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ORIGINAL ARTICLE

Left Ventricular Myocardial Performance Index and its Relationship with Presystolic Wave in Prediabetic Patients

Prediyabetik Hastalarda Sol Ventriküler Miyokardiyal Performans İndeksi ve Presistolik Dalga ile İlişkisi

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Abstract

Introduction: In this study, we aimed to investigate the effect of prediabetes on the cardiovascular system and the relationship between MPI and PSW by using myocardial performance index (MPI) and presystolic wave (PSW) and the usability of both parameters as a screening test.

Methods: A total of 113 participants, that is, 59 prediabetic patients and 54 healthy volunteers, aged 18–79 years, who applied to cardiology and endocrinology polyclinics between March 2020 and September 2020, were included in the present study. The groups were compared in demographic and clinical data, left ventricular functions, left ventricular MPI, PSW, and laboratory results.

Results: Left ventricular diastolic dysfunction (p=0.001), MPI (p<0.001), and PSW (p=0.003) were higher in the prediabetic group. A positive correlation was observed between fasting blood glucose and MPI index (r=0.509, p<0.001) and between PSW and MPI (r=0.405, p=0.001).

Discussion and Conclusion: This study is the first in the literature to examine the effects of prediabetes on the cardiovascular system using MPI and PSW. We think that these parameters may be associated with left ventricular diastolic dysfunction in prediabetics.

Keywords: Diastolic dysfunction; Myocardial performance index; Prediabetes; Presystolic wave

The incidence of cardiovascular diseases (CVDs) increases day by day globally because of increasing life expectancy. It ranks first among all causes of death and creates a significant medical and economic burden.[1] Among the risk factors, besides genetic factors, sedentary life, and negative behaviors such as smoking and poor diet, there are diseases such as diabetes mellitus (DM), hypertension (HT), and dyslipidemia. DM is a worldwide health problem that negatively affects all age groups. If DM and its complications are not diagnosed and treated in time, mortality

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rates increase. The statement "diabetes is accepted as a risk equivalent for CVD" is included in the current DM diagnosis and treatment guidelines.[2] Unfortunately, several patients have concomitant CVD when DM is diagnosed.[3] Hence, it is crucial to diagnose and take necessary preventive measures in the prediabetic phase before DM develops.

Prediabetes is when the fasting blood glucose (FBG) value is below the limit values for the diagnosis of DM and above the normal glucose value. Two forms of prediabetes have been described as impaired fasting glucose (IFG) and impaired glucose tolerance (IGT).[4] Current evidence has shown that prediabetes is related to increased cardiovascular risk and mortality.[5] The myocardial performance index (MPI) is an index that can be used to evaluate systolic and diastolic functions, which has prognostic value in several heart diseases and provides information regarding the global performance of the left ventricle.[6] Various studies have shown that MPI can be used to evaluate cardiac functions in dilated cardiomyopathy, congestive heart failure, cardiac amyloidosis, and many diseases with cardiac involvement.[7–9] Additionally, it has been found that MPI can predict cardiovascular outcomes in DM.[10]

Similarly, MPI was found to be related to cardiovascular outcomes in prediabetics.[11] A Doppler examination can detect a presystolic wave (PSW) by scanning the left ventricular outflow tract (LVOT). PSW often occurs in the late diastolic phase and can theoretically be related to poor left ventricular compliance and increased left ventricular stiffness.[12,13]

Preventing complications caused by any disease is directly related to early diagnosis and early detection of damage to the end organs. Hence, we aim to examine the effect of prediabetes on the cardiovascular system using MPI and PSW to investigate the relationship between MPI and PSW and the usability of both parameters as a screening test.

Materials and Methods

The study was designed prospectively as a single-center study. The study was designed as a single-center and prospective study. Ethics committee approval was received from Kırıkkale University Clinical Research Ethics Committee with the decision number 2020/04 dated 20.02.2020. Between March 2, 2020, and September 1, 2020, individuals between the ages of 18 and 79 years who applied to our hospital's cardiology and endocrinology polyclinics were diagnosed with prediabetes and indicated echocardiography were included in the study. Fifty-nine prediabetes patients and 54 age- and sex-matched healthy volunteers were included in the study. Those with FBG of 100–125 mg/dl were defined as IFG, and those whose blood glucose was 140–199 mg/dl at the second hour after OGTT with 75 g glucose were defined as IGT. Those with IFG, IGT, or both (IAG+IGT) constituted the prediabetic patient group. Those with FBG of <100 mg/dl and 2 h glucose values of <140 mg/dl were included in the control group.

The following patients were excluded:

Those describing known coronary artery disease (CAD), heart failure (left ventricular ejection fraction (LVEF) <55%), moderate and severe heart valve diseases, acute and chronic renal failure, active angina pectoris, atrial fibrillation, Type I and Type II patients with a diagnosis of DM, pregnant women, severe hepatic failure, or thyroid disorders; those with active infections or those who have had an infection in the last 2 weeks and have received treatment for it; and those with a hemoglobin value of <11.0 g/dl and poor image quality.

General Evaluation and Measurements

Medical histories of all individuals included in the study were taken, and physical examinations were performed. The waist circumference, weight, and height of the individuals were measured, and their body mass index (BMI) was calculated using the formula BMI=weight (kg)/[height (m)]^2. Blood samples were taken from all individuals included in the study after a 12 h fast. Complete blood count measured hemoglobin, platelet, white blood cell, neutrophil, and lymphocyte levels. In biochemical analysis, FBG, creatinine, sodium, potassium, blood urea nitrogen, liver function tests, thyroid-stimulating hormone, and HbA1c levels were measured.

Echocardiographic Examination

GE (General Electric Company, Indianapolis, Indiana USA) Vivid E9 echocardiography device was used for echocardiographic examination. All visualization was performed in the left lateral decubitus position, with monitoring, by the American Society of Echocardiography recommendations. Separate measurements were made from the apical two- and four-chamber views using the modified Simpson method, and the average of both values was accepted as LVEF. A transmitral flow sample was obtained with the PW Doppler sample volume placed at the tip of the mitral leaflets in the apical four-chamber window. The mitral E, A waves, and the deceleration time of the E wave were obtained from the sample obtained. E/A ratios were calculated for each patient utilizing these measurements. Simultaneous ECG follow-up was performed in all cases via Doppler echocardiography. Measurements were made by placing

the tissue Doppler sample volume on the septal and lateral edges of the mitral annulus in the apical four-chamber window. Early diastolic peak (Em), late diastolic peak (Am), and systolic flow peak velocities (Sm) were evaluated from the annulus of the septal and lateral walls, respectively. Isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT), and ejection times (ETs) were determined. MPI was calculated by dividing the sum of IVCT and IVRT obtained with these measurements by ET (Fig. 1). The LVOT continuous waveform was scanned with Doppler (CW) and the PSW velocity was measured. All standard and tissue Doppler measurements were determined for five sequential cardiac cycles, and the averages of the obtained values were used for statistical analysis.

Statistical Method

SPSS 20.0 (SPSS, Inc., Chicago, Illinois, USA) computer program was used for statistical analysis while evaluating the results obtained in the study. Continuous variables were recorded as mean±standard deviation for parametric variables and as median and 25%–75% quartiles for non-parametric variables. Categorical variables were stated as frequency and percentage (%). Data distribution was interpreted utilizing the Kolmogorov–Smirnov test. Variables showing a normal distribution among the groups were compared using the Student t-test. The variables not showing normal distribution were compared using the Mann–Whitney-U test. The Chi-square test was used to compare categorical variables. Finally, correlation analysis was done using Spearman or Pearson correlation test. For all statistical evaluations, $p<0.05$ was considered significant.

Results

Of all the participants included in the study, 67 were female and 46 were male. The average age of prediabetics was higher than that of the healthy group, and it was not statistically significant (44.2±10.7 years vs. 40.0±9.7 years, p=0.07, respectively). Mean weight and BMI were significantly higher in the prediabetic group than in the control group (80. 3±14. 9 kg vs 72±12. 5 kg, p=0.02) (28.9±5.5 kg/m^2 vs 25.3±4.1 kg/m^2 ($p<0.001$). There was no statistically significant difference between the groups regarding sex, age, family history of CAD, smoking, HT, and hyperlipidemia. Table 1 shows the demographic and clinical characteristics of the patients.

In laboratory analyzes, as expected, FPG and HbA1c were significantly higher in the prediabetic group than in the control group (111±6 mg/dl vs. 89±6 mg/dl and 5.7%±0.4% vs. 5.3%±0.3%) ($p<0.001$ and p=0.009, respectively). Although the total cholesterol level was higher in the prediabetic group (p=0.017), there was no significant difference between other laboratory parameters (Table 2).

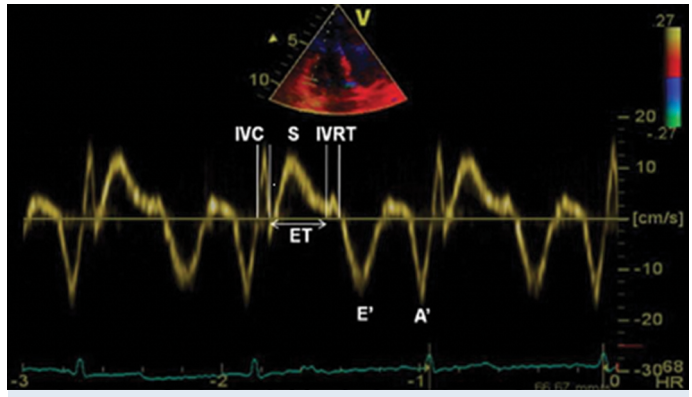

Figure 1. CTissue Doppler Visualization demonstrated myocardial Sm, Em, and Am waves as well as IVCT, IVRT, and ET.

Table 1. Demographic and clinical data of the patients

	Prediabetics (n=59)	Normal (n=54)	p
Male, n (%)	22 (37)	24 (44)	0.45
Female, n (%)	37 (63)	30 (56)	
Age (year)	44.2±10.7	40.0±9.7	0.07
Height (m)	166.8±8.4	168.7±7.7	0.20
Weight (kg)	80.3±14.9	72±12.5	**0.002**
BMI (kg/m^2)	28.9±5.5	25.3±4.1	<**0.001**
Family history of CAD, n (%)	7 (12.1)	5 (9.3)	0.63
Smoking, n (%)	12 (20.7)	9 (16.7)	0.58
Hypertension, n (%)	19 (32.8)	10 (18.5)	0.08
Hyperlipidemia, n (%)	6 (10.3)	1 (1.9)	0.06

BMI: Body mass index; CAD: Coronary artery disease.

Table 2. Laboratory measurements of patients

	Prediabetics (n=59)	Normal (n=54)	p
WBC (10^3/µl)	7.0±1.7	7.3±1.9	0.27
Hemoglobin (g/dl)	14±1.4	13.5±2.1	0.24
Platelet (10^3/µl)	269±57	256±66	0.28
Fasting glucose (mg/dl)	111±6	89±6	<**0.001**
Urea (mg/dl)	27±8	25±8	0.32
Creatinine (mg/dl)	0.84±0.17	0.85±0.17	0.80
Total cholesterol (mg/dl)	208±38	187±40	**0.017**
LDL (mg/dl)	122±31	109±39	0.10
HDL (mg/dl)	50±11	49±11	0.64
Triglyceride (mg/dl)	168 (101–191)	143 (76–201)	0.24
HbA1c (%)	5.7±0.4	5.3±0.3	**0.009**

WBC: White blood cells; LDL: Low-density lipoprotein; HDL: High-density lipoproteins.

Table 3. Echocardiographic measurements of the patients

	Prediabetics (n=59)	Normal (n=54)	p
LVEF (%)	65±3	66±3	0.46
Diastolic dysfunction, n (%)	18 (31)	3 (5.6)	**0.001**
IVCT (msn)	60±11	46±11	<**0.001**
IVRT (msn)	93±13	69±14	<**0.001**
ET (msn)	229±15	287±18	<**0.001**
MPI	0.56±0.11	0.45±0.10	<**0.001**
PSW velocity (m/sn)	0.52±0.12	0.43±0.12	**0.003**

LVEF: Left ventricular ejection fraction; IVCT: Isovolumetric contraction time; IVRT: Isovolumetric relaxation time; ET: Ejection time; MPI: Myocardial performance index; PSW: Presystolic wave.

Table 3 shows a comparison of echocardiographic data. LVEF was similar in both groups, and the number of patients with diastolic dysfunction was higher in the prediabetic group (18 vs. 3, p=0.001). IVCT and IVRT were higher in the prediabetic group. Average IVCT; 60±11 ms vs. 46±11 ms, and mean IVRT, respectively; 93±13 ms vs. 69±14 ms (both p<0.001). ET was significantly lower in the prediabetic group (229±15 ms vs. 287±18 ms, p<0.001).

MPI was calculated significantly higher in the prediabetic group compared to the control group (0.56±0.11 vs. 0.45±0.10 p<0.001) (Fig. 2a). PSW, again, was found to be higher in the prediabetic group (0.52±0.12 m/s vs 0.43±0.12 m/s, p=0.003) (Fig. 2b).

A positive and significant correlation was found between MPI and PSW (r=0.405, p=0.001) (Fig. 2c).

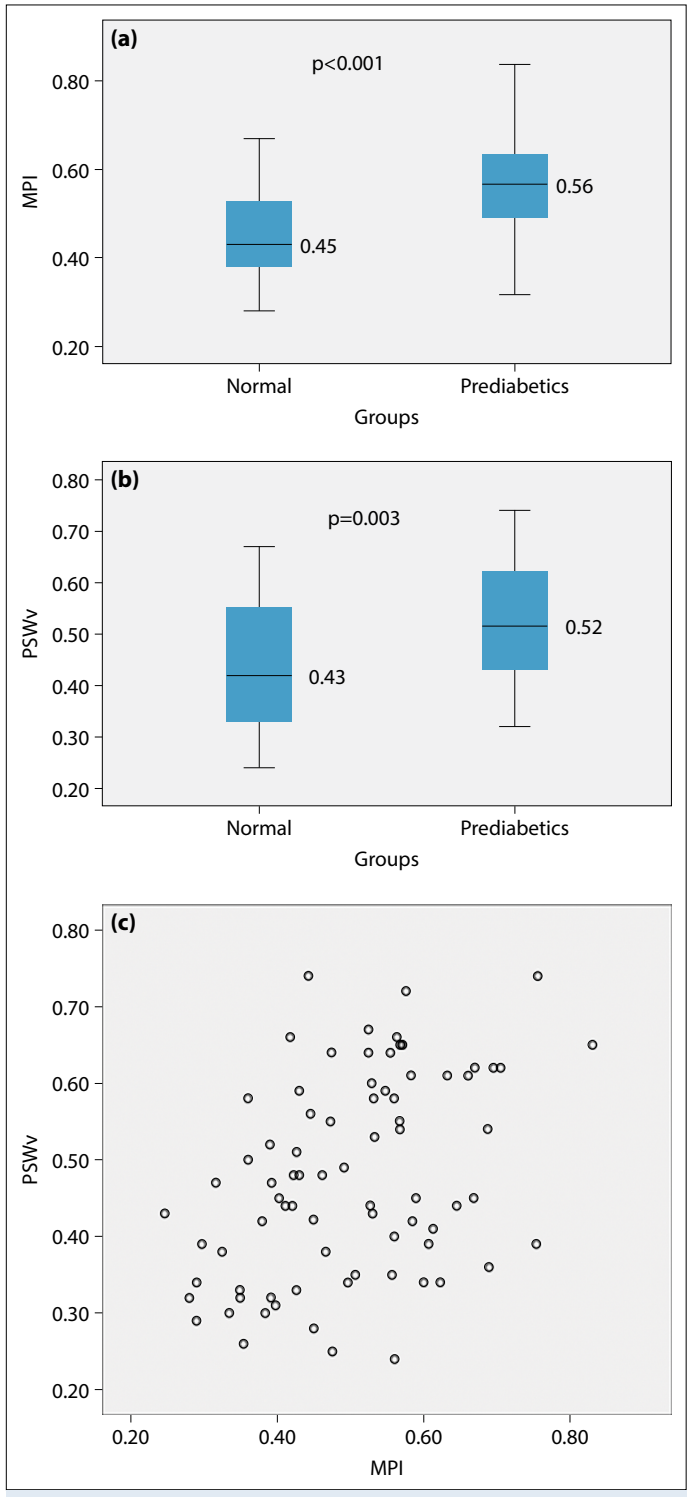

Figure 2. (a) Comparison of mean MPI values between groups. **(b)** Comparison of mean PSW velocity values between groups. **(c)** Scatter plot of the relationship between MPI and PSW velocity.

Discussion

The present study found that MPI and its constituent parameters, IVCT and IVRT, were prolonged in the prediabetic group, whereas ET was shortened. Additionally, we found that PSW, an indicator of decreased left ventricular compliance and increased stiffness, was higher in prediabetic patients, and a positive correlation was seen among MPI and PSW. Hence, this study is the first in the literature to examine the effects of prediabetes on the cardiovascular system by using MPI and PSW parameters together.

It is known that DM and prediabetes adversely affect the systolic and diastolic functions of the heart.[14,15] Since DM has an important place in the etiology of diastolic dysfunction, it is in the group of diseases at high risk for developing heart failure. Nevertheless, it does not have structural defects in the myocardium. Prediabetes, which is a precursor to DM, has also been associated with increased cardiovascular risk and mortality.[16] For this reason, early recognition of prediabetes and prevention of possible complications, especially in vital organs that cause increased mortality, is very crucial.

MPI is a repeatable and easily measurable echocardiographic parameter that provides information regarding the sys-

tolic and diastolic functions of the heart.[6] MPI can be measured by conventional methods as well as by tissue Doppler technique. In previous studies, MPI was calculated with more conventional methods, and the tissue Doppler imaging technique was used in this study. In a study, tissue Doppler imaging was a better alternative in preventing possible false results in cases with high heart rates.[17] MPI is a parameter that has been shown to have prognostic value in several diseases such as dilated cardiomyopathy, infiltrative cardiomyopathy, and pulmonary HT.[9,18–20] MPI is also increased in patients with CAD, diabetes, and hypertension and those with moderate to severe obstructive sleep apnea syndrome.[11,21,22] Patients with any of the diseases affecting MPI mentioned above were not included in this present study.

The longer duration of IVRT, one of the components of MPI, in the prediabetic group is one of the reasons why MPI is higher in the prediabetic group. IVRT, which is an energetically active period, is adenosine triphosphate (ATP) dependent. In this phase, the sodium, potassium, and calcium pumps are actively functioning by consuming ATP. ATP, which cannot be formed sufficiently in the cell due to ischemia, increases lactic acid accumulation due to anaerobic respiration, restricts diastole, and prolongs IVRT. This may occur in ischemia and in conditions such as prediabetes that affect left ventricular functions and cause indirect ischemia. It is known that myocyte hypertrophy, fibrous tissue increase, microangiopathy together with microvascular dysfunction, impaired relaxation, and increased passive diastolic stiffness develop in the diabetic heart.

Nevertheless, there are limited studies on these mechanisms in prediabetes, and possible mechanisms have been mentioned in a few studies. One of them is that transforming growth factor β1 increases in the left ventricle with the effect of hyperinsulinemia and hyperglycemia in prediabetic rats. Hence, fibrosis develops in the myocardial tissue.[23] Again, certain studies have shown that insulin levels increase in prediabetics, which increases hypertrophy and fibrosis by stimulating myocytes and fibroblasts.[24] These reasons may be the reasons for the higher incidence of diastolic dysfunction in the prediabetic group. The fact that MPI, a predictor of diastolic dysfunction, was higher in the prediabetic group may be due to the reasons mentioned above in the prediabetic heart.

The number of studies examining the connection between PSW and left ventricular dysfunction is limited in the literature. In a study by Akyuz AR et al.,[25] it was shown that the presence of PSW in asymptomatic hypertensive individuals might be an independent predictor of subclinical LV dysfunction. In another study, the relationship between non-dipper HT and PSW was examined. It was thought that the presence of PSW or increased PSW velocity might be associated with non-dipper HT and the risk of severe end-organ damage.[26] In a study examining the relationship between carotid intima media thickness, which is a direct marker of atherosclerosis, and PSW, it was found that increased PSW velocity was associated with carotid intima media thickness.[27] Kul et al.[21] evaluated subclinical left ventricular dysfunction with MPI in patients with type 2 DM. They showed that the presence of PSW may be associated with increased MPI. In the present study, unlike Kul et al., prediabetic patients were examined. Similarly, the presence of PSW and the increase in velocity were associated with abnormal MPI values. It has been thought that PSW may be associated with decreased left ventricular compliance and increased left ventricular stiffness. The increased left ventricular stiffness seen in prediabetes may cause the presence of PSW and increased velocity. Thus, the presence of PSW may be a parameter that can predict subclinical LV dysfunction in prediabetes patients.

Although many studies in the literature examine the effects of diabetes on cardiac functions, the number of studies evaluating cardiac functions in the prediabetic period is less. In a study by Stahrenberg et al.,[28] individuals with impaired glucose metabolism and hyperinsulinemia were screened with conventional echocardiography. No difference was found in left ventricular systolic functions when compared with the control group. By contrast, deterioration in diastolic functions was found. In another similar study, it was found that there was a significant deterioration in diastolic functions in prediabetics with Doppler echocardiography.[29] Similar to other studies, in this study, after excluding etiologies that may cause diastolic dysfunction, echocardiographic examination revealed more diastolic dysfunction in prediabetic patients than in the normal group. Several factors such as myocyte hypertrophy, myocardial fibrosis, microvascular dysfunction, impaired relaxation, increased diastolic stiffness, and metabolic changes can cause these disorders. A recent study showed that ventricular repolarization parameters are impaired in prediabetic patients, and the risk of arrhythmia may be high.[30] We think that the possible cause of this situation may be the changes in the cellular level of the myocardium due to impaired glucose metabolism.

The fact that the weight, BMI and total cholesterol values of the prediabetic group were significantly higher than the healthy group in the present study suggested that obesity and insulin resistance contribute to the development of diastolic dysfunction and the classical pathophysiological bases.

It is known that high blood glucose level is related with worse clinical outcomes. Hyperglycemia is associated with increased hospitalization even without DM, and hyperglycemia alone is a significant risk factor for heart failure. Moreover, it has been shown that every 1% increase in HbA1c levels increases the risk of HF by 12%.[31] In this study, it was suggested that high blood glucose levels and HbA1c values also affected diastolic dysfunction, which was more common in the prediabetic group.

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