The Relationship Between Electrocardiographic P Wave Parameters and Left Atrial Volume and Volume Indices in Patients with Hypertension

İnanç Artaç[1](İD), Bahattin Balcı[1](İD), Serdar Sevimli[2](İD), Ahmet Karakurt[1](İD), İbrahim Rencüzoğulları[1](İD), Metin Çağdaş[4](İD), Yavuz Karabağ[1](İD), Doğan İliş[3](İD)

[1] Department of Cardiology, Kafkas University Faculty of Medicine, Kars, Türkiye
[2] Department of Cardiology, Atatürk University Faculty of Medicine, Erzurum, Türkiye
[3] Clinic of Cardiology, Kars Harakani State Hospital, Kars, Türkiye
[4] Clinic of Cardiology, Gebze Fatih State Hospital, Kocaeli, Türkiye

ABSTRACT

Introduction: This study was designed to evaluate the relationship between left atrial volume index, which is an important indicator of left ventricular diastolic dysfunction, and electrocardiographic parameters such as P wave duration, P wave dispersion (PW_{DISP}), P wave terminal force (PWTF), and P wave peak time (PWPT) in hypertensive patients.

Patients and Methods: A total of 58 patients with a diagnosis of hypertension between June 2017 and April 2018 were included in this retrospective study. Age-sex matched 58 healthy subjects constituted the control group. The patients without diastolic dysfunction and stage I diastolic dysfunction were included in the normal left atrial pressure (NLAP) group, while stage II and stage III diastolic dysfunction patients constituted the high left atrial pressure (HLAP) group.

Results: The PWD_{max}, PW_{DISP}, and PWPT which are calculated from the lead DII ($PWPT_{DII}$) were found to be longer in the group of hypertensive patients ($p< 0.05$, for all). Electrocardiographic parameters of PWD-max, PW_{DISP}, PWTF, $PWPT_{DII}$, and $PWPT_{VI}$ were found to be longer in patients with HLAP. Both $PWPT_{VI}$ ($p= 0.008$ $r= 0.395$) and $PWPT_{DII}$ ($p< 0.001$ $r= 0.456$) were significantly correlated with left atrial volume index.

Conclusion: In this study, the relationship between PWPT and diastolic dysfunction was revealed for the first time in the literature. In addition, the PWPT was found to be increased in patients with increased left atrial pressure (LAP). Our findings deserve attention because electrocardiography is an inexpensive and easily accessible diagnostic method that can be used to detect diastolic dysfunction in hypertensive patients.

Key Words: P wave; p wave peak time; diastolic dysfunction; hypertension; left atrium

Hipertansiyonlu Hastalarda Elektrokardiyografik P Dalga Parametreleri ile Sol Atriyal Hacim ve Hacim İndeksleri Arasındaki İlişki

ÖZET

Giriş: Bu çalışma, hipertansif hastalarda sol ventrikül diyastolik disfonksiyonunun önemli bir göstergesi olan sol atriyum hacim indeksi ile P dalgası tepe zamanı (PDTZ), P dalga süresi, P dalga dağılımı ($PD_{DİSP}$), P dalga terminal kuvveti (PDTK) gibi elektrokardiyografik parametreler arasındaki ilişkiyi değerlendirmek amacıyla planlandı.

Hastalar ve Yöntem: Bu retrospektif çalışmaya Haziran 2017 ile Nisan 2018 arasında hipertansiyon tanısı alan toplam 58 hasta dahil edildi. Kontrol grubunu yaş-cinsiyet uyumlu 58 sağlıklı birey oluşturdu. Diyastolik disfonksiyonu olmayan ve evre I diyastolik disfonksiyonu olan hastalar normal sol atriyal basınç (NLAP) grubuna dahil edilirken, evre II ve evre III diyastolik disfonksiyon hastaları yüksek sol atriyal basınç (HLAP) grubunu oluşturdu.

Bulgular: DII derivasyonundan hesaplanan PDD_{max}, $PD_{DİSP}$ ve PDTZ hipertansif hasta grubunda daha uzun bulundu (tümü için $p< 0.05$). HLAP'li hastalarda PDD_{max}, $PD_{DİSP}$, PDTZ, PDPZD2 ve PDPZV1 elektrokardiyografik parametreleri daha uzun bulundu. Hem PDTZV1 ($p= 0.008$ $r= 0.395$) hem de PDTZD2 ($p< 0.001$ $r= 0.456$) sol atriyal hacim indeksi ile anlamlı şekilde koreleydi.

Sonuç: Bu çalışmada PDTZ ile diyastolik disfonksiyon arasındaki ilişki literatürde ilk kez ortaya konmuştur. Ayrıca LAB artışı olan hastalarda PDTZ'nın yükseldiği bulundu. Hipertansif hastalarda diyastolik disfonksiyonu saptamak için elektrokardiyografi ucuz ve kolay bir tanı yöntemi olarak kullanılabilir.

Anahtar Kelimeler: P dalga; p dalga pik süresi; diyastolik disfonksiyon; hipertansiyon; sol atriyum

Cite this article as: *Artaç İ, Balcı B, Sevimli S, Karakurt A, Rencüzoğulları İ, Çağdaş M, et al. The relationship between electrocardiographic p wave parameters and left atrial volume and volume indices in patients with hypertension. Koşuyolu Heart J 2022;25(2):177-186.*

Correspondence

İnanç Artaç

E-mail: inancartac@hotmail.com
Submitted: 06.12.2021
Accepted: 22.02.2022
Available Online Date: 20.08.2022

INTRODUCTION

The left ventricular ejection fraction (LVEF) is nearly normal in half of the patients diagnosed with heart failure, and it is referred to as heart failure with preserved ejection fraction (HFpEF)[1]. HFpEF is associated with increased mortality and morbidity, and hypertension is the most common cause of HFpEF[2,3]. Hypertension causes increasing in afterload, which leads to progressive left ventricular hypertrophy and fibrosis, deteriorating myocardial relaxation and compliance, eventually leading to increased filling pressures in the left heart chambers. Although an invasive left end-diastolic pressure measurement is the gold standard for a diagnosis of left ventricular diastolic dysfunction (LVDD), echocardiography is the most commonly used diagnostic tool in clinical practice.

Electrocardiography (ECG) is the most commonly used diagnostic tool in patients with ischemic heart diseases and arrhythmias. In the ECG, the P wave refers to atrial depolarization. Previous studies revealed that impaired atrial pressure and/or volume are closely related to P wave morphology. Although there is data on the association between the P wave duration maximum (PWD_{max}), P wave dispersion (PW_{DISP}), and P wave terminal force (PWTF) and diastolic dysfunction, it is unknown whether there is any relation between the P wave peak time (PWPT) and diastolic dysfunction[4,5]. For this reason, we aimed to investigate the relationship between the PWPT and diastolic dysfunction in patients with hypertension.

PATIENTS and METHODS

Study Population

A total of 58 patients with a diagnosis of hypertension who presented to the cardiology department of Kafkas University between June 2017 and April 2018 were included in this retrospective study. Age-sex matched 58 healthy subjects constituted the control group. The patients who had a coronary artery disease, chronic atrial fibrillation (AF), or have been previously diagnosed with AF, valvular heart disease, pericardial disease, left ventricular systolic dysfunction, pulmonary disease, connective tissue disease, diabetes mellitus, thyroid dysfunction, malignancy, and cerebrovascular disease were excluded from the study. All patients received medical therapy per current guidelines.

Electrocardiographic Analysis

A standard 12-lead ECG with 25 mm/sec paper and 10 mm/mV (Nihon-Kohden-Cardiofax-S, Tokyo, Japan) was performed for each patient. All ECG strips were scanned and digitized. All uploaded records were magnified and analyzed using a digital image processing software (https://imagej.nih.gov/ij/index.html). Two experienced cardiologists who were blinded to the patient's clinical data evaluated all ECG recordings. In the event of a dispute, the opinion of a third cardiologist was consulted, and the conclusion was reached by a consensus. The maximum value of QRS duration was considered as the beginning of the QRS to the J point. Fragmentation of QRS (fQRS) was accepted as the presence of QRS <120 msec and RSR' patterns or notching in the S or R wave in at least two adjacent leads in the absence of a typical branch block[6]. Electrocardiographic left ventricular hypertrophy was defined using Sokolow-Lyon and Cornell voltage criteria. The maximum and minimum P wave duration (PWD_{max} and PWD_{min}, respectively) were measured from the lead DII. The PW_{DISP} was accepted as the difference between the PWD_{max} and PWD_{min}[7]. PWTF was calculated by multiplying the depth and the duration of the terminal negative component of the P wave in the lead V1, and the abnormal PWTF was defined as PWTF≥ 40 ms. PWPT was defined as the duration from the beginning to the peak of the P wave and measured from the leads DII and V1. P wave amplitude (PWamp) was calculated from the lead DII by measuring the distance from the peak point of the P wave to the isoelectric line (millimeter) (Figure 1)[8].

Echocardiographic Examinations

All echocardiographic examinations were performed by an experienced imaging cardiologist using a Vivid S6 echocardiography device (GE, Vingmed Ultrasound AS, Horten, Norway). Standard imaging techniques were performed in accordance with the American Society of Echocardiography (ASE)[9]. Left atrial volume measurement was performed using the biplane disk summation technique. Left ventricular mass index (LVMI) was measured with the truncated ellipsoid technique using the two-dimensional echocardiographic images. The left atrial diameter was measured by taking three measurements from the parasternal long-axis and apical four-chamber images. Standard two-dimensional echocardiography, color Doppler examination, continuous and pulse wave doppler flows, and tissue Doppler measurements of mitral and lateral annulus were performed in all patients. The presence and staging of diastolic dysfunction in hypertensive patients were evaluated according to the current ASE guidelines. The presence of diastolic dysfunction was accepted if two or more of the following parameters were detected: E/Em> 14, Em-septal< 7 cm/sec or Em-lateral< 10 cm/sec, tricuspid regurgitation peak velocity (Tr-vlc)> 2.8 m/sec and left atrium volume index (LAVI)> 34 mL/m2. The severity of left atrial pressure (LAP) and the degree of diastolic dysfunction was evaluated by measuring E velocities, E/A ratio, E/Em ratio, Tr-vlc, and LAVI in the presence of the diastolic dysfunction (Figure 2). Stage I diastolic dysfunction was accepted if the E/A ratio was≤ 0.8 and E≤ 0.5 ms. Stage II diastolic dysfunction was accepted if E/A≤ 0.8 and E> 0.5 or 0.8< E< 2, and two or more

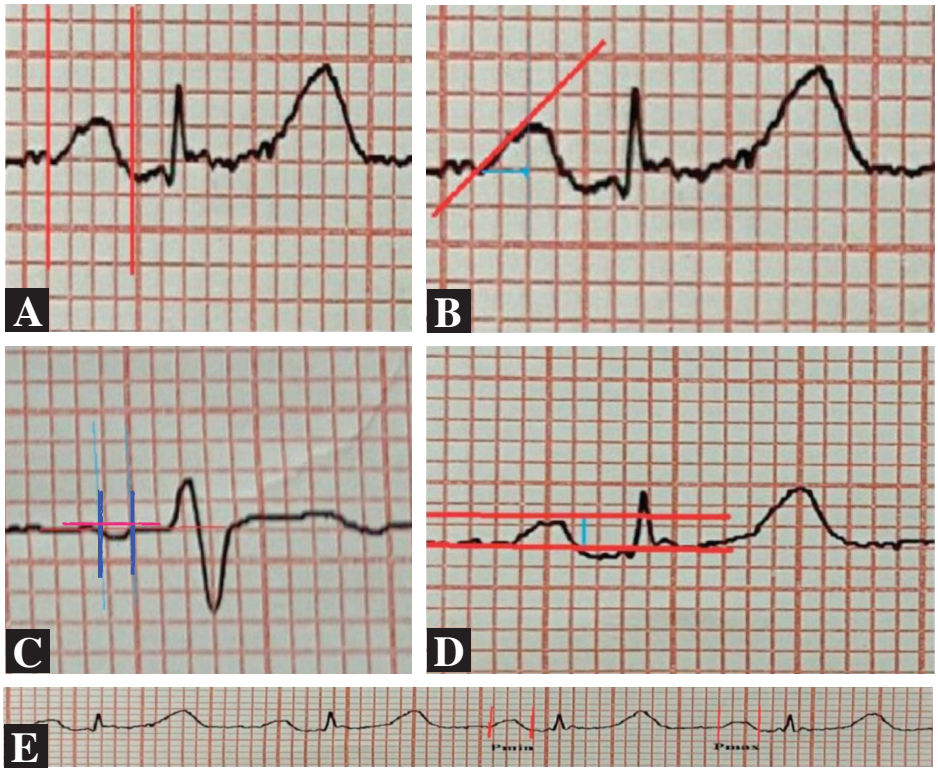

Figure 1. The measurements of the p-wave parameters. **A**: P duration, **B**: P wave peak time, **C**: P wave terminal force V1, **D**: Dispersion (P_{max}-P_{min}).

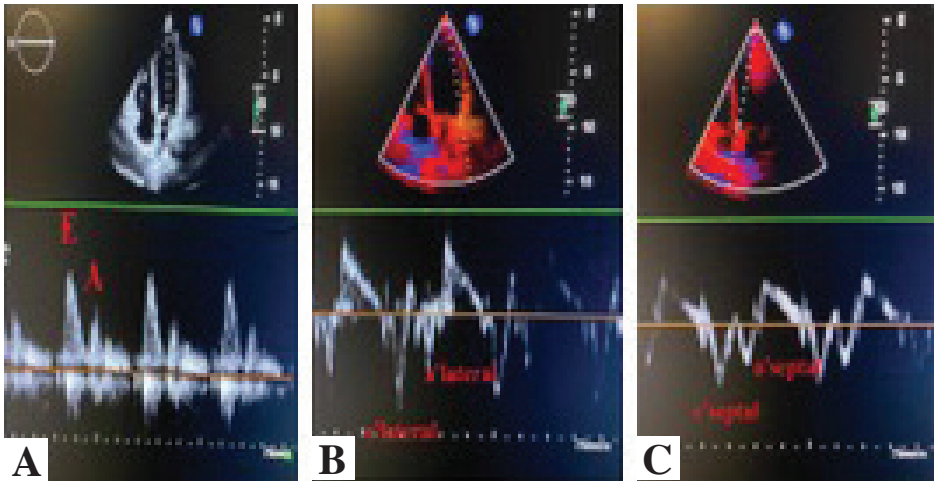

Figure 2. Mitral inflow and tissue Doppler velocities measurements. **A**: Mitral inflow velocities, **B**: Lateral tissue Doppler velocitles of the mitral annulus, **C**: Septal tissue Doppler velocities of the mitral annulus.

of the following were detected: 'E/Em ratio> 14, Tr-vlc> 2.8 m/sec, and LAVI> 34 mL/m^2'. Stage III diastolic dysfunction was accepted when the E/A ratio was >2. Left atrial pressures were considered to be elevated in patients with the presence of stage II and III diastolic dysfunction.

Statistical Analysis

For statistical analysis, SPSS version 17 (SPSS Inc., Chicago, Illinois) was used, and statistical significance was accepted as $p< 0.05$. Continuous variables were evaluated by the Kolmogorov-Smirnov test. Mean and standard deviations were given for continuous variables with normal distribution, and median and 25-75% were given for those without. Both numbers and percentage were used to define categorical variables. The continuous variables between the two groups were compared with the Mann-Whitney U test when the Student's t-test did not meet the normal distribution. Categorical data

were compared with Chi-square or Fisher's exact test. Continuous variables with normal distribution were analyzed using Pearson's test, and variables without normal distribution were analyzed by the Spearman test. The best threshold values predicting the increased left atrial pressure were determined by the receiver operating characteristic (ROC) curve analysis. The De Long method was used for ROC curve comparisons.

RESULTS

Comparison of Baseline Characteristics, Echocardiographic and Electrocardiographic Data of All Patients

Baseline demographic characteristics and laboratory findings of all patients are depicted in Table 1. There was no difference in terms of mean age, gender, BMI, and smoking between the groups ($p< 0.05$, for all). Systolic and diastolic blood pressure, urea, and creatinine levels were found to be higher in the hypertensive patient group ($p< 0.05$, for all). Table 2 shows the echocardiographic and electrocardiographic data of both groups. LVMI, LAVI, A, and E/Em ratios were elevated, whereas E, E/A ratio, Em-septal, and Em-lateral parameters were decreased in the hypertensive group. A comparison of electrocardiographic findings revealed that the proportion of prolonged QRS duration and QRS fragmentation was higher in hypertensive patients. PAMP-DII (P wave amplitude in lead II) was also higher in the hypertensive group. Pmax, Pdisp, and PWPT-DII were found to be longer in the hypertensive group ($p< 0.05$, for all). Of note, negative and biphasic P wave morphology in the lead V1 was more commonly observed in the hypertensive group.

Comparison of Patients with Normal vs. Increased Left Atrial Pressure

In the hypertensive patient group, diastolic dysfunction was detected in 52 (89.7%) out of 58 patients. The patients without diastolic dysfunction and patients with stage I diastolic dysfunction (n= 42, 72.4%) were included in the normal left atrial pressure (NLAP) group, and patients with Stage II (n= 13, 22.4%) and III (n= 3, 5.2%) diastolic dysfunction con-

Table 1. Demographic and laboratory features of patient and control groups

	Control Group n= 58	Hypertansive Group n= 58	p
Age, year	54.2 ± 7.1	56.4 ± 5.0	0.149
Woman gender, n (%)	40 (69.0)	36 (62.1)	0.435
Body Surface Area, m^2	1.86 ± 0.17	1.86 ± 0.18	0.377
Smoking, n (%)	10 (17.2)	17 (29.3)	0.124
Systolic Blood Pressure, mmHg	124 ± 13	143 ± 11	<0.001
Dyastolic Blood Pressure, mmHg	73 ± 11	87 ± 12	<0.001
Hemoglobin, gr/dL	13.5 ± 1.5	13.9 ± 1.3	0.781
White Blood Cell, $10^3/\mu L$	6.3 ± 1.5	7.1 ± 2.6	0.068
Glucose, mg/dL	90 ± 18	97 ± 24	0.109
Creatine, mg/dL	0.74 ± 0.19	0.80 ± 0.17	0.026
Ürea, mg/dL	33 ± 12	36 ± 11	0.042
Sodium, mmol/L	139 ± 3	139 ± 2	0.503
Potassium, mmol/L	4.3 ± 0.3	4.3 ± 0.4	0.749
Calcium, mmol/L	9.6 ± 0.3	9.6 ± 0.4	0.594
Aspartate aminotransferase, U/L	20 ± 9	19 ± 6	0.509
Total Cholesterol, mg/dL	190 ± 43	199 ± 55	0.389
Low density lipoprotein, mg/dL	112 ± 35	121 ± 51	0.32
High density lipoprotein, mg/dL	52 ± 14	47 ± 12	0.06
Triglycerides, mg/dL	119 (70-201)	128 (94-219)	0.1
Uric acid, mg/dL	4.3 (3.7-5.1)	4.4 (3.8-5.6)	0.179
C-reactive protein, mg/L	0.25 (0.18-0.39)	0.27 (0.17-0.75)	0.178
Thyroid stimulating hormone, mLU/L	1.67 (1.12-2.20)	1.61 (1.01-2.46)	0.649

Table 2. Echocardiographic and electrocardiographic characteristics of patient and control groups

		Control Group n= 58	Hypertension Group n= 58	p
Left ventricular mass index, gr/m^2		63 (54-71)	67 (62-89)	0.016
Left ventricular ejection fraction, %		66 ± 5	67 ± 3	0.867
Left atrial volume index, mL/m^2		23.4 ± 5.7	32.5 ± 8.2	<0.001
E, m/sec		0.69 (0.62-0.75)	0.58 (0.53-0.74)	0.004
A, m/sec		0.66 (0.56-0.76)	0.84 (0.66-0.91)	<0.001
E/A ratio		1.15 (0.81-1.24)	0.7 (0.63-0.89)	<0.001
Emseptal, cm/sec		0.1 (0.08-0.00)	0.08 (0.07-0.09)	<0.001
Emlateral, cm/sec		0.14 (0.11-0.18)	0.11 (0.08-0.12)	<0.001
E/Em ratio		6.02 (4.97-7.05)	7.01 (5.5-8.6)	0.005
Tricuspid insufficiency velocity, m/sec		2.4 ± 0.4	2.6 ± 0.5	0.176
Heart rate, per/minute		71 ± 11	72 ± 11	0.866
QRS duration, msec		88 ± 17	96 ± 12	0.004
Fragmentation, n (%)		4 (6.9)	30 (51.7)	<0.001
Left axis deviation, n (%)		6 (10.3)	6 (10.3)	0.995
V1SV6R, mm		18.3 ± 7.3	18.8 ± 8.3	0.72
V2SV6R, mm		19.4 ± 5.2	20.1 ± 7.2	0.58
MAXRMAXS, mm		21.8 ± 7.7	23 ± 8.2	0.432
aVLRV3S, mm		11.9 ± 4.3	14.5 ± 6.4	0.011
Maximum P wave duration, msec		99 ± 16	109 ± 17	0.001
Minimum P wave duration, msec		80 ± 12	76 ± 11	0.086
P wave dispersion, msec		19 ± 11	33 ± 12	<0.001
P wave amplitude in lead DII, mm		1.1 ± 0.3	1.1 ± 0.3	0.486
P wave peak time in lead DII, msec		49 ± 13	67 ± 14	<0.001
P wave morphology V1, n (%)	Negative	0 (0)	8 (13.8)	0.005
	Pozitive	24 (41.4)	14 (24.1)	
	Biphasic	34 (58.6)	36 (62.1)	
P wave peak time in lead V1, msec		54 ± 14	60 ± 17	0.055
V1 P wave terminal force, mm x msec		29 ± 16	33 ± 14	0.136
V1 P wave terminal force≥ 40, n (%)		8 (23.5)	13 (29.5)	0.42

stituted the high left atrial pressure (HLAP) group. Baseline demographic characteristics and laboratory parameters of all patients stratified according to LAP are demonstrated in Table 3. Between the two groups, there was no difference in terms of mean age, gender, and BMI. Systolic and diastolic blood pressure levels were elevated, and the use of an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker was more frequent in the HLAP group (p< 0.05, for all). Echocardiographic and electrocardiographic findings of all patients stratified according to LAP are shown in Table 4. LVMI, LAVI, E/Em ratio, and Tr-vlc were found to be elevated, and Em-lateral was lower in the HLAP group. Pmax, PWPT-DII, and PWPT-V1 were longer and more patients had PWTF≥ 40 in the HLAP group.

Correlation of Electrocardiographic Parameters with Echocardiographic Diastolic Dysfunction Parameters

A correlation analysis was performed between the electrocardiographic P wave parameters and echocardiographic diastolic dysfunction parameters (Table 5). There was a moderate correlation between Pmax and Em-lateral, E/Em ratio, and

Table 3. Demographic and laboratory features of patients with normal leftatrial pressure and high left atrial pressure

	Hypertension Group (n= 58)	Normal Left Atrial Pressure (n= 42)	High Left Atrial Pressure (n= 16)	p
Age, year	56 ± 5	57 ± 6	56 ± 3	0.606
Woman gender, n (%)	36 (62.1)	26 (61.9)	10 (62.5)	0.889
Body surface area, m^2	1.86 ± 0.18	1.86 ± 0.18	1.88 ± 0.21	0.917
Smoking, n (%)	17 (29.3)	12 (28.6)	5 (31.3)	0.841
Acetylsalicylicacid, n (%)	10 (17.2)	7 (16.7)	3 (18.8)	0.851
Statin, n (%)	2 (3.4)	2 (4.8)	0 (0.0)	0.371
ACEI/ARB, n (%)	44 (75.9)	29 (69.0)	15 (93.8)	0.049
Beta-blocker, n (%)	20 (34.5)	15 (35.7)	5 (31.3)	0.749
Calcium channel blocker, n (%)	20 (34.5)	14 (33.3)	6 (37.5)	0.765
Thiazides, n (%)	25 (43.1)	16 (38.1)	9 (56.3)	0.212
Systolic blood pressure, mmHg	143 ± 11	141 ± 9	151 ± 12	0.003
Diastolic blood pressure, mmHg	87 ± 12	85 ± 12	94 ± 8	0.009
Hemoglobin, gr/d	13.9 ± 1.3	14.0 ± 1.2	13.7 ± 1.6	0.767
White blood cell, $10^3/\mu L$	7.1 ± 2.6	7.4 ± 2.9	6.3 ± 1.3	0.329
Glucose, mg/dL	97 ± 24	97 ± 24	97 ± 27	0.138
Urea, mg/dL	36 ± 11	35 ± 11	37 ± 10	0.508
Creatinine, mg/dL	0.80 ± 0.17	0.80 ± 0.17	0.81 ± 0.17	0.781
Sodium, mmoL/L	139 ± 2	139 ± 2	140 ± 2	0.503
Potassium, mmoL/L	4.3 ± 0.4	4.3 ± 0.4	4.2 ± 0.4	0.109
Calsium, mmoL/L	9.6 ± 0.4	9.6 ± 0.4	9.5 ± 0.4	0.373
Aspartate amino transferase, U/L	19 ± 6	19 ± 6	18 ± 5	0.637
Total Cholesterol, mg/dL	199 ± 55	201 ± 53	195 ± 63	0.365
Low density lipoprotein, mg/dL	121 ± 51	119 ± 49	126 ± 56	0.862
High density lipoprotein, mg/dL	47 ± 12	47 ± 13	45 ± 11	0.614
Triglycerides, mg/dL	128 (94-219)	135 (94-235)	128 (77-166)	0.153
Uric acid, mg/dL	4.4 (3.8-5.6)	4.3 (3.7-5.5)	4.9 (3.9-5.7)	0.497
C-reaktive protein, mg/L	0.27 (0.17-0.75)	0.27 (0.13-0.75)	0.34 (0.17-0.74)	0.807
Thyroid stimulating hormone, mLU/L	1.61 (1.01-2.46)	1.66 (0.92-2.46)	1.27 (1.01-1.89)	0.1

ACEI: Angiotensin converting enzyme inhibitors, ARB: Angiotensin receptor blockers.

LVMI. All 'p wave' parameters other than Pmin were correlated with LAVI. There was a weak correlation between PWPT-DII and Em-lateral, and an intermediate correlation between PWPT-DII and LVMI.

ROC Curve Analysis

ROC analysis was performed to determine the optimal cut-off values of PWPT-DII and PWPT-V1 for predicting the LAP (Figure 3). The optimal cut-off value of PWPT-DII for predicting the LAP was 58.8 ms with a sensitivity of 93.7% and a specificity of 45.2% (area under the curve (AUC= 0.704, p= 0.0047). The optimal cut-off value of PWPT-V1for predicting the LAP was 54.4 ms with a sensitivity of 93.3% and a specificity of 44.8% (AUC= 0.74, p= 0.0067). The areas under the curves between PWPT-DII and PWPT-V1 were compared with P_{max}, P_{dis}, and PWTF. The AUC of PWPT-DII and PWPT-V1 were greater than the AUC of P_{max}, P_{dis}, and PWTF.

Table 4. Echocardiographic and electrocardiographic characteristics of hypertensive patients with normal and high left atrial pressure

		High Left Atrial Pressure (n= 42)	Normal Left Atrial Pressure (n= 16)	p
Left ventricular mass index, gr/m^2		67 ± 14	98 ± 33	0.002
Left ventricular ejection fraction, %		67 ± 3	66 ± 1	0.332
Left atrial volume index, mL/m^2		29 ± 4.3	41.7 ± 8.9	<0.001
E, m/sec		0.58 (0.53-0.70)	0.59 (0.53-1.13)	0.475
A, m/sec		0.85 (0.66-0.92)	0.84 (0.76-0.88)	0.702
E/A ratio		0.67 (0.62-0.89)	0.71 (0.64-1.31)	0.164
Emseptal, cm/sn		0.08 (0.07-0.09)	0.08 (0.06-0.09)	0.324
Emlateral, cm/sn		0.11 (0.08-0.13)	0.09 (0.07-0.11)	0.063
E/Em ratio		6.56 (5.42-8.44)	8.4 (6.25-14.70)	0.021
Tricuspid insufficiency velocity, m/sec		2.4 ± 0.4	3.02 ± 0.28	<0.001
Heart rate, per/minute		72 ± 11	74 ± 11	0.554
QRS duration, msec		95 ± 12	101 ± 11	0.02
Fragmentation, n (%)		20 (47.6)	10 (62.5)	0.311
Left axis deviation, n (%)		4 (9.5)	2 (12.5)	0.739
V1SV6R, mm		16.5 ± 5.1	24.8 ± 11.8	0.018
V2SV6R, mm		18.34 ± 5.98	24.68 ± 8.38	0.009
MAXRMAXS, mm		20.76 ± 5.99	28.9 ± 10.41	0.002
AVLRV3S, mm		12.97 ± 4.34	18.69 ± 8.89	0.023
Maximum P wave duration, msec		105.51 ± 15.02	117.58 ± 19.63	0.036
Minimum P wave duration, msec		74.08 ± 7.92	81.5 ± 16.75	0.047
P wave dispersion, msec		31.44 ± 11.66	36.08 ± 10.93	0.091
P wave amplitude in lead DII, mm		1.04 ± 0.18	1.32 ± 0.45	0.043
P wave peak time in lead DII, msec		63 ± 13	75 ± 16	0.017
P wave morphology V1, n (%)	Negative	8 (19)	0 (0)	0.008
	Pozitive	13 (31)	1 (6.3)	
	Biphasic	21 (50)	15 (93.8)	
P wave peak time V1, msec		55 ± 16	70 ± 16	0.021
V1 P wave terminal force, mm x msec		29.28 ± 10.86	39.9 ± 16.81	0.022
V1 P wave terminal force≥ 40, n (%)		5 (17.2)	8 (53.3)	0.013

DISCUSSION

Our study findings demonstrated that PWPT measured from the leads DII and V1 were prolonged in patients with hypertension compared to healthy subjects. In addition, this parameter was found to be associated with elevated LAP measured by means of echocardiography in hypertensive patients.

Increased left ventricular afterload due to increased blood pressure leads to left ventricular hypertrophy and interstitial fibrosis. As expected, we noted an increase in the left ventricular wall thickness and LVMI in the hypertensive group compared to the control group. In the present study, there was no significant difference between the groups in terms of electrocardiographic hypertrophy parameters such as the S wave in the lead V1, R wave in the lead V5-6, maximal S wave in the lead V1, and maximal S wave in the lead V5-6. These findings might be due to the low number of patients enrolled in our study and also the low sensitivity and specificity of electrocardiographic left ventricular hypertrophy criteria[10]. Myocardial hypertrophy disrupts repolarization in the left ventricular tissue and slows down transmural conduction. The deceleration of electrical im-

Table 5. Correlation table between electrocardiographic P wave parameters and echocardiographic diastolic dysfunction parameters in hypertension group

		E/A Ratio	Emseptal	Emlateral	E/Em Ratio	LAVI	LVMI	Tricuspid Insufficiency Velocity
Maximum P wave duration, msec	KK	-0.286	-0.216	-0.42	0.32	0.346	0.315	0.220
	p	0.030	0.104	0.001	0.014	0.008	0.016	0.097
	n	58	58	58	58	58	58	58
P wave dispersion, msec	KK	-0.053	-0.142	-0.352	0.278	0.273	0.259	0.190
	p	0.692	0.287	0.007	0.034	0.038	0.049	0.154
	n	58	58	58	58	58	58	58
P wave peak time in lead DII, msec	KK	-0.242	-0.100	-0.28	0.153	0.456	0.32	0.210
	p	0.067	0.453	0.033	0.251	0.000	0.014	0.114
	n	58	58	58	58	58	58	58
P wave peak time in lead V1, msec	KK	0.175	0.082	-0.038	-0.017	0.395	0.130	0.277
	p	0.256	0.596	0.808	0.911	0.008	0.402	0.069
	n	44	44	44	44	44	44	44
P wave terminal force V1, mm x msec	KK	0.073	0.053	-0.028	-0.238	0.406	0.594	0.148
	p	0.636	0.731	0.858	0.120	0.006	0.000	0.338
	n	44	44	44	44	44	44	44

LAVI: Left atrial volume index, LVMI: Left ventricular mass index.

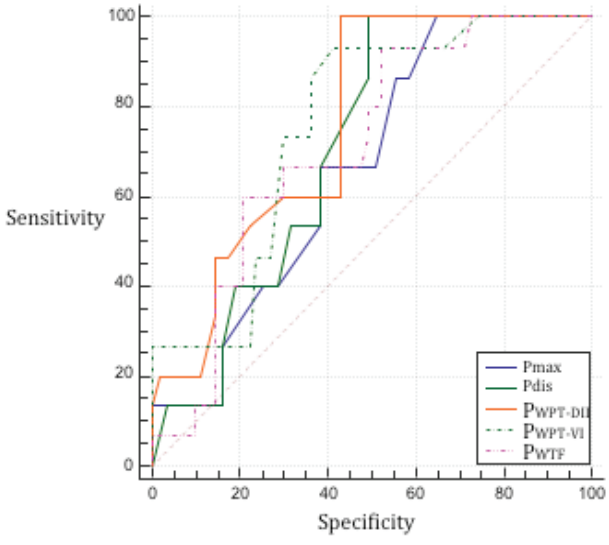

Figure 3. ROC curve analysis and ROC curve comparison for predicting increased left atrial pressure of $P_{maximum}$, $P_{dispersion}$, P_{WTF}, $P_{WPT-DII}$, and P_{WPT-V1}.

pulses in the ventricle is associated with prolongation and fragmentation of QRS duration[11-13]. In accordance with the literature, we found that QRS duration was longer and the frequency of fragmented QRS was higher in the hypertensive group.

In the early stages of diastolic dysfunction, the left ventricle's early passive filling reduces due to impaired relaxation, and the contribution of atrial contracture increases. Our results also supported this pathophysiology; we observed that the early mitral flow velocity decreased, atrial contracture velocity increased, and therefore E/A ratio decreased in the hypertensive group. Furthermore, we found that tissue Doppler velocities were lower, and the E/Em ratio was higher in the hypertensive group, which was consistent with the findings of previous studies[14]. Increased left atrial pressure due to increased left ventricular diastolic pressure cause atrial remodeling and fibrosis. This leads to a volume overload and an increase in the size of the left atrium. Similarly, we noted that the LAVI increased in the hypertensive group[15]. As seen in our study, increased left atrial volume and fibrosis cause a delay in conduction time, which results in a prolongation of P_{max} and P_{dis} [16]. Additionally, we have determined that PWPT, measured from the leads D2 and V1 was also prolonged.

Although an invasive left ventricular end-diastolic pressure measurement is the gold standard in the diagnosis of LVDD, the most commonly used method in daily clinical practice is echocardiography. According to previous studies, the incidence of LVDD in hypertensive patients may range from 18 to 84% because of the varying echocardiographic imaging techniques

and diagnostic criteria used[17]. Therefore, the ASE has recommended an algorithm based on the mitral flow velocities (E, A), tissue Doppler rates (Em-septal, Em-lateral), E/A ratio, E/Em ratio, LAVI, and Tr-vlc for detection and grading of diastolic dysfunction and determination of LAP elevation[9]. By using this diagnostic algorithm, we found that 89.7% (n= 52) of the hypertensive patients had diastolic dysfunction, and 38.1% of these patients had high LAP. Also, we observed that systolic and diastolic blood pressures were higher and the use of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker was higher in patients with increased LAP. This may be attributable to the need for higher anti-hypertensive drug doses in the HLAP patient group due to the increased systolic and diastolic blood pressures and LVMI[18]. In the group with HLAP, echocardiographic parameters used for the staging of diastolic dysfunction such as LAVI, E/Em ratio, and Tr-vlc were found to be higher as excepted. In addition, it was observed that the LVMI, which was not included in the staging of diastolic dysfunction, was also elevated in the HLAP group.

Electrocardiographic voltage criteria for left ventricular hypertrophy were evaluated in both subgroups, and we found that these parameters were higher in the HLAP group. Previous studies have shown that Sokolow-Lyon and Cornell voltage criteria may be related to diastolic dysfunction[19,20]. Left ventricular hypertrophy and interstitial fibrosis in hypertension can lead to an intraventricular conduction delay and hence QRS prolongation may be observed. As in our study, there are reports in the literature showing that the prolongation of QRS duration may be related to diastolic dysfunction[21]. Increased left ventricular diastolic pressure as a result of LVDD raises left atrial pressure, and chronically elevated LAP causes remodeling, resulting in an increase in LAVI. As seen in our study, the LVDD is closely associated with the increase in the LAVI.

The relationship between left atrial dilatation and P wave duration prolongation has been known for a long time and is called 'P mitrale'[22]. Wei-Chung Tsai and his colleagues found in their study of 270 patients that prolonged P wave duration and P wave dispersion were related to diastolic dysfunction and an increase of the LAVI[23]. In our study, P_{max} and P_{min} were associated with increased left atrial pressure, but we didn't observe any relation with P_{dis} and HLAP. In a previous study, the PWTF, calculated from the lead V1, was found to be related to the severity of diastolic dysfunction in hypertensive patients with normal left ventricular systolic function[24]. Also, we found that P_{max} and PWTF were associated with increased LAP in accordance with the literature as mentioned above. Furthermore, P_{max}, P_{dis}, and the PWTF, calculated from the lead V1, were positively correlated with LAVI in our study.

The PWPT has been recently described in the literature, and it has been demonstrated that prolonged PWPT is associated with no-reflow in patients with acute coronary syndrome. The authors claimed that the prolongation in the PWPT duration might be associated with high left atrial and left ventricular end-diastolic pressure in patients with no-reflow[8]. However, in this study, there were no invasive measurements and echocardiographic parameters for diastolic functions. In our study, the PWPT, calculated from the lead D2 and V1, was longer in patients with HLAP compared to those with NLAP. In addition, there was a positive correlation between PWPT-DII and PWPT-V1 with the LAVI and a negative correlation between PWPT-DII and Em-lateral. It is well-known that the process of remodeling, which causes structural and electrical changes in the atrium, is triggered when the atrium is exposed to pressure and/or volume load. Increased left atrial volume and inter-intra atrial conduction delays results of the atrial remodeling, increase P wave duration, P wave dispersion, and PWTF[25]. We thought that the prolongation of PWPT duration in the lead D2 and V1 depends on these possible mechanisms.

Limitations

Our study is a cross-sectional study with no long-term follow-up data on clinical outcomes. Therefore, the effect of PWPT on the prognosis and clinical outcome of hypertension patients has not been investigated. Since individuals in hypertension and control groups live in a limited geographical area, the results of the study may not be generalized to the general population. Invasive left ventricular end-diastolic pressure, pulmonary capillary wedge pressure, and the relationship between P wave parameters were not evaluated as the gold standard for the diagnosis of diastolic dysfunction. Natriuretic peptide levels which have an important role in the diagnosis of diastolic dysfunction have not been studied and the relationship with P wave parameters could not be evaluated. PWPT should be validated in larger patient populations for clinical use in detecting diastolic dysfunction.

CONCLUSION

The PWPT was found to be longer in hypertensive patients than in healthy controls in our study for the first time in the literature. In addition, the P wave peak duration was increased in patients with elevated LAP. Moreover, we observed that the LAVI was positively correlated with PWPT. The findings of our study could be useful because the PWPT, Pmax, and PWTF are simple and easy ECG parameters for detecting diastolic dysfunction in hypertensive patients.

Ethics Committee Approval: This study was approved by Kafkas University Faculty of Medicine (Decision no: 80576354-050-99/107, Date: 30.05.2018).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - İA, Dİ; Analysis/Interpretation - İA, Dİ, YK; Data Collection - İA, Dİ; Writing - İA, MÇ; Critical Revision - İA, BB; Final Approval - İA, MÇ, BB; Statistical Analysis - İA, YK; Overall Responsibility - İA, YK.

Conflict of Interest: The authors declared that there was no conflict of interest during the preparation and publication of this article.

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

REFERENCES

1. Zile M, Brutsaert D, New concepts in diastolic dysfunction and diastolic heart failure: Part I. Diagnosis, prognosis, and measurements of diastolic function. Circulation 2002;105:1387-93. [Crossref]
2. Bhatia RS, Tu JV, Lee DS, Austin PC, Fang J, Haouzi A, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355(3):260-9. [Crossref]
3. Leite-Moreira AF, Correia-Pinto J, Gillebert TC. Diastolic dysfunction and hypertension. N Engl J Med 2001;344:1401-2. [Crossref]
4. Labovitz A, Pearson A. Evaluation of left ventricular diastolic function:clinical relevance and recent electrocardiographic insights. Am Heart J 1987;114:836-51. [Crossref]
5. Vasan RS, Levy D. Defining diastolic heart failure: a call for standardized diagnostic criteria. Circulation 2000;101(17):2118-21. [Crossref]
6. Das MK, MaskounW, Shen C, Michael MA, Suradi H, Desai M, et al. Fragmented QRS on twelve-lead electrocardiogram predicts arrhythmic events in patientswith ischemicand non-ischemic cardiomyopathy. Hear Rhythm 2010;7:74-80. [Crossref]
7. Dilaveris PE, Gialafos EJ, Sideris S, Theopistou AM, Andrikopoulos GK, Kyriakidis M, et al. Simple electrocardiographic markers for the prediction of paroxysmal idiopathic atrial fibrillation. Am Heart J 1998;135:733-8. [Crossref]
8. Çağdaş M, Karakoyun S, Rencüzoğulları İ, Karabağ Y, Yesin M, Gürsoy MO, et al. P wave peak time; a novel electrocardiographic parameter in the assessment of coronary no-reflow. J Electrocardiol 2017;50:584-90. [Crossref]
9. Nagueh SF, Smiseth OA, Appleton CP, Byrd 3rd BF, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American society of echocardiography and the European association of cardiovascular imaging. Eur Heart J Cardiovasc Imaging 2016;17:1321-60. [Crossref]
10. Manolis AJ, Hamodraka ES, Poulimenos LE. Electrocardiography for the diagnosis of left ventricular hypertrophy: Revisiting an old friend in times of austerity. J Hypertens 2012;30:1325-7. [Crossref]
11. Hill JA. Hypertrophic reprogramming of the left ventricle: Translation to the ECG. J Electrocardiol 2012;45:624-9. [Crossref]
12. Bacharova L, Szathmary V, Kovalcik M, Mateasik A. Effect of changes in left ventricular anatomy and conduction velocity on the QRS voltage and morphology in left ventricular hypertrophy: A model study. J Electrocardiol 2010;43:200-8. [Crossref]
13. Yesin M, Kalçık M, Çağdaş M, Karabağ Y, Rencüzoğulları İ, Gürsoy MO, et al. Fragmented QRS may predict new onset atrial fibrillation in patients with ST-segment elevation myocardial infarction. J Electrocardiol 2018;51:27-32. [Crossref]
14. An WS, Lee SM, Park TH, Kim SE, Kim KH, Park YJ, et al. Association between diastolic dysfunction by color tissue doppler ımaging and vascular calcification on plain radiographs in dialysis patients. Kidney Blood Press Res 2012;35:619-26. [Crossref]
15. Tsang TSM, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. Am J Cardiol 2002;90:1284-9. [Crossref]
16. Ermis N, Acikgoz N, Cuglan B, Cansel M, Yagmur J, Tasolar H, et al. Comparison of atrial electromechanical coupling interval and P-wave dispersion in non-dipper versus dipper hypertensive subjects. Blood Press 2011;20(1):60-6. [Crossref]
17. Galderisi M. Diagnosis and management of left ventricular diastolic dysfunction in the hypertensive patients. Am J Hypertens 2011;24:507-17. [Crossref]
18. Dobrowolski P, Klisiewicz A, Prejbisz A, Florczak E, Rybicka J, Bieleń P, et al. Factors associated with diastolic dysfunction in patients with resistant hypertension: Resist-POL study. Am J Hypertens 2015;28:307-11. [Crossref]
19. Hsu PC, Tsai WC, Lin TH, Su HM, Voon WC, Lai WT, et al. Association of arterial stiffness and electrocardiography-determined left ventricular hypertrophy with left ventricular diastolic dysfunction. PLoS One 2012;7(11):e49100. [Crossref]
20. Krepp JM, Lin F, Min JK, Devereux RB, Okin PM. Relationship of electrocardiographic left ventricular hypertrophy to the presence of diastolic dysfunction. Ann Noninvasive Electrocardiol 2014;19:552-660. [Crossref]
21. Wilcox JE, Rosenberg J, Vallakati A, Gheorghiade M, Shah SJ. Usefulness of electrocardiographic QT interval to predict left ventricular diastolic dysfunction. Am J Cardiol 2011;108:1760-6. [Crossref]
22. Sodi-Pollares D, Bisteni A, Fishleder BL, Medrano GA. Importance of the unipolar morphologies in the interpretation of the electrocardiogram: The theoretical basis of the unipolar morphologies and its correlation with vectorial analysis, with cardiac activation, and with the potential variations at the epicardial surface of the heart. Am heart J 1959;57:590-605. [Crossref]
23. Tsai WC, Lee KT, Wu MT, Chu CS, Lin TH, Hsu PC, et al. Significant correlation of P-wave parameters with left atrial volume index and left ventricular diastolic function. Am J Med Sci 2013;346:45-51. [Crossref]
24. Tanoue MT, Kjeldsen SE, Devereux RB, Okin PM. Relationship between abnormal P-wave terminal force in lead V1 and left ventricular diastolic dysfunction in hypertensive patients: The LIFE study. Blood Press 2017;26:94-101. [Crossref]
25. De Jong AM, Maass AH, Oberdorf-Maass SU, Van Veldhuisen DJ, Van Gilst WH, Van Gelder IC. Mechanisms of atrial structural changes caused by stretch occurring before and during early atrial fibrillation. Cardiovasc Res 2011;89:754-65. [Crossref]