10.5152/turkjnephrol.2021.4334

Original Article

Turkish Journal of Nephrology

Volume Status, Echocardiographic Findings, and Endothelial Functions in Primary Hypertension Patients Who Do Not Have Kidney Failure

Hasan Görkem[1], Oğuzhan Sıtkı Dizdar[1], Ali Yeşiltepe[2], Engin Dondurmacı[3], Eyüp Özkan[3], Ali İhsan Günal[1]

[1]Department of Internal Medicine, Kayseri City Hospital, Kayseri, Turkey
[2]Department of Intensive Care, Erciyes University School of Medicine, Kayseri, Turkey
[3]Department of Cardiology, Kayseri City Hospital, Kayseri, Turkey

ABSTRACT

Objective: Due to hypertension, the organs may get damaged over time, and with the damage of end-organ, the prognosis of the disease may get negatively affected. The intent of this study is to identify the contribution of hypervolemia to uncontrolled hypertension and how it affects endothelial function and echocardiographic findings in patients who have primary hypertension and who are not suffering from kidney failure.
Methods: This cross-sectional study was performed on patients who were going through a follow-up with a diagnosis of primary hypertension. The patient's volume status was determined with the help of a body composition monitor. The patient's ambulatory blood pressure was monitored for 24 h. Flow-mediated dilation (FMD), carotid intima-media thickness, and echocardiographic evaluation measurements were performed.
Results: The study included a total number of 101 patients out of which 63.4% of patients had an average blood pressure of less than 135/85 mmHg for 24 h, and 51% patients had non-dipper hypertension. The mean of hydration status value of patients was -0.25 ± 0.86 L, and 40.6% ($n = 41$) were identified as hypervolemic. The multiple logistic regression analysis of the factors for uncontrolled hypertension showed that the non-dipper and hypervolemic patients were 2.7 (1.1-6.5) times and 3.3 times, respectively, more likely to have greater mean blood pressure. Regarding mean FMD values and echocardiographic measurements, we failed to find any significant difference after observing both the uncontrolled and controlled hypertension groups. A positive correlation between carotid intima-media thickness and mean systolic arterial blood pressure was determined.
Conclusions: The significance of control of volume in terms of blood pressure control among patients with primary hypertension, who do not have a failure of the kidney, has been shown. However, this study could not establish the significance of volume control concerning endothelial and cardiac functions as opposed to patients who are suffering from kidney failure.
Keywords: Hypertension, hypervolemia, echocardiography, flow-mediated dilation, carotid intima-media thickness

Corresponding author: Hasan Görkem ✉ drhgorkem@gmail.com
Received: March 3, 2020 **Accepted:** January 3, 2021

Cite this article as: Görkem H, Dizdar OS, Yeşiltepe A, Dondurmacı E, Özkan E, Günal İA. Volume status, echocardiographic findings, and endothelial functions in primary hypertension patients who do not have kidney failure. *Turk J Nephrol.* 2021; 30(3): 205-212.

INTRODUCTION

The prevalence of hypertension ranges from 30 to 45% in different studies.[1,2] Hypertension is projected to affect around 1 billion individuals worldwide, and about 13% (7.1 million) of deaths that happen each year are assumed to be related to hypertension.[3] Due to high blood pressure, the organ may get damaged over time, and the existence of end-organ damage negatively affects the diagnosis of the disease. Therefore, early diagnosis and treatment of end-organ damage among individuals who have hypertension gain more importance.

An increase in sympathetic activity and activation of the renin-angiotensin-aldosterone system together with a reduction in renal natriuresis are the main mechanisms that are outlined in the case of hypertension pathogenesis. Ultimately, hypertension will develop as the kidney fails to excrete sodium. Even if vasodilators are used that do not have any effect on the volume status of patients, they may decrease the blood pressure without decreasing the cardiovascular events at the same rate. We have detailed information about the importance of volume status within patients of anuric dialysis. Cardiovascular events are uncommon in patients who are normotensive only by volume control without any usage of antihypertensive drugs compared to the patients who received vasodilator only.[4,5] However, there are a limited number of studies on the importance of volume control among patients who are primary hypertensive and not suffering from kidney failure.[6] In our other study which was prospective interventional and the follow-up period was 1 year, we showed how significant can negative hydration status be in terms of blood pressure control, endothelial, and cardiac functions.[6]

The endothelium has effects on blood pressure, vascular tone, coagulation system, and blood flow.[7] If hypertension is not controlled, it can affect endothelial function and facilitate atherosclerosis adversely.[8] Further, uncontrolled hypertension is known to damage cardiac function (e.g., left ventricular hypertrophy).[9]

This study was aimed to determine hypervolemia contributed to uncontrolled hypertension and its effects on cardiac and endothelial functions among patients who are primary hypertensive without kidney failure.

METHODS

Design and Participants

This is a cross-sectional study performed among patients admitted to the cardiology clinics, nephrology, and internal medicine of a tertiary research hospital between May and December 2015, who were on follow-up with a primary hypertension diagnosis. This study was conducted only on primary hypertension patients. Patients have secondary hypertension, which cause by renal failure, renovascular disease, aldosteronism, pheochromocytoma, etc., were not included in the study. Patients having a glomerular filtration rate (GFR) below 60 mL/min/1.73 m^2, those who are pregnant, having malignant tumors and diabetic, who did not give consent, and who are bedridden or require care were not included in the study. The study protocol (2015/219) was approved by the clinical research ethics committee of Erciyes University. All patients were informed about the study, and a written statement was collected from each one of them.

The whole blood count, creatinine, uric acid, blood urea nitrogen, potassium, sodium, chlorine and glucose levels, height (cm), weight (kg), arterial blood pressure, and medications they use were recorded of each patient. Individuals who had a body mass index below 30 kg/m^2 were considered to be at low risk, while individuals with higher values were considered to be at high risk for hypertension.

At first, the volume status of the patients was determined by a body composition monitor, and 24-h ambulatory blood pressure monitoring of the patients was performed. Then, flow-mediated dilation (FMD), echocardiographic evaluation, and carotid intima-media thickness were performed.

Body Composition Monitoring

With the help of a body composition monitor, first body weight (kg) is measured and then the measurement of height (cm) is also collected and arterial blood pressure (systolic and diastolic mmHg) is also checked, urea distribution volume, hydration status, fatty tissue index, intercellular fluid, total body fluid, non-fatty tissue index, body cell mass were also measured with the body composition monitor from Fresenius Medical Care, GmbH, Germany.

The fluid status was represented by the overhydration (OH) value (L). Measurements were accomplished following the device instructions, and values of OH and others were provided by the body composition monitor software. Depending on the patient's hydration status measurements, those with values over 0 were considered as positively hydrated (hypervolemia), those with values below 0 were assessed as negatively hydrated. The hydration status measurements were decided using the approach described by Moissl et al.[10] The relative hydration status was described as hydration status (OH value)/ extracellular water (ECW).

Ambulatory Blood Pressure Monitoring

Using Mobil-O-Graph NG and Melograph PWA (I.E.M. GmbH, Stolberg, Germany), ambulatory blood pressure monitoring was performed. To record blood pressure measurements every 30 min during the daytime and every 60 min during nighttime, ambulatory blood pressure devices were programmed. The ambulatory blood pressure monitor cuff was positioned on the non-dominant arm. Participants were also provided training to have the arm with the attached cuff static (standing or sitting) at the time when the reading was taken. Uncontrolled hypertension was defined as a mean blood pressure value of 135/85 mmHg or higher. A blood pressure drop of 10% compared with blood pressure readings that are taken during the daytime was called dipper blood pressure, while if the drop is less than 10%, it is termed as "non-dipper blood pressure."

Echocardiographic Evaluation

Two-dimensional, M-mode, and Doppler echocardiographic evaluations were done for each patient for the determination of functional parameters and cardiac structure. Using the modified Simpson's rule, ejection fraction was determined. The left ventricular mass index (LVMI) is determined by the Devereux formula.[11-13] Values below 115 g/m^2 among males and 95 g/m^2

among women were considered normal, while values above were considered as hypertrophic.[1]

Flow-mediated dilation (FMD)

The FMD of the brachial artery was measured using ultrasound. The brachial artery of the left arm was visualized and scanned in a longitudinal section where the best image was obtained. The mean of 3 different measurements of post-flow brachial artery lumen diameter (endothelial-dependent vasodilator response [EDVR]) was calculated and recorded. The expansion in interior width as a result of responsive hyperemia was communicated as the level of the standard vessel distance across (BD) (%FMD). FMD was determined with the formula:

FMD = [(EDVR) − BD)/BD] × 100 equation.

Carotid Intima-Media Thickness

An ultrasound device was used for examination of the carotid arteries. Carotid intima-media thickness was estimated in 3 matched portions of both right and left regular carotid vein, carotid bulb, and interior carotid corridor. Three measurements of the maximal intima-media thickness were averaged in each segment, and the average intima-media thickness was calculated. Fragments with atherosclerotic plaques were not utilized. Patients with carotid intima-media thickness of 0.9 mm or more were considered to be at cardiovascular risk, and those with < 0.9 mm were considered normal.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics 22.0 (IBM SPSS Corp.; Armonk, NY, USA) statistical software. Descriptive statistics provided are unit counts (*n*), percentage (%), and mean ± standard deviation. Normality of the distribution of numerical variables was evaluated with Shapiro–Wilk normality test and Q-Q graphs. Between-group comparisons were made using the independent samples *t*-test for variables with normal distribution. Associations between numerical variables were evaluated with Pearson correlation analysis. Relationships between categorical variables were investigated using the chi-square exact test method. Binary logistic regression analysis with backward elimination method was used to identify the factors in effect over the dependent categorical variable. The level of statistical significance was set as $P < .05$.

RESULTS

A total of 101 patients, followed-up for essential hypertension, were included for the examination. Of the participants, whose mean age was 53.84 ± 9.61 years, 34.7% (*n* = 35) were males and 65.3% (*n* = 66) were females. Every patient was using at least 1 antihypertensive medication, out of which17.8% were using 1, 58.4% were using 2, 21.8% were using 3, and 2% were using 4 antihypertensive medications. A diuretic treatment (hydrochlorothiazide or chlorthalidone) was used by 70.3% (*n* = 71) of the patients. As per the ambulatory blood pressure monitoring results, 63.4% (*n* = 64) had 24-h average blood pressure below 135/85 mmHg, and 51.5% (*n* = 52) had non-dipper hypertension.

The mean FMD value of the patients was 11.71% ± 3.61 (4.59-22). The mean carotid intima-media thickness was 0.81 ± 0.12 (0.52-1.2) mm, where 20.8% (*n* = 21) of the patients were considered to be at cardiovascular risk with carotid intima-media thickness greater than 0.9 mm. In light of the echocardiography results, 42.6% (*n* = 43) of the patients had hypertrophic left ventricle. While the mean hydration status of patients, measured with body composition monitor, was −0.25 ± 0.86 [(−2.1) − 2.5] L, 40.6% (*n* = 41) were identified as positively hydrated (Hypervolemic). It was observed that the patients with mean blood pressure greater than 135/85 mmHg were more likely to present with hypervolemia and non-dipper hypertension (Table 1). The patients with mean blood pressure greater than 135/85 mmHg were observed to have higher hydration status measurement values compared to those with mean blood pressure less than 135/85 mmHg (0.119 ± 0.98 L and −0.475 ± 0.70 L, respectively; *P* = .001). The relative hydration status was significantly higher in patients with mean blood pressure greater than 135/85 mmHg (*P* = .001). As for mean echocardiographic

Table 1. Comparison of Patients According to Mean Blood Pressure

	Mean Blood Pressure		
	<135-85 mmHg, (*n* = 64) *n* (%)	**≥135-85 mmHg, (*n* = 37), *n* (%)**	***P***
Body mass index			
<30 kg/m²	28 (43.8)	15 (40.5)	.836
>30 kg/m²	36 (56.8)	22 (59.5)	
Left ventricle hypertrophy	25 (39.1)	18 (48.6)	.406
Carotid intima-media thickness (mm)			
<0.9	51 (79.7)	29 (78.4)	1.000
>0.9	13 (20.3)	8 (21.6)	
Dipper, non-dipper			
Dipper	37 (57.8)	12 (32.4)	.022
Non-dipper	27 (42.2)	25 (67.6)	
Hydration status			
Hypervolemic	19 (29.7)	22 (59.5)	.006
Normovolemic	45 (70.3)	15 (40.5)	
Diuretic usage			
Receiving	44 (62.0)	27 (66.7)	.822
Not receiving	20 (38.0)	10 (33.3)	

Table 2. Demographic and Other Characteristics of Patients According to Mean Blood Pressure

	Mean Blood Pressure		
	<135/85 mmHg, (*n* = 64)	≥135/85mmHg, (*n* = 37)	*P*
Age (year)	54.5 ± 9.8	52.62 ± 9.3	.335
FMD (%)	12.0 ± 3.7	11.1 ± 3.38	.275
Carotid intima-media thickness (mm)	0.80 ± 0.12	0.84 ± 0.13	.193
Decline in sleep blood pressure (%)	10.40 ± 6.46	7.08 ± 7.65	.023
Body mass index (kg/m^2)	30.92 ± 4.64	31.99 ± 4.93	.281
LVMI (g/m^2)	96.02 ± 27.58	102.24 ± 20.56	.235
Hydration status (L)	−0.475 ± 0.70	0.119 ± 0.98	.001
Relative hydration status (OH/ECW)	−3.284 ± 4.49	0.297 ± 5.45	.001
EF (%)	62.06 ± 5.30	63.81 ± 5.58	.121
Septum thickness (mm)	10.96 ± 1.67	11.25 ± 1.78	.408
Diastolic diameter (mm)	46.17 ± 5.94	47.16 ± 5.61	.413
Systolic diameter (mm)	31.32 ± 5.65	30.80 ± 6.16	.667
Left atrium diameter (mm)	30.67 ± 4.33	31.71 ± 3.49	.215
Aort diameter (mm)	29.58 ± 3.37	30.54 ± 3.41	.174

Data are expressed as the mean ± SD. FMD, flow-mediated dilation; LVMI, left ventricular mass index, EF, ejection fraction, ECW, extracellular water.

estimations and FMD, no critical distinction was seen between the groups (Table 2).

Logistic regression analysis was utilized to decide the relative risks of developing uncontrolled hypertension. Only the variables with a statistically significant association in the simple logistic regression model were included in the multiple logistic regression model. Multiple logistic regression analysis showed that the non-dipper patients were 2.7 (1.1-6.5) times more likely to have higher mean blood pressure compared to dipper patients (P = .028), and hypervolemic patients were 3.3 times more likely than normovolemic patients to have higher mean blood pressure (P = .007) (Table 3). There was no significant difference in LVMI value between dipper and non-dipper patients (97and 99.5 g/m^2, respectively; P = .620). Hypervolemia was more frequent among patients received no diuretic drug (Table 4). Patients on diuretic treatment did not differ significantly from those who did not receive diuretics concerning FMD and echocardiographic measurements (Table 4).

Table 3. Logistic Regression Analysis of Risk Factors for Uncontrolled Hypertension

	Odds Ratio	95% CI	*P*
Univariate Analysis			
Non-dipper, present or not	2.9	1.2-6.7	.015
Hypervolemi, present or not	3.4	1.5-8.1	.004
Diuretic usage, present or not	0.8	0.3-1.9	.655
Gender, male/female	1.8	0.7-4.2	.170
Body mass index, kg/m^2	1.1	0.9-1.1	.279
Age, year	0.9	0.9-1.0	.332
Ejection fraction, %	1.1	0.9-1.1	.122
LVMI, g/m^2	1.0	0.9-1.1	.234
Creatinine, mg/dL	1.4	0.1-17.4	.790
Multivariate Analysis			
Non-dipper, present or not	2.7	1.1-6.5	.028
Hypervolemi, present or not	3.3	1.4-7.9	.007

LVMI, left ventricular mass index.

The characteristics of patients according to volume status are shown in Table 5. Hypervolemic patients had a wider aorta

Table 4. Assessment of Risk Factors According to Diuretic Usage of Patients

	Not Receiving Diuretics (*n* = 30)	Receiving Diuretics (*n* = 71)	*P*
Left ventricle hypertrophy	15 (50.0)	28 (39.4)	.381
Hidration status			
Normovolemic	12 (40.0)	48 (67.6)	.014
Hypervolemic	18 (60.0)	23 (32.4)	
Dipper, non-dipper			
Dipper	16 (53.3)	33 (46.5)	.664
Non-dipper	14 (46.7)	38 (53.5)	
Carotid intima-media thickness (mm)			
<0.9	22 (73.3)	58 (81.7)	.422
>0.9	8 (26.7)	13 (18.3)	
FMD	10.9 ± 2.9	12.1 ± 3.8	.154
EF	63.5 ± 6.1	62.4 ± 5.1	.342

Data are expressed as the mean ± SD or *n* (%).
FMD, flow-mediated dilation; EF, ejection fraction.

Table 5. Characteristics of Patients According to Volume Status

	Hypervolemic (≥0 L), (*n* = 41)	Normovolemic (<0 L), (*n* = 60)	*P*
Age (year)	54.51 ± 11.49	53.38 ± 8.14	.565
FMD (%)	11.06 ± 3.32	12.16 ± 3.75	.133
Carotid intima-media thickness (mm)	0.82 ± 0.13	0.81 ± 0.12	.533
LVMI (g/m^2)	96.37 ± 22.57	99.62 ± 27.13	.529
Glucose (mg/dL)	100.49 ± 14.86	103.07 ± 16.56	.425
Uric acid (mg/dL)	6.07 ± 1.66	5.42 ± 1.32	.075
EF (%)	62.07 ± 5.78	63.03 ± 5.21	.340
Septum thickness (mm)	10.96 ± 1.52	11.14 ± 1.83	.596
Diatolic diameter (mm)	46.30 ± 6.33	46.70 ± 5.49	.738
Left atrium diameter (mm)	30.95 ± 4.38	31.12 ± 3.85	.837
Posterior wall thickness (mm)	11.53 ± 1.67	11.42 ± 1.87	.770
Systolic diameter (mm)	31.11 ± 5.88	31.15 ± 5.83	.971
Aort diameter (mm)	30.79 ± 3.56	29.35 ± 3.19	.037
Mean systolic BP (mmHg)	130.63 ± 15.38	125.32 ± 15.39	.091
Mean diastolic BP (mmHg)	82.00 ± 10.93	78.03 ± 10.44	.069
Percentage decrease in sleep blood pressure (%)	7.27 ± 7.48	10.49 ± 6.51	.024
White blood cell (/µL)	7907 ± 1933	8043 ± 1789	.718
Hemoglobin (g/dL)	14.56 ± 1.73	14.12 ± 1.44	.169
Creatinine (mg/dL)	0.81 ± 0.18	0.75 ± 0.14	.071
BUN (mg/dL)	14.95 ± 3.96	15.43 ± 4.69	.591
Glomerular filtration rate (mL/min/1.73 m^2)	93.79 ± 14.5	93.75 ± 13.9	.987
Sodium (mmol/L)	139 ± 2.68	138 ± 2.48	.064
Potassium(mmol/L)	4.23 ± 0.36	4.26 ± 0.35	.655

Data are expressed as the mean ± SD.
FMD, flow-mediated dilation; LVMI, left ventricular mass index; EF, ejection fraction; ECW, extracellular water; BP, blood pressure; BUN, blood urea nitrogen.

diameter compared to normovolemic patients with a less decline in sleep blood pressure (Table 5). FMD and other echocardiographic finding comparisons did not yield significantly different results. The groups did not differ significantly in terms of laboratory parameters either.

The correlation analysis showed that FMD had a negative correlation with age (r = –0.205, P = .040) and L VESd (r = –0.198, P = .047). The percentage decline in the sleep blood pressure was negatively correlated to both age (r = –0.239, P = .016) and hydration status (r = –0.249, P = .012). Taking the 0.9 mm threshold for carotid intima-media thickness, no significant relationship was determined between uncontrolled hypertension and carotid intima-media thickness. However, the correlation analysis yielded a positive correlation between mean systolic arterial blood pressure and carotid intima-media thickness (r = 0.255, P = .010). A positive correlation was also observed between mean systolic blood pressure and septum diameter (r = 0.207, P = .038).

DISCUSSION

It has been reported that left ventricular hypertrophy, expanded carotid intima-media thickness, and other target organ damages that can develop among hypertensive patients are more strongly correlated with ambulatory blood pressure rather than office blood pressure measurements.[9] Even though hypertension has crucial outcomes, the quantity of patients effectively accomplishing the treatment targets is still low. Different investigations report that the rate of patients attaining goals varies between 27 and 66%.[14,15] Along with the leading factors of low awareness of hypertension and over-consumption of sodium, many factors impact this low success rate and the differences between the success rates of countries. In our investigation, 63.4% of the 101 patients had arrived at their treatment objectives. This generally high achievement pace of our examination contrasting with the clinical literature might be related to the investigation being directed at a tertiary community and the included patients were chosen from a group of patients who were consistently appearing for their subsequent meet-ups.

Also, it ought to be viewed as this is not an epidemiologic investigation and the quantity of patients is lower in contrast with epidemiologic examinations. A strong association has been demonstrated between mean 24-h blood pressure and the risk of death or developing disease due to hypertension.[16] Hence, we decided to utilize a highly standard method, such as ambulatory blood pressure measurement, to research how hypertension was related to volume and its negative effects on the heart and endothelium.

If dialysis patients only received antihypertensive treatment, but not a volume-reducing drug, amelioration in the cardiovascular mortality and LVMI did not occur. On the other hand, when the volume control was established, there was a reduction in LVMI.[4] In another study, patients attaining normotension with volume control had significant amelioration on echocardiography findings.[5] Hypervolemia is one of the most significant variables in expanding LVMI.[17,18] In our examination, there was not a noteworthy difference between the left ventricle mass indices of hypervolemic and normovolemic patients. Just the aorta diameter was more extensive among the hypervolemic patients. Since our participants consisted of patients with normal renal functions and often controlled blood pressure, we believe that hypervolemia had not yet affected the LVMI negatively.

Although bioimpedance device might have important roles in the planning of hypertension treatment, especially diuretic usage, a few studies investigated the use of volume measurement with bioimpedance and appropriate diuretic administration in the treatment of uncontrolled hypertension in patients who did not have kidney failure.[19,20] Taler et al.'s[20] study reported success rates in hypertension treatment to be 56% in the group regulated with bioimpedance device and 33% in the other group. In Smith et al.'s[21] study, patients whose volume control was attained via the help of thoracic impedance had a significantly higher success rate (77%). Sodium consumption has a negative impact on hypertension.[22,23] In our investigation, we established that the patients with mean blood pressure at target values also had favorable volume status, and this volume status was closely associated with diuretic use. In social orders with high sodium consumption, as in Turkey, diuretics might be considered as an aspect of the standard treatment, as shown in this examination.[24] FMD is one of the clinical methods used to evaluate endothelial functions.[25] FMD was significantly lower in hypervolemic dialysis patients.[26] In any case, our investigation is one of the first reports in clinical literature meant to assess the relationship between volume and FMD among essential hypertension patients without kidney failure. We did not find a significant relationship between hypervolemia and FMD.

Hypervolemic kidney failure patients are reported to have a more prominent carotid intima-media thickness,[27] however, we have restricted data on the relationship between carotid intima-media thickness and hypervolemia among essential hypertension patients without kidney failure. We did not identify a significant relationship between hypervolemia and carotid intima-media thickness among essential hypertension patients without kidney failure. Although we found a relationship between hypervolemia and uncontrolled hypertension in our study, its impact on cardiac and endothelial functions was not clear. This condition suggests that this patient group has a different characteristic than kidney failure patients, who are more exposed to hypervolemia and respond more weakly to it. In corresponding with the decrease in GFR in kidney failure patients, impaired renal capacity results in a failure to effectively handle water and salt, leading to fluid overload. The effect of hypervolemia on cardiac or endothelial functions in essential hypertension patients without kidney failure should be checked with planned randomized controlled investigations.

Non-dipper hypertension prevalence changed between 17 and 69% among different hypertensive patient cohorts in various examinations.[28,29] This rate was 51.5% in our investigation. Patients with non-dipper hypertension have a higher target organ damage risk. Non-dipper hypertensive cases have an increased risk of developing left ventricular hypertrophy, heart failure, and cardiovascular diseases regardless of blood pressure control.[30-32] Despite the more hypertrophic left ventricles of the non-dipper hypertension patients compared to dipper hypertension patients, the difference was not statistically significant in our study. The small sample size and the high number of target meeting patients may have contributed to this finding.

The possible causes of non-dipper hypertension are sleep disorders, obstructive sleep apnea, obesity, high salt intake among salt-sensitive individuals, orthostatic hypotension, autonomic dysfunction, chronic kidney disease, diabetic neuropathy, and aging.[1]

Additionally, non-dipper hypertension is likewise demonstrated to be related to melatonin concentration.[3,33] In our examination, the significantly lower decline in sleep blood pressure of hypervolemic patients is significant in demonstrating that hypervolemia may have a role in the development of non-dipper hypertension.

In this study, the most important risk factors for uncontrolled hypertension among primary hypertension patients were determined to be volume overload and the presence of non-dipper hypertension. Patients with volume overload were found to be 3.3 times more likely to have uncontrolled hypertension compared to those without volume overload.

This examination makes significant commitments to the treatment and development of hypertensive patients. The most significant limitations of our investigation were that echocardiographic information was collected by many physicians, the 24-h sodium excretion in urine was not assessed, and its cross-sectional nature.

CONCLUSION

The significance of volume control in terms of blood pressure control among primary hypertension patients who do not have kidney failure has been shown. It was indicated that diuretics should be a part of the routine antihypertensive treatment. However, this study could not demonstrate the significance of volume control with respect to endothelial and cardiac functions within this patient group as opposed to patients suffering from kidney failure. While a difference is expected between primary hypertension patients with and without kidney failure, these results emphasize the need for further randomized controlled studies on this topic with larger patient populations.

Ethics Committee Approval: Ethics committee approval was received from the Ethics Committee of Erciyes University (2015-219).

Informed Consent: Written informed consent was obtained from all participants who participated to this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.I.G.; Design - A.I.G.; Supervision - A.I.G.; Resource - H.G., A.Y., E.D., E.O.; Materials - H.G., A.Y., E.D., E.O.; Data Collection and/or Processing - H.G., A.Y., E.Y.; Analysis and/or Interpretation - H.G., O.S.D.; Literature Search - H.G., A.Y.; Writing - H.G., O.S.D.; Critical Reviews - O.S.D.

Acknowledgments: We are grateful for support of our hospital radiology clinic.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Mancia G, Fagard R, Narkiewicz K, et al. 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*. 2013;31(7):1281-1357. [CrossRef]
2. Nwankwo T, Yoon SS, Burt V, Gu Q. Hypertension among adults in the United States: national Health and Nutrition Examination Survey, 2011-2012. *NCHS Data Brief*. 2013;133(133):1-8.
3. Mathers CSG, Mascarenhas M. *Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks*. Geneva, Switzerland: World Health Organization; 2009.
4. Gunal AI, Kirciman E, Guler M, Yavuzkir M, Celiker H. Should the preservation of residual renal function cost volume overload and its consequence left ventricular hypertrophy in new hemodialysis patients? *Ren Fail*. 2004;26(4):405-409. [CrossRef]
5. Gunal AI, Karaca I, Aygen B, et al. Strict fluid volume control and left ventricular hypertrophy in hypertensive patients on chronic haemodialysis: a cross-sectional study. *J Int Med Res*. 2004;32(1):70-77. [CrossRef]
6. Yeşiltepe A, Dizdar OS, Gorkem H, et al. Maintenance of negative fluid balance can improve endothelial and cardiac functions in primary hypertensive patients. *Clin Exp Hypertens*. 2017;39(6):579-586. [CrossRef]
7. Cooke JP. The endothelium: a new target for therapy. *Vasc Med*. 2000;5(1):49-53. [CrossRef]
8. Li H, Förstermann U. Nitric oxide in pathogenesis of vascular disease. *J Pathol*. 2000;190(3):244-254. [CrossRef]
9. Gaborieau V, Delarche N, Gosse P. Ambulatory blood pressure monitoring versus self-measurement of blood pressure at home: correlation with target organ damage. *J Hypertens*. 2008;26(10):1919-1927. [CrossRef]
10. Moissl UM, Wabel P, Chamney PW, et al. Body fluid volume determination via body composition spectroscopy in health and disease. *Physiol Meas*. 2006;27(9):921-933. [CrossRef]
11. Lang RM, Badano LP, Mor-Avi V, et al. 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*. 2015;28(1):1-39.e14. [CrossRef] 211
12. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr*. 2005;18(12):1440-1463. [CrossRef]
13. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol*. 1986;57(6):450-458. [CrossRef]
14. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA*. 2010;303(20):2043-2050. [CrossRef]
15. Joffres M, Falaschetti E, Gillespie C, et al. Hypertension prevalence,awareness, treatment and control in national surveys from England, the USA and Canada, and correlation with stroke and ischaemic heart disease mortality: a cross-sectional study. *BMJ Open*. 2013;3(8):e003423. [CrossRef]
16. Dolan E, Stanton A, Thijs L, et al. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. *Hypertension*. 2005;46(1):156-161. [CrossRef]
17. Harnett JD, Kent GM, Barre PE, Taylor R, Parfrey PS. Risk factors for the development of left ventricular hypertrophy in a prospectively followed cohort of dialysis patients. *J Am Soc Nephrol*. 1994;4(7):1486-1490. [CrossRef]
18. Mailloux LU, Haley WE. Hypertension in the ESRD patient: pathophysiology, therapy, outcomes, and future directions. *Am J Kidney Dis*. 1998;32(5):705 -719. [CrossRef]
19. Covic A, Voroneanu L, Goldsmith D. Routine bioimpedance-derived volume assessment for all hypertensives: a new paradigm. *Am J Nephrol*. 2014;40(5):434-440. [CrossRef]
20. Taler SJ, Textor SC, Augustine JE. Resistant hypertension: comparing hemodynamic management to specialist care. *Hypertension*. 2002;39(5):982-988. [CrossRef]
21. Smith RD, Levy P, Ferrario CM, Consideration of Noninvasive Hemodynamic Monitoring to Target Reduction of Blood Pressure Levels Study Group. Value of noninvasive hemodynamics to achieve blood pressure control in hypertensive subjects. *Hypertension*. 2006;47(4):771-777. [CrossRef]

22. Elliott P, Stamler J, Nichols R, et al. Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. Intersalt Cooperative Research Group. *BMJ*. 1996;312(7041):1249-1253. [CrossRef]
23. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ*. 2013;346:f1326. [CrossRef]
24. Erdem Y, Arici M, Altun B, et al. The relationship between hypertension and salt intake in Turkish population: SALTURK study. *Blood Press*. 2010;19(5):313-318. [CrossRef]
25. Esper RJ. Interrogando al endotelio. *Rev Argent Cardiol*. 2000;68:429-439.
26. Tang W, Xue T, Lu XH, Luo YJ, Wang T. Factors contributing to formation of edema in volume overloaded continuous ambulatory peritoneal dialysis patients. *Perit Dial Int*. 2011;31(2):160-167. [CrossRef]
27. Demirci MS, Demirci C, Ozdogan O, et al. Relations between malnutrition-inflammation-atherosclerosis and volume status: the usefulness of bioimpedance analysis in peritoneal dialysis patients. *Nephrol Dial Transplant*. 2011;26(5):1708-1716. [CrossRef]
28. Verdecchia P, Schillaci G, Porcellati C. Dippers versus non-dippers. *J Hypertens Suppl*. 1991;9(8):S42-S44.
29. Fujii T, Uzu T, Nishimura M, et al. Circadian rhythm of natriuresis is disturbed in nondipper type of essential hypertension. *Am J Kidney Dis*. 1999;33(1):29-35. [CrossRef]
30. Ingelsson E, Björklund-Bodegård K, Lind L, Arnlöv J, Sundström J. Diurnal blood pressure pattern and risk of congestive heart failure. *JAMA*. 2006;295(24):2859-2866. [CrossRef]
31. Verdecchia P, Schillaci G, Gatteschi C, et al. Blunted nocturnal fall in blood pressure in hypertensive women with future cardiovascular morbid events. *Circulation*. 1993;88(3):986-992. [CrossRef]
32. Fan HQ, Li Y, Thijs L, et al. Prognostic value of isolated nocturnal hypertension on ambulatory measurement in 8711 individuals from 10 populations. *J Hypertens*. 2010;28(10):2036-2045. [CrossRef]
33. Zanchetti A, Bond MG, Hennig M, et al. Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis: principal results of the European Lacidipine Study on Atherosclerosis (ELSA), a randomized, double-blind, long-term trial. *Circulation*. 2002;106(19):2422-2427. [CrossRef]