Original Article

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Arterial Stiffness and Mean Arterial Pressure (MAP) and Their Relationship with Renin and Aldosterone Levels in Primary Hyperparathyroidism

Primer Hiperparatiroidizmde Arteriyel Sertlik ve Ortalama Arteriyel Basınç (MAP) ile Renin ve Aldosteron Düzeyleri Arasındaki İlişki

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ABSTRACT

Objective: Primary hyperparathyroidism (PHPT) is associated with cardiovascular mortality and hypertension. Arterial stiffness is a predictor of cardiovascular events. The aim of this study is to investigate arterial stiffness, and daytime and nighttime mean arterial pressures in patients with PHPT using 24-hour ambulatory blood pressure monitoring (ABPM) and to reveal their relationship with renin, aldosterone, and other biochemical parameters.

Methods: Thirty-five patients with PHPT and 32 healthy control subjects participated. All study participants were fitted with an ABPM device for 24 hours. Renin and aldosterone levels were measured and other necessary biochemical tests were performed. Ambulatory pulse wave velocity (PWV) and augmentation index (AIX) were used to evaluate arterial stiffness.

Results: Mean renin levels were statistically higher in patients than in controls ($p<0.05$). Daytime mean arterial pressure and nighttime mean arterial pressure were higher in the patients than in the control group ($p<0.05$). PWV and AIX of the two groups were statistically similar ($p>0.05$). Daytime and nighttime mean arterial pressures were positively correlated with 25-hydroxy vitamin D level, but not with calcium, parathyroid hormone or

ÖZ

Amaç: Primer hiperparatiroidizm (PHPT), kardiyovasküler mortalite ve hipertansiyon ile ilişkilidir. Arteriyel sertlik, kardiyovasküler olayların bir öngörücüsüdür. Bu çalışmanın amacı, PHPT'li hastalarda 24 saatlik ambulatuvar kan basıncı izlemi (ABPM) yöntemi kullanarak, arteriyel sertliği ve gündüz ve gece ortalama arteriyel basınçlarını araştırmak ve bunların renin, aldosteron ve diğer biyokimyasal parametrelerle ilişkisini ortaya koymaktır.

Yöntemler: Çalışmaya PHPT'li 35 hasta ve 32 sağlıklı kontrol katıldı. Tüm çalışma katılımcılarına 24 saatlik ABPM cihazı takıldı. Renin ve aldosteron seviyeleri ölçüldü ve diğer gerekli biyokimyasal testler yapıldı. Arteriyel sertliği değerlendirmek için nabız dalga hızı (PWV) ve augmentasyon indeksi (AIX) kullanıldı.

Bulgular: Hastaların ortalama renin seviyeleri kontrol grubuna göre anlamlı olarak daha yüksekti ($p<0,05$). Hastaların gündüz ve gece ortalama arteriyel basınçları kontrol grubundan anlamlı olarak daha yüksekti ($p<0,05$). İki grubun PWV ve AIX sonuçları arasında istatistiksel olarak bir fark saptanmadı ($p>0,05$). Gündüz ve gece ortalama arter basınçları 25-hidroksi D vitamini seviyesiyle pozitif korelasyon gösterdi, ancak kalsiyum, paratiroid hormonu veya

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ABSTRACT

renin, aldosterone levels. Five patients were newly diagnosed with hypertension based on ABPM.

Conclusion: Our study shows that arterial stiffness is not elevated in PHPT patients at low cardiovascular risk, as shown by ABPM. PHPT is associated with increased mean arterial pressure and increased renin levels. ABPM may detect hypertension early in PHPT. The finding of a positive correlation of 25-hydroxy vitamin D level with mean arterial pressure in PHPT needs to be supported by further studies.

Keywords: Primary hyperparathyroidism, arterial stiffness, pulse wave velocity (PWV), augmentation index (AIX), renin, aldosterone, mean arterial pressure (MAP)

ÖZ

renin, aldosteron seviyeleriyle anlamlı korelasyon göstermedi. Beş hastaya ABPM'ye göre yeni hipertansiyon tanısı konuldu.

Sonuç: Çalışmamız, düşük kardiyovasküler riske sahip olan PHPT hastalarında ABPM ile saptanan arteriyel sertliğin yüksek olmadığını göstermektedir. PHPT, artmış ortalama arter basıncı ve artmış renin seviyeleri ile ilişkilidir. ABPM, PHPT'de hipertansiyonu erken tespit edebilir. PHPT'de 25-hidroksi D vitamini seviyesi ile ortalama arter basıncı arasındaki pozitif korelasyonun daha fazla çalışma ile desteklenmesi gerekmektedir.

Anahtar Kelimeler: Primer hiperparatiroidizm, arteriyel sertlik, nabız dalga hızı (PWV), augmentasyon indeksi (AIX), renin, aldosteron, ortalama arter basıncı (MAP)

Introduction

Primary hyperparathyroidism (PHPT) is associated with hypertension (HT) and cardiovascular disease (1). There are several studies investigating the effects of parathyroid hormone (PTH) on vascular function, such as vascular reactivity, endothelial cell and vascular smooth muscle cell function, and large vessel compliance (1-4). Arterial stiffness (AS) is a marker of increased cardiovascular disease risk, including myocardial infarction, heart failure, all-cause mortality, stroke and kidney disease (5,6). It is known that pulse wave velocity (PWV) can be used to assess AS, and augmentation index (AIX) is an indicator of AS that can be influenced by hemodynamics and ventricular ejection (7). Twenty-four-hour ambulatory blood pressure monitoring (ABPM) is a non-invasive method to detect arterial changes associated with cardiovascular risk (8). With the advancement of technology, ABPM can be used to perform pulse wave analysis in addition to blood pressure measurement (9). Vascular parameters such as PWV and AIX can be measured in this way (9). Another parameter that can be measured with ABPM is ambulatory pulse pressure, which is known to be associated with AS and cardiovascular outcomes (10). Although AS is measured by different methods in studies, it was found to be elevated in PHPT, even in mild cases (1-4,11). Factors such as diabetes, hyperlipidemia, age, gender, smoking, and HT are known to influence AS (1,12-16). Most studies in the literature have included hypertensive patients with PHPT (17). The aim of this study is to investigate AS and mean arterial pressure (MAP) in patients with PHPT who are at low cardiovascular risk (patients without diabetes, HT, hyperlipidemia and smoking history) using 24-hour ABPM and to reveal their relationship with the levels of renin, aldosterone, calcium (Ca), PTH, phosphorus (P) and 25-hydroxyvitamin D (25OHD).

Methods

This study was conducted by the Department of Endocrinology and Metabolic Diseases and Internal Medicine of the University of Health Sciences Türkiye, Antalya Training and Research Hospital between December 2020 and March 2022. The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Antalya Training and Research Hospital (date: 26/11/2020, number: 18/11) and written informed consent was obtained from all patients. The report followed the Declaration of Helsinki. The study was conducted on newly diagnosed PHPT patients aged 18-75 years and a control group consisting of healthy volunteers. Patients with secondary hyperparathyroidism, diabetes, HT, hyperlipidemia, morbid obesity, coronary heart disease, cerebrovascular disease, primary hyperaldosteronism, congestive heart failure, liver disease, kidney disease or diseases that cause secondary HT (hypothyroidism, hyperthyroidism, congenital adrenal hyperplasia, pheochromocytoma), patients with a history of thyroid or parathyroid surgery, patients who smoke, patients with a 24-hour urinary Ca of less than 100 mg/day and patients taking medications (antihypertensives, diuretics, oral Ca preparations, lithium, etc.) that affect the renin-angiotensin-aldosterone system (RAAS) or Ca and PTH levels were excluded from the study. Thirty-five newly diagnosed PHPT patients and 32 healthy controls who did not smoke, had no medical conditions and were not taking any medications participated in the study, and data from a total of 67 subjects were analysed. The subjects' weight and height were measured, and after a 5-minute rest, blood pressure was measured manually twice. No HT was detected during the manual measurements (blood pressure ≤140/90).

Laboratory Analysis

Blood samples from the entire study group were collected after at least 8 hours of fasting. From the blood samples collected, PTH, Ca, P, magnesium, blood urea nitrogen, creatinine, 25OHD, albumin, total protein, thyroid stimulating hormone (TSH), fasting blood glucose (FBG), total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride (TG) levels were measured in the laboratory of our hospital. In addition, venous blood samples were simultaneously taken from the patients to determine renin and aldosterone levels. These venous blood samples were centrifuged at 3500 rpm for 10 minutes, and the serums were separated and stored in 1.5-mL lidded Eppendorf tubes at -80 °C for later analysis. The separated serums of all subjects were thawed at room temperature on the study day to determine renin and aldosterone levels. To exclude familial

hypocalciuric hypercalcemia in the patients, 24-hour urinary Ca levels were examined. Renin levels in human serum (LDN immunoassay and services, Nordhorn, Germany) were analyzed with commercial ELISA kits (intraassay coefficient of variation <5%, interassay coefficient of variation <7%, detection range: 0.8-128 pg/mL, sensitivity: 0.8 pg/mL). Aldosterone levels in human serum (DiaMetra, Spello, Italy) were analyzed using commercial ELISA kits (intraassay <10%, interassay <10%, detection range: 86-1520 pg/mL, sensitivity: 80 pg/mL.

Analysis of 24-hour Ambulatory BP Monitoring

All participants in the study were fitted with an ABPM device for 24 hours in the nephrology clinic. All measurements were performed with the Mobil-O-Graph 24-h PWA monitor (I.E.M. Industrielle Entwicklung Medizintechnik und Vertriebsgesellschaft mbH, Stolberg, Germany). This device can be used to perform pulse wave analysis as well as central aortic and brachial BP measurements. A cuff size was chosen that was suitable for the arm of all patients. The device was programmed to measure BP every 30 minutes during the day and once per hour at night during sleep. The following patient values were recorded with ambulatory monitoring: Daytime systolic BP (SBP) and diastolic BP (DBP), and MAP; nighttime SBP, DBP, and MAP, brachial artery PWV, pulse pressure and AIX. PWV and AIX were used to assess AS. Ambulatory HT was identified as 24-hour mean BP ≥130/80 mmHg (18).

Statistical Analysis

Categorical variables were given with frequency (n) and percentage (%). The relationship between categorical variables was examined with the Pearson chi-square test and the Fisher's exact test. The assumption of normal distribution was checked with the Shapiro-Wilk test. Normally distributed continuous variables were presented as mean ± standard deviation and non-distributed ones as median (interquartile range: 25^{th}-75^{th} percentile). The Mann-Whitney U test and the Independent t-test were used to compare continuous variables according to study groups. The Spearman correlation test was performed to determine the relationship between laboratory parameters and ambulatory results of the patients. Data were analyzed with the IBM SPSS 23.0 package program (IBM Corp Armonk, NY). P-values less than 0.05 were considered statistically significant.

Results

The general characteristics and laboratory parameters of the patient and control groups are shown in Table 1. The mean age of the patient group was higher than that of the control group. The FBG (p=0.002), TG (p=0.001) and TSH (p=0.012) levels

Table 1. General characteristics and laboratory parameters of the control and patient groups

Variables	Control (n=32)	Patient (n=35)	p
Age (years)	47.31±11.13	55.91±15.57	**0.012**
Gender			
Female	20 (62.5)	27 (77.1)	0.191
Male	12 (37.5)	8 (22.9)	
BMI (kg/m²)	27.39±3.42	28.86±5.51	0.192
FBG (mg/dL)	88 (83.5-90)	91 (87-95)	**0.002**
Total-C (mg/dL)	205.44±36.74	211.97±43.35	0.510
LDL-C (mg/dL)	128.16±30.72	121.75±33.13	0.416
TG (mg/dL)	101.5 (78.5-136.5)	152 (113-210)	**0.001**
HDL-C (mg/dL)	54.06±11.93	60.06±14.65	0.072
Creatinine (mg/dL)	0.89±0.11	0.88±0.16	0.726
GFR (mL/min./1.73 m²)	86.25±12.99	80.14±21.54	0.161
Ca (mg/dL)	9.67±0.41	11.27±1.92	**<0.001**
P (mg/dL)	3.4±0.49	2.6±0.51	**<0.001**
25OHD (ug/L)	16.89 (9.43-26.5)	18.32 (14.47-26.27)	0.429
Magnesium (mg/dL)	2.1 (2-2.2)	2.1 (2-2.3)	0.390
PTH (ng/L)	43 (34-54)	136 (84-181)	**<0.001**
TSH (uIU/mL)	1.92±0.59	2.43±0.99	**0.012**
Renin (pg/mL)	5.51 (3.98-14.91)	14.24 (5.7-30.37)	**0.023**
Aldosterone (pg/mL)	81.34 (42.23-176.86)	51.49 (30.9-120.12)	0.082
Urine Ca (mg/day)	-	252 (150-380)	

Results are given as mean ± standard deviation, median (interquartile range), or n (%). Mann-Whitney U test, Independent t-test, Pearson chi-square test, Fisher's exact test. BMI: Body mass index, FBG: Fasting blood glucose, Total-C: Total cholesterol, LDL-C: LDL cholesterol, TG: Triglyceride, HDL-C: HDL Cholesterol, GFR: Glomerular filtration rate, 25OHD: 25-hydroxyvitamin D, TSH: Thyroid stimulating hormone, Ca: Calcium, P: Phosphorus, PTH: Parathormone

of the patients were higher than those of the control group. The median renin level of PHPT patients was statistically higher than that of the control group (p=0.023). After adjustment for age, the significance of the parameters TSH (p=0.060), renin (p=0.263) and P (p=0.477) levels disappeared. The results of the participants' ABPM are shown in Table 2. It was found that the daytime MAP, nighttime MAP and nighttime SBP of the patients were significantly higher than those of the control subjects (p=0.012, p=0.003 and p=0.025, respectively). Pulse pressure was increased in PHPT compared to controls (p=0.033). The PWV and AIX of the two groups were not statistically different. After adjusting for age, daytime MAP (p=0.026) and nighttime MAP (p=0.010) were still significantly different between the groups. However nighttime SBP (p=0.064) and pulse pressure (p=0.128) did not differ significantly between groups. There was a positive correlation between nighttime MAP and daytime MAP with 25OHD levels (r=0.410; p=0.014 and r=0.392; p=0.020, respectively). There was no correlation between MAP and Ca, P or PTH levels. The results of the correlation analysis are shown in Table 3. Patients diagnosed with HT were not included in our study. Manual BP measurements were performed twice before ABPM, and patients were confirmed as normotensive with blood pressure measurements and then included in the study. However, in our study, 5 patients were diagnosed with HT using the 24-hour ABPM method (18). In the analysis performed by removing these 5 patients; the age (p=0.051), gender (p=0.189) and BMI (p=0.239) were similar between the groups. Renin levels were higher in patients than controls (p=0.019) (Table 4).

Table 2. Ambulatory results of the control and patient groups

Variables	Control (n=32)	Patient (n=35)	p
Daytime SBP (mmHg)	118.5 (113-128.5)	120 (114-125)	0.451
Daytime DBP (mmHg)	77.5 (70-82)	74 (70-82)	0.985
Daytime MAP (mmHg)	91.5 (83.8-96.1)	97 (90-103)	**0.012**
Nighttime SBP (mmHg)	110.5 (102.5-116)	115 (112-121)	**0.025**
Nighttime DBP (mmHg)	66.5 (62-76)	71 (64-78)	0.336
Nighttime MAP (mmHg)	85 (77.83-90)	92 (86-96)	**0.003**
Pulse pressure (mmHg)	41 (34.5-46)	46 (39-52)	**0.033**
PWV (m/s)	6.5 (5.7-7.05)	6.2 (4.8-7.6)	0.459
AIX (%)	24.13±10.48	25.51±6.22	0.519

Results are given as mean ± standard deviation or median (interquartile range). Mann-Whitney U test, Independent t-test. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, PWV: Pulse wave velocity, AIX: Augmentation index

Table 3. Correlation between laboratory findings and the results of ambulatory blood pressure monitoring in the patient group (n=35) (suppl)

Variables		Daytime SBP (mmHg)	Daytime DBP (mmHg)	Daytime MAP (mmHg)	Nighttime SBP (mmHg)	Nighttime DBP (mmHg)	Nighttime MAP (mmHg)	Pulse pressure (mmHg)	PWV (m/s)	AIX (%)
FBG (mg/dL)	r	0.087	0.065	0.102	0.202	0.156	0.201	-0.099	-0.003	0.183
	p	0.617	0.713	0.559	0.244	0.372	0.247	0.570	0.988	0.293
TG (mg/dL)	r	-0.118	0.129	0.008	-0.213	-0.028	-0.138	-0.169	-0.289	-0.102
	p	0.499	0.461	0.962	0.219	0.872	0.429	0.333	0.092	0.559
Ca (mg/dL)	r	-0.171	-0.029	-0.107	-0.162	-0.150	-0.176	-0.133	-0.238	-0.324
	p	0.326	0.869	0.541	0.352	0.389	0.312	0.448	0.169	0.057
P (mg/dL)	r	-0.010	-0.052	-0.015	-0.047	0.045	0.021	-0.045	0.068	0.199
	p	0.955	0.765	0.934	0.791	0.797	0.907	0.797	0.696	0.252
25OHD (ug/L)	r	0.400	0.282	0.392	0.365	0.384	0.410	0.152	0.550	0.367
	p	**0.017**	0.100	**0.020**	**0.031**	**0.023**	**0.014**	0.384	**0.001**	**0.030**
PTH (ng/L)	r	-0.156	-0.056	-0.173	-0.224	-0.183	-0.162	-0.104	-0.293	-0.524
	p	0.371	0.748	0.320	0.196	0.293	0.353	0.551	0.087	**0.001**
Renin (pg/mL)	r	-0.219	-0.234	-0.256	-0.336	-0.221	-0.293	-0.330	-0.323	-0.378
	p	0.207	0.177	0.138	0.049	0.203	0.088	0.053	0.059	**0.025**

Spearman correlation test. FBG: Fasting blood glucose, Total-C: Total cholesterol, LDL-C: LDL cholesterol, TG: Triglyceride, HDL-C: HDL cholesterol, GFR: Glomerular filtration rate, 25OHD: 25-hydroxyvitamin D, TSH: Thyroid stimulating hormone, Ca: Calcium, P: Phosphorus, PTH: Parathormone, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, PWV: Pulse wave velocity, AIX: Augmentation index

In ambulatory measurement results; there were no significant differences in PWV, AIX and pulse pressure and daytime MAP (p=0.033) and nighttime MAP (p=0.017) were higher in the patients compared to control group (Table 5).

Discussion

Patients with PHPT have an increased risk of death due to cardiovascular disease (19,20). AS reflects ageing of the cardiovascular system and loss of elastic properties of the arterial wall (21). AS has an independent predictive value for cardiovascular disease morbidity and mortality (21). Studies in the general population show an association between PTH and AS (22,23). A meta-analysis shows elevated AS even with mild PHPT and a significant reduction in AS after parathyroidectomy (21). Ambulatory PWV and AIX are simple and non-invasive measures of AS. Of the methods used to measure AS, they are closely related to cardiovascular structural changes such as atherosclerosis and mortality (24). A study by Schillaci et al. (2) found that PWV was higher in patients with PHPT than in

Table 4. Laboratory findings of control and patient groups after excluding hypertensive patients

Variables	Control (n=32)	Patients (n=30)	p
Age (years)	47.31±11.13	51.85±12.17	0.051
Gender			
Female	20 (62.5)	23 (76.6)	0.189
Male	12 (37.5)	7 (23.3)	
BMI (kg/m²)	27.39±3.42	27.46±4.25	0.239
FBG (mg/dL)	88 (83.5-90)	91 (85.25-95.00)	**0.015**
Total-C (mg/dL)	205.44±36.74	212.37±48.25	0.544
LDL-C (mg/dL)	128.16±30.72	121.52±35.80	0.459
TG (mg/dL)	101.5 (78.5-136.5)	164.0 (106.3-207.5)	**0.003**
HDL-C (mg/dL)	54.06±11.93	60.70±15.58	0.076
Creatinine (mg/dL)	0.89±0.11	0.88±0.15	0.567
GFR (mL/min./1.73 m²)	86.25±12.99	85.20±21.02	0.820
Ca (mg/dL)	9.67±0.41	11.10±2.23	**0.001**
P (mg/dL)	3.4±0.49	2.60±0.49	**<0.001**
25OHD (ug/L)	16.89 (09.28-26.84)	19.17 (12.09-25.16)	0.508
Magnesium (mg/dL)	2.1 (2-2.2)	2.1 (2.0-2.40)	0.091
PTH (ng/L)	43 (34-54)	141.5 (103.2-179.25)	**<0.001**
TSH (uIU/mL)	1.92±0.59	2.20±0.93	0.170
Renin (pg/mL)	5.51 (3.98-14.91)	14.94 (5.85-42.70)	**0.019**
Aldosterone (pg/mL)	81.34 (42.23-176.86)	66.63 (37.72-136.65)	0.325
Urine Ca (mg/day)	-	268 (154.0-394.25)	

Results are given as mean ± standard deviation, median (interquartile range), or n (%). Mann-Whitney U test, Independent t-test. FBG: Fasting blood glucose, Total-C: Total cholesterol, LDL-C: LDL cholesterol, TG: Triglyceride, HDL-C: HDL Cholesterol, GFR: Glomerular filtration rate, 25OHD: 25-hydroxyvitamin D, TSH: Thyroid stimulating hormone, Ca: Calcium, P: Phosphorus, PTH: Parathormon, BMI: Body mass index

Table 5. Comparison of ambulatory results of the control and patient groups after excluding hypertensive patients

Variables	Control (n=32)	Patient (n=30)	p
Daytime SBP (mmHg)	118.5 (113-128.5)	119 (112-125)	0.868
Daytime DBP (mmHg)	77.5 (70-82)	74 (70-82)	0.987
Daytime MAP (mmHg)	91.5 (83.8-96.15)	97 (90-102.5)	**0.033**
Nighttime SKB (mmHg)	110.5 (102.5-116)	115 (109-120)	0.100
Nighttime DKB (mmHg)	66.5 (62-76)	71 (63.25-75.75)	0.595
Nighttime MAP (mmHg)	85 (77.83-90)	92 (86-94.75)	**0.017**
Pulse pressure (mmHg)	41 (34.5-46)	42 (38-47.5)	0.344
PWV (m/s)	6.5 (5.7-7.05)	6.1 (4.65-7.40)	0.182
AIX (%)	24.13±10.48	24.91±6.17	0.746

Results are given as mean ± standard deviation (SD) or median (interquartile range). Independent t-test (AIX), Mann-Whitney U test. Results are given as mean ± SD or median (interquartile range). Mann-Whitney U test, Independent t-test. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, PWV: Pulse wave velocity, AIX: Augmentation index

control subjects with similar sex, age and blood pressure values. In their study of 28 hypertensive and 16 normotensive patients with PHPT, Rosa et al. (3) also showed higher PWV and AS, especially in hypertensive patients. In this study, no correlation was found between PWV and Ca or PTH levels. A study by Wetzel et al. (4) showed that there was a direct interaction between PTH levels and PWV. The study by Rubin et al. (17) found a strong correlation between serum PTH levels and AIX, but no correlation between serum Ca levels and AIX. The methods used to measure PWV and AIX were different in the studies, and these studies did not exclude diabetics, smokers or hypertensive patients. In our study, PWV and AIX were statistically similar between the patient and control groups. We can argue that in patients at low risk of cardiovascular disease, AS is not increased in PHPT and that Ca and PTH levels are not independently associated with AS.

Another finding was that patients' blood pressure could be normal when measured manually, but could be high when measured using ABPM. With ABPM, HT could be diagnosed early in these patients. The prevalence of HT is higher in PHPT patients (25), and the study by Letizia et al. (26) showed that almost half of patients with PHPT had HT. There are several mechanisms such as hypercalcemia, high PTH, renal damage, activation of the sympathetic nervous system and RAAS that are responsible for HT in PHPT (5,27,28). Letizia et al. (26) showed a correlation between serum Ca level and mean 24-hour DBP and daytime DBP. A study conducted on 3002 patients over a follow-up period of 9 years showed that higher PTH levels were associated with an increased risk of HT (27). Another study showed that intracellular Ca plays an important role in smooth muscle cell contraction in the pathogenesis of essential HT. In this study, hypertensive patients with PHPT were found to have higher intracellular Ca levels compared with normotensive patients with PHPT and the control group (25). Our ABPM results in PHPT patients without concomitant HT showed that MAP was elevated in PHPT. However, we found no significant difference in systolic and diastolic pressure values between patients and the control group. Since no correlation between MAP and Ca, PTH or renin levels was found in our study, it could not be concluded that the increased MAP in PHPT was related to these parameters. However, the intracellular Ca level, which was not measured in our study, could be related to increased blood pressure, in contrast to the serum Ca levels described in the literature (25).

The study's first analysis revealed a significant difference in pulse pressure between the two groups. Pulse pressure is a sign of deteriorating cardiovascular health and naturally increases with age due to arteriosclerosis (29). However, this analysis shows that the patient group is older than the control group, and the significance of this parameter disappeared in the age-adjusted analysis. Excluding hypertensive patients, the second analysis showed no difference between the groups in pulse pressure results. However, in this analysis, the difference between the two groups in age also disappeared. It is therefore hypothesized that increasing age or the presence of HT are the main factors influencing pulse pressure in PHPT, rather than the disease itself.

A positive correlation was found between 25OHD level and MAP in PHPT. Contemporary studies have generally shown that vitamin D deficiency is associated with HT (30,31). Studies have shown that vitamin D deficiency in PHPT leads to increased Ca and PTH levels (32,33). A study on PHPT conducted in our country also showed that vitamin D deficiency was a risk factor for the development of HT in PHPT (34). Long-term exposure to vitamin D deficiency in PHPT may be associated with an increased risk of HT. However, it appears that there are insufficient studies investigating the risk of HT in PHPT with low vitamin D levels. In our study, the early diagnosis and the small number of patients might be the reasons for this result. However, the limited number of studies on this topic in the literature make it difficult to discuss this finding. Unlike in the general population, new studies are needed to reveal the association between 25OHD levels and HT in PHPT patients.

In our study, we found increased FBG and TG levels in PHPT patients compared to the control group, and this result may confirm the literature. In the study by Luboshitzky et al., the incidence of metabolic syndrome and insulin resistance was significantly higher in patients with severe PHPT than in patients with mild PHPT and the control group (35). Procopio et al. (36) performed an oral glucose tolerance test in 105 PHPT patients and showed that the prevalence of impaired glucose tolerance and diabetes was higher in the PHPT group than in the healthy control group. Diabetics and patients with morbid obesity were not included in the study, so we cannot comment on the prevalence of these conditions, but we found no significant difference in BMI between patients and controls.

Some studies have shown that the renin-aldosterone system plays a role in the development of HT in PHPT. In particular, these studies indicate that renin and aldosterone levels tend to be high in hypertensive PHPT patients (37,38). Brinton et al. (37) showed that plasma renin activity was elevated in 4 of 7 patients with PHPT and HT, whereas plasma renin activity was normal in PHPT patients with normal blood pressure. Gennari et al. (38) studied 34 patients with PHPT. Ten of these 34 patients were hypertensive. Plasma renin and aldosterone levels were found to be higher in hypertensive patients with PHPT than in normotensive patients with PHPT. Our results showed that patients with PHPT had higher renin levels than healthy controls, regardless of HT. However, in our study, no significant difference was found between the patient and control groups in terms of aldosterone levels. This could be due to the fact that aldosterone is also controlled by mechanisms other than renin.

Study Limitations

The most important limitation is the small number of patients. In addition, AS was studied using a non-invasive method such as 24-hour ABPM, and no additional methods were used, which is another limitation.

Conclusion

Consequently, in our study, we found that MAP increased in PHPT regardless of HT and age. There was no correlation between MAP with Ca, PTH or renin levels. The finding of a positive correlation of 25OHD level with MAP in PHPT needs to be supported by further studies. PWV, pulse pressure and AIX, which are cardiovascular risk markers, were not elevated in PHPT patients with low cardiovascular risk. New studies with a larger number of patients are needed to substantiate these findings.

Information: This study is a thesis study. University of Health Sciences Türkiye, Antalya Training and Research Hospital has financially contributed to the study for biochemical tests and renin and aldosterone kit.

This study was presented as an oral presentation at the 44th Endocrinology and Metabolic Diseases Congress (İstanbul/Türkiye).

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Türkiye, Antalya Training and Research Hospital (date: 26/11/2020, number: 18/11).

Informed Consent: Written informed consent was obtained from all patients.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: H.G.B., I.K.S., A.İ., Concept: I.K.S., Design: I.K.S., A.İ., Data Collection or Processing: H.G.B., Analysis or Interpretation: I.K.S., A.İ., Literature Search: H.G.B., I.K.S., Writing: H.G.B., I.K.S., A.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

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