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Independent predictors of true positivity of positive myocardial perfusion imaging

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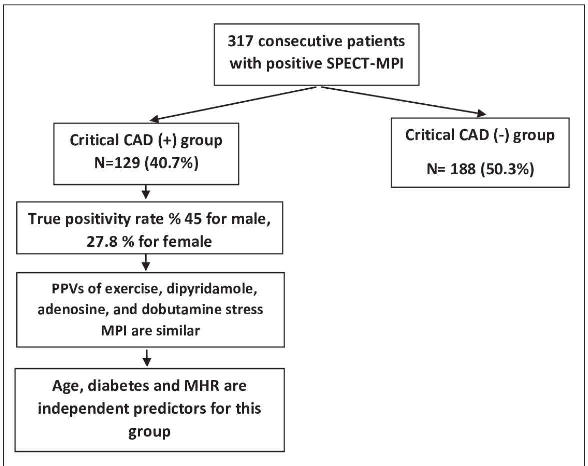
Abstract. – OBJECTIVE: The primary aim of the present study was to determine the success of single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) in detecting critical coronary artery disease (CAD) as identified by invasive coronary angiography (ICA), as well as to compare the positive predictive values (PPV) of different stress methods. Our secondary aim was to investigate demographic, laboratory, electrocardiographic, and echocardiographic variables that could predict true positive results.

PATIENTS AND METHODS: The study was conducted with 317 consecutive patients. Exercise, dipyridamole, adenosine, or dobutamine were used as stress methods. According to the results of ICA, patients with and without critical CAD were divided into two groups and compared statistically. The independent predictors of true positive results of positive SPECT-MPI were determined using univariate and multivariate logistic regression analysis (MLRA).

RESULTS: Among the patients, 129 (40.7%) were found to have critical CAD (+) and 188 (50.3%) critical CAD (-). The PPVs of different stress methods were similar. Age, diabetes, and monocyte to HDL ratio (MHR) were found to be independent predictors of critical CAD in MLRA (*p*<0.005, *p*=0.002, and *p*<0.005, respectively). ROC curve analysis revealed 81.4% sensitivity and 47.3% specificity (AUC: 0.683) at a cut-off of 57 for age and 72.1% sensitivity and 54.3% specificity (AUC: 0.649) for MHR at a cut-off of 9.7.

CONCLUSIONS: The true positivity rate of SPECT-MPI is low. Moreover, this rate is much lower for women. The PPVs of different stress methods are similar. Age, presence of diabetes, and MHR ratio are independent predictors for true positive results of SPECT-MPI.



Graphical Abstract. Graphical abstract of the study.

Key Words:
Myocardial perfusion imaging, True-positivity, Monocyte to HDL ratio, SPECT, Coronary artery disease, Frontal QRS-T angle, Positive predictive value.

Abbreviations

CAD: Coronary artery disease; f-QRS-T: frontal plane QRS-T angle; ICA: Invasive coronary angiography; IV: Intravenous; MPI: Myocardial perfusion imaging; MHR: Monocyte to high-density lipoprotein cholesterol; N/L: Neutrophil/lymphocyte; PPV: Positive predictive value; P/L: Platelet/lymphocyte; ROC: Receiver operating characteristic; SII: Systemic immune inflammation index; SPECT: Single-photon emission computed tomography.

Introduction

Coronary artery disease (CAD) continues to be the leading cause of death worldwide[1]. Therefore, accurate and safe diagnosis of CAD is of utmost importance. Cardiac imaging serves as a fundamental basis for medical decision-making in patients with known or suspected heart disease. While invasive coronary angiography (ICA) is considered the gold standard for CAD diagnosis, non-invasive tests are preferred as initial assessments.

Myocardial perfusion imaging (MPI) performed with single-photon emission computed tomography (SPECT) is one of the most commonly used stress tests in CAD diagnosis[2]. Previous studies[3,4] have demonstrated that exercise and pharmacological stress SPECT-MPI have sensitivities of 87-88% and specificities of 73-75% in diagnosing

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critical CAD (stenosis >50%) as detected by ICA. In certain cases (such as breast and diaphragm attenuation and left ventricular hypertrophy), the limited spatial resolution of SPECT-MPI leads to its high false positivity rates[5-7].

Studies investigating the true positivity rates of positive MPI and the superiority of different stress methods over each other are limited. The primary aim of our current study was to determine the success of SPECT-MPI in detecting critical CAD as identified by ICA and also to compare the positive predictive values (PPV) of different stress methods. Our secondary aim was to investigate demographic, laboratory, electrocardiographic, and echocardiographic parameters that could predict true positive results in patients who underwent ICA based on a positive SPECT-MPI result.

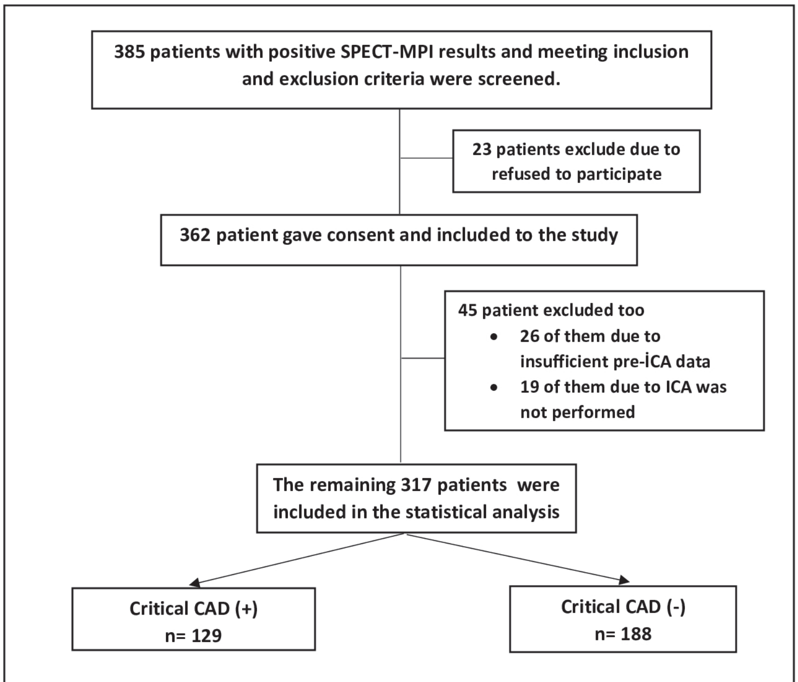
Patients And Methods

Study Population

Our study is designed as a prospective cross-sectional study. The study was approved by the local ethics committee. Inclusion criteria were patients preliminary diagnosed with chronic coronary syndrome who were scheduled for ICA based on positive SPECT-MPI results, and aged 18 or older. Exclusion criteria were previous bypass surgery, acute coronary syndrome patients, those with infections or inflammatory diseases, those with a history of malignancy, recent surgical or traumatic history, patients who had used steroids within the past three months, patients with white blood cell count (WBC) >12,000 or <4,000, and those who refused to provide consent. Between January 2023 and August 2023, a total of 385 consecutive patients who met the inclusion identified; 23 of these patients declined to participate in the study. Written informed consent was obtained from the remaining 362 patients and included in the study. 26 patients were excluded as pre-procedure electrocardiography and/or echocardiography could not be performed. Another 19 patients were excluded due to last-minute cancellations of ICA procedures. Ultimately, 317 patients were included in the statistical analysis (Figure 1).

Myocardial Perfusion Imaging

Patients underwent SPECT-MPI at the Nuclear Medicine Department of Bursa Yüksek İhtisas Training and Research Hospital (C.CAM Imaging System, Siemens Medical Solutions USA Inc, Hoffman, Estates, IL, USA). Exercise, dipyridamole, adenosine, or dobutamine were used as stress methods. Technetium-99m



CAD: Coronary artery disease, ICA: Invasive coronary angiography, MPI: Myocardial perfusion imaging.

Figure 1. Study flowchart.

methoxyisobutyl isonitrile (Tc-99m MIBI) was used as the radiopharmaceutical in all procedures. 0.31 mCi/kg Tc-99m MIBI was used for MPI. Axial, sagittal, and coronal SPECT images were obtained from patients during stress and at rest. Rest imaging was performed 24 hours after stress imaging with the same dose of Tc-99m MIBI. SPECT-MPI results were reported by two experienced nuclear medicine specialists, blinded to the patient's data, using the standard 17-segment model. Positive MPI was defined in the MPI report as the presence of inducible ischemia.

For exercise stress imaging, the Bruce protocol was used. When patients reached at least 85% of the target heart rate, stress-gated SPECT imaging was performed at the 20^{th} minute after intravenous (IV) injection of Tc-99m MIBI.

For dipyridamole stress imaging, stress-gated SPECT imaging was performed at the 20^{th} minute after the application of 0.56 mg/kg IV dipyridamole, followed by Tc-99m MIBI.

For adenosine stress imaging, Tc-99m MIBI injection was made at the 3^{rd} minute during a continuous infusion of 140 mg/kg/min adenosine for 6 minutes, followed by stress-gated SPECT imaging 20 minutes later.

For dobutamine SPECT MPI, dobutamine was initially administered IV at a rate of 10 μg/kg/min, increased by 10 μg/kg/min every 3 minutes up to a maximum of 40 μg/kg/min, and Tc-99m MIBI was injected at the final stage. Stress-gated SPECT images were taken 20 minutes later.

Laboratory Analysis

Fasting blood tests of all patients were performed before the angiography procedure. Patients' blood test results were recorded. Neutrophil/lymphocyte (N/L) ratio, platelet/lymphocyte (P/L) ratio, systemic immune inflammation index (SII=neutrophil/lymphocyte*platelet), and monocyte/high-density lipoprotein ratios (MHR=monocyte/HDL*1000) were calculated from the patients' blood test results.

Electrocardiography

12-lead electrocardiograms (ECGs) of patients were taken at a speed of 25 mm/second before the ICA procedure (MAC 2000, GE Medical System Information Technologies, Milwaukee, WI, USA). The frontal plane QRS-T (f-QRS-T) angle was calculated from the difference between the QRS and T angles automatically provided by the device, the QTc distance was recorded. The Tp-e interval was measured manually, and the Tp-e/QT and Tp-e/QTc ratios were calculated and recorded.

Echocardiography

All patients underwent two-dimensional (2D) transthoracic echocardiography (TTE) before the coronary angiography procedure. Echocardiography was performed by a single echocardiography expert blinded to the patient's data. The Vivid E95 platform with a 3.5 MHz transducer (GE Vingmed Ultrasound AS, Horten, Norway) was used for the procedure. Echocardiographic parameters were assessed according to the recommendations of the American Society of Echocardiography (ASE) guidelines[8].

Invasive Coronary Angiography

317 patients included in the statistical analysis underwent ICA (Siemens Axiom Artis zee, München, Germany), within two weeks after SPECT-MPI. The results of the ICA were reported by two experienced interventional cardiologists unaware of the patients' clinical characteristics. Stenoses of 50% and above for the left main coronary artery and 70% and above for other major coronaries were considered critical. Syntax scores were obtained using an online calculator (www.syntaxscore.com, version 2.1).

Statistical Analysis

All statistical analyses were performed using MedCalc 20.0.4 software (MedCalc Software Ltd, Ostend, Belgium). Continuous variables with normal distribution were expressed as mean ± standard deviation, continuous variables with non-normal distribution were expressed as median (25^{th}-75^{th} percentile), and categorical variables were expressed as count and percentages (n, %). Critical CAD (+) and (-) groups based on ICA results were compared using the Independent Samples *t*-test for continuous variables with normal distribution and the Mann-Whitney U test for continuous variables with non-normal distribution. The Chi-square test was used for comparing categorical variables. Variables that were statistically significant in the difference tests were subjected to univariate and multivariate logistic regression analyses to identify independent variables that could predict true positivity. Subsequently, appropriate sensitivity and specificity ratios for these independent variables were determined using ROC curve analysis. A two-tailed $p<0.05$ was considered statistically significant.

Results

The mean age of the 317 patients included in the study was 61.22±10.64 (range: 30-89) years. Of these patients, 238 (75.1%) were male and 79 (24.9%) were female. Stress SPECT-MPI was performed using exercise in 26 (8.2%) patients, dipyridamole in 37 (11.7%) patients, adenosine in 116 (36.6%) patients, and dobutamine in 138 (43.5%) patients. Among the entire study population, 129 (40.7%) were found to have critical stenosis, while 188 (50.3%) did not exhibit critical CAD. When comparing the different stress methods, the PPVs were as follows: exercise: 57.7%, dipyridamole: 32.4%, adenosine: 37.1%, and dobutamine: 42.8%, with no statistically significant difference between them (p=0.169). Among male patients, 107 (45%) were diagnosed with critical CAD, whereas among female patients, 22 (27.8%) had critical CAD, demonstrating a statistically significant difference between these proportions (p=0.007). Electrocardiography of 58 (18.3%) patients showed left bundle branch block, right bundle branch block or left anterior hemiblock. Critical CAD rates were similar when comparing the group with and without bundle branch block (p=0.859). The results remained similar when comparing the group of patients with only left bundle branch block 15 (4.7%) to the group without this condition (p=0.552).

Comparison of demographic data between patients with and without critical CAD revealed that mean age, male gender, hypertension, and diabetes rates were statistically higher in the critical CAD group (p<0.005, p=0.007, p<0.005, and p<0.005, respectively).

Comparison of electrocardiographic data among patients revealed that the f QRS-T angle (except for patients with unifascicular and bifascicular bundle branch blocks), QTc interval, and pathological Q wave ratio were statistically higher in the critical CAD group (p=0.007, 0.018, and 0.007, respectively). Among the echocardiographic variables, the ejection fraction (EF) was lower, and the left ventricular hypertrophy (LVH) rate was higher in the critical CAD group (p=0.019 and p<0.005, respectively) (Table I).

When comparing laboratory results, the critical CAD (+) group had statistically lower levels of eGFR, sodium, aspartate aminotransferase (AST), total cholesterol (TC), and low-density lipoprotein (LDL) (p<0.005, p=0.013, p=0.028, p=0.040, and p=0.018, respectively). White blood cell counts, neutrophil and monocyte counts, N/L ratio, SII levels, and MHR ratio were statistically higher in the critical CAD group

Table I. Comparison of demographic, electrocardiographic and echocardiographic variables of CAD.

Variables	Critical CAD (+) Group n=129	Critical CAD (-) Group n=188	*p*-value
Age, mean±SD	65.34±8.61	58.39±10.99	**<0.005**
Male ratio, n (%)	107 (82.9)	131 (69.7)	**0.007**
Active smoking, n (%)	44 (34.1)	71 (37.8)	0.515
BMI, median (25^{th}-75^{th})	28.68 (26.75-32.04)	29.40 (26.66-31.69)	0.712
Hypertension, n (%)	94 (72.9)	90 (47.9)	**<0.005**
Diabetes, n (%)	63 (48.8)	48 (25.5)	**<0.005**
QRS-T angle, median(25^{th}-75^{th})	38.14 (15-59.50), n=106	26 (12-42), n=153	**0.007**
QT interval, ms, mean±SD	385.89±30.51	381.70±28.82	0.215
QTc interval, ms, mean±SD	428.70±26.54	421.37±27.08	**0.018**
Tp-e interval, ms, median (25^{th}-75^{th})	80 (70-90)	80 (70-90)	0.763
Tp-e/QT ratio, median (25^{th}-75^{th})	0.20 (0.18-0.22)	0.20 (0.18-0.23)	0.486
Tp-e/QTc ratio, median (25^{th}-75^{th})	0.18 (0.16-0.20)	0.19 (0.16-0.21)	0.313
ST elevation, n (%)	9 (7)	14 (7.4)	0.883
Pathological Q wave, n (%)	10 (7.8)	3 (1.6)	**0.007**
ST depression, n (%)	16 (12.4)	13 (6.9)	0.096
T negativity, n (%)	8 (6.2)	11 (5.9)	0.916
MPI ischemia ratio, % median (25^{th}-75^{th})	12 (10-16)	12 (10-14)	0.916
MPI EF, %, median (25^{th}-75^{th})	52.50 (43-60)	55 (49-60)	0.184
ECHO EF, %, median (25^{th}-75^{th})	60 (50-63.5)	60 (56.5-64.75)	**0.019**
LVH, n (%)	73 (56.6)	62 (33)	**<0.005**

(+) and (-) groups. BMI: body mass index, CAD: coronary artery disease, MPI: myocardial perfusion imaging, ECHO: echocardiograhy, LVH: left ventricle hypertrophy.

Table II. Comparison of blood test results of critical CAD (+) and critical CAD (-) groups.

Variables	Critical CAD (+) Group n=129	Critical CAD (-) Group n=188	*p*-value
CrCl† mL/min, median (25th-75th)	80.44 (61.13-94.54)	92.71 (77.79-101.94)	**<0.005**
Sodium, mmol/L, median (25th-75th)	138 (137-139)	139 (137-140)	**0.013**
Potassium, mmol/L, median (25th-75th)	4.3 (4.1-4.7)	4.2 (4-4.5)	0.107
AST, IU/L, median (25th-75th)	17 (14-21)	18 (16-23)	**0.028**
ALT, IU/L, median (25th-75th)	18 (14-22)	18 (13-24)	0.223
Total Cholesterol, mg/dL, mean±SD	181.85±44.28	191.78±40.60	**0.040**
LDL cholesterol,mg/dL mean±SD	102.65±38.20	112.68±35.87	**0.018**
HDL cholessterol, mg/dL, mean±SD	45.42±11.47	47.99±11.54	0.052
Triglyceride, mg/dL, median (25th-75th)	150 (115-216.5)	141.50 (104.25-206)	0.117
Hemoglobin, g/dL; mean±SD	13.70±1.89	13.81±1.68	0.6
White blood cell, × 10^3/µL, mean±SD	8.36±2.4	7.47±2.18	**0.001**
Neutrophils × 10^3/µL, mean±SD	5.18±1.91	4.44±1.71	**<0.005**
Lymphocytes × 10^3/µL, mean±SD	2.39±0.91	2.34±1.42	0.889
Platelet, ×10^3/µL, mean±SD	265.64±94.25	261.34±70.74	0.620
Monocyte, ×10^3/µL, median (25th-75th)	0.55 (0.43-0.64)	0.46 (0.37-0.54)	**<0.005**
Eosinofyl, ×10^3/µL median (25th-75th)	0.20 (0.12-0.28)	0.18 (0.11-0.26)	0.204
Basofil, ×10^3/µL median (25th-75th)	0.03 (0.02-0.04)	0.03 (0.02-0.05)	0.751
RDW, % median (25th-75th)	13.9 (13.2-14.8)	13.6 (13.1-14.6)	0.086
MPV, fL, mean±SD	10.59±1.32	11.12±5.83	0.310
PDW, % median (25th-75th)	16.20(16-16.4)	16.20 (15.9-16.4)	0.501
Platecrit, % median (25th-75th)	0.26 (0.22-0.31)	0.27 (0.23-0.31)	0.362
N/L ratio median (25th-75th)	2.2 (1.76-2.91)	1.89 (1.39-2.42)	**<0.005**
P/L ratio median (25th-75th)	112.78 (89.12-146.48)	114.31 (89.50-151.39)	0.823
SII median (25th-75th)	554.32 (380.31-778.92)	479.31 (331.88-663.19)	**0.008**
MHR, median (25th-75th)	12.06 (9.24-16.23)	9.37 (7.76-13.12)	**<0.005**
TSH mIU/L, median (25th-75th)	1.2 (0.75-1.81)	1.32 (0.86-1.95)	0.363

ALT: alanine aminotransferase, AST: aspartate aminotransferase, CrCl: creatinine clearance, HDL: high-density lipoprotein, LDL: low-density lipoprotein, MHR: monocytes to HDL ratio, MPV: mean platelet volume, N/L: neutrophil to lymphocyte, PDW: platelet distribution width, P/L: platelet to lymphocyte, RDW: red cell distribution width, SD: standard deviation, SII: systemic immune-inflammation index, TSH: thyroid-stimulating hormone; †Calculated with modification of diet in renal disease study.

(*p*=0.001, *p*<0.005, *p*<0.005, *p*<0.005, *p*=0.008, and *p*<0.005, respectively) (Table II).

Univariate logistic regression and then multivariate logistic regression analyses were performed for the variables that showed a significant difference in the comparison of the groups with critical CAD (+) and (-). Age, diabetes, and MHR were found to be independent predictors of critical CAD (Table III).

ROC curve analysis revealed 81.4% sensitivity and 47.3% specificity (AUC: 0.683 (CI: 0.629-0.734, *p*<0.0001) for critical CAD detection at the cut-off of 57 for age. With a cut-off of 9.6 for MHR, 72.1% sensitivity and 54.3% specificity were detected (AUC: 0.649, CI: 0.594-0.701, *p*<0.0001) (Figure 2).

Discussion

Among the preliminary diagnosed patients with chronic coronary syndrome who underwent ICA based on positive SPECT-MPI results, true positivity (critical CAD ratio=PPV) was detected in only 40.7% of cases. It was concluded that the different stress methods used for SPECT-MPI did not affect PPV in these patients. Age, diabetes, and MHR were identified as independent predictors for predicting critical CAD. Additionally, it was found that SPECT MPI had a higher PPV in males. To the best of our knowledge, our study is the first to evaluate the relationship between true positive results of SPECT-MPI and f QRS-T angle, N/L ratio, SII, and MHR ratios in the literature.

In a study conducted by McGee et al[9], critical CAD was detected in 54% of patients who underwent ICA based on positive SPECT-MPI results. In this study, critical CAD was found in 66% of males and 29% of females. Similarly, in another study[10], both SPECT and CAD were positive in 67% of males and 33% of females, which is quite similar to our results, especially in terms of the low PPV in females (40.7% in all patients, 45% in males, and 27.8% in females in the current study). In a meta-analysis conducted by Iskandar and colleagues, it was concluded that gender did

Table III. Logistic regression analysis for identifying predictors of critical CAD.

Variables	Univariate Analysis OR	95% CI	*p*-value	Multivariate Analysis OR	95 % CI	*p*-value
Age	1.073	1.046-1.100	**<0.005**	1.095	1.050-1.143	**<0.005**
Male ratio	2.116	1.216-3.684	**0.008**	2.666	0.995-5.160	0.051
Diabetes	2.784	1.730-4.482	**<0.005**	0.351	0.183-0.673	**0.002**
Hypertension	2.924	1.806-4.736	**<0.005**	0.516	0.255-1.043	0.065
QTc interval	1.010	1.002-1.019	**0.019**	1.013	0.999-1.027	0.066
QRS-T angle	1.012	1.004-1.020	**0.004**	1.006	0.996-1.016	0.232
Pathological Q wave	0.191	0.051-0.712	**0.014**	0.200	0.036-1.016	0.200
LVH	0.377	0.238-0.599	**<0.005**	0.702	0.368-1.338	0.282
CrCl	0.993	0.962-0.985	**<0.005**	1.006	0.986-1.027	0.543
LDL cholesterol	0.993	0.986-0.999	**0.019**	0.995	0.986-1.003	0.205
N/L ratio	1.169	0.967-1.414	0.107			
MHR	1.118	1.064-1.174	**<0.005**	1.159	1.074-1.250	**<0.005**
SII	0.487	1.000-1.001	0.062			

CAD: coronary artery disease, CI: confidence interval, CrCL: creatinine Clearance, LDL: low-density lipoprotein, LVH: left ventricle hypertrophy, MHR: monocytes to HDL cholesterol ratio, N/L: neutrophil to lymphocyte, SII: systemic immune-inflammation index, OR: odds ratio.

not affect the accuracy of SPECT-MPI when stenosis degree >50% was considered[11]. However, in our study, the true positive rate of SPECT-MPI was statistically higher in males compared to females (p=0.007). When analyzing the stenosis rate as >50%, critical CAD was detected in 49.2% of males and 32.9% of females, showing a statistically significant difference (p=0.012). Population differences in the current study, especially the relatively low ratio of women and the number of subjects may have caused different results from this study. According to all these results, the positive predictive value of SPECT-MPI is quite low. Therefore, it can be inferred that SPECT-MPI may inappropriately increase the need for ICA, which carries certain risks.

It is known that patients with obstructive CAD are older and have higher rates of diabetes[12-14]. It was not surprising that in the current study, traditional risk factors such as age and diabetes were found to be independent predictors of true positive results.

In recent studies[15], MHR has emerged as a new and widely usable cardiovascular prognostic biomarker that is strongly associated with inflammation and oxidative stress. Monocytes play a significant role in the release of pro-inflammatory and pro-oxidative cytokines in the inflammatory area[16]. Inflammation and lipid accumulation are two fundamental features of atherosclerosis[17]. Dyslipidemia, especially elevated TC, triglycerides, LDL, and low HDL levels, are well-known risk factors for cardiovascular diseases[18]. Low HDL is associated with increased inflammation levels[19,20]. In our study, consistent with the literature, the MHR ratio was identified as an independent predictor for true positive results of SPECT-MPI. The threshold of 9.6 had a sensitivity of 72.1% and a specificity of 54.3% for true positive results.

A previous study[21] concluded that fragmented QRS could predict positive results of SPECT-MPI. In another study[22], Tp-e interval, Tp-e/QTc ratio, and f(QRS-T) were shown to be associated with high syntax scores in stable CAD patients. In our study, these variables were found to be

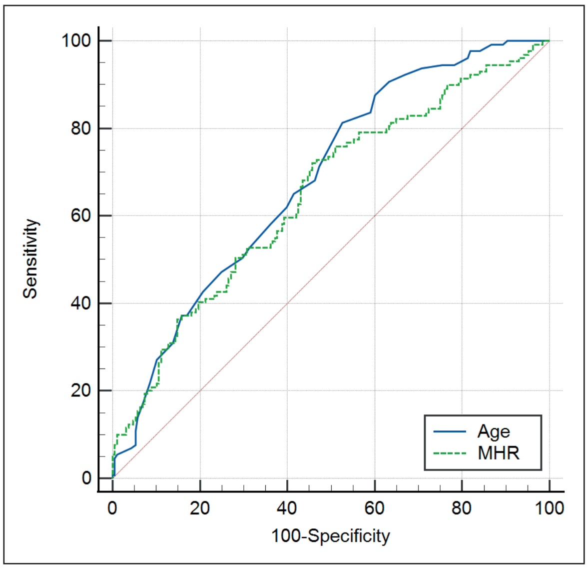


Figure 2. ROC curve analyzes of age and monocyte to HDL cholesterol (MHR) ratio.

significantly higher in the critical CAD (+) group. However, none of the electrocardiographic variables were found to be independent predictors in multivariate logistic regression analysis.

In recent times, the developed cadmium zinc telluride camera technology has been proven to have high sensitivity and accuracy in detecting critical CAD, reducing radiation exposure and imaging time, thus enhancing patient comfort[23]. Furthermore, quantitative assessment has been shown to improve the repeatability and diagnostic accuracy of MPI[24,25]. Positron emission tomography (PET) MPI is superior to SPECT-MPI in terms of higher spatial resolution and the ability to correct for attenuation. It is also highly useful due to its capability to measure myocardial blood flow and flow reserve[26]. A multicenter study[27] demonstrated that comprehensive coronary CT angiography (CCTA) is superior to SPECT-MPI in functionally detecting critical CAD.

Considering the results of all the aforementioned studies and the current study, it becomes evident that SPECT-MPI leads to a high rate of false positives in CAD diagnosis. If feasible, the use of new MPI technologies or more accurate tests such as PET-MPI and CCTA could provide more accurate results in CAD diagnosis and enhance patient comfort.

Limitations of the Study

Angiographic stenosis is no longer considered the gold standard for hemodynamically significant CAD. Nowadays, methods such as fractional flow reserve, instantaneous wave-free ratio, microvascular resistance, and intravascular ultrasound have emerged as primary options for assessing hemodynamically significant CAD, as recommended by chronic coronary syndrome guidelines. The limitation of our study lies in not being able to employ one of these methods and relying solely on coronary angiography (ICA) images to detect critical CAD. Additionally, our study focused on investigating true positive rates and did not provide interpretations for sensitivity and specificity. Moreover, in the literature, >50% stenosis rates have been considered critical CAD.

Conclusions

The true positivity rate of SPECT-MPI is low. Moreover, this rate is much lower for women. The PPVs of different stress methods such as exercise, dipyridamole, adenosine, or dobutamine are similar. Age, presence of diabetes, and MHR ratio are independent predictors for true positive results of SPECT-MPI. Hence, these variables may be considered when making decisions regarding ICA for patients. Improved clinical assessment and better non-invasive tests are needed for a more accurate diagnosis of CAD. Further research is required to support and corroborate these findings.

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Informed Consent
Informed consent was obtained from all subjects involved in the study.

Ethics Approval
The study protocol was approved by the Local Clinical Research Ethics Committee, Bursa, Sağlık Bilimleri Üniversitesi Bursa Yüksek İhtisas Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulu with Ethics Approval acceptance number 2011-KAEK-25 2023. The study conforms to the principles outlined in the Declaration of Helsinki.

Conflicts of Interest
The authors declare no conflict of interest.

Data Availability
The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Authors' Contributions
Conceptualization, FK; methodology, FK, GÖ; software, FK; validation, GÖ; formal analysis, FK, GÖ; investigation, FK; data curation, FK; GÖ; writing-original draft preparation, FK, GÖ; writing-review and editing, FK, GÖ; visualization, FK, GÖ; supervision, GÖ; project administration, FK.

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