Dicle Tıp Dergisi / Dicle Med J (2022) 49 (1) : 12-20

www.diclemedj.org

Original Article / Özgün Araştırma

Prognostic Significance of Monocyte to High-density Lipoprotein Ratio in Patients With Chronic Coronary Artery Occlusion

Muhammed Demir[1], Mehmet Özbek[1], Adem Aktan[2], Tuncay Güzel[3], Burhan Aslan[3], Hakkı Şimşek[1]

1 Department of Cardiology, Dicle University School of Medicine, Diyarbakir, Turkey

2 Department of Cardiology,Mardin State Hospital, Mardin, Turkey

3 Department of Cardiology,Gazi Yaşargil Training and Research Hospital, Diyarbakır, Turkey

Received: 04.10.2021; Revised: 14.01.2022; Accepted: 21.01.2022

Abstract

Objective: Monocyte to high-density lipoprotein ratio (MHR) is a biomarker of inflammatory response. In this study, we investigated the relationship between MHR and mortality in patients with chronic coronary artery occlusion (CTO).

Method: Retrospective observational study including 493 patients over a follow up period of 73 months. Blood samples were taken before cardiac catheterization for coronary angiography.

Results: Median follow-up was 48 months(26-73) . Patients were seperated into two groups: (I) MHR <17.68 (n=278, 95 females) and (II) MHR ≥17.68 (n=215, 45 females). Mortality was considerably higher in MHR II than in MHR I (n=70 vs. n=43; p<0,001). MHR was an independent predictor of mortality (OR: 1.089, 95% [CI]: 1.055-1.124, p<0,001). Lower survival rates were found in MHR II on Kaplan-Meier analyses when compared to that of MHR I (75.223±2.670 vs. 89.220±2.102, p<0,001).

Conclusions: As a simple, easy applicable and universal marker, MHR may be a parameter that predicts mortality risk and survival time in CTO patients.

Keywords: Prognosis, inflammation, mortality, atherosclerosis

DOI: 10.5798/dicletip.1085926

Correspondence / Yazışma Adresi: *Muhammed Demir, Department of Cardiology, Dicle University School of Medicine, Diyarbakir, Turkey. e-mail: drmdemirr@gmail.com*

Monosit/HDL Değerinin Koroner Kronik Total Oklüzyon Hastalarında Prognostik önemi

Öz

Amaç: Kronik total oklüzyon (KTO) gelişimi her aşaması farklı histopatolojik özellikler içeren çok sayıda histolojik evrelerden oluşur. Monosit/HDL oranı (MHO) inflamatuvar yanıtın derecesini gösteren faydalı bir parametredir. KTO hastalarında MHO'nun sağkalım süresi ve uzun dönem mortalite üzerine etkisini araştırdık.

Yöntemler: 2011 Ocak ile 2019 Aralık arasında 73 aya kadar takibi yapılan 493 KTO hastası çalışmaya alındı. Periprosedüral kan örneklerinden MHO hesaplanıp detaylı klinik datalar elde edildi.

Bulgular: Medyan takip süresi 48 ay olup hastalar MHO değerine göre MHO I <17.68 (N:278, 95 kadın) ve MHO II ≥17.68 (N:215, 45 kadın) olacak şekilde iki gruba ayrıldı.Mortalite MHO II grubunda MHO grup I'e göre belirgin olarak daha fazla bulundu (n=70 vs. n=43; p<0,001). MHO değeri mortalitenin bağımsız öngördürücüsü olarak bulundu (OR: 1.089, 95% [CI]: 1.055-1.124, p<0,001). Kaplan-Meier analizinde MHO II grubunda daha düşük sağkalım süresi tespit edildi (75.223±2.670 vs. 89.220±2.102, p<0,001).

Sonuç: KTO hastalarında basit, kolay uygulanabilir, evrensel bir marker olarak MHO, mortalite riski ve sağkalım süresini öngördüren bir parametre olabilir.

Anahtar kelimeler: Prognoz, enflamasyon, mortalite, ateroskleroz.

INTRODUCTION

Chronic total occlusion (CTO) is defined as occlusion of a coronary artery for more than three months period. CTO is a clinical condition commonly detected during routine angiography and has a prevalence of 18-52%[1-3]. According to the National Heart, Lung, and Blood Institute (NHLBI) Dynamic Registry, CTO is most commonly seen in the right coronary artery and least commonly in the circumflex artery. The incidence of CTO increases with age, with a reported incidence of 37% in patients aged less than 65 years, 40% in patients aged between 65-79 years, and 41% in patients aged over 85 years[4].

The development of CTO consists of multiple histological stages, with distinct histopathological features for each stage. In most cases, CTO is triggered by thrombus caused by sudden rupture of an atherosclerotic plaque[5]. The progression of coronary artery disease (CAD) and its evolution to a CTO lesion is caused by numerous conditions such as immunological upregulation, inflammatory indicators (cytokines, leukocytes, C-reactive protein [CRP]), endothelial dysfunction, and cholesterol saving.

Monocytes have a basic part in the early phase of atherosclerosis[6]. These cells bind to adhesion particles expressed on injuried endothelial cells through immune-mediated mechanisms[7]. Subsequently, they transmigrate to the subendothelial area and convert into macrophages and thereby internalize oxidized low-density lipoprotein (LDL) and class A scavenger receptors[8]. Afterwards, they convert into foam cells, thereby causing the release of proinflammatory and prooxidant cytokines[9]. Unlike monocytes, high-density lipoprotein (HDL) is a heterogeneous lipid and protein particle which has been displayed to have antioxidant, anti-inflammatory, anti-apoptotic, anti-thrombotic and anti-atherosclerotic properties[10-11].

Various parameters can be used to show the burden of coronary artery disease[12]. The monocyte to HDL ratio (MHR) has recently emerged as a novel, inexpensive, and accessible marker of inflammation and oxidative effect. MHR has also been associated with adverse cardiac outcomes in patients with acute

myocardial infarction (AMI)[13], stable angina pectoris (SAP)[14], atrial fibrillation (AF)[15], coronary slow-flow phenomenon (CSFP)[16], rheumatic mitral stenosis (RMS)[17], and hypertrophic cardiomyopathy (HCM)[18].

To the best of our knowledge, there is no study in the literature reporting on a direct relationship between MHR and mortality in CTO patients. The objective of this study was to explore the relationship between MHR and mortality in CTO patients.

METHOD

Research design

The research was planned as an observational, retrospective and included cases that had a diagnosis of SAP, unstable angina pectoris (USAP), non-ST-elevated myocardial infarction (NSTEMI), and ST-elevated myocardial infarction (STEMI) or asymptomatic patients that were incidentally diagnosed with CTO during a routine angiography prior to cardiovascular surgery between the calendar years of 2011 and 2019. Cases with hematological disorders, inflammatory disorders, malignancies, infections, chronic liver or kidney disorder, autoimmune disorders, and a CTO vessel diameter <2 mm were excluded from the study. The study protocol was validated by the local ethics committee. The study was approved by the ethics committee of our hospital on 7.1.2021. The reference number of research is 81.

Definitions

Chronic total occlusion (CTO) was described as a coronary occlusion with TIMI (thrombolysis in myocardial infarction) grade 0 flow for at least three months. During admission, a detailed medical history including cardiovascular risk factors was obtained from each patient. Hypertension (HT) was accepted as either systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mm Hg on two different measurements or taking anti-hypertensive therapy. Diabetes mellitus (DM) was described as a fasting glucose level ≥126 mg/dL on two different evaluation or taking antidiabetic medication. Dyslipidemia was defined as a total cholesterol of ≥200 mg/dl. Current smoking was defined as smoker. Positive family history was accepted as the history of a cardiovascular event in first-degree family members before age 55 in males and before age 65 in females. Cerebral hemorrhage and ischemic stroke were defined as cerebrovascular events. Chronic kidney disease was defined as having a glomerular filtration rate (GFR) of lower than 60 ml/min/1.73 m2 over a date of more than three months with no renal impairment or as a structural and functional disorder in the kidney lasting for more than three months regardless of a decrease in GFR.

Biochemical and Hematological parameters

Laboratory analysis were performed on the blood specimens taken from patients instantly before coronary angiography. Blood samples were analyzed using a hematological apparatus (Abbott Cell-Dyn 3700; Illinois, USA). Laboratory analyses were performed using routine methods and MHR was calculated for each patient.

Follow-up

The survival time was defined as the period from initial admission to our hospital for angiography to demise of patient. Data on patients' death were accessed by telephone interviews or were retrieved from the state's registration records.

Statistical process

SPSS for Windows was utilized for data analyses (version 25.0, Armonk, NY: IBM Corp.). Normality of dispersion was assessed with Kolmogorov-Smirnov test. Categorical variables were stated as percentages (%) and were matched using Chi-square test. Continuous variables with normal dispersion were reported

as mean ± standard deviation (SD) and group differences were analyzedusing Student's t-test. Continuous factors with non-normal distribution were reported as median (25th-75th percentile) and group differences were analyzedusing Mann-Whitney U. Independent predictors of mortality were described using univariate and multivariate logistic regression analysis and only with a p value <0.05 were included in the multivariate analysis. The results were reported as odds ratio (OR) and 95% confidence interval (CI). The optimum MHR cut-off for the mortality prediction was established utilizing receiver operating characteristic (ROC) analysis. Correlations were investigated using Spearman's correlation coefficient. Survival analyses were carried out using Kaplan-Meier analysis. A p value of <0.05 was designated as statistical significance cut off.

RESULTS

353 (71.6%) men and 140 (28.4%) women were included with an average age of 63.03±10.88 years. Median follow-up period was 48 months (interquartile range [IQR]: 26-73). Patients were separated into two groups: (I) MHR <17.68 (n=278) and (II) MHR ≥17.68 (n=215). Table 1 presents the demographic and clinical characteristics of patients in both groups. Out of all patients, 254 (51.5%) underwent percutaneous coronary intervention (PCI), 104 (21.1%) underwent medical treatment alone, 61 (12.4%) had a failed CTO intervention, and 74 (15%) underwent coronary artery bypass grafting. A statistically significant difference was found between the two groups in variables including gender, mortality, smoking status, and clinical symptomatology (p=0.001, p<0.001, p=0.006, and p=0.035, respectively). Table 2 presents the hematological and biochemical parameters for both groups. White blood cell (WBC), red cell distribution width (RDW), lymphocyte, monocyte, and neutrophil counts, urea, creatinine, and total cholesterol were significantly higher and HDL level was considerably lower in MHR I (MHR <17.68) compared to MHR II.

Table I: Clinical characteristics of the patients

	Total N=493	MHR <17,68 N=278	MHR ≥17,68 N=215	P value
Age (Years)	63.03±10.88	63.33±10.79	62.65±11.00	0.490*
Follow-up time (Months)	48 (26-73)	48,5 (27,75-70,25)	48 (22-76)	0.891
Male gender	353 (71.6%)	183 (65.8%)	170 (79.1%)	0,.001
Mortality	113 (22.9%)	43 (15.5%)	70 (32.6%)	<0.001
Hypertension	172 (34.9%)	90 (32.4%)	82 (38.1%)	0.183
Diabetes mellitus	143 (29%)	73 (26.3%)	70 (32.6%)	0.126
Hyperlipidaemia	31 (6.3%)	14 (5%)	17 (7.9%)	0.193
Smoker	132 (26.8%)	61 (21.9%)	71 (33%)	0.006
Chronic renal disease	27 (5.5%)	12 (4.3%)	15 (7%)	0.198
Family history	28 (5.7%)	15 (5.4%)	13 (6%)	0.757
Cerebrovascular events	13 (2.6%)	6 (2.2%)	7 (3.3%)	0.451
LVEF	50 (40-60)	55 (45-60)	50 (40-60)	0.016
Symptomatology Asymptomatic SAP USAP NSTEMI STEMI	 1 (0.2%) 230 (46.7%) 120 (24.3%) 126 (25.6%) 16 (3.2%)	 1 (0.4%) 144 (51.8%) 65 (23.4%) 58 (20.9%) 10 (3.6%)	 0 86 (40%) 55 (25.6%) 68 (31.6%) 16 (3.2%)	0.035**
Clinical approach Medical treatment PCI Failed CTO intervention CABG	 104 (21.1%) 254 (51.5%) 61 (12.4%) 74 (15%)	 54 (19.4%) 152 (54.7%) 32 (11.5%) 40 (14.4%)	 50 (23.3%) 102 (47.4%) 29 (13.5%) 34 (15.8%)	0.454**

*Data are expressed as mean ± SD, number (percentage) or median (interquartile range)as appropriate. *Independent Samples t Test. **Chi Square Test. CABG: coronary artery bypass graft, CTO: chronic total occlusion, LVEF: left ventricule ejection fraction, NSTEMI: non-ST elevated myocardial infarction, PCI: percutaneous coronary intervention, SAP: stable angına pectoris, STEMI: ST elevated myocardial infarction, USAP: unstable angına pectoris.*

Table II: Baseline haematological and biochemical parameters of the patients

	Total N=493	MHR <17,68 N=278	MHR ≥17,68 N=215	P value
White blood cell count (× 10^3 µL)	8.75 (7.35-10.79)	7.81 (6.6-9.55)	10.19 (8.63-1.,7)	<0.001
Hemoglobin (g/dl)	13.80 (12.45-15)	13.70 (12.50-14.80)	13.90 (12.40-15.30)	0.287
Hematocrit (%)	41.21±5.54	41.10±5.36	41.35±5.78	0.619*
RDW (%)	12.4 (11.7-15.2)	12.2 (11.6-14.72)	13.92 (11.8-16)	0.003
Platelets (× 10^3 µL)	240 (201-291)	240 (202-291)	240 (198-293)	0.873
Lymphocytes (× 10^3 µL)	1.87 (1.64-2.72)	1.99 (1.54-2.49)	2.41 (1.74-3)	<0.001
Monocytes (× 10^9 L)	640 (499-791)	521 (430-623)	817 (690-951)	<0.001
Neutrophils (× 10^3 µL)	6.14 (4.37-7.08)	4.84 (3.89-6.31)	6.26 (5.15-8)	<0.001
eGFR (ml/min/1,73m^2)	75 (70-101)	88 (72-101)	84 (67-100)	0.346
Glucose (mg/dl)	126 (95-165)	119 (94-167)	113 (97-165)	0.891
Urea(mg/dl)	48 (30-49)	37 (29,7-48,2)	40 (31-51)	0.011
Creatine (mg/dl)	0.97 (0.77-1.05)	0.84 (0.76-1.02)	0.89 (0.77-1.11)	0.044
Sodium (mmol/L)	137 (135-139)	138 (136-139)	137 (135-139)	0.092
Potassium (mmol/L)	4.4 (4-4.7)	4.4 (4.1-4.8)	4.4 (4-4.7)	0.331
Lactate dehydrogenase (U/L)	259 (188-319)	226,5 (188-309)	239 (190-346)	0.206
Serum albumin (g/dl)	3.3 (3.3-3.9)	3.7 (3.4-3.9)	3.6 (3.2-3.9)	0.144
Total cholesterol (mg/dl)	164 (146-210)	178,5 (149-217)	169 (141-199)	0.004
Triglyserides (mg/dl)	122 (101-214)	143,5 (98-210)	154 (104-219)	0.371
LDL (mg/dl)	100 (77-132)	103 (78-136)	99 (77-125)	0.198
HDL (mg/dl)	34 (32-44)	42 (35-47)	34 (29-38)	<0.001
NLR	3.13 (1.82-3.69)	2.52 (1.82-3.46)	2.51 (1.82-3.98)	0.267

*Data are expressed as mean ± SD and median (interquartile range) as appropriate. *Independent Samples t Test. eGFR: estimated glomerular filtration rate, HDL: high density lipoprotein LDL: low density lipoprotein, NLR: neutrophil to lymphocyte ratio. MHR: monocyte to high density lipoprotein ratio, RDW: red cell distribution width.*

On multivariate logistic regression analysis, MHR, albumin, and age were detected to be independent predictors of long-term mortality (OR: 1.091, 95% CI: 1.058-1.126, p<0.001, OR: 0.318, 95% CI: 0.176-0.573, p<0,001, OR: 1.048, 95% CI: 1.023-1.075, p<0.001, respectively; Table 3). MHR ≥17.68 determined mortality in CTO patients with a sensitivity of 61% and specificity of 62% ([AUC]: 0.679, 95% CI: 0.623-0.735; Figure 1). Positive correlation was found among MHR and the neutrophil-to-lymphocyte ratio (NLR) (r=0.103, p=0.22; Figure 2). The

Kaplan-Meier analysis indicated higher surveillance in group I (MHR <17.68) (p<0.001; Figure 3).

Table III: Predictors of mortality in univariate and multivariate logistic regression analysis

	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Hypertension	1.699	1.101-2.620	0.017	1.094	0.659-1.818	0.728
Diabetes mellitus	1.382	0.879-2.174	0.161			
Hyperlipidaemia	0.490	0.169-1.442	0.197			
MHR	1.093	1.064-1.123	<0.001	1.091	1.058-1.126	<0.001
Hemoglobin	0.786	0.702-0.881	<0.001	0.926	0.801-1.072	0.304
Platelet	0.999	0.996-1.002	0.459			
Glucose	1.002	0.999-1	0.174			
Serum albumin	0.171	0.103-0.283	<0.001	0.318	0.176-0.573	<0.001
Total cholesterol	0.994	0.989-0.999	0.013	1	0.994-1.005	0.876
NLR	1.154	1.068-1.248	<0.001	1.070	0.974-1.175	0.160
Age	1.065	1.042-1.089	<0.001	1.048	1.023-1.075	<0.001
Gender	0.879	0.545-1.418	0.597			

CI: confident interval, MHR: monocyte to high density lipoprotein ratio, NLR: neutrophil to lymphocyte ratio, OR: odds ratio.

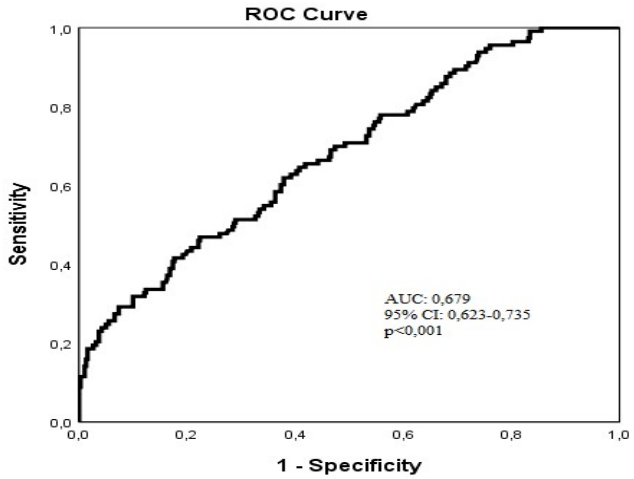

Figure 1. Receiver-operating characteristic (ROC) curve for preprocedural monocyte count to high density lipoprotein ratio for predicting mortality on patients with chronic total occlusions. AUC: Area under the curve, CI: confident interval.

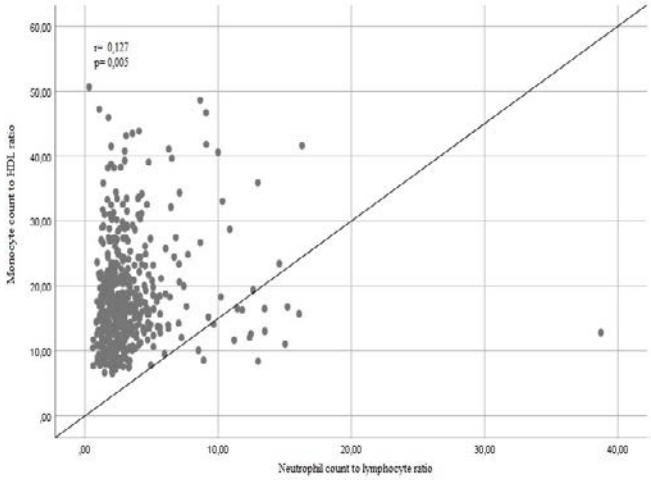

Figure 2. Correlation analysis of monocyte to high-density lipoprotein ratio with neutropil count to lymphocyte ratio level

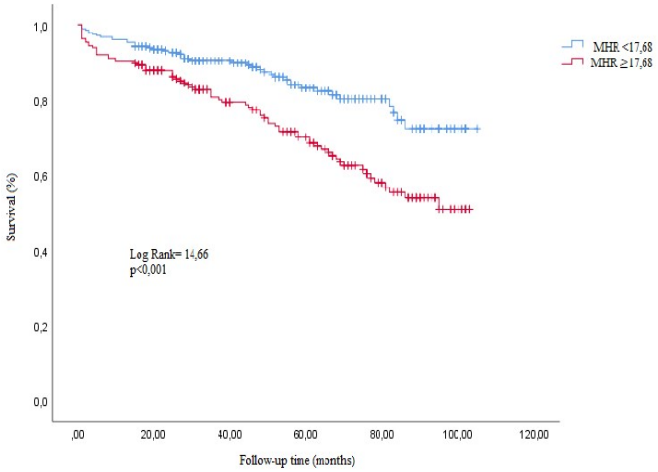

Figure 3. Kaplan-Meier survival analysis. During long-term follow-up (median 48 months) period patients group with MHR≥ 17,68 had significantly worse survival than patients group with MHR< 17,68 (p<0,001). Mean survival time MHR <17,68 and MHR≥17,68(89,220±2,102; 75,223±2,670, p<0,001) respectively.

DISCUSSION

In addition to risk models used in mortality prediction, practical, low-cost, and reliable novel markers are needed and could be beneficial in terms of treatment management and prognostication. The present study aimed to investigate whether a simple and easily calculated parameter such as MHR could be used in predicting mortality and survival in

CTO. Our results indicate that increased MHR is associated with mortality and survival rate decreases as MHR value increases. Additionally, MHR has been shown to be a predictor of mortality.

High MHR has been reported to be a risk element for CTO in CAD cases[19]. A recent study indicated that MHR predicted mortality in patients with ischemic stroke[20]. Similarly, Efe et al. showed the prognostic importance of MHR in predicting early mortality in acute pulmonary embolism patients[21]. Another study reported that MHR predicted adverse cardiac outcomes in HCM patients[18]. The aforementioned study, as in our current study, found higher WBC, neutrophil, and lymphocyte levels to be associated with advanced MHR values. In a similar way, Wu et al. suggested that MHR could be a long-term prognostic marker in CAD patients undergoing PCI[22]. Unlike the study by Wu et al.,our study included CTO patients only and and along with the treatment modalities other than PCI such as coronary artery bypass grafting, medical treatment, and failed CTO intervention.

The mechanism of the relationship between MHR and poor prognosis in CTO patients remains unclear. Monocytes have a key role in atherosclerosis development [6]. These cells bind to adhesion molecules expressed on damaged endothelial cells[7]. Subsequently, they transmigrate to the subendothelial area and convert into macrophages and thereby internalize oxidized LDL and class A scavenger receptors [8]. Afterwards, they convert into foam cells, thereby causing the release of proinflammatory and prooxidant cytokines[9]. In recent studies, HDL has been shown to act in the opposite direction in the development of atherosclerosis and to play an main role in monocyte activation, adhesion, and inflammation and further to act as a natural protective barrier against the proinflammatory effects of monocytes by taking part in the control of the reproduction of progenitor cells that distinguish into monocytes[23-25]. Low HDL value and high monocyte count appear to be indirect indicators of inflammation. Accordingly, using these two parameters in combination by calculating their ratios to each other provides more precious knowledge about the presence of inflammation and oxidation balance. On the other hand, heart failure could be a reason for the relationship between high MHR and poor prognosis in CTO patients. Wrigley et al. indicated that the monocyte count raised in cases with acute and stable heart failure[26]. In this study, in line with the literature, a significant correlation was found between higher MHR value and lower ejection fraction. Additionally, we suggest that cardiac arrhythmia could be a reason for the relationship between MHR and poor prognosis in CTO patients[18].

One of the important parameters predicting clinical outcomes in CTO patients is NLR. In a study by Li et al., it has been shown that higher NLR levels were associated with advers cardiac events in the CTO patient population[27]. This study was conducted in a homogeneous patient population with stable coronary disease. However, our study was conducted in a wide spectrum cohort which ranges from stable coronary artery disease to acute coronary syndromes. Similar to this study, NLR is one of the independent predictor parameter of all-cause mortality in CTO patients.

Both the studies above mentioned and our study found an association between high MHR value and mortality, which implicates that MHR could be a predictor of unfavorable cardiac consequences in high-risk cases. We also found that MHR could be a novel markerin addition to conventional parameters for the prediction of mortality in CTO patients.

Study Limitations

The main limitation of this study is single center retrospective study design with a limited number of patients. Second, the calculation of MHR was performed from the single blood sample taken prior to the procedure and the MHR value could have varied if it had been calculated from multiple blood samples. Another important limitation was that the study was conducted on a heterogeneous patient population. By various clinical status that may affect the MHR, planning a study with a more homogeneous patient population will yield more valuable results in terms of clinical outcomes. Finally, inflammatory markers including interleukin-6, thromboxane A2, and C-reactive protein (CRP) were not studied, and a correlation analysis was performed with NLR only.

CONCLUSİON

Increased MHR (≥17.68) is associated with increased mortality and poor survival in CTO patients. Accordingly, MHR could be used as a practical biomarker for survival of CTO patients.

Acknowledgements

All the authors declare no conflict of interest. All authors made very important contributions to data collection, writing, statistics, graphics and drawing and final approval of the version to be published.

Ethics Committee Approval: The study protocol was validated by the local ethics committee. The study was approved by the ethics committee of our hospital on 7.1.2021. The reference number of research is 81.

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Fefer P, Knudtson ML, Cheema AN, et all. Current perspectives on coronary chronic total occlusions: the Canadian Multicenter Chronic Total Occlusions Registry. J Am Coll Cardiol 2012; 59: 991–7.

2. Jeroudi OM, Alomar ME, Michael TT, et all. Prevalence and management of coronary chronic total occlusions in a tertiary Veterans Affairs hospital. Catheter Cardiovasc Interv 2014; 84:637–43.

3. Stone GW, Kandzari DE, Mehran R, et all. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: part I. Circulation 2005; 112:2364–72.

4. Cohen HA, Williams DO, Holmes DR, et all. NHLBI Dynamic Registry. Impact of age on procedural and 1-year outcome in percutaneous transluminal coronary angioplasty: a report from the NHLBI Dynamic Registry. Am Heart J. 2003; 146:513-9.

5. Godino C, Sharp AS, Carlino M, Colombo A. Crossing CTOs-the tips, tricks, and specialist kit that can mean the difference between success and failure. Catheter Cardiovasc Interv. 2009; 74: 1019–46.

6. Ammirati E., Moroni F., Magnoni M., et all. Circulating CD14+ and CD14 high CD16-classical monocytes are reduced in patients with signs of plaque neovascularization in the carotid artery. Atherosclerosis, 2016; 255: 171–8.

7. Aukrust P., Halvorsen B., Yndestad A., et all. Chemokines and cardiovascular risk. Arteriosclerosis, Thrombosis, and Vascular Biology. 2008; 28: 1909–19.

8. Tani S., Matsumoto M., Anazawa T., et all. Development of a model for prediction of coronary atherosclerotic regression: Evaluation of high-density lipoprotein cho esterol level and peripheral blood monocyte count. Heart and Vessels,2012; 27: 143–50.

9. Acikgoz N., Kurtoğlu E., Yagmur J., et all. Elevated monocyte to high-density lipoprotein cholesterol ratio and endothelial dysfunction in behçet disease. Angiology. 2017; 69: 65–70.

10. Ganjali S., Momtazi A. A., Banach M., et all. HDL abnormalities in familial hypercholesterolemia: Focus on biological functions. Progress in Lipid Research. 2017; 67, 16–26.

11. Gomaraschi M., Basilico N., Sisto F., et aLl. High-density lipoproteins attenuate interleukin-6 production in endothelial cells exposed to pro-inflammatory stimuli. Biochimica et Biophysica Acta. 2005; 1736: 136–43.

12. D. Muhammed, Ö. Mehmet, A. Adem, E. Faruk. Fibrinogen to Albumin Ratio Predicts Burden of Coronary Artery Disease in Patients with NSTEMI. Dicle Med J 2021; 48:688-95.

13. Cetin EH, Cetin MS, Canpolat U, et all. Monocyte/HDL-cholesterol ratio predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Biomark Med. 2015; 9:967-77.

14. Fan Z, Ji H, Li Y, et al. Relationship between monocyte-to-lymphocyte ratio and coronary plaque vulnerability in patients with stable angina. Biomark. Med. 2017; 11: 979–90.

15. Canpolat U, Aytemir K, Yorgun H, et all. The role of preprocedural monocyte-to-high-density lipoprotein ratio in prediction of atrial fibrillation recurrence after cryoballoon-based catheter ablation. Europace. 2015; 17:1807-15.

16. Canpolat U, Çetin EH, Cetin S, et al. Association of Monocyte-to-HDL Cholesterol Ratio with Slow Coronary Flow is Linked to Systemic Inflammation. Clin Appl Thromb Hemost. 2016; 22:476-82.

17. Demir V, Samet Y, Akboga MK. Association of lymphocyte-monocyte ratio and monocyte-to-high-density lipoprotein ratio with the presence and severity of rheumatic mitral valve stenosis. Biomark. Med.2017; 11: 657–63.

18. Ekizler FA, Cay S, Açar B, et all. Monocyte to high-density lipoprotein cholesterol ratio predicts adverse cardiac events in patients with hypertrophic cardiomyopathy. Biomark Med. 2019; 13:1175-86.

19. Surya I.K.R., Wita I.W., Iswari I.S., et all. High Ratio of Monosit: High-Density Lipoprotein as a Risk Factor Of chronic Total Occlusion in Patients Coronary Artery Disease. Asian Journal of Pharmaceutical and Clinical Research, 2020;13:155-8.

20. Bolayir A, Gokce SF, Cigdem B, et al. Monocyte/high-density lipoprotein ratio predicts the mortality in ischemic stroke patients. Neurol Neurochir Pol. 2018; 52:150-5.

21. Efe T, Arslan E, Ertem A, ve ark. Akut Pulmoner Emboli Hastalarında Monosit/HDL Oranının Kısa Dönem Mortaliteyi Ön Gördürmedeki Prognostik Değeri. Koşuyolu Heart Journal. 2016; 19: 149-53.

22. Wu TT., Zheng YY., Chen Y., et all. Monocyte to high-density lipoprotein cholesterol ratio as long-term prognostic marker in patients with coronary artery disease undergoing percutaneous coronary intervention. Lipids Health Dis 2019;18, 180.

23. Murphy AJ, Chin-Dusting JP, Sviridov D, Woollard KJ. The anti-inflammatory effects of high density lipoproteins. Curr Med Chem. 2009; 16:667-75.

24. Murphy AJ, Woollard KJ. High-density lipoprotein: a potent inhibitor of inflammation. Clin Exp Pharmacol Physiol. 2010; 37:710-18.

25. Yvan-Charvet L, Pagler T, Gautier EL, et all. ATP-binding cassette transporters and HDL suppress hematopoietic stem cell proliferation. Science 2010;328:1689-93.

26. Wrigley BJ, Shantsila E, Tapp LD, Lip GY. CD14++CD16+ monocytes in patients with acute ischaemic heart failure. Eur J Clin Invest. 2013 Feb; 43:121-30.

27. Li, Chenguang, et al. "Impact of neutrophil to lymphocyte ratio (NLR) index and its periprocedural change (NLRΔ) for percutaneous coronary intervention in patients with chronic total occlusion." Angiology 68.7 (2017): 640-6.