Araştırma Makalesi *Research Article*

Pamukkale Tıp Dergisi
Pamukkale Medical Journal

doi:https://dx.doi.org/10.31362/patd.910961

Myocardial performance index is associated with Systematic Coronary Risk Estimation (SCORE) system in chronic coronary syndrome

Kronik koroner sendromda miyokardial performans indeks Sistematik Koroner Risk Tahmini (SCORE) ile ilişkilidir

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Gönderilme tarihi:07.04.2021 Kabul tarihi:28.04.2021

Abstract

Purpose: The Systematic Coronary Risk Estimation (SCORE) system is used to determine 10-year cardiovascular risk. Myocardial performance index (MPI), a well-accepted echocardiographic parameter, is used to provide any information about the global function of the ventricle. We aimed to investigate the relationship between MPI and SCORE.

Materials and methods: A total of 168 participants with chronic coronary syndrome (CCS) presented to cardiology outpatient clinic between 1 June and 31 December 2020 were retrospectively enrolled in the study. Cardiovascular risk estimation was calculated by SCORE assessment. The participants were divided into two groups as 46 patients with low cardiovascular risk, and 122 patients with moderate-high-very high risk, according to the SCORE. Laboratory parameters and echocardiography findings of the patients were recorded.

Results: There was no difference in body mass index, office systolic, and diastolic blood pressure between the groups. While blood glucose was 94.5 (83.0-110.3) in the low-risk group, it was 101.0 (90.0-130.5) in the moderate-high risk patient group (p=0.007). Similarly, Urea, creatinine, lactate dehydrogenase, total cholesterol, NT pro-BNP, and Troponin T in the moderate-high risk group were significantly higher than was the low-risk group. MPI was significantly higher in the moderate-high risk patient group (p<0.001). MPI (OR=2.358, 95% CI:1.033-5.382, p=0.042), urea (OR=1.090, 95% CI:1.019-1.166, p=0.012), and glucose (OR=1.023, 95% CI:1.003-1.043, p=0.025) were independently associated with the moderate-high SCORE.

Conclusion: We found that MPI predicted a moderate-high SCORE system. Further studies are warranted to better clarify the association of SCORE with echocardiographic parameters including MPI.

Key words: Myocardial performance index, Systematic Coronary Risk Estimation (SCORE) system, chronic coronary syndrome, cardiovascular risk.

Harbalioglu H, Genc O, Yildirim A. Myocardial performance index is associated with Systematic Coronary Risk Estimation (SCORE) system in chronic coronary syndrome. Pam Med J 2021;14:818-827.

Öz

Amaç: Sistematik Koroner Risk Tahmin (SCORE) sistemi, 10 yıllık kardiyovasküler riski belirlemek için kullanılır. Kabul gören bir ekokardiyografik parametre olan miyokardiyal performans indeksi (MPI), ventrikülün global işlevi hakkında bilgi sağlamak için kullanılır. Biz; MPI ve SCORE arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve yöntem: 1 Haziran-31 Aralık 2020 tarihleri arasında kardiyoloji polikliniğine başvuran kronik koroner sendromlu (KKS) toplam 168 hasta retrospektif olarak çalışmaya alındı. Kardiyovasküler risk tahmini SCORE değerlendirmesi ile hesaplandı. SCORE'a göre hastalar düşük kardiyovasküler riskli 46 hasta ve orta-yüksek-çok yüksek riskli 122 hasta olarak iki gruba ayrıldı. Hastaların laboratuvar parametreleri ve ekokardiyografi bulguları kaydedildi.

Bulgular: Gruplar arasında vücut kitle indeksi, ofis sistolik ve diyastolik kan basıncı açısından fark yoktu. Kan şekeri düşük risk grubunda 94,5 (83,0-110,3) iken, orta-yüksek riskli hasta grubunda 101,0 (90,0-130,5) idi (p=0,007). Benzer şekilde, orta-yüksek risk grubundaki Üre, kreatinin, laktat dehidrogenaz, total kolesterol, NT pro-BNP ve Troponin T, düşük risk grubuna göre anlamlı olarak daha yüksekti. Orta-yüksek riskli hasta grubunda MPI anlamlı olarak daha yüksekti (p<0,001). MPI (OR=2,358, %95 CI:1,033-5,382, p=0,042), üre (OR=1,090, %95 CI:1,019-1,166, p=0,012) ve glikoz (OR=1,023, %95 CI:1,003 -1,043, p=0,025) bağımsız olarak orta-yüksek SCORE ile ilişkilendirildi.

Sonuç: MPI'nin orta-yüksek SCORE sistemini öngördüğünü bulduk. SCORE ile MPI de dahil olmak üzere ekokardiyografik parametreler arasındaki ilişkiyi daha iyi açıklığa kavuşturmak için ileri çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Miyokardiyal performans indeks, Sistematik Koroner Risk Tahmin (SCORE) sistemi, kronik koroner sendrom, kardiyovasküler risk.

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Harbalıoğlu H, Genç Ö, Yıldırım A. Kronik koroner sendromda miyokardial performans indeks ile Sistematik Koroner Risk Tahmini (SCORE) arasındaki ilişki. Pam Tıp Derg 2021;14:818-827.

Introduction

Cardiovascular diseases, the leading cause of mortality in both men and women, account for 46% of deaths in Europe [1]. There are many risk factors associated with cardiovascular events such as male gender [2], advanced age [2], high blood pressure [3], high low-density lipoprotein (LDL) [4], smoking [5], and diabetes mellitus [6]. Various risk scores have been developed to select patients at moderate-high risk to receive primary preventive treatment approaches including lipid-lowering therapy and lifestyle change. The Systematic Coronary Risk Estimation (SCORE) scoring tool, calculated using age, sex, total cholesterol, systolic blood pressure, and smoking parameters, is recommended by the European Society of Cardiology to determine 10-year cardiovascular risk [7]. This scoring aims to reduce cardiovascular deaths via measures and treatment protocols to be practiced according to the determined risk level.

Myocardial performance index (MPI), which is a doppler-derived echocardiographic parameter easy to obtain, is calculated by summing the isovolumetric relaxation time and the isovolumetric contraction time and dividing it by the ejection time [8]. The ratio of isovolumetric contraction time to ejection time reflects the systolic function of the ventricle, while the ratio of isovolumetric relaxation time to ejection time reveals the diastolic function of the ventricle [9]. Many studies reported that the increase in MPI, which provides information about both systolic and diastolic function of the ventricle, is associated with diseases that affect the cardiovascular system, such as hypertension [10], coronary artery disease [11], congestive heart failure [12], pulmonary hypertension [13], chronic obstructive pulmonary disease [14], and cardiac amyloidosis [15]. Since MPI is less affected by the image quality and also demonstrates diastolic dysfunction, it enables us to better evaluate global left ventricular (LV) function, compared to ejection fraction [16]. There are few studies on echocardiographic parameters that may be related to the SCORE and even might predict a higher SCORE. We, therefore, believe this point should be clarified. Thus, in order to overcome this deficiency, to some extent, we aimed to investigate the relationship between MPI and SCORE, which reflects cardiovascular risk.

Materials and methods

Study population and design

168 patients with chronic coronary syndrome (CCS) who admitted to Düzce Atatürk State Hospital cardiology outpatient clinic between 1 June and 31 December 2020 were retrospectively included in the study. The diagnosis of CCS was made after the confirmation by imaging procedures (myocardial perfusion scintigraphy (MPS) or coronary CT angiography) or a positive exercise test for patients with effort-related typical chest pain (localized to retrosternal/anterior chest, arm, shoulder, jaw, and relieved by rest or nitrate or shortness of breath, equivalent to angina) [17]. Of the study population, 95 patients were positive for exercise test, 38 patients for MPS, and 35 patients for coronary computed tomography. The participants were divided into two groups as 46 patients with low cardiovascular risk, and 122 patients with moderate-high-very high risk according to the SCORE assessment tool. Demographic data of the study population consisting of age, gender, comorbidities, smoking, and body mass index were recorded. Laboratory parameters including hemogram, glucose, urea, creatinine, lipid profile, Troponin T both on admission and peak, N-terminal pro-BNP, C-reactive protein (CRP), and lactate dehydrogenase (LDH) were analyzed. Glomerular filtration rate (GFR) was calculated by the Modification of Diet in Renal Disease (MDRD) method [18]. Echocardiography findings of the patients were recorded. Cardiovascular risk estimation was calculated by SCORE assessment. The study was conducted in accordance with the Declaration of Helsinki. Patients were excluded if they had coronary artery disease, diabetes mellitus, cerebrovascular disease, peripheral artery disease, moderate-severe chronic renal failure (GFR<60 ml/min /1.73 m^2), heart failure with reduced EF (EF<50%), severe valve insufficiency, active infection or malignancy.

An institutional ethics committee, Çukurova University Faculty of Medicine Clinical Research Ethics Committee, approved the study protocol. The need for written informed consent was waived due to the retrospective nature of the study.

SCORE algorithm

In the European Society of Cardiology's guideline on cardiovascular disease prevention in clinical practice, the risk algorithm of countries has been determined by a 10-year cardiovascular risk assessment [7]. SCORE was calculated for each patient using age, sex, smoking status, systolic blood pressure, and total cholesterol levels according to the European high-risk chart. Determination of cardiovascular risk algorithm was as follows; those with a SCORE of < 1 as low-risk, those with a SCORE of 1 ≤ to <5 as intermediate-risk, those with a SCORE of 5 ≤ to <10 as high-risk, and those with a SCORE of >10 as very high-risk patients.

Echocardiographic findings

Measurements were taken from the participants in the left decubitus position with a VIVID 7 (GE-Vingmed, Horten, Norway) echocardiography device using a 3.5 MHz cardiac probe. Ejection fraction (EF) was measured by using the modified Simpson method [19]. In echocardiographic evaluation, left atrial diameter, left ventricular systolic volume, left ventricular diastolic volume, interventricular wall thickness, and posterior wall thickness were recorded. MPI was calculated by measuring isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT), and ejection time (ET), with the (IVCT + IVRT) / ET formula [20] (Figure 1).

Statistical analysis

An analytical (Kolmogorov–Smirnov test) method and visual methods (histograms and probability plots) were used to test the normality of distribution. Categorical variables were

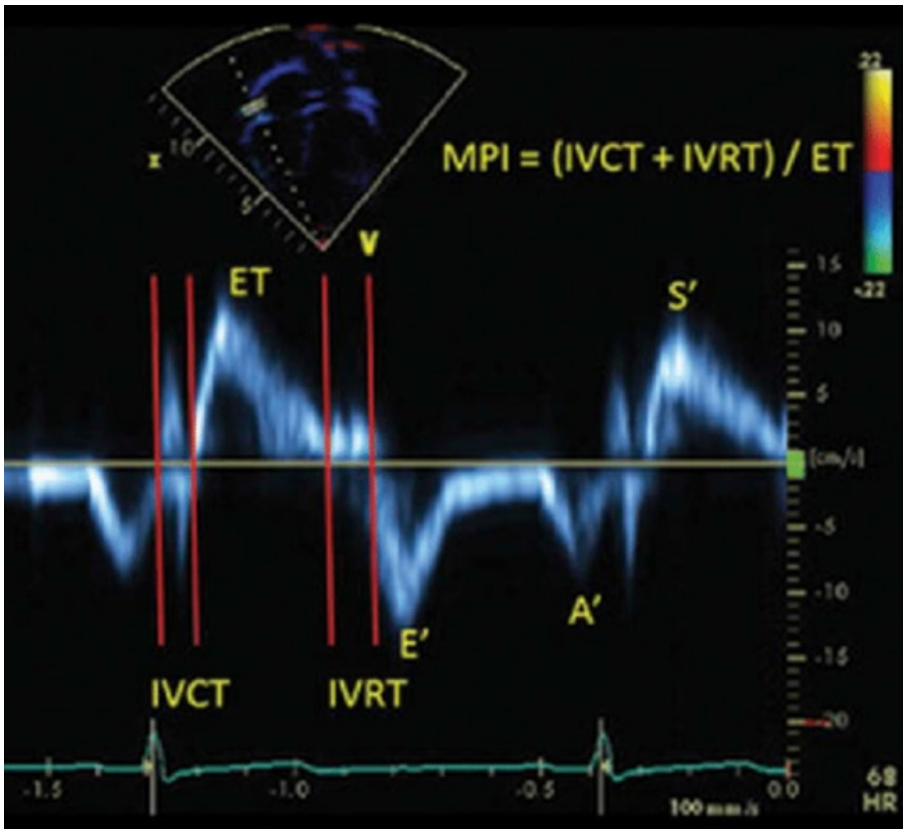

Figure 1. Illustration of how to calculate MPI in echocardiographic evaluation.
IVRT: isovolumetric relaxation time, IVCT: isovolumetric contraction time, ET: ejection time

expressed as numbers and percentages (%), while continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range). Fisher's exact test and The Chi-square test were utilized to compare categorical variables. The Student t-test and the Mann-Whitney U test were used to compare continuous variables where appropriate. All of the significant parameters in the univariate analysis with p<0.1 were selected for the multivariable model and stepwise logistic regression analysis with backward selection was used to identify the independent association of a high SCORE. The odds ratio (OR) and 95% confidence interval (CI) of each independent variable were calculated. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off value of MPI level for determining high SCORE with the Youden index (Youden index = Max ([sensitivity] + [specificity] − 1). A 2-tailed p-value of <0.05 was considered significant throughout the study. In all statistical analyses; SPSS 20.0 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc statistical software v19.5.6 (Ostend, Belgium) were utilized.

Results

A total of 168 individuals participated in our retrospective cohort, 46 of whom were at low risk in SCORE assessment. The mean age in the low-risk group was lower than in the moderate-high risk group (45.4±5.9 vs 57.0±10.4, p<0.001). There was no difference in body mass index, office systolic, and diastolic blood pressure between the groups. In comorbidities, Hypertension and chronic obstructive pulmonary disease were similar between the two groups. While blood glucose was 94.5 (83.0-110.3) in the low-risk group, it was 101.0 (90.0-130.5) in the moderate-high risk patient group (p=0.007). Similarly, Urea, creatinine, lactate dehydrogenase, total cholesterol, NT pro-BNP, and Troponin T in the moderate-high risk group were significantly higher than the low-risk group. SCORE was 2 (1-9) in the study population and 4 (1-15) in the moderate-high SCORE group. The demographic data and laboratory parameters of the patients are shown in detail in Table 1. EF was higher in the low-risk patient group (p=0.02). MPI was significantly higher in the moderate-high risk patient group (p<0.001). However, no difference was observed in other echocardiographic parameters (Table 2). SCORE system was positively correlated with MPI (r:0.325, p<0.001), fasting blood glucose (r:0.369, p<0.001), and urea (r:0.311, p<0.001) (Table 3). These relationships are demonstrated more clearly in the scatter plot analysis (Figure 2).

In the stepwise logistic regression analysis; MPI (OR=2.358, 95% CI:1.033-5.382, p=0.042), urea (OR=1.090, 95% CI:1.019-1.166, p=0.012), and glucose (OR=1.023, 95% CI: 1.003-1.043, p=0.025) were independently associated with the moderate-high SCORE assessment (Table 4). The association of NT pro-BNP with SCORE was close to statistical significance after adjustment (OR=1.006, 95% CI:0.999-1.013, p=0.074). In receiving operating characteristics (ROC) curve analysis; MPI value of >0.57, based on the youden-index, determined moderate-high SCORE system, with 93.2% sensitivity and 41.3% specificity (AUC:0.709, 95% CI, p<0.001) (Figure 3).

Discussion

This is the first study to reveal the relationship between SCORE assessment, which is used to determine estimated cardiovascular risk, and MPI, a popular doppler-derived echocardiographic parameter for demonstrating global LV function. The main result of our study was that MPI was independently associated with moderate-high SCORE system.

In a study with a mean age of 70 years, co-morbidities and echocardiographic findings of the patients were evaluated and patients were followed up for an average of 6.8 years. As a result of the study, it has been found that MPI predicted cardiovascular mortality [21]. This inference has been attributed to the association of MPI with left ventricular hypertrophy, arterial compliance, and peripheral resistance as well as left ventricular functions. In another study by Kılıç et al. [22], compared cardiac syndrome X, a syndrome which is characterized by abnormal coronary flow reserve, insulin resistance, abnormal autonomic control, increased sodium hydrogen exchange, angina-like chest pain, microvascular spasm, positive cardiac stress test, and normal coronary arteries, with the control group, EF was similar between the two groups, while MPI was significantly higher in the cardiac syndrome X group. That conclusion

Table 1. Demographic and laboratory parameters of the study population

	Low SCORE (n:46)	Moderate-high SCORE (n:122)	All patients (n:168)	*p* value
Age (years)	45.43±5.99	57.00±10.41	53.83±10.72	<0.001
Sex (male), n (%)	17 (36.9)	62 (50.8)	79 (47.0)	0.108
Body mass index (kg/m^2)	29.36±5.15	29.37±5.68	29.37±5.52	0.993
Systolic blood pressure (mmHg)	115.66±13.55	119.41±13.61	118.44±13.65	0.126
Diastolic blood pressure (mmHg)	75.14±9.98	74.79±8.87	74.88±9.14	0.831
Current smoker, n (%)	10 (21.7)	37 (30.3)	47 (28.0)	0.170
Hypertension n (%)	16 (34.8)	54 (44.3)	70 (41.7)	0.266
COPD, n (%)	2 (4.3)	13 (10.7)	15 (8.9)	0.243
Laboratory parameters				
Fasting blood glucose (mg/dL)	94.50 (83.00-110.25)	101.00 (90.00-130.50)	99.00 (88.00-123.00)	0.007
Urea (mg/dL)	23.00 (19.00-27.00)	29.50 (25.10-35.95)	27.50 (23.00-35.00)	<0.001
Creatinine (mg/dL)	0.70 (0.60-0.90)	0.80 (0.70-0.90)	0.80 (0.70-0.90)	0.022
Lactate dehydrogenase (U/L)	212.00 (187.00-303.75)	263.00 (207.00-338.00)	252.00 (196.50-335.50)	0.043
Total cholesterol (mg/dL)	179.58±35.12	200.81±46.71	194.79±44.67	0.002
HDL (mg/dL)	44.04±22.31	45.98±12.46	45.43±15.84	0.485
LDL (mg/dL)	118.73±30.78	130.00±37.62	126.80±36.08	0.073
Triglyceride (mg/dL)	159.22±72.72	179.06±87.77	173.43±84.03	0.176
CRP (mg/L)	0.20 (0.10-0.50)	0.30 (0.10-0.57)	0.20 (0.10-0.50)	0.273
Hemoglobin (g/dL)	14.00 (12.45-15.00)	13.95 (13.00-15.25)	14.00(12.97-15.02	0.814
White blood cell (10^3/uL)	7.23 (6.49-8.60)	7.27 (5.80-9.06)	7.21 (5.90-8.76)	0.581
Platelet count (10^3/uL)	259.90±65.47	251.83±66.98	253.94±66.45	0.517
NT pro-BNP (pg/ml)	68.10 (36.00-110.00)	84.56 (55.57-173.70)	77.77 (50.87-147.50)	0.003
Troponin T (ng/mL)	3.92 (0.00-6.80)	8.00 (3.90-11.47)	6.39 (3.47-10.38)	0.001
Drugs, n (%)				
Angiotensin converting enzyme inhibitor	5 (11.6)	7 (6.2)	12 (7.7)	0.314
Angiotensin receptor blocker	5 (11.6)	22 (19.5)	27 (17.3)	0.247
Beta blocker	5 (11.6)	13 (11.5)	18 (11.5)	1.000
Calcium channel blocker	3 (7.0)	8 (7.1)	11 (7.1)	1.000
Diuretic	5 (11.6)	18 (15.9)	23 (14.7)	0.498
Acetylsalicylic acid	4 (9.3)	12 (10.6)	16 (10.3)	1.000

COPD, chronic obstructive pulmonary disease; HDL, high-density lipoprotein; LDL, low-density lipoprotein;
CRP, C-reactive protein; NT pro-BNP, N-terminal pro-Brain natriuretic peptide.
Note: those with a SCORE of < 1 are at low SCORE group, those with a SCORE of ≥ 1 are at moderate-high SCORE group

Table 2. Echocardiography parametres of the study population

	Low SCORE (n:46)	Moderate-high SCORE (n:122)	All patients (n:168)	*p* value
Ejection fraction (%)	62.97±3.90	60.53±6.45	61.21±5.94	0.020
Left atrium diameter (cm)	3.45±0.44	3.49±0.36	3.48±0.38	0.570
Left ventricular systolic volume (ml)	35.37±10.94	39.63±17.09	38.78±16.11	0.130
Left ventricular diastolic volume (ml)	107.80±34.87	101.49±36.36	103.33±35.93	0.328
Interventricular wall thickness (cm)	1.04±0.17	1.00±0.20	1.01±0.19	0.344
Posterior wall thickness(cm)	0.97±0.21	0.91±0.19	0.93±0.19	0.100
Myocardial perfomance index	0.66±0.18	0.80±0.18	0.76±0.19	<0.001

Note: those with a SCORE of < 1 are at low SCORE group, those with a SCORE of ≥ 1 are at moderate-high SCORE group

Table 3. Association of SCORE assessment tool with glucose, MPI and urea

	r*	*p*
MPI	0.325	**<0.001**
Urea (mg/dL)	0.311	**<0.001**
Glucose (mg/dL)	0.369	**<0.001**

*Spearman's rho correlation coefficient. MPI: Myocardial performance index

Table 4. Univariate and multivariate regression analysis of independent risk factors for SCORE system

Variable	**Univariate Analysis**		**Multivariate Analysis**	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Glucose (mg/dL)	1.017 (1.004-1.030)	**0.011**	1.023 (1.003-1.043)	**0.025**
Urea (mg/dL)	1.119 (1.061-1.180)	<0.001	1.090 (1.019-1.166)-	**0.012**
Lactate dehydrogenase (U/L)	1.002	0.126	**-**	-
B-type natriuretic peptide (pg/ml)	(0.999-1.005) 1.008	**0.018**	1.006 (0.999-1.013)	**0.074**
	(1.001-1.015)			
Troponin T (ng/mL)	1.094 (1.018-1.176)	**0.014**	**-**	-
Ejection Fraction (%)	0.918 (0.852-0.987)	**0.022**		
MPI	3.875 (2.021-7.430)	**<0.001**	2.358 (1.033-5.382)	**0.042**

p-value <0.05 was considered significant. MPI: Myocardial performance index. Nagelkerke R^2:0.172. *p*<0.001

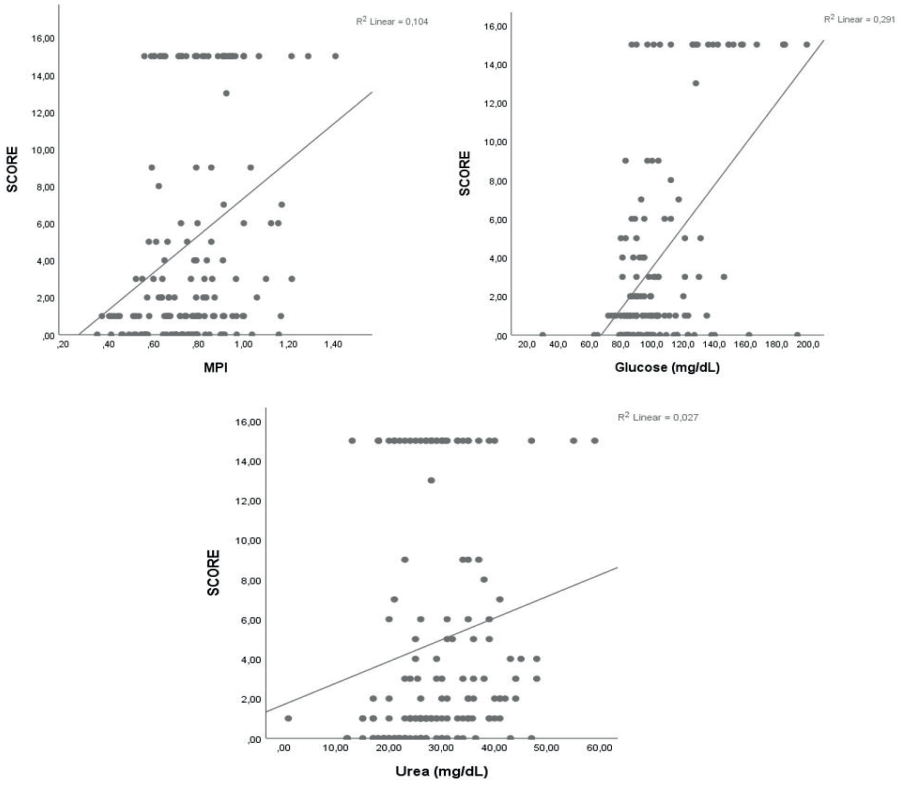

Figure 2. Scatter plot graphs that indicate the association of SCORE system with MPI, urea and, fasting blood glucose

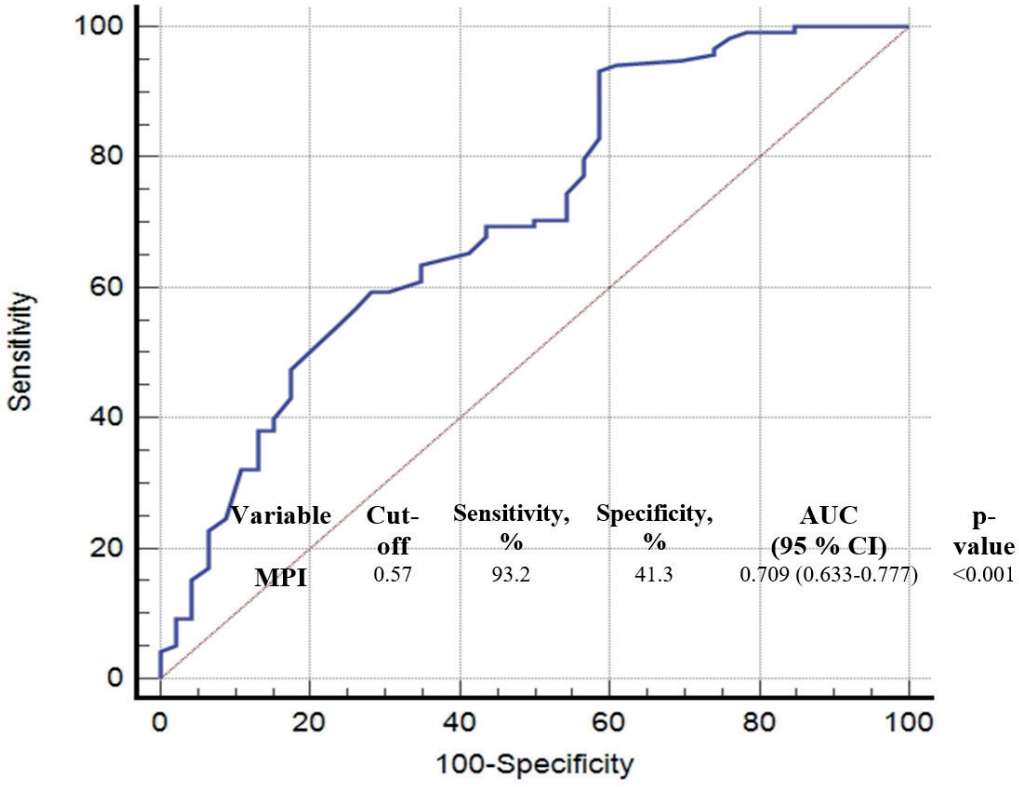

Figure 3. ROC curve analysis of MPI for determining moderate-high SCORE system in patients with chronic coronary syndrome.

AUC: area under the curve, CI: confidence interval, MPI: myocardial performance index

is not surprising since myocardial ischemia caused by increased oxidative stress and radical oxygen species in cardiac syndrome X patients impairs cardiac functions, which is associated with an increase in MPI. As stated before, the fact that MPI shows both systolic and diastolic functions and hereby provides more insight into total cardiac performance compared to ejection fraction has made its relationship with SCORE more important. Therefore, the association of SCORE, which is determined by demographic and laboratory parameters, with that echocardiographic parameter may give us a clinical and pathophysiological approach.

In one study Al Daydamony et al. [23], 24-hour Holter monitoring was applied to type-2 DM patients without a history of heart failure or coronary artery disease, and ST changes were observed. Patients with ST-elevation or depression were diagnosed with silent ischemia and MPI was significantly higher in patients with a diagnosis of silent ischemia. Prolonged IVCT and shortened ET have been reported in heart failure patients with myocardial infarction (MI). In addition, MPI predicted the severity of the disease and the development of heart failure following MI [24]. Similarly, MPI is successful in predicting in-hospital major adverse cardiac events consisting of death, heart failure, post-MI angina, and arrhythmia in patients with MI [25]. After percutaneous coronary intervention, a significant decrease in MPI, which could be associated with improvement in LV systolic function, was detected in patients with stable coronary artery disease [26].

Despite systolic functions at the physiological limit, diastolic dysfunction is frequently reported in diabetic patients [27, 28]. Underlying neurohumoral changes, cardiovascular diseases, microangiopathies, interstitial fibrosis, and extracellular collagen deposition may impair myocardial relaxation in DM [29, 30]. Consistent with this result, there is a positive correlation between albuminuria and MPI [31].

In hypertensive patients, deterioration in myocardial functions might be associated with other reasons such as left ventricular mass increase without hypertrophy, change in collagen matrix density in myocardial tissue and left ventricular architecture, and increased ‘afterload’, apart from classical physiopathological explanations [32]. The study by Yılmaz et al. [33] that compares hypertensive patients with different left ventricular geometries with healthy individuals revealed that MPI was significantly higher in all hypertensive patient groups. The fact that hypertension, one of the parameters used in SCORE calculation, is also responsible for the increase in MPI supports the theory of our study. Smoking is a firmly established risk factor for coronary and peripheral vascular disease. Most significantly, smoking is associated with impaired coronary blood flow responses during increased myocardial demand and might thereby contribute to myocardial ischemia in patients with CAD [34]. Studies indicating that MPI increases with smoking are also in line with our conclusion [35, 36]. This increase in MPI is thought to be due to impaired diastolic filling and prolonged IVRT. Taking precautions according to the SCORE assessment is considerable in preventing cardiovascular diseases. In this regard, the association of increased MPI with SCORE provides us with a different perspective for identifying a population at moderate-high cardiovascular risk and offers a new approach in determining treatment priority.

As a result; we found that MPI was independently associated with SCORE, a well-established tool in the assessment of 10-year cardiovascular risk. This result is crucial in terms of providing a perspective that an echocardiographic parameter could also be used for risk assessment in outpatient clinic conditions. Comprehensive prospective investigations, however, are required to test this conclusion.

Limitations

The limitations of the study could be listed as follows; (i) Although we documented ischemia by various imaging methods, we did not confirm this via coronary angiography, which may be considered as the major limitation of our study, (ii) The retrospective observational study design prevented us from obtaining follow-up data, (iii) The present study with a small sample size makes statistical analysis poor, (iv) Because of retrospective nature, as stated above, echocardiographic evaluation was performed by different echocardiographers in our cardiology outpatient clinic, not by a previously determined

independent echocardiographer, intra and inter-observer analysis, therefore, could not be conducted.

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

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Ethics committee approval: An institutional ethics committee, Çukurova University Faculty of Medicine Clinical Research Ethics Committee, approved the study protocol. (Meeting number:107, decision number 75, date:22 Jan 2021)

Contributions of the authors to the article

H.H. constructed the main idea and hypothesis of the study. H.H. and Ö.G. developed the theory and organized the material method section. H.H., Ö.G. and A.Y. analyzed the data in the results section. The discussion section of the article was written by H.H., Ö.G. and A.Y. reviewed, made the necessary corrections, and approved. Also, all authors discussed the whole study and approved its final version.