic organ damage. Future studies may clarify the relationship between HT and biomarkers, and methods indicating organ damage and NGAL may lead to changes in our clinical practice. This can guide us in which patients we should treat more aggressively and in which patients we should behave more conservatively. Prospective and more extensive studies are needed in this regard.

Ethics Committee Approval: The research, conveyed based on the Declaration of Good Clinical Practice and the Declaration of Helsinki, was confirmed by the Gazi University Faculty of Medicine Clinical Research Ethics Committee (approval number: 25.09.2017/427). Prior to taking part in the study, all patients were required to sign the informed consent form.

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.Ş.; Design – A.Ş., S.G.N., S.Ü.; Supervision – A.Ş.; Materials – S.G.N., S.Ü, B.Ş.; Data Collection and/or Processing – S.G.N, S.Ü., B.Ş., B.T.A., M.H.R.; Analysis and/or Interpretation – A.Ş., S.G.N., B.T.A., B.Ş.; Literature Review – A.Ş., M.H.R.; Writing – S.G.N, S.Ü, B.Ş, B.T.A.; Critical Review – A.Ş., M.H.R., S.Ü., S.G.N.

Acknowledgments: This article was derived from the thesis of Serdar Gökhan Nurkoç, which was accepted and approved by the Gazi University Faculty of Medicine in 2017. We would like to thank the staff of the Cardiology, Ophthalmology, and Biochemistry Departments of Gazi University Hospital for their support. All authors contributed to the drafting of the manuscript and gave final approval for submission.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: This study was funded by the Directorate of Scientific Research, Gazi University (project decision no; 012018/03). The funding sources had no role in the design of the study; in the collection, analysis, and interpretation of data; or the writing of the manuscript.

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