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The Relationship between Coronary Thrombus Burden and Monocyte to High-Density Lipoprotein Cholesterol Ratio in Patients with Acute Non-ST Elevation Myocardial Infarction

Non-ST Eleve Miyokard Infarklarda Koroner Trombüs Yükü ile Monosit Yüksek Dansiteli Lipoprotein Kolesterol Oranı İlişkisi

Gündüz Durmuş

Haseki Training and Research Hospital, Clinic of Cardiology, İstanbul, Turkey

ABSTRACT

Introduction: Non-ST-segment elevation myocardial infarction (NSTEMI) is a condition that constitutes a large part of acute coronary syndromes and has a high mortality rate with diffuse vascular disease. The aim of this study was to examine the association between monocyte to high-density lipoprotein cholesterol ratio (MHR) and thrombus burden, which is indicative of inflammation and cardiovascular endpoints in patients with NSTEMI.

Methods: We retrospectively evaluated 205 consecutive patients who underwent coronary angiography for NSTEMI in our tertiary center. Complete blood count and biochemical analysis were performed using blood samples. Angiographic thrombus burden was classified as previously described by thrombolysis in the myocardial infarction (TIMI) study group.

Results: Patients with high thrombus burden had higher monocyte count, MHR and platelet count compared to the group with low thrombus burden. TIMI and Syntax scores were also higher in the high thrombus burden group. Multiple logistic regression analysis revealed that TIMI and MHR values were independently related to high thrombus burden. [Odds ratio (OR): 1.678 (1.120-2.515) p=0.012) and OR: 1.432 (1.102-1.861), p=0.007) respectively.]

Conclusion: In our study, we found that MHR was closely related to thrombus burden in patients with NSTEMI. With further studies, MHR may be a helpful parameter for risk scoring informing long-term morbidity and mortality.

Keywords: Monocyte to high-density lipoprotein cholesterol ratio, HDL-C, MHR, myocardial infarction

ÖZ

Amaç: Non-ST elevasyonlu miyokard infarktüsü (NSTEMI) akut koroner sendromların geniş bir kısmını oluşturan ve yaygın damar hastalığıyla yüksek mortaliteye sahip bir durumdur. Enflamasyonun aterosklerozun gelişiminden başlayan etkisi plak rüptürü sonucu trombüs oluşumuna kadar sürmektedir. Yüksek trombüs yükü ile kötü sonlanım noktaları arasında yakın ilişki vardır. Amacımız NSTEMI hastalarında enflamasyonun ve kardiyovasküler sonlanım noktalarının göstergesi olan monosit yüksek dansiteli lipoprotein oranı (MHR) ile trombüs yükü arasındaki ilişkiyi incelemektir.

Yöntemler: Tersiyer merkezimizde NSTEMI tanısı ile koroner anjiyografi yapılmış 205 ardışık hastayı retrospektif olarak değerlendirdik. Kan örneklerinden tam kan sayımı ve biyokimyasal analizler yapıldı. Anjiyografik trombüs yükü, miyokard enfarktüsü (TIMI) çalışma grubunda tromboliz ile daha önce tanımlandığı gibi sınıflandırıldı.

Bulgular: Yüksek trombüs yükü olan hastalarda düşük gruba göre daha yüksek monosit sayısı, MHR ve platelet sayısı mevcuttu. Ayrıca TIMI ve Syntax skorları da yüksek trombüs yükü olan grupta daha yüksekti. Çoklu lojistik regresyon analizi MR ve TIMI değerlerinin bağımsız olarak yüksek trombüs yükü ile ilişkili olduğunu ortaya çıkardı. [Odds ratio (OR): 1,678 (1,120-2,515) p=0,012) ve OR: 1,432 (1,102-1,861), p=0,007) sırasıyla].

Sonuç: Çalışmamızda MHR'nin NSTEMI hastalarında trombüs yükü ile yakından ilişkili olduğunu tespit ettik. Yapılacak ek çalışmalar ile MHR uzun dönem morbidite ve mortalite hakkında bilgi veren risk skorlamalarına yardımcı bir parametre olabilir.

Anahtar Kelimeler: Yüksek dasiteli lipoprotein kolesterol oranı, HDL-C, MHR, miyokard enfarktüsü

Address for Correspondence/Yazışma Adresi: Gündüz Durmuş MD, Haseki Training and Research Hospital, Clinic of Cardiology, İstanbul, Turkey
Phone: +90 212 533 34 61 **E-mail:** drgd28@hotmail.com **ORCID ID:** orcid.org/0000-0002-2232-2858

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Introduction

Acute coronary syndrome (ACS) is defined as unstable coronary artery diseases (CADs), including unstable angina pectoris and acute myocardial infarction (AMI) that occurs in response to plaque rupture and vascular inflammation that results in thrombosis (1). Compared with ST-segment elevation AMI (STEMI), non-(N)STEMI patients tend to be older and have more comorbidity with varied CAD severity (2,3). The role of inflammation is essential in the progression and destabilization of atherosclerosis, and eventually in the initiation of the ACS by leading to plaque erosion and rupture (4,5). Intracoronary thrombosis is closely related to no-reflow, distal embolization and ultimately low procedurally success with thrombus size (6). In accordance with this, there was a close correlation between high thrombus burden and 1-year mortality rate and stent thrombosis (7).

Monocyte to high-density lipoprotein cholesterol ratio (MHR) is a prognostic marker that is associated with cardiovascular outcomes in numerous cardiovascular diseases (8,9). Monocytes play a role in the pathophysiology of CAD by transforming into macrophils as they take part in the inflammatory process (10). The function of HDL is to remove the cholesterol in the peripheral tissue and inhibit the monocytes.

There are no studies examining the relationship between thrombus burden and MHR in patients with NSTEMI. Being aware of this relationship may help us estimate the risk of cardiovascular events and obtain information about prognosis and possible additional therapies.

Methods

Two hundred and five consecutive patients who underwent coronary angiography in our tertiary center for the diagnosis of NSTEMI were retrospectively enrolled and the study was undertaken in compliance with the principles of the Declaration of Helsinki. The medical records of consecutive patients hospitalized between January 2015 and December 2017 at Haseki Training and Research Hospital were reviewed.

Patients, who were diagnosed with NSTEMI and had coronary angiography with or without percutaneous coronary intervention (PCI), were enrolled in our study. Using hospital records, baseline clinical and demographic characteristics of patients including diabetes mellitus, hypertension (HT), CAD, family history of CAD, dyslipidemia, smoking, chronic obstructive pulmonary disease and history of CAD or CAD equivalent, such as peripheral arterial disease, were obtained. The medical records of 321 patients were retrospectively reviewed and analyzed. Finally, 205 patients were included in the study. Patients with a history of CAD, malignancy, active infection, connective tissue disorder, end-stage renal disease or receiving hemodialysis, and patients with no significant CAD or with other causes of coronary pain, such as major myocardial bridging or diffuse coronary spasm during angiography and any missing information were excluded from the study.

The diagnosis of NSTEMI uses the American College of Cardiology/American Heart Association guidelines as a basis, and it is diagnosed in a patient with typical chest pain or an equivalent symptom, high troponin and without a ST-segment elevation in ECG. All patients in the emergency department were given 300 mg oral aspirin, 70 U/kg unfractionated heparin and a loading dose 600 mg clopidogrel intravenously, and radial or femoral routes were used to perform coronary angiographies where two different plane images were used to display individual coronary arteries. Two experienced and independent interventional cardiologists (blinded to the data) analyzed digital angiograms. Angiographic thrombus burden was classified as previously defined by thrombolysis in myocardial infarction (TIMI) study group. The grades according to this classification are as follows: grade 0: no evidence of thrombus, grade 1: suspected thrombus (reduced contrast density, haziness, irregular lesion contour, or a smooth convex "meniscus" at the site of occlusion), grade 2: definite thrombus with greatest dimensions ≤ 1/2 vessel diameter, grade 3: definite thrombus with greatest linear dimension >1/2 but <2 vessel diameters, grade 4: definite thrombus with greatest linear dimension ≥2 vessel diameters, and grade 5: total thrombotic occlusion. The patients were grouped into two categories as low thrombus burden (grades 0-3) and high thrombus burden (grades 4 and 5) (11).

Blood samples taken by antecubital vein puncture on admission to emergency room were used for biochemical analysis and complete blood count. An automated blood cell counter (Beckman Coulter analyzer, Brea, CA, USA) was used to determine blood count parameters of hemoglobin, neutrophils, monocytes, white blood cells, platelets and lymphocytes. The targeted biochemical parameters were creatine, low-density lipoprotein cholesterol, glucose, total cholesterol and triglycerides.

Statistical Analysis

Statistical Package for the Social Sciences version 24.0 (SPSS, Chicago, Illinois) was used for statistical analysis. Continuous variables were given as mean ± standard deviation (normal distribution) and median (interquartile range) (non-normal distribution). Categorical variables were provided as percentages. Chi-square (χ^2) test was used to compare categorical variables between groups. Kolmogorov-Smirnov test was used to determine the distribution of variables and Student's t-test or Mann-Whitney U tests were used to compare the continuous variables between the groups in relation to normal distribution. In order to determine independent predictors for high thrombus burden, variables that were found to be associated with a p level of <0.1 by univariate analysis were included in the multivariate logistic regression analysis. Receiver operating characteristic curve analysis was performed to determine the optimal cut-off value for MHR in relation to high thrombus burden. P<0.05 was considered statistically significant at 95% confidence interval.

Results

A total of 205 patients were included in the study. One hundred and seven patients (52.1%) were male and the mean age was 56.8±12 years.

Patients with high thrombus burden had higher monocyte count, MHR and platelet count compared to the group with low thrombus burden. TIMI and Syntax scores were also higher in the high thrombus burden group.

Univariate regression analysis showed that TIMI, platelet and MHR at p<0.1 were found to be significant. Multiple logistic regression analysis

revealed that TIMI and MHR values were independently related to high thrombus burden [Odds ratio (OR): 1.678 (1.120-2.515) p=0.012) and OR: 1.432 (1.102-1.861), p=0.007) respectively] (Table 2).

Analysis of the receiver-operating characteristic found an optimal MHR cut-off value to be 1.75 with a sensitivity of 71.4% and specificity of 64% (AUC: 0.61; 95% CI: 0.51-0.70) in predicting a high thrombus burden score (Figure 1).

Discussion

The study found that MHR was closely related to thrombus burden in patients with NSTEMI.

The main pathophysiology of ACS is the onset of the formation of the thrombus and rupture of the atherosclerotic plaque. In spite of a successful PCI, the amount of thrombus formed has a close relationship between the distal coronary perfusion and the drop in EF (11,12). There was a close relationship with major adverse cardiac events in patients with an elevated thrombus burden (13-15).

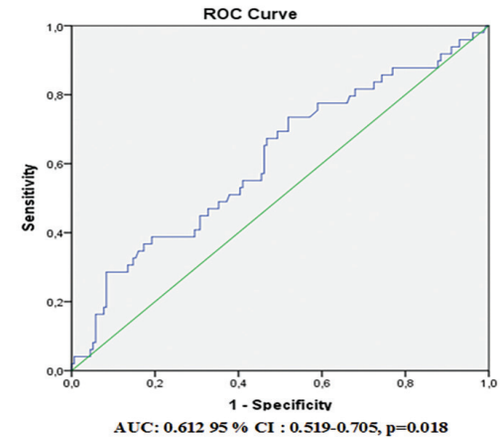

Figure 1. ROC curve of the MHR in predicting the high thrombus burden

ROC: receiver operating characteristic, MHR: monocyte to high-density lipoprotein cholesterol ratio

Table 1. Demographic, clinical and laboratory parameters of study cohort

	Low thrombus burden, (n=155)	High thrombus burden, (n=50)	p
Age, years	56.9±10.9	56.6±12.4	0.84
Male, n (%)	125 (80.6)	40 (80)	0.85
BMI, kg/m^2	26.6±3.0	26.8±3.0	0.69
HT, n (%)	82 (52.3)	25 (52)	0.85
DM, n (%)	43 (27.7)	14 (28)	0.97
HL, n (%)	22 (14.3)	10 (20.4)	0.3
Smoking	92 (59.4)	28 (56)	0.7
Glucose, mg/dL	139.4±58.6	155.6±75.7	0.12
GFR, mL/min/1.73 m^2	89.4±21.7	89.4±24.8	0.99
TC, mg/dL	207.6±45.8	203.1±64.7	0.58
TG, mg/dL	216.4±159.1	186.2±104	0.21
HDL, mg/dL	39.8±9.7	39.6±9.5	0.92
LDL, mg/dL	127.7±42.1	131.8.2±41.2	0.54
Monocyte, (10^3/µL)	0.64±0.3	0.83±0.36	<0.001
MHR, (X100)	1.61±0.81	1.96±0.82	0.006
Neutrophil, (10^3/µL)	9.2±3.5	7.5±2.6	0.72
Lymphocyte, (10^3/µL)	3.5±1.2	2.8±1.8	0.70
Platelet, (10^3/µL)	231.7±72.2	256.3±75.3	0.04
Grace score	95.2±25.6	101.8±26.7	0.12
TIMI score	3.7±1.4	4.2±1.2	0.01
Syntax score 1	13.1±9.1	23.9±9.2	<001

BMI: body mass index, HT: hypertension, DM: diabetes mellitus, HL: hyperlipidemia, GFR: glomerular filtration rate, TC: total cholesterol, TG: triglycerides, HDL: high density lipoprotein, LDL: low density lipoprotein, MHR: monocyte to high-density lipoprotein cholesterol ratio, TIMI: thrombolysis in the myocardial infarction

Table 2. Independent predictors of high thrombus burden

Variables	Univariate		Multivariate	
	OR (95% CI)	p	OR (95% CI)	p
MHR	1.746 (1.185-2.572)	0.02	1.701 (1.088-2.657)	0.02
Platelet	1.004 (1.000-1.008)	0.05	1.004 (0.999-1.009)	0.09
TIMI	1.372 (1.070-1.760)	0.01	1.420 (1.098-1.836)	0.007

OR: odds ratio, CI: confidence interval, MHR: monocyte to high-density lipoprotein cholesterol ratio, TIMI: thrombolysis in the myocardial infarction

The roles of monocyte activation and mature macrophage forms are vital in the development and exacerbation of the atherosclerotic process, which is a lipid directed inflammatory disease (16). Blood monocytes enter the intimal/sub-intimal layers of the vessel wall, then differentiate into foam cells via up-taking oxidized LDL and other lipids through scavenger receptors. Patients diagnosed with hypercholesterolemia have been found to have accelerated monocyte migratory properties (17). Secretion of matrix metalloproteinases, pro-inflammatory cytokines, and tissue factors into the vessel wall occurs. Plaque rupture is caused digestion of the internal elastic lamina by metalloproteinases and the tissue factor that is released and contacts with circulating blood and causes the formation of thrombus (18). Anti-inflammatory and anti-thrombotic effects on human monocytes are exhibited by HDL-C, which counteracts activation and migration. Reddy et al. (19) showed how lower levels of HDL cholesterol, theoretically related to the inadequate limitation of inflammatory response, had a relationship with increased in-hospital patient deaths preceding AMI. MHR is now considered to be a vascular inflammatory marker and a reliable predictor for atherosclerosis formation, progression and cardiovascular outcomes. Furthermore, its value in acute STMI has been studied in previous clinical investigations. Karataş et al. (9) showed that admission MHR values were independently correlated with inpatient major adverse cardiovascular outcomes and death following a primary PCI. Similarly Çiçek et al. (20) recently showed that in-hospital mortality rates, late mortality, re-infarction, target vessel revascularization, major adverse cardiovascular events, and stroke were higher in the group with a greater MHR in comparison to the other MHR groups. They subsequently concluded that admission MHR was significantly and independently related with long-term and short-term mortality in STEMI. Furthermore, Cetin et al. (21) has verified that MHR is an innovative marker of inflammation and that it appears to be an independent predictor of stent thrombosis for STEMI patients. Finally, Balta et al. (22) found a relationship between MHR and no-reflow phenomenon in STEMI patients.

Study Limitations

The most important primary limitations of this study were the small number of patients and the research being conducted in a single center. Additional limitations were the mean age of the study population being fairly young, all of the study data being accumulated at a single point in time, and thus may not be representative of variations over time.

Conclusion

If we can better understand the relationship between basic biochemical tests and the thrombus burden closely related to the prognosis in NSTEMI patients with obtained MHR value, data about the risk of short- and long-term morbidity and mortality, which may be valid in compiling risk scores, can be obtained.

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

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References

1. Braunwald E. Unstable angina: An etiologic approach to management. Circulation.1998; 98: 2219-22.
2. Amstardam EA, Wenger NK, Brindis RG, Casey DE, Ganiats TG, et al. 2014 AHA/ACC Guideline for the management of patients with non-ST-elevation acute coronary syndromes: A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. JACC 2014; 64: 139-228.
3. Chang H, Min JK, Rao SV, Patel MR, Simonetti OP, Ambrosio G, et al. Non-ST-Segment elevation acute coronary syndromes: Targeted imaging to refne upstream risk stratifcation. Circ Cardiovasc Imaging. 2012; 5: 536-46.
4. Wada H, Dohi T, Miyauchi K, Doi S, Naito R, Konishi H, et al. Independent and combined effects of serum albumin and C-reactive protein on long-term outcomes of patients undergoing percutaneous coronary intervention. Circ J 2017; 81: 1293-300.
5. Koenig W, Rosenson RS. Acute-phase reactants and coronary heart disease. Send to Semin Vasc Med. 2002; 2: 417-28.
6. Kurt M, Karakas MF, Buyukkaya E, Akc¸ay AB, Sen N. Relation of angiographic thrombus burden with electrocardiographic grade III ischemia in patients with ST-segment elevation myocardial infarction. Clin Appl Thromb Hemost. 2014; 20: 31-6.
7. Sianos G, Papafaklis MI, Daemen J, et al. Angiographic stent thrombosis after routine use of drug-eluting stents in STsegment elevation myocardial infarction: the importance of thrombus burden. J Am Coll Cardiol. 2007; 50: 573-83.
8. Canpolat U, Aytemir K, Yorgun H, Şahiner L, Kaya EB, Çay S, et al. The role of preprocedu ral monocyte-to-high-density lipoprotein ratio in prediction of atrial fibrillation recurrence after cryoballoon-based catheter ablation. Europace. 2015; 17: 1807-15.
9. Karataş MB, Çanga Y, Özcan KS, İpek G, Güngör B, Onuk T, et al. Monocyte to high-density lipoprotein ratio as a new prognostic marker in patients with STEMI undergoing primary percutaneous coronary intervention. Am J Emerg Med. 2016; 34: 240-4.
10. Hansson GK. Inflammatory mechanisms in atherosclerosis. J Thromb Haemost 2009; 7: 328-31.
11. Gibson CM, de Lemos JA, Murphy SA, Marble SJ, McCabe CH, Cannon CP, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. Circulation. 2001; 103: 2550-4.
12. Tanboga IH, Topcu S, Aksakal E, Kalkan K, Sevimli S, Acikel M. Determinants of angiographic thrombus burden in patients with ST-segment elevation myocardial infarction. Clin Appl Thromb Hemost. 2014; 20: 716-22.
13. Tungsubutra W, Towashiraporn K, Tresukosol D, Chotinaiwattrakul C, Phankingthongkum R, Wongpraparut N, et al. One-year clinical outcomes of ST segment elevation myocardial infarction patients treated with emergent percutaneous coronary intervention: the impact of thrombus burden. J Med Assoc Thai 2014; 97: 139-46.
14. Sianos G, Papafaklis MI, Serruys PW. Angiographic thrombus burden classification in patients with ST-segment elevation myocardial infarction treated with percutaneous coronary intervention. J Invasive Cardiol. 2010; 22: 6-14.
15. Singh M, Berger PB, Ting HH, et al. Influence of coronary thrombus on outcome of percutaneous coronary angioplasty in the current era (the Mayo Clinic experience). Am J Cardiol. 2001; 88: 1091-6.
16. Hilgendorf I, Swirski FK, Robbins CS. Monocyte fate in atherosclerosis. Arterioscler Thromb Vasc Biol. 2015; 35: 272-9.
17. Bath PM, Gladwin A-M, Martin JF. Human monocyte characteristics are altered in hypercholesterolaemia. Atherosclerosis 1991; 90:175-81.

18. Moreno PR, Purushothaman KR, Fuster V, O'Connor WN. Intimomedial interface damage and adventitial inflammation is increased beneath disrupted atherosclerosisin the aorta: implications for plaque vulnerability. Circulation 2002; 105: 2504-11.

19. Reddy VS, Bui QT, Jacobs JR, Begelman SM, Miller DP, French WJ, et al. Relationship between serum low-density lipoprotein cholesterol and in hospital mortality following acute myocardial infarction (the lipid paradox). Am J Cardiol 2015; 115: 557-62.

20. Çiçek G, Kundi H, Bozbay M, Yayla C, Uyarel H. The relationship between admission monocyte HDL-C ratio with short-term and long-term mortality among STEMI patients treated with successful primary PCI. Coron Artery Dis. 2016; 27:176-84.

21. Cetin EHO, Cetin MS, Canpolat U, Aydin S, Topaloglu S, Aras D, et al. Monocyte/HDLcholesterol ratio predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Biomark Med. 2015; 9: 967-77.

22. Balta S, Celik T, Ozturk C, Kaya MG, Aparci M, Yildirim AO, et al. The relation between monocyte to HDL ratio and no-reflow phenomenon in the patients with acute ST-segment elevation myocardial infarction. Am J Emerg Med. 2016; 34: 1542-7.