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CORRELATION BETWEEN P WAVE DISPERSION FROM 12-LEAD ECG AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS DIAGNOSED WITH HYPERTENSION

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Abstract

Background: Patients diagnosed with hypertension generally have diastolic dysfunction of the left ventricle which causes an increase in LVEDP as well as in the dimension of the left atrium. Changes in the structure of the left atrium can be detected through P wave dispersion on a 12-lead Electrocardiography. The purpose of this study was to determine the correlation of P wave dispersion on the 12-lead Electrocardiography with diastolic dysfunction in patients diagnosed with hypertension in the outpatient clinic of Cardiac Center Adam Malik General Hospital in Medan.

Method: This is a cross-sectional study conducted from February 2019 till August 2019. Patients with hypertension who met the inclusion criteria was examined electrocardiographically to obtain P wave dispersion value. Then echocardiography examination was performed to assess the grades of diastolic dysfunction and other parameters. Analysis of correlation between P wave dispersion values and diastolic dysfunction was then conducted.

Results: Significant differences in P-wave dispersion are found among diastolic dysfunction groups. Grade I diastolic dysfunction is found to have P wave dispersion value of 43 ms, grade II diastolic dysfunction has P wave dispersion value of 53 ms, and grade III diastolic dysfunction has P wave dispersion value of 56 ms, Significance of p value is <0.001. There is a strong correlation between P wave dispersion and diastolic dysfunction grade (r = 0.7 (P <0.001)). Cut off point of P-wave dispersion > 50.5 ms can discriminate patients who have increased LAP with a sensitivity of 83% and specificity of 93%.

Conclusion: P-wave dispersion is a simple screening tool which is widely available to detect grades of left ventricular diastolic dysfunction, especially in areas where echocardiography is not available.

Keywords: Diastolic dysfunction, P wave dispersion, Electrocardiography.

Introduction

The increasing prevalence of hypertension every year is a major problem in both developed and developing countries. It is estimated that in 2025 the percentage of hypertensive patients will increase by 24% in developed countries. Whereas in developing countries the percentage of people with hypertension increases much higher at around 80%[1]. Indonesia is an example of a developing country with a high prevalence of hypertension. The average prevalence of hypertension throughout Indonesia is 29.8%[2].

Hypertension will progress into hypertension heart disease that begins with left ventricular hypertrophy and diastolic dysfunction before eventually deteriorates into systolic dysfunction. Diastolic dysfunction of the left ventricle is responsible for the increased LVEDP and enlarged dimension of the left atrium [3,4]. That is why the focus of many studies about diastolic dysfunction is directed to size and abnormality of the left atrium. Increased dimension of the left atrium results in changes of the left atrial tissue structure, and this is also followed by inhomogeneous fibrosis in the left atrium which eventually causes interference with the impulse delivery from the SA node. This can be detected from the morphology of the P wave and also from the PR interval[5].

P wave dispersion is the substraction between the maximum and minimum duration of the P wave on a 12 lead ECG. P-wave dispersion is a subject that's often studied. This is mainly due to the ability of P wave dispersion to describe conduction disturbances in the atrium or between atria [6,7]. One study conducted by Tushar et al found that maximum duration of P wave increased significantly in patients with diastolic dysfunction (119.60 ± 8.2 ms vs 114.0 ± 6.4 ms, p = 0.001), and the minimum duration of P waves increased significantly in patients without diastolic dysfunction (72.60 ± 7.5 ms vs 62.7 ± 7.4 ms, p = 0.001) compared to their normal counterpart, The study also found that P-wave dispersion increases significantly in patients with diastolic dysfunction (56.6 ± 6.3 ms vs. 41.5 ± 5.2 ms, p = 0.001) [5]. Based on that, this study aimed to look further into the relationship of P wave dispersion and left ventricular diastolic dysfunction in patients with hypertension.

Methods

This study is a cross-sectional diagnostic study conducted in the outpatient clinic of Department of Cardiology and Vascular Medicine, H. Adam Malik Teaching Hospital. Sample collection was carried out from March 2019 to August 2019. The inclusion criteria were subjects with BP ≥ 140/90 or patients with normal blood pressure but routinely taking hypertension medication. Exclusion Criteria were patients with arrhythmia, heart valve abnormalites due to rheumatic heart disease, severe functional disorders of the mitral or aortic valve, congenital heart disease, pericardial abnormalities, patients who could not lie on their backs, and poor echo window.

Patients who met the inclusion criteria were then conducted anamnesis and physical examination to obtain clinical baseline data and patient's history, then electrocardiographic examination with a speed of 50 mm / s and a scale of 20 mm / mV. P-wave dispersion is measured as the substraction between the maximum and minimum P-wave duration on a 12-lead ECG. Measurements were made manually using a 150 mm Krisbow vernier caliper micrometer (KW0600352) and a magnifying glass. Measurement results are reported in ms units. The patient then performed an echocardiographic examination, data such as ejection fraction and a complete LV study, left ventricular diastolic function as assessed by the ratio E / A, septal e ', lateral e', E / e 'ratio, LAVI (mL / mm2), and TR Velocity were recorded. Then the patients were divided into three groups of diastolic dysfunction grades which refers to the diastolic dysfunction guidelines issued by ASE in 2016[8].

Data was presented byfrequency distribution and percentage for categorical data while numerical data is presented by displaying the mean (average) ± standard deviation and median (middle value) and minimum - maximum values. Baseline characteristics will be compared between groups with One Way Anova or Kruskal Wallis test and post hoc with Bonferroni or Games Howell for numeric variables and Chi-Square or Fisher's Exact Test for categorical variables. The correlation of P wave dispersion and left ventricular diastolic function was then assessed by the Pearson or Spearman correlation test. With the ROC method, the Area under the curve (AUC) will be calculated, and the cutoff value, sensitivity and specificity values for the desired variables were found. Statistical data analysis used SPSS software version 23, p value <0.05 was said to be statistically significant.

Results

A total of 93 samples who fulfilled the inclusion criteria were enrolled in this study , and they were divided into three groups according to the grades of diastolic dysfunction. The mean age of the subjects was 60 years and no significant differences were found between the three diastolic dysfunction grades. In terms of gender, male were found more frequently (70 people (75%)), compared with female (22 people (23%)), no significant differences were found between diastolic dysfunction groups.

Table 1.Clinical characteristics

Clinical Parameters	Diastolic dysfunction grade I (n = 31)	Diastolic dysfunction grade II (n = 31)	Diastolic dysfunction grade III (n = 31)	P value
Age (years)*	61,5 ± 8,1	59,7 ± 8,9	58,8 ± 10,2	0,491
Genders :				
Men ***	25 (80%)	24 (77%)	22(70%)	0,659

Women ***	6 (19 %)	7(22%)	9(29%)	
Smoking***	18 (58%)	19 (61%)	19 (61%)	0,956
DM ***	10 (32 %)	12 (38 %)	9 (29%)	0,713
Dislipidemia***	21 (67%)	22 (70%)	21 (67%)	0,951
HT duration (years)**	12 (7-17)	11 (10 – 14)	13 (7 – 17)	0,737
BW (kg)*	71,8 ± 14,2	74,3 ± 14,6	66,8 ± 11,2	0,088
Height 9 (cm)**	164 (143 – 176)	165(153-176)	160 (150-170)	0,239
BMI (kg/m^2)**	27,1 (19 – 34)	27,3 (19-32)	25,5(18,9–34,8)	0,161
SBP (mmHg)*	130 ± 12,38	128,7 ± 10,24	130,9 ± 11,6	0,733
DBP (mmHg)*	78,3 ± 9,64	75,8 ± 10,2	77,4 ± 10,3	0,598
Heart Rate (bpm)*	78,4 ± 10,6	75,7 ± 11,1	75,1 ± 10,9	0,447
Beta blocker***	22 (70%)	20 (64%)	19 (61%)	0,716
Ace Inhibitor***	25 (80%)	27 (87%)	26 (83%)	0,788
CCB ***	18 (58%)	20 (64%)	18 (58%)	0,836
Diuretik***	18 (58%)	19 (61%)	16 (51%)	0,672

* : Mean ± SD
** : Median (minimum – maximum)
*** : n (%)

There were no significant differences in risk factors between the three diastolic dysfunction groups. The subjects had an average systolic blood pressure of 129 and a diastolic blood pressure of 77, with an average pulse rate of 77 times per minute. The most consumed medication by the patients is ACE Inhibitor with 78 users or 83% of the research subjects. When compared between diastolic dysfunction groups, no difference was found between blood pressure, pulse, or classes of antihypertensive drugs consumed.

From the analysis of echocardiography parameters, there was a significant difference in left ventricular ejection fraction (36.5 ± 7.7%) of the grade III diastolic dysfunction group compared to the other two diastolic dysfunction groups. Left ventricular end diastolic dimension as well as all diastolic dysfunction parameters were also found to differ between grade I, II, and III groups.

Table 2. Echocardiography characteristic

Echocardiography Parameters	Diastolic dysfunction grade I (n = 31)	Diastolic dysfunction grade II (n = 31)	Diastolic dysfunction grade III (n = 31)	P Value
EF (%)*	55,2 ± 9,6	50,3 ± 11,9	36,5 ± 7,7	< 0,001
LVEDD (cm)**	4,5 (3,2 – 6,7)	5,0 (3,5-6,7)	5,7 (3,2-6,8)	< 0,001
LA (cm)**	3,4 (2,2 – 4,5)	3,2 (2,6 – 4,8)	4 (2,4 – 4,6)	< 0,001
Ao (cm)*	2,31 ± 0,24	2,32 ± 0,42	2,37 ± 0,45	0,84
E/A**	0,79 (0,4-1,7)	1,2 (0,56 – 1,9)	2,5 (2,0-2,59)	< 0,001
LAVI (ml/m^2)**	31,5 (18-42)	33,6 (25,3– 51,3)	34,1 (26,4 – 38,2)	0,027
E/E'**	7,5 (5,4 – 15)	15,6 (10,8–17,6)	19,8 (13,4 – 25,6)	< 0,001
E' Septal (cm/sec)**	6 (3 – 9)	4 (1-8)	4 (2-6)	< 0,001
E' Lateral (cm/sec)**	5 (2-15)	8 (5-17)	7 (5-13)	0,001
TR V max > 2,8 m/s***	0(0%)	6(19%)	8 (25%)	0,009

* : Mean ± SD
** : Median (minimum – maximum)
*** : n (%)

From the baseline characteristics of the ECG, significant differences were found in the minimum P wave duration, which in grade I diastolic dysfunction group it was 62 ms, in grade II diastolic dysfunction it was 52 ms and in grade III diastolic dysfunction it was 51 ms, with a P value< 0.001. Significant differences were also found in P wave dispersion, it was 43 ms in grade I diastolic dysfunction, 53 ms in grade II diastolic dysfunction, and 56 ms in grade III diastolic dysfunction with a significant P value of <0.001. PR interval and QT dispersion value were also found different between the three diastolic dysfunction groups. Then a post hoc analysis was performed significant differences in the P wave dispersion between groups I and II, groups I and III, or groups II and III were found.

Table 3. ECG Characteristics of study subject

ECG Parameters	Diastolic dysfunction gradeI (n = 31)	Diastolic dysfunction grade II (n = 31)	Diastolic dysfunction grade III (n = 31)	P value
P max*	103,4 ± 9,2	103,0 ± 9,5	106,6 ± 9,5	0,269
P min**	62 (32-79)	52 (34-79)	51 (32-75)	<0,001
P dispersion**	43 (22-57)	53 (35-59)	56 (48-66)	<0,001
QTc (ms)*	386,9 ± 38	381,1 ± 36,7	474 ± 37,1	<0,001
LVH Voltage ***	18 (58%)	14 (45%)	12 (38%)	0,299
LVH Strain ***	17 (54%)	17 (54%)	21 (67%)	0,396

* : Mean ± SD
** : Median (minimum – maximum)
*** : n (%)

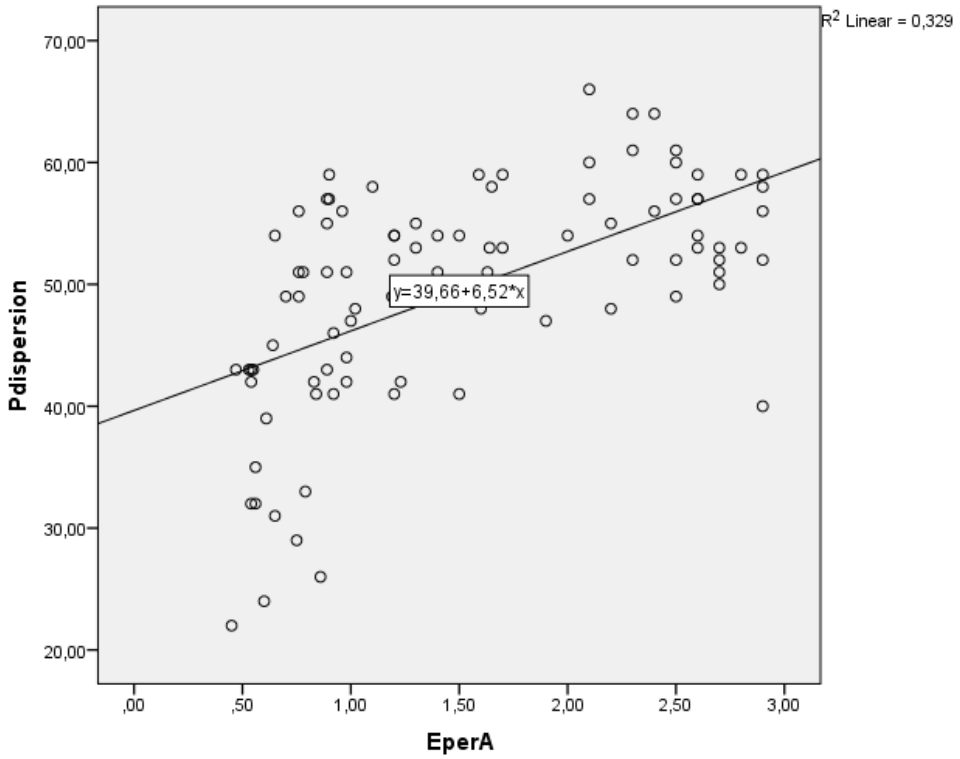
Table 4. Post hoc analysis of the ECG

ECG Parameters	DD grade I vs DD grade II	DD grade I vs DD grade III	DD grade II vs DD grade III
Dispersi gel. P	P : < 0,001	P : < 0,001	P : 0,008
P min	P : < 0,001	P : < 0,001	P : 0,740
PR Interval	P : < 0,001	P : < 0,001	P : 0,226
QTc	P : 0,816	P : < 0,001	P : < 0,001

From the correlation analysis between P wave dispersion and diastolic dysfunction, a strong correlation was found with an R value of 0.7 (P <0.001). While from correlation analysis between P wave dispersion and each component of diastolic dysfunction, there is a moderate correlation between P wave dispersion with E / A, and E / E ', and also weak correlation between P wave dispersion and LA anteroposterior dimensions.

Table 5. Correlation between P dispersion and diastolic parameters

Correlation	R	P
P dispersion with diastolic dysfunction	0,70	P < 0,001
P dispersion with E/A ratio	0,59	P < 0,001
P dispersion with E/E'	0,59	P < 0,001
P dispersion with LA dimension	0,29	P < 0,004

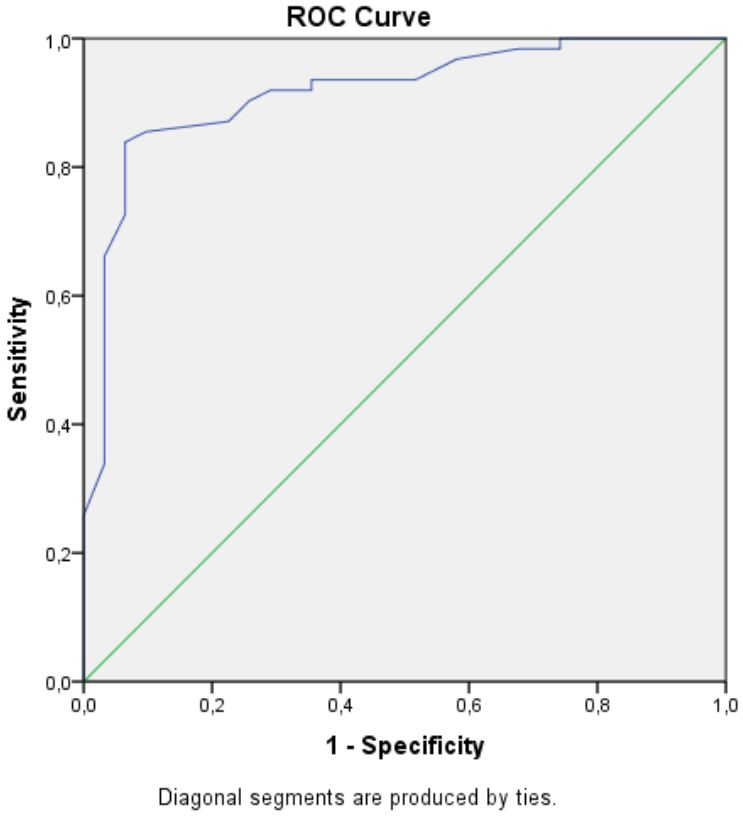


Picture 1. Scatter plot of P dispersion and E/A ratio

Cutoff value to distinguish diastolic dysfunction without increased LAP (grade I), with diastolic dysfunction with increased LAP (grade II and grade III) is then sought, from the analysis of ROC curve, the area under the curve is 0.916 with a P value <0.001. The best P-wave dispersion cutoff point to detect an increased LAP in diastolic dysfunction is 50.5 ms which has a sensitivity of 83%, specificity 93%, positive predictive value 96%, and negative predictive value 74%.

Table 6. Cut off point of P wave dispersion to determine Diastolic dysfunction with increased LAP

AUC	P value	P dispersion cut off point	Sensitivity	Spesificity
0,916	< 0,001	50,5 ms	83 %	93 %



Picture 2. ROC curve of P dispersion and diastolic dysfunction with increased LAP

Discussion

This is a cross-sectional diagnostic study that aimed to examine the relationship between P wave dispersion from 12-lead ECG and diastolic dysfunction in hypertensive patients. Based on the characteristics of the study subjects, the average age of the subjects was 60 years old, this is in accordance with previous study by Gunduyz et al, which the age of the subjects ranged between 50-60 years, from the study also, no significant differences were found in the age of the study subjects among the three diastolic dysfunction groups. The aging process is thought to play a role as a substrate in the pathophysiology of diastolic dysfunction, although it is not yet fully understood. The aging process in diastolic dysfunction is evidenced by the presence of fibrosis on histopathological examination [10,11].

From this study, the duration of hypertension in each group was more than 10 years. However, there was no significant difference in the duration of hypertension between the diastolic dysfunction groups. Hypertension with duration of> 5 years is proven to cause extensive left ventricular remodeling processes which will eventually increase the stiffness of the left ventricle so that it affects diastolic function [12]. The effect of hypertension duration on diastolic dysfunction grade itself varies. Research by Abdul et al showed patients with hypertension duration of more than 8 years, as many as 73% do not suffer from diastolic dysfunction. Therefore this difference is likely related to differences in the study population [13]. From the results of echocardiography significant differences in the EF of the research subjects was found. In patients with grade III diastolic dysfunction group, the mean EF was 36.5%, while in the mild diastolic dysfunction grade, the average EF was 50-55%. This is in accordance with previous research by Galderisi et al who stated that restrictive filling pattern with a drastic increase of LVEDP in patients with HF is associated with a more severe category of heart failure, with a significant decrease in systolic function and even many subjects has fallen into advanced/ end stage of heart failure [14].

In this study significant differences were found between the minimum duration of the P wave and the dispersion of the P wave in each diastolic dysfunction group. This is in accordance with the research by Abdullah Dogan et al. In which they encountered a value of minimum P wave duration and P wave dispersion differed in subjects with impaired left ventricular relaxation function and those who did not, in another study by Tushar et al. Also found differences in the duration of the P wave minimal among the three diastolic dysfunctions [5]. In this study, the median P-wave dispersion among diastolic dysfunction groups was 43 ms in grade I diastolic dysfunction, 53 ms in grade II diastolic dysfunction, and in grade III diastolic dysfunction, the value was 56 ms , the significance of the P value is <0.001. This is in accordance with research by Husein Gunduz et al, in which the dispersion for grade I diastolic dysfunction group in the study was 48 ms, grade II diastolic dysfunction was 54 ms, and grade III diastolic dysfunction was 58 ms [9]. From several previous studies , correlation between P wave dispersion and some diastolic dysfunction parameters were found, such as research by Randa A. Soliman regarding the correlation between P wave dispersion and diastolic dysfunction in a group of patients with coronary heart disease, P wave dispersion was found to correlate with LA's anteroposterior dimension, E / A ratio, LAVI, E / E 'septal, and also LVEDP 16. Likewise with research by Abdullah Dogan, that found a correlation between the dispersion of the P wave with the ratio E / A, IVRT, and deceleration time [15]. In this study, a strong correlation was found between P wave dispersion and diastolic dysfunction grade, and moderate correlation with E / A and E / E ratios' ratio, also weak correlation with LA's anteroposterior dimension was found.

In this study a cut off point to detect diastolic dysfunction with increased LAP is 50.5 ms which has high sensitivity and specificity. In patients with a chronic increase in LVEDP will also result in increased LAP. Other studies have found significant differences in P wave dispersion between patients with LVEDP <15 and LVEDP> 15 mmHg, although there is no mention of the cutoff point but the mean P dispersion in groups with LVEDP > 15 in the study was 70 ms, and this number is greater than the cut off point of LAP increase in this study, but overall the average P wave dispersion in the study was also greater than the average P dispersion in this study (65 ms vs 49 ms) [16]. Nevertheless, this study has several limitations, one of them is its single center nature, so we hope that further research about the same topic can be conducted in multiple centers in order to increase the reliability and strength of the results. Another limitation is the ECG examination was carried out manually so there was a potential to produce measurement errors. Next research should utilize digital measurement software to minimize the probability of this type of error.

Conclusion

Based on the results of this study, it can be concluded that P wave dispersion obtained from the 12 lead ECG has correlations with left ventricular diastolic dysfunction grades, E / A ratio, E / E ', and LA Dimension. P-wave dispersion cutoff values of ≥ 50.5 ms have good sensitivity and specificity in determining the presence of diastolic dysfunction with increased LAP. Therefore, P-wave dispersion is a simple screening tool, which are widely available and has the ability to detect grades of left ventricular diastolic dysfunction, especially in areas where echocardiography is not readily available.

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