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The Relationship between Coronary Artery Calcium Score and Monocyte to High-Density Lipoprotein Cholesterol Ratio in Patients with Stable Angina Pectoris

Stabil Angina Pektorisli Hastalarda Koroner Arter Kalsiyum Skoru ile Monosit/Yüksek-Yoğunluklu Lipoprotein Kolesterol Oranı Arasındaki İlişki

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: Coronary artery calcification is a cornerstone marker for coronary atherosclerosis. Therefore, the calculation of the coronary artery calcium score has become a routine method in diagnosing coronary artery disease in recent years. Monocyte to high-density lipoprotein cholesterol ratio reflects proatherogenic and antiatherogenic balance, and this ratio is associated with coronary atherosclerosis and cardiovascular events. This study aimed to investigate the value of monocyte to high-densitylipoprotein cholesterol ratio in predicting coronary atherosclerosis, which coronary artery calcium score determines.

Methods: A total of 276 patients with chest pain who underwent coronary computed tomography angiography were enrolled in the study. The patients were divided into 3 groups according to coronary artery calcium score [coronary artery calcium score=0 for very low risk (n=121), coronary artery calcium score=1-99 for low risk (n=100), coronary artery calcium score ≥ 100 for moderate-high risk (n=55)]. The monocyte to high-density lipoprotein cholesterol ratio, neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, and platelet-to-lymphocyte ratio were calculated from venous blood samples.

Results: Monocyte to high-density lipoprotein cholesterol ratio values were significantly higher in patients with moderate-high coronary artery calcium score (1.29 ± 0.59 vs 1.41 ± 0.56 vs 1.56 ± 0.58, *P* = .009). However, there were no differences between the groups in terms of other inflammatory markers (neutrophil-to-lymphocyte ratio, systemic immune-inflammation index, and platelet-to-lymphocyte ratio). Age (odds ratio: 1.178; 95% CI: 1.107-1.253; *P* < .001), dyslipidemia (odds ratio: 14.252; 95% CI: 5.459-37.211; *P* < .001), smoking (odds ratio: 2.893; 95% CI: 1.317-6.358; *P* = .008), and monocyte to high-density lipoprotein cholesterol ratio (odds ratio: 2.082 per 1-point increase; 95% CI: 1.016-4.268; *P* = .045) were independent predictors of coronary artery calcium score in multivariate analysis.

Conclusion: Our data showed that high monocyte to high-density lipoprotein cholesterol ratio is significantly associated with increased coronary artery calcium score. Monocyte to high-density lipoprotein cholesterol ratio indicates that it can be applied easily and swiftly in clinics to help predicting the coronary artery disease.

Keywords: Agatston, atherosclerosis, coronary calcium score, monocyte to high-density-lipoprotein cholesterol ratio

ÖZET

Amaç: Koroner arter kalsifikasyonu, koroner ateroskleroz için önemli bir belirteçtir. Bu nedenle koroner arter kalsiyum skorunun (CCS) hesaplanması son yıllarda koroner arter hastalığı tanısında rutin bir yöntem haline gelmiştir. Monosit/yüksek yoğunluklu lipoprotein kolesterol oranı (MHR), proaterojenik ve antiaterojenik dengeyi yansıtır ve bu oran koroner ateroskleroz ve kardiyovasküler olaylarla ilişkilidir. Bu çalışma, CCS'nin belirlediği koroner aterosklerozu öngörmede MHR'nin değerini araştırmayı amaçladı.

Yöntemler: Koroner BT anjiyografisi yapılan göğüs ağrısı olan toplam 276 hasta çalışmaya alındı. Hastalar CCS'ye göre [CCS=0 çok düşük risk (n: 121), CCS=1-99 düşük risk (n: 100), CCS ≥ 100 orta-yüksek risk (n: 55) olarak] üç gruba ayrıldı. Venöz kan örneklerinden MHR, nötrofil-lenfosit oranı (NLR), sistemik immün-enflamasyon indeksi (SII) ve trombosit-lenfosit oranı (PLR) hesaplandı.

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Bulgular: MHR değerleri orta-yüksek CCS'li hastalarda anlamlı olarak daha yüksekti (1,29 ± 0,59'a karşı 1,41 ± 0,56'ya karşı 1,56 ± 0,58, *P* = ,009). Ancak diğer enflamatuvar belirteçler (SII, NLR, PLR) açısından gruplar arasında fark yoktu. Yaş (OR: 1,178; %95 CI: 1,107-1,253; *P* <.001), dislipidemi (OR: 14,252; %95 CI: 5,459-37.211; *P* < ,001), sigara (OR: 2,893; %95 CI: 1,317-6,358; *P* = ,008) ve MHR (OR: 1 puanlık artış başına 2,082; %95 CI: 1,016-4,268; *P* = ,045), çok değişkenli analizde CCS'nin bağımsız öngörücüleriydi.

Sonuç: Verilerimiz, yüksek MHR'nin artan CCS ile önemli ölçüde ilişkili olduğunu göstermektedir. MHR, koroner arter hastalığının öngörülmesine yardımcı olmak için kliniklerde kolay ve hızlı bir şekilde uygulanabilir.

Anahtar Kelimeler: Agatston, ateroskleroz, koroner kalsiyum skoru, monosit/yüksek yoğunluklu lipoprotein kolesterol oranı

Calcification is a marker of coronary atherosclerosis and a crucial cardiac risk predictor.[1] Coronary artery calcium scoring (CCS) is a non-invasive imaging technique that measures coronary artery calcification (CAC) and helps to predict cardiovascular mortality and adverse events. In the beginning, fluoroscopy, chest x-ray, and then electron beam computed tomography (CT) and currently, multi-detector CT is used to determine the extent of calcification in the atherosclerotic plaque.[2-4] The most commonly used method for CCS is the Agatston score. The total plaque area and the maximum calcium density in the plaque determine the Agatston score. The predictive effectiveness of the Agatston score (Agatston = 0 very low risk, Agatston = 1-99 low risk, Agatston = 100-299 moderate risk, and Agatston ≥300 high risk) for cardiovascular events has served it to be used in clinical practice.[5]

Inflammation, oxidative stress, and endothelial dysfunction have essential roles at the onset and progression of the atherosclerotic process.[6] Monocytes are necessary components of the inflammatory process in atherosclerotic plaques.[7] Monocytes, the source of many cytokines and inflammatory mediators, interact with endothelial cells and platelets, leading to the onset and exacerbation of inflammation and atherosclerosis.[8] Conversely, high-density lipoprotein cholesterol (HDL-C) participates in the transfer of cholesterol from the peripheral regions to the liver, thereby exhibiting an antiatherosclerotic effect.[9] Monocyte to HDL-C ratio (MHR) is a newly used inflammation and oxidative stress marker and calculated as the monocyte count ratio to HDL-C level.[10]

In this study, we aimed to investigate the value of MHR in predicting coronary atherosclerosis determined by CCS in patients presenting with chest pain.

ABBREVIATIONS

CAC	Coronary artery calcification
CAD	Coronary artery disease
CCS	Coronary artery calcium scoring
CRP	C-reactive protein
CT	Computed tomography
HDL-C	High-density lipoprotein cholesterol
HU	Hounsfield Units
ICA	Invasive coronary angiography
LDL-C	Low-density lipoprotein cholesterol
MHR	Monocyte to HDL-C ratio
NLR	Neutrophil-to-lymphocyte ratio
PLR	Platelet-to-lymphocyte ratio
SII	Systemic immune-inflammation index
STEMI	ST-segment elevation myocardial infarction

Methods

Study Population

Two hundred eighty-nine patients with suspicion of coronary artery disease (CAD) underwent coronary CT angiography between January 2020 and January 2021 and were retrospectively screened. Patients with known CAD,[7] acute or chronic inflammatory or autoimmune disease,[3] chronic infectious disease,[1] and whose cardiac CT could not be evaluated due to the poor image quality[2] were excluded. Finally, 276 patients constituted the study population. All patients provided written informed consent, and the study protocol was reviewed and approved by the ethics committee of University of Health Sciences, Derince Education and Research Hospital and conducted by the Declaration of Helsinki.

Medical history and medications in all patients were recorded in detail. Hypertension is defined as a systolic blood pressure of ≥140 mmHg, a diastolic blood pressure of ≥90 mmHg, or the use of blood pressure medications. Diabetes mellitus diagnosed with a fasting blood glucose >126 mg/dl and/or the presence of antidiabetic drug use. Dyslipidemia was considered as total cholesterol level >200 mg/dL, low-density lipoprotein cholesterol (LDL-C) level >130 mg/dL, triglyceride level >150 mg/dL, or receiving lipid-lowering medication. Smoking status was defined as never, former, and current smoker. A family history of CAD is defined as in a parent or sibling diagnosed under the age of 55 for men and 65 years for women. The mortality of the patients and adverse cardiovascular events after CT angiography were screened using the national health and social service registry.

Laboratory Parameters

Venous blood samples were obtained from all patients on admission to determine the biochemical parameters and complete blood count. Blood samples were collected in ethylene diamine tetra acetic acid (EDTA) tubes for complete blood count and dry tubes for biochemical parameters. Complete blood counts were measured using a Horiba Pentra DX 120 automated blood cell counter (Horiba Medical, Montpellier, France), and biochemical parameters were measured using a Roche Cobas C501 auto analyzer system (Roche Diagnostics, Indianapolis, Ind, USA). The MHR (the MHR ratio was multiplied by 100 for straightforward interpretation), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII, defined as neutrophil × platelet/lymphocyte), and platelet-to-lymphocyte ratio (PLR) were calculated from complete blood counts.

Coronary Calcium Score

Coronary CT imaging was performed using a 64-slice CT scanner (Aquilion 64, Toshiba Medical Systems, Japan). Electrocardiogr

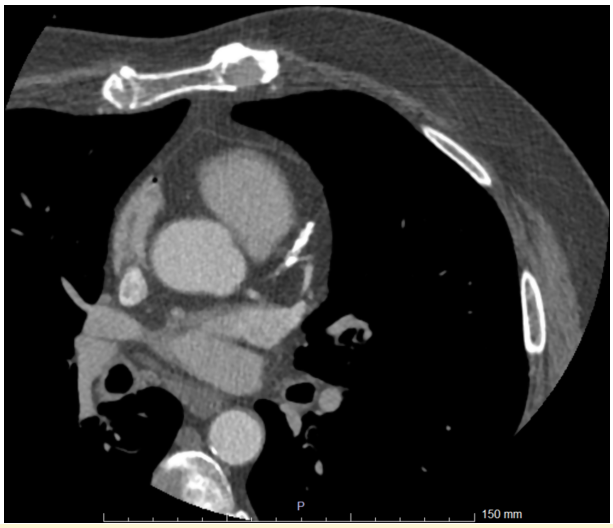

Figure 1. An example of diffuse calcification on left anterior descending artery.

am-gated CT calcium score was obtained by prospective gating with collimation (4 × 3.0 mm) with 3-mm reconstructed slice thickness. Tube current and tube voltages were 300 mA and 120 kV, respectively, and gantry rotation time was 0.4 seconds. Coronary artery calcium score was calculated using the software (Vitrea2 version 3.0.9.1, Vital Images, Minnesota). Calcium level based on the Agatston method was defined as the presence of a lesion with an area greater than 1 mm^2 and peak intensity greater than 130 Hounsfield Units (HU), which are automatically identified and marked with color by the software (Figure 1). All lesions are added to calculate the total CCS by the Agatston method. During the procedure, all patients were in sinus rhythm, and beta-blockers were given to the patients with heart rates above 60 to improve the imaging quality.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences software 22.0 version (IBM Corp.; Armonk, NY, USA). The continuous variables with a normal distribution were presented as mean ± standard deviation, whereas those without a normal distribution were presented as median (interquartile range). Categorical variables were presented as numbers and percent (%). Continuous variables between the 3 groups were compared with the analysis of variance or Kruskal–Wallis test according to their distribution. Categorical data were compared using the chi-square or Fisher's exact test. Correlations between different variables were assessed by Pearson's correlation test for continuous variables and Spearman's test for non-continuous variables. Statistical significance was defined as a $P < .05$. Multivariate logistic regression analysis was performed to identify the independent predictors of moderate-high CCS using variables showing marginal association with it on univariate testing. Receiver-operating characteristic analysis was used to detect the cutoff value of MHR in the prediction of intermediate-high CCS.

Results

A total of 276 patients (122 males, 44.2%; mean age: 56 ± 10 years) were enrolled. The patients were divided into 3 groups according to CCS [CCS = 0 for very low risk (n = 121), CCS = 1-99 for low risk (n = 100), CCS ≥100 for moderate-high risk (n = 55)]. Baseline characteristics and clinical and laboratory parameters of the study population are demonstrated in Table 1. Age, male gender, diabetes mellitus, hypertension, dyslipidemia, and smoking were significantly higher in patients with moderate-high CCS. Similarly, diuretics, beta-blockers, statin, and antiplatelet use were also significantly associated with moderate-high CCS. Creatinine levels were high, and HDL-C levels were low in patients with moderate-high CCS (48 ± 11 vs 43 ± 9 vs. 42 ± 10, $P < .001$). Monocyte to HDL-C ratio values were significantly higher in patients with moderate-high CCS (1.29 ± 0.59 vs. 1.41 ± 0.56 vs 1.56 ± 0.58, $P = .009$). However, there were no differences between the groups in terms of other inflammatory markers (SII, NLR, and PLR). In addition, the patients were stratified into tertiles according to MHR (MHR ≤1.08, n = 92; 1.08 < MHR < 1.59, n = 92; MHR ≥ 1.59, n = 92). Median CCS values of the patients with the highest tertile were significantly higher than the others [0 (0-24); 3 (0-51); 8 (0-160); respectively, $P = .019$].

Univariate analysis showed that older age, male gender, hypertension, dyslipidemia, smoking, and increased MHR values were significantly associated with CCS. In multivariate analysis, age (odds ratio (OR): 1.178; 95% CI: 1.107-1.253, $P < .001$), dyslipidemia (OR: 14.252; 95% CI: 5.459-37.211, $P < .001$), smoking (OR: 2.893; 95% CI: 1.317-6.358, $P = .008$), and MHR (OR: 2.082 per 1-point increase; 95% CI: 1.016-4.268, $P = .045$) were found to be independent predictors of CCS (Table 2).

Receiver-operating characteristic analysis was performed to determine the best MHR cutoff value for predicting moderate-high CCS. Monocyte to HDL-C ratio cutoff value of 1.19 and above had 69.1% sensitivity and 47.5% specificity for predicting moderate-high CCS (area under curve: 0.621, 95% CI: 0.561-0.678, $P = .003$) (Figure 2).

Mortality and acute myocardial infarction were not observed during an average of 10 months of follow-up. No patients with very low-risk CCS underwent invasive coronary angiography (ICA). Sixty-one patients (22.1%) underwent ICA and 70.5% (n = 43) of these patients had moderate-high CCS, while 29.5% (n = 18) had low CCS. Thirty-seven (13.4%) patients were revascularized. Patients with moderate-high CCS had a higher rate of revascularization compared to the other 2 groups [0% (n = 0) vs 6% (n = 6) vs 56.4% (n = 31), $P < .001$]. Patients with high MHR tertiles had higher ICA rates than other tertiles [18.5% (n = 17) vs 17.4% (n = 16) vs. 30.4% (n = 28), $P = .061$]. Per 1-point increase in MHR was associated with a 1.478-fold (95% CI 0.950-2.299, $P = .083$) increase in the need for revascularization.

Discussion

To the best of our knowledge, this is the first study demonstrating the association of MHR with CCS. In the present study, we found that MHR is a contributive parameter in predicting CAC in symptomatic patients with suspected CAD.

Evidence in studies has shown that CAC can significantly improve CAD and mortality risk prediction beyond traditional risk factors

Table 1. The Baseline Clinical and Laboratory Characteristics of the Patients According to CCS

	CCS = 0 (Very Low Risk) (n = 121)	CCS = 1-99 (Low Risk) (n = 100)	CCS ≥ 100 (Moderate-High Risk) (n = 55)	Total (n = 276)	*P*
Age	52 ± 10	57 ± 9	65 ± 9	56 ± 10	<.001
Gender (male), n (%)	32 (35.2)	48 (48)	42 (76.4)	122 (44.2)	<.001
Diabetes mellitus, n (%)	13 (10.7)	26 (26)	14 (25.5)	53 (19.2)	.007
Hypertension, n (%)	30 (24.8)	40 (40)	39 (70.9)	109 (39.5)	<.001
Dyslipidemia, n (%)	11 (9.1)	31 (31)	44 (80)	86 (31.2)	<.001
Family history, n (%)	17 (14)	17 (17)	13 (23.6)	47 (17)	.292
Smoking, n (%)					
Never	91 (75.2)	63 (63)	13 (23.6)	167 (60.5)	<.001
Former	18 (14.9)	26 (26)	31 (56)	75 (27.2)	
Current	12 (9.9)	11 (11)	11 (20)	34 (12.3)	
ACEI/ARBs, n (%)	30 (24.8)	38 (38.4)	33 (60)	101 (36.7)	<.001
Calcium channel blockers, n (%)	21 (17.4)	29 (29)	17 (30.9)	67 (24.3)	.058
Diuretics, n (%)	23 (19)	24 (24)	21 (38.2)	68 (24.6)	.002
Beta-blockers, n (%)	31 (25.6)	29 (29)	29 (52.7)	89 (32.2)	.001
Statins, n (%)	8 (6.6)	30 (30)	39 (70.9)	77 (27.9)	<.001
Antiplatelet, n (%)	24 (19.8)	42 (42)	41 (74.5)	107 (38.8)	<.001
Anticoagulant, n (%)	3 (2.5)	6 (6)	3 (5.5)	12 (4.3)	.400
Fasting blood glucose, mg/dL	98 (90-108)	102 (93-114)	100 (93-121)	100 (91-110)	.270
Creatinine, mg/dL	0.8 ± 0.1	0.8 ± 0.2	0.9 ± 0.2	0.8 ± 0.2	<.001
Total cholesterol, mg/dL	206 ± 39	205 ± 41	207 ± 57	206 ± 43	.708
LDL-C, mg/dL	129 ± 30	125 ± 32	128 ± 42	127 ± 33	.530
HDL-C, mg/dL	48 ± 11	43 ± 9	42 ± 10	45 ± 10	<.001
Triglyceride, mg/dL	131 (98-179)	150 (105-203)	154 (89-206)	138 (99-198)	.251
CRP, mg/dL	0.5 (0.2-1.3)	0.7 (0.3-1.6)	0.6 (0.2-1)	0.6 (0.2-1.3)	.594
White blood cell count, 10^3/μL	7.4 ± 1.8	7.6 ± 1.7	7.1 ± 1.6	7.4 ± 1.7	.203
Hemoglobin, g/dL	13.7 ± 1.4	13.8 ± 1.5	13.9 ± 1.3	13.8 ± 1.4	.614
Neutrophil count, 10^3/μL	4.1 ± 1.2	4.3 ± 1.3	3.9 ± 1.3	4.1 ± 1.3	.110
Lymphocyte count, 10^3/μL	2.4 ± 0.7	2.5 ± 0.9	2.3 ± 0.7	2.4 ± 0.8	.420
Platelet count, 10^3/μL	256 ± 62	242 ± 63	234 ± 57	247 ± 62	.024
Monocyte count, 10^3/μL	0.58 ± 0.21	0.58 ± 0.18	0.62 ± 0.19	0.59 ± 0.19	.607
MHR*	1.29 ± 0.59	1.41 ± 0.56	1.56 ± 0.58	1.39 ± 0.58	.009
SII	460 ± 231	466 ± 254	440 ± 277	458 ± 248	.678
NLR	1.77 ± 0.66	1.9 ± 0.79	18.9 ± 1.03	1.85 ± 0.79	.641
PLR	113.2 ± 41.1	105.3 ± 41.2	109.7 ± 40.3	109.6 ± 41	.473
CAG, n (%)	0 (0)	18 (18)	43 (78.2)	61 (22.1)	<.001
Revascularization, n (%)	0 (0)	6 (6)	31 (54.6)	37 (13.4)	<.001

CAG, coronary angiogram; CCS, coronary artery calcium score; ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin II receptor blockers; LDL-C, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; CRP, C-reactive protein; SII, systemic immune-inflammation index; MHR, monocyte to HDL-C ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.
*MHR × 100.

and scores. Agatston score is the most commonly used scoring method and defines CCS as the calcium level within the coronary arterial system as 130 HU or higher. The predictive efficacy of CCS, which was measured by the Agatston score, has been proven to predict cardiovascular events and mortality in many studies. Agatston score has high sensitivity in determining obstructive CAD.[11,12] In our study, we divided the patients into risk classification with the Agatston score.

Table 2. Univariate and Multivariate Logistic Regression Analysis of CCS

	Univariate Analysis			Multivariate Analysis		
Variable	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age	1.129	1.085-1.174	<.001	1.178	1.107-1.253	<.001
Gender (male)	4.483	2.259-8.895	<.001	-	-	-
Diabetes mellitus	1.593	0.793-3.204	.191	-	-	-
Hypertension	5.258	2.753-10	<.001	-	-	-
Dyslipidemia	17.048	8.123-35.775	<.001	14.252	5.459-37.211	<.001
Smoking	2.772	1.850-4.154	<.001	2.893	1.317-6.358	.008
MHR	1.804	1.123-2.899	.015	2.082	1.016-4.268	.045

OD, odds ratio; MHR, monocyte to HDL-C ratio.

Coronary artery calcification, which was measured by cardiac CT, has high sensitivity and negative predictive power for CAD, but its specificity is limited. Budoff et al[12] reported that patients with 0 CAC scores did not have any obstruction in ICA (negative predictive power of 98%). The prognostic value of CCS in asymptomatic patients is independent of traditional risk factors in the Multi-Ethnic Study of Atherosclerosis and Coronary Artery Risk Development in Young Adults studies.[13] Silverman et al[14] showed that the individuals who did not have traditional risk factors but have a high CAC burden are associated with an elevated adverse cardiovascular event rate. However, high-risk factors in the absence of CAC are associated with a low event rate.[14] Following the results of individual studies, findings from meta-analyses showed that CAC was an independent predictor of CAD.[15] CAC's ability to predict future coronary events in symptomatic individuals has been demonstrated in many studies. Detrano et al[16] demonstrated that high CAC was associated with an increased risk of coronary events within 30 months.[16] Kennedy et al[17] also reported that atherosclerotic plaque burden is a more critical marker rather than the severity of stenosis. Besides, CAC was found to be a more reliable predictor than the sum of traditional risk factors in determining future events. Since calcified atherosclerotic plaque may also be present in non-obstructive coronary lesions, the presence of CAC in asymptomatic individuals is not justification for revascularization. However, it provides risk factor modification and possible advanced functional evaluation.

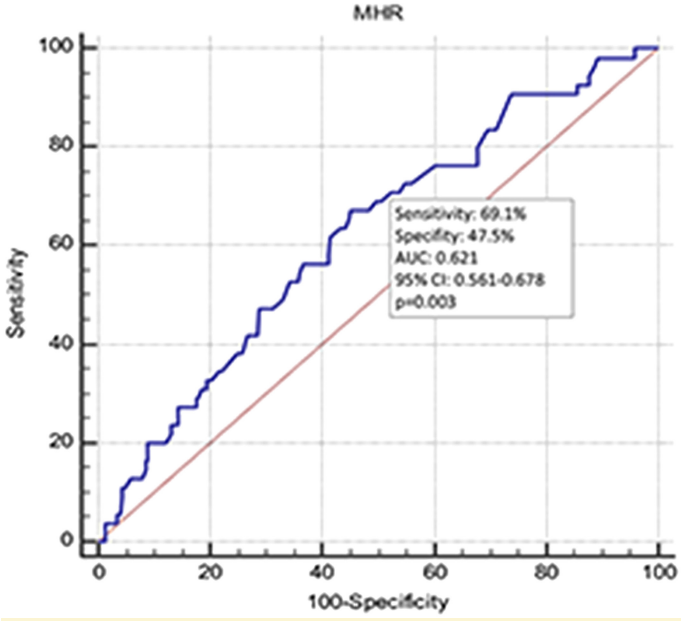

Figure 2. ROC analysis performed to determine the best MHR cutoff value for predicting moderate-high CCS. ROC, receiver-operating characteristic; MHR, monocyte to high-density lipoprotein cholesterol ratio; CCS, coronary artery calcium score.

Inflammation has an essential role in the progression of atherosclerosis and cardiovascular diseases. Monocytes play a crucial role in inflammation. Monocytes are activated by binding to adhesion molecules that are expressed on the damaged endothelium and play an essential role in the progression of atherosclerosis.[18] Activated monocytes migrate to the subendothelial layer and turn into macrophages. Macrophages phagocyte oxidized LDL-C molecules and become foam cells, and these foam cells secrete pro-inflammatory and pro-oxidant cytokines.[19,20] In a study, Gratchev et al[21] found that the number of circulating monocytes is the source of tissue macrophages and foam cells are a determinant for the development of new atherosclerotic plaque. Another study by Nozawa et al[22] indicated that circulating monocytes play an essential role in the progression of coronary plaque in acute myocardial infarction. In our study, monocyte count was found higher in moderate-high CCS, although it was not statistically significant.

In contrast to the effects of monocytes described above, HDL-C reduces monocyte activation and adhesion, regulates the endothelial adhesion molecule release, reverses the effects of oxidized LDL-C, and causes vasodilation by NO release.[23,24] High-density lipoprotein cholesterol reduces the risk of cardiovascular events with these anti-inflammatory effects.[25] Protective effects of the HDL-C on atherosclerotic cardiovascular diseases are demonstrated in several studies. The most striking results among these studies are presented in an analysis by the Emerging Risk Factors Collaboration. In this analysis, 68 long-term prospective studies were included, and it was found that HDL-C and non-HDL-C levels were firmly (in opposite directions) associated with CAD risk.[26] In this study, HDL-C levels decreased significantly as the risk of CCS increased, and this result was consistent with the literature.

High monocyte count and low HDL-C levels are indirect indicators of inflammation. Many studies in recent years demonstrated that the MHR is an indicator of inflammatory and atherosclerotic metabolic balance and is strongly related to CAD. Çiçek et al[27] examined that MHR was independently and significantly associated with long-term mortality in patients with ST-segment elevation myocardial infarction (STEMI) treated with percutaneous coronary intervention. In another study conducted by Çağdaş et al[28] high MHR levels in STEMI patients were associated with high SYNTAX and SYNTAX II scores. Also, Kalyoncuoglu et al[29] found that high MHR is associated with a slow flow/no-reflow phenomenon in patients with non-ST-elevated myocardial infarction. In the studies mentioned above, MHR is associated with CAD prevalence, mortality rate, and complications that may develop in acute coronary syndrome.

On the other hand, the number of studies with stable angina pectoris is minimal. Kundi et al[7] reported that MHR was independently and significantly associated with SYNTAX score in stable CAD patients. Similarly, Akboga et al[30] examined the MHR of 1229 patients with stable CAD and compared the SYNTAX scores. They showed that there was a significant and independent relationship between high MHR and high SYNTAX scores. In a recent study, inflammatory markers, including MHR, were studied in patients with stable angina pectoris. As a result of this study, 421 patients who underwent ICA had high MHR levels in patients with significant CAD.[31] In our study, MHR was associated with increased CCS, and the increase in MHR values toward moderate-high CCS was statistically significant.

Two hundred seventy-six stable patients were included in our study. Sixty-one patients underwent ICA, and 37 patients were revascularized. In accordance with the literature, CCS was associated with ICA requirements and revascularization. When patients are separated according to MHR tertiles, ICA and revascularization might be related to MHR values. In our study, advanced age, dyslipidemia, smoking, and MHR are determined as independent predictors of moderate-high CCS.[32]

In light of the current literature, the relationship between CCS and MHR has not been studied. The presence and degree of atherosclerosis were determined by ICA in all studies. However, ICA is a lumenography, and the absence of obstruction in the lumen does not mean that there is no atherosclerosis. Therefore, high CCS is associated with undesirable events independent of obstruction severity. In this study, CCS was used to determine coronary atherosclerosis, and MHR levels were found to be significantly higher in patients with moderate-high CCS. The relationship between CCS and other inflammatory markers, such as C-reactive protein (CPR), SII, NLR, and PLR, has been studied. However, other inflammatory markers were not found to be significant in predicting the severity of coronary atherosclerosis determined by CCS. Notwithstanding that the number of patients who needed ICA and revascularization was low, we found that patients with high MHR were more frequently revascularized.

The present study has several limitations. First, it has a cross-sectional design. Second, the number of patients who underwent ICA and revascularization was relatively low; therefore, robust data on the prognostic value of MHR could not be obtained. In clinical practice, the rate of ICA is very limited in patients with low and very low CCS, and the presence of CAD in this group may have been underestimated. All potential factors that could affect the interaction between monocytes and HDL-C could not be evaluated. Monocytes have different subtypes, and the behavior of these subtypes also varies.[33] In this study, monocytes were not separated according to their subtypes. A similar situation applies to HDL-C. Apart from the amount of HDL-C, they were also classified according to their sizes as small, medium, and large.[34] The biological activity of the subtypes of HDL-C differs, and this may affect the outcome of the study. Finally, the high-sensitivity CRP level, a good indicator of basal inflammation, could not be measured.

Conclusion

This study shows that high MHR values may be helpful to reveal the CAD. The detection of high MHR is significantly associated with increased CCS in patients with stable angina pectoris. Besides this data, MHR may aid in determining the patients for revascularization need.

Ethics Committee Approval: The study was approved by the medical ethics committee of University of Health Sciences, Derince Education and Research Hospital.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.İ.Ç; Design – A.İ.Ç., T.B.; Supervision – M.Ç., R.C.; Resources – A.İ.Ç., T.B.; Materials – A.İ.Ç.; Data Collection and/or Processing – A.İ.Ç.; Analysis and/or Interpretation – M.Ç., M.B.K.; Literature Search – A.İ.Ç., R.C.; Writing Manuscript – A.İ.Ç., M.B.K.; Critical Review – M.Ç., T.B.

Declaration of Interests: The authors have no conflicts of interest to declare.

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