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## Research Article

# THE RELATIONSHIP OF BLOOD PRESSURE WITH PLASMA ATHEROGENIC INDEX IN TYPE 2 DIABETES MELLITUS PATIENTS

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### ABSTRACT

**Objective:** Type 2 Diabetes Mellitus (T2DM) patients have the abnormal distribution of body fat and a high visceral fat area, which was associated with plasma atherogenic index (PAI). PAI is a valuable marker for the cardiovascular disease and cardiac risk. The aim of this study was to evaluate the role and clinical use of PAI in the cardiac risk in hypertensive T2DM patients compared to normotensive T2DM.

**Methods:** A total of 124 patients were included in the study. The patients were separated two groups that normotensive T2DM (n: 58) and hypertensive T2DM (n: 66). PAI was measured as a logarithmic value of triglyceride to high-density cholesterol ratio. Baseline demographic and clinical characteristics of patients were recorded and by used automated soft ware and compared between the groups.

**Results:** Some demographic variables of the groups were similar in our study (such as age, gender, smoker, presence of chronic disease, fasting glucose and hemoglobin A1C). Lipid profile, PAI and systolic and diastolic blood pressure significantly impaired in hypertensive group ( $p < 0,005$ ). Also, we found that a significant relationship between blood pressure and PAI used the correlation analysis ( $p < 0,001$ ).

**Conclusion:** Hypertension and diabetes mellitus are two major risk factors for cardiovascular morbidity and mortality. Epidemiological evidence shows the frequent association between hypertension and T2DM. In our study, we showed that PAI values were higher in hypertensive T2DM patients compared to normotensive T2DM patients. According to the correlation analysis, there was a positive correlation between the PAI levels and blood pressure in hypertensive T2DM patients.

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### INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become a significant global health care problem and its reported incidence is increasing at an alarming rate. Type 2 diabetes mellitus specifically increases the risk for cardiovascular mortality nearly fivefold. When hypertension is combined with diabetes, the risk of CVD is even greater<sup>1</sup>. Despite adequate glycemic and blood pressure control, diabetic hypertensives remain at increased cardiovascular risk compared to normotensive diabetic patients<sup>2</sup>.

Plasma atherogenic index (PAI) is a value defined by Dobiasova and Frohlich and is defined as the logarithmic transformation of molar TG and HDL-K ratio<sup>3</sup>. PAI is positive by HDL-K fractional esterification, negatively correlated with LDL-C particle size and cardiovascular provides additional benefits when assessing risk factors. It was suggested that PAI

values between -0.3 and 0.1 are lower, values between 0.1-0.24 and values greater than 0.24 are associated with high cardiovascular risk<sup>4</sup>.

Studies have shown the importance of high LDL-C and low HDL-C levels in the pathogenesis of atherosclerosis. In addition, high triglyceride levels have recently been shown to be an independent risk factor for coronary heart disease. Several studies have been carried out on the relationship between TG and HDL-C and there is a strong relationship between high TG / HDL-C ratio and coronary artery disease<sup>5</sup>. This rate was found to be a strong predictor of myocardial infarction<sup>6</sup>. The aim of this study was to evaluate the role and clinical use of PAI in the cardiac risk in hypertensive T2DM patients.

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## METHODS

### Study Groups

Patients with T2DM, referred to the internal medicine department between March 2018 and November 2018 and who had no target organ damage and met the study inclusion and exclusion criteria, were enrolled. The patients were separated into two groups: normotensive T2DM and hypertensive T2DM.

The following definitions were used; Type 2 Diabetes Mellitus: A fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, 2-hr PG  $\geq$ 200 mg/dL (11.1 mmol/L) during oral glucose tolerance test (OGTT, 75-g uptake) or higher, glycated hemoglobin A1c  $\geq$ 6.5 mg/dl or higher and/or glucose lowering treatment<sup>7</sup>. The definition of hypertension was considered as systolic BP  $\geq$ 140 mm Hg and/or diastolic BP  $\geq$ 90 mm Hg, previously diagnosed hypertension, or use of antihypertensive drugs.

Smokers were defined as participants who reported smoking currently and regularly (at least five cigarettes per day). Cerebrovascular events have been questioned as ischemic and hemorrhagic events. Atherosclerotic heart disease is coronary angiography detected signs of stenosis was defined as patients who have undergone PTCA (percutaneous transluminal coronary angioplasty) or stenting and coronary bypass surgery. BMI weight in kilograms divided by the square of height in meters was obtained.

The basic clinical and laboratory features of the patient and the control groups were examined and recorded. PAI was measured as a logarithmic value of triglyceride to high-density cholesterol ratio. In addition, medications of all patients were noted.

Participants who were older than 18 years and younger than 80 years were included. Patients with any of the following were excluded from the study: type 1 diabetes mellitus, hepatorenal dysfunction, thyroid dysfunction, malignancy, age outside the specified range, active infection, any anti-lipid drug usage.

### Statistical Analysis

The SPSS for Windows software package (ver. 22; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Local ethics committee approval and informed consent form were obtained from all participants.

The variables were investigated using visual (histogram, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Correlation between quantitative variables were assessed using Pearson's X<sup>2</sup> test. The Mann-Whitney U test was used to compare for non-normal distributed variables between the groups. Also while investigating the associations between non-normally distributed and/or ordinal variables, the correlation coefficients and their significance were calculated using the Spearman test. The results were evaluated at a confidence interval of 95% and significance level at p <0.05 significance level.

## RESULTS

There was no significant difference between the patient and control groups in terms of their ages, gender, smoker, have a chronic disease and BMI values. The drug use, laboratory results and all variables of patients are shown in Table 1. Among the groups included in the study, the PAI value was significantly higher in the hypertensive T2DM group (p <0.001). In addition we showed that lipid profiles of hypertensive T2DM group was significantly higher compared to normotensive T2DM. Correlation analysis showed a significant correlation between blood pressure and PAI values (p <0,001) (Figure 1). Patients correlation analyses were given in table-2.

**Table 1** Baseline demographic and clinical characteristics of normotensive and hypertensive T2DM patients

Variables	HT-2DM+ (n:58) Mean $\pm$ SD	HT+T2DM+ (n:66) Mean $\pm$ SD	P value
Male n (%)	30(51.7)	28(42.4)	0.32*
Women n (%)	28(48.2)	38(57.6)	
Smokers (%)	15(25.8)	16(24.2)	0.83*
Non-smokers (%)	43(74.2)	50(75.8)	
Age (years)	51.4 $\pm$ 6.8	53.63 $\pm$ 5.2	0.74*
BMI (kg/m <sup>2</sup> )	28.08 $\pm$ 1.7	28.07 $\pm$ 2.07	
DM duration	4.07 $\pm$ 4.11	4.47 $\pm$ 4.51	0.214*
Fasting glucose (mg/dl)	161.6 $\pm$ 20.5	159.4 $\pm$ 20.1	0.57**
HbA1c (mg/dl)	7.89 $\pm$ 0.82	7.79 $\pm$ 0.9	0.354**
Kreatinin (mg/dl)	0.82 $\pm$ 0.22	0.84 $\pm$ 0.17	0.641**
Office SBP (mmHg)	125.3 $\pm$ 6.3	140.7 $\pm$ 13.9	0.001**
Office DBP (mmHg)	70.37 $\pm$ 4.3	87.30 $\pm$ 5.18	0.001**
Total Kolesterol (mg/dl)	258.26 $\pm$ 19.3	273.95 $\pm$ 25.1	0.001**
Triglycerid (mg/dl)	270.5 $\pm$ 25.7	322.43 $\pm$ 58.3	0.001**
HDL kolesterol (mg/dl)	45.5 $\pm$ 5.9	38.51 $\pm$ 5.1	0.001**
LDL kolesterol (mg/dl)	158.7 $\pm$ 19.1	170.9 $\pm$ 21.4	0.001**
PAI ratio	1.78 $\pm$ 0.15	2.11 $\pm$ 0.24	0.001**
OAD n (%)	42(72.4)	48(72.7)	0.904*
OAD+Insüline n (%)	12(20.68)	13(19.6)	0.78*
Insüline n (%)	4(6.89)	5(7.57)	0.97*

\*Ki-kare Test \*\* Independent Samples Mann-Whitney U test # p <0,05 statistical significance **HT:** Hypertension; **BMI:** body mass index; **T2DM:** type 2 diabetes mellitus, **SBP:** systolic blood pressure, **DBP:** diastolic blood pressure, **HbA1c:** glycated hemoglobin, **PAI:** plasma atherogenic index, **OAD:** oral anti-diabetic

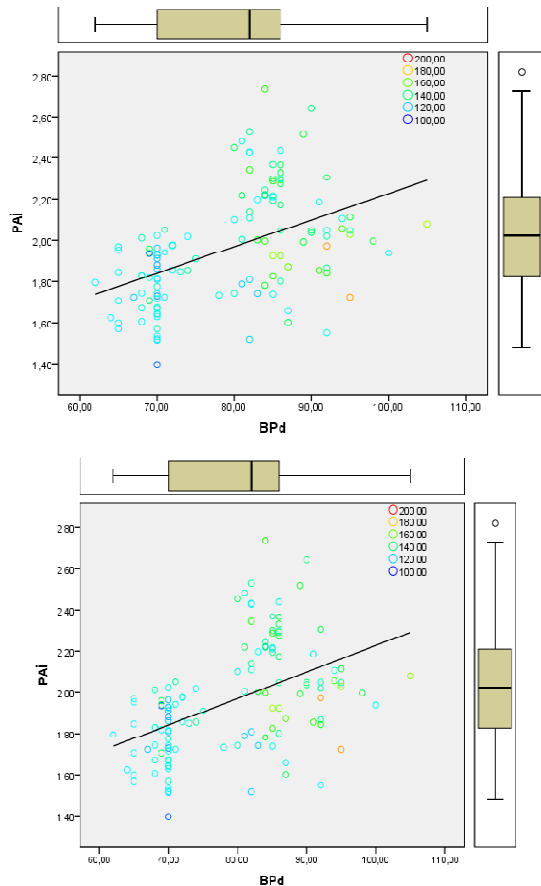
**Table 2** Patients correlation analyses

		PAI
PAI	Correlation Coefficient	1,000
	Sig. (2-tailed)	.
HBA1C	Correlation Coefficient	,117
	Sig. (2-tailed)	,194
F.GLUCOSE	Correlation Coefficient	,121
	Sig. (2-tailed)	,181
HT	Correlation Coefficient	-,652**
	Sig. (2-tailed)	,000
BMI	Correlation Coefficient	,137
	Sig. (2-tailed)	,128
BPs	Correlation Coefficient	,403**
	Sig. (2-tailed)	,000
BPd	Correlation Coefficient	,487**
	Sig. (2-tailed)	,000
TG	Correlation Coefficient	,837**
	Sig. (2-tailed)	,000
	N	124

LDL	Correlation Coefficient	,303**
	Sig. (2-tailed)	,001
	N	124
HDL	Correlation Coefficient	-,848**
	Sig. (2-tailed)	,000
	N	124
KREATİNİN	Correlation Coefficient	-,080
	Sig. (2-tailed)	,379
	N	124

\*Correlation is significant at the 0.05 level (2-tailed).-

\*\*Correlation is significant at the 0.01 level (2-tailed).



**Figure 1** Correlation analysis showed a significant correlation between blood pressure and PAI values.

## DISCUSSION

In our study, we showed that PAI values were higher in hypertensive T2DM patients compared to normotensive T2DM patients. According to the correlation analysis, there was a positive correlation between the PAI levels and blood pressure in hypertensive T2DM patients.

Triglyceride primarily contains LDL and HDL and the alterations in the lipid profile possess a risk for AS development and cardiovascular diseases. TG contains small dense LDL, which a highly atherogenic molecule. Atheroma, which develops due to the accumulation of the cholesterol crystals in the inner layers of the atherosclerotic arteries, causes the narrowing and blockage of the lumen. Systemic inflammation, increased oxidative stress, and alteration in the lipid profile are important in the development and the progression of the process<sup>8</sup>. There are studies in which the TG and HDL and the ratio of TG and HDL can be used to calculate the PAI. Niroumand *et al.* determined that PAI can be used as

an indicator of the cardiovascular diseases<sup>9</sup>. Onat *et al.* showed that PAI predicts CHD independently, type 2 diabetes mediated by obesity in men and in women, high blood pressure, metabolic syndrome, and CHD potentially mediated by involvement in a proinflammatory status reflected by CRP<sup>10</sup>.

Manohar *et al.* showed that PAI may be particularly useful as atherogenic risk predictors in newly diagnosed patients with T2DM<sup>11</sup>. Hermans *et al.*, proposed PAI as a simple means to estimate atherogenic dyslipidemia and the residual cardiovascular risk in T2DM<sup>12</sup>. A recent study by Rao *et al.*, emphasizes the importance of PAI in predicting cardiovascular disease (CVD) risk associated with newly diagnosed diabetes<sup>13</sup>. Hypertension and diabetes mellitus are 2 major risk factors for cardiovascular morbidity and mortality. Epidemiological evidence shows the frequent association between hypertension and diabetes mellitus, indicating a substantial overlap in the pathophysiology of the 2 diseases, and leading to additive increases in the risk of cardiovascular events<sup>14</sup>. In patients at high risk for cardiovascular complications, the SPRINT (Systolic Blood Pressure Intervention Trial) recently showed that targeting a systolic blood pressure (SBP) of <120 mm Hg, as compared with the standard <140 mm Hg, results in lower rates of fatal and nonfatal major cardiovascular events and death from any cause<sup>15</sup>. In our study, PAI was found higher in normotensive and hypertensive diabetic patients. Hypertensive diabetic patients have a higher risk of CVD. When we did a literature review, we could not find any study that examined the PAI rates of this patient group. A significant increase in the PAI value in patients with hypertensive T2DM especially compared to normotensive T2DM, we think this group of patients may explain why the risk of CVD is higher.

### Limitations of the Study

The main limitation of our study is the small number of patients enrolled in the study.

### Conflict of Interest

None declared

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