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Original Article

Relationship between monocyte to high-density lipoprotein ratio and contrast-induced nephropathy in patients with non-st elevation myocardial infarction

Monosit/yüksek-dansiteli lipoprotein oranının st elevasyonu olmayan miyokard enfarktüslü hastalarda kontrasta bağlı nefropatiyle ilişkisi

Onur BAYDAR* , Alparslan KILIC

Koc University Hospital, Department of Cardiology, Istanbul/TURKEY

Abstract

Aim: Contrast-induced nephropathy (CIN) is associated with worse prognosis in patients with non-ST-elevation myocardial infarction (NSTEMI). Early identification patients with a high risk of CIN are very crucial to improve outcomes. The monocyte to high-density lipoprotein ratio (MHR) is a novel inflammatory marker. We aimed to investigate the MHR had a predictive role for CIN development in patients with NSTEMI.

Material and Methods: NSTEMI who underwent percutaneous coronary intervention (PCI) were included in the study. MHR was calculated and CIN was defined as an increase in serum creatinine 25% or 0.5 mg/dl from baseline in the first 48- 72 hours.

Results: A total of 370(200, 54.1% men) patients were included in this study and 104 (28.1%) of them had DM. 25 (6.7%) of patients had CIN.MHR was significantly higher in patients with CIN (0.014± 0.004 vs 0.011± 0.006-respectively, p: 0.017). MHR was also significantly correlated with creatinine levels after PCI (r:0,104, p: 0.047). CIN group also experienced a more complicated in-hospital clinical course. Additionally; weight and MHR were detected as independent risk factors of CIN in logistic regression analysis.

Conclusion: Preprocedural MHR may be used as cheap, easy and simple marker of CIN. It may help with the early identification of patients with NSTEMIwho are at high risk of CIN.

Keywords: myocardial infarction; contrast-induced nephropathy; monocyte to high-density lipoprotein ratio.

Corresponding Author*: Onur Baydar, Koc University Hospital, Department of Cardiology, Istanbul/TURKEY
E-mail: obaydar@kuh.ku.edu.tr
Received:23.10.2019 Accepted : 22.02.2020
ORCİD: 0000-0003-1555-0489
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Öz

Amaç: Kontrast madde kullanımına bağlı nefropati (KBN) gelişimi perkutan koroner girişim (PKG) yapılan ST elevasyonu olmayan miyokard enfarktüsü (NON-STEMI) geçiren hastalarda sık görülmekte olup artmış mortalite ve morbidite ile ilişklidir. KBN açısından yüksek riskli hastaların önceden tespiti ve tedavisi, klinik sonuçların iyileşmesinde etkili olacaktır. Monosit yüksek dansiteli lipoprotein (HDL) oranı (MHO) klinikte yeni tanımlanan inflamasyon belirteçlerinden biridir. Çalışamızda işlem öncesi MHO' nın PKG yapılmış NON-STMI hastalarında KBN gelişimi arasıdaki ilişki araştırılmıştır.

Gereç ve Yöntemler: Çalışmamızda retrospektif olarak NON-STEMI tanısıyla PKG yapılanhastalar incelenmiştir. Hastaneye başvuruşunda alınan örneklerden MHO oranın hesaplanmış ve KBN; işlemden 48-72 saat sonra bakılan serum kreatininde bazal değere göre % 25 ya da 0,5 mg/dl artış olarak tanımlanmıştır.

Bulgular: Toplam 370(200, %54.1 erkek) hasta geriye dönük incelenmiş, 25 (%6.7) hastada KBN geliştiği saptanmıştır. Ayrıca hastaların 104'ünde (%28.1) Diabetes Mellitus (DM) olduğu görülmiştür. MHO; KBN gelilşen grupta gelişmeyen gruba göre anlamlı olarak yüksek saptandı (sırasıyla 0.014± 0.004 ve 0.011± 0.006, p: 0.017). Ek olarak MHO ile PKG sonrası kreatinin değerleri arasında pozitif korelasyon saptandı (r:0,104, p: 0.047). Beklendiği gibi KBN gelişen hastların yatışları sırasında daha çok komplikasyon olduğu görüldü. Ayrıca; kiloveMHO değerleri KBN gelişimi için bağımsız risk faktörleri olarak bulundu.

Sonuç: MHO ucuz, basit ve kolay şekilde saptanabilen inflamasyon belirteci olup, PKG yapılan NON-STEMI hastlarında KBN'nin saptanmasında ve tedavinin yönlendirilmesinde faydalı olabilir.

Anahtar Kelimeler: miyokard enfarktüsü; kontrast madde kullanımına bağlı nefropati; monosit yüksek dansiteli lipoprotein oranı

Introduction

Contrast-induced nephropathy(CIN), is afrequent complication of contrast use, after coronary procedures such as percutaneous coronary interventions (PCI) in patients with acute coronary syndromes (ACS) including non- ST elevation myocardial infarction (NSTEMI) and strongly associated with high mortality and morbidity (1-6).The aetiology of CIN is not clearly clarified.Although many risk factors for the development of CIN have been demonstrated such as chronic kidney disease (CKD), diabetes mellitus (DM), reduced left ventricular systolic function, nephrotoxic drugs and age over 70 years (6-8), the main pathophysiology of CIN is still underinvestigation. Thepossible causes of CIN developmentincludesincreased oxidative stress,endothelial dysfunction,direct tubular toxicity,inflammation andrenal parenchymal hypoxia (9,10). Recently studies have shown that The platelet to-lymphocyte ratio (PLR), elevated preprocedural high sensitive- C-reactive protein (Hs-Crp), and the neutrophil-to-lymphocyte ratio (NLR) have been shown to be associated with increased risk of CIN levels were associated with CIN in patients with ACS(11-13).

Monocyte to high density lipoprotein cholesterol (HDL-C) ratio (MHR)has been entered a new inflammatory marker and several studies have shown that there is strongcorrelation between MHR various adverse cardiovascular events (14-16). Although the relationship between the risk of developing CIN and MHR was demonstratedin small sized patients with ST-segment elevation myocardial infarction(STEMI) (17), whether there is a relationship between MHR and CIN in the patient with NSTEMIis still unclear. Thus, the aim of this study was to assess whether there is a relationship MHR and CIN after urgent PCI in patients with NSTEMI.

Materials and methods

Study population

370 consecutive patients who admitted withNSTEMIundergoing urgent PCI were retrospectively enrolled in the study, between February 2015 and December 2017at the Avicenna Hospital Cardiology Depratment. All patients were administered with (PCI).Patients with cardiac arrest, active infection or previously proven systemic inflammatory disease, contrast medium administration within the previous 10 days, end-stage renal failure (serum creatinine >3 mg/dl), advanced stage liver (alanine aminotransferase >50 IU/L) or malignancy and patients using lipid-lowering drugs were excluded from the study.Patients were identified as NSTEMI: Anginal symptoms occurringat rest, with positive cardiac enzymes and markers, deficiency of ST-segment elevation on theelectrocardiogram. Unstable angina pectoris

was defined as (a) the absence of ST-segment elevation as defined 1mm or more, (b) negative cardiac enzymes and markers, and (c) angina pectoris with at least one of three characteristic: 1) chest pain happen at rest and often for a prolonged period (usually> 20 min); 2) chest pain being severe and usually described as frank pain, or 3) chest pain happen with a crescendo pattern. Diabetes mellitus was defined by fasting serum glucose levels of at least 126 mg/ dl, a random plasma glucose level of >200 mg/dl and/or if the patient was taking oral anti-diabetic drugs, or insulin. Hypertension was described as a systolic blood pressure (BP) > 140 mmHg and/or a diastolic BP > 90 mmHg on two different occasions or treatment with any antihypertensive drugs for a known diagnosis of hypertension. Hypercholesterolaemia was described as baseline total cholesterol greater than 200 mg/ dl and/or a low-density lipoprotein cholesterol (LDL-C) level greater than 130 mg/dl or previously diagnosed and treated hypercholesterolemia.Current smokers are respondents who have smoked regularly in the previous 6 months. A family history of coronary artery disease was described as a coronary event occurring in men before 55 years old or a coronary event occurring in women before 65 years of age.The hospital local ethics committee approved our study. Our study was performed in accordance with the Helsinki Declaration.

Coronary angiography and intervention

Coronary angiography(CA) and PCI (Siemens Axiom Artis zee 2006; Siemens Healthcare, Erlangen, Germany) were performed by a percutaneous femoral approach according to standard clinical practice. Patients underwent CA within the 1-72 hours after admission.All patients, nonionic, low-osmolar contrast media (iohexol, Omnipaque 350 mg/ml; GE Healthcare, Cork, Ireland) was used. All patients were administered acetylsalicylic acid (loading dose of 300 mg) and clopidogrel (loading dose of 600 mg) before PCI.All patients were recommended aspirin 100 mg daily plus clopidogrel 75 mg daily for at least 12 months. Unfractionated heparin (a first bolus dose of 60 U/kg) was administered in the emergency department and followed by additional intraprocedural boluses in order to achieve an activated clotting time >250 seconds.Culprit lesion was treated with according to standard PCI technique by using a6-French guiding catheter (Launcher; Medtronic, Minneapolis, Minnesota, USA).The type of stents used (bare metal or drug eluting) and the decision to use glycoprotein IIb/IIIa antagonists were of the interventional cardiologist choice. All nephrotoxic drugs were stopped upon admission.After the PCI, all patients were treated with intravenous hydration (isotonic 0.9% saline intravenously at a rate of 1 ml/kg per hour for 6-12 hours). The infusion rate was reduced to 0.5 mL/kg per hour if severeleft ventricular dysfunction or overt heart failure was present.We performed echocardiography (Vivid 3; GE Medical System, Horten, Norway) to all patients within 48 hours of admission to the hospital. The left ventricular systolic performance was calculated usingthe modified Simpson's method. Other medical treatments (adrenergic blocking agents, renin-angiotensin-aldosterone system inhibitors, statins, diuretics) were determined by the physicians according to suggestions of the international guidelines.Contrast-induced nephropathy was described as an increase in serum creatinine of 0.5 mg/dl, or a 25%relative increase from baseline at 48-72 hours after the PCI .

Laboratory analysis

Blood samples were drawn by antecubital venipuncture into EDTAtreatedor plain tubes according to hospital protocol. The results offasting blood samples collected within the 24-h of hospitalizationwere used in the analyses. Patients whose lipoprotein levels werenot measured within the 24-h of hospitalization were excluded fromthe study. For definition of CIN, creatinine levels were measureddaily. Complete blood count (CBC) measurements were conductedusing Cell-Dyn 3700 (MAPSS Laser Differential; Abbott Laboratories,Abbott Park, IL, USA) for hemoglobin, total white blood cell count(WBC), monocyte, neutrophil and lymphocyte counts. Total cholesterol,HDL-C and triglyceride levels were measured enzymatically(Hitachi 7350 autoanalyzer, Hitachi Ltd., Tokyo, Japan) and LDL-Clevels were measured from these lipid parameters with Friedewaldformula. Monocyte to HDL-C ratio was calculated by dividing monocytecount (109/L) to HDL-C level (mmol/L) and reported as 109/mmol.The serum creatinine level was measured in allpatients upon hospital admission (prior to CA),daily for the three days after PCI, upon dischargefrom the coronary care unit and upon hospital discharge.WBC and differential counts were measuredat the time of admission before the patients weretransferred to the catheter laboratory. The total numbers ofneutrophils and lymphocytes were determined using anautomated blood cell counter (XE-2100, Sysmex Inc., Kobe,Japan), and NLR were automatically calculated by loading allthe data to the statistical program used. The estimated glomerularfiltration rate (eGFR) was calculated using the Modificationof Diet in Renal Disease formula [20] and utilizingthe baseline creatinine level.

Statistical analysis

All analyses were performed using SPSS version 22 for Windows (SPSS Inc, Chicago, Illinois). Numerical variables are Presented as mean ± standart deviation or median (minimum-maximum levels) according to distributions of parameters and nominals as percentages. All variables were subjected to Kolmogorov Smirnov testing to determine whether they were normally distributed. The independent samples t test was used to compare the values of continuous variables between the 2 groups. Nonparametric values were compared using the Mann-Whitney U test. The chi-square test was used to compare categorical data. To evaluate the effects of various factors on CIN development, we performed multivariate regression analyses using the backward Logistic Regression (LR) method. Variables for which the unadjusted P <0 .05 was considered significant.

Results

A total of 370(200, 54.1% men) patients were included in this studyand 104 (28.1%) of them had DM. 25 (6.7%) of patients had CIN. There was not significant difference between the patients with and without CIN in terms of weight, age and gender.General risk factors that DM, smoking and hypertension were same in both groups. Additionally; previous medications, Grace scores, HbA1c, peak troponin levels, left ventricular ejection fraction(LVEF), contrast volume, numbers of PCI and CABG rates were not differed between two groups. The baseline clinical and procedural characteristics of patients were shown in Table I and II. MHR, PLR, NLR and high sensitive C reactive protein (Hs-Crp) were significantly higher in patients with CIN (Table II) (Figure 1 and 2). MHR was also significantly correlated with creatinine levels after PCI (r:0,104, p: 0.047). Additionally,patients developed CIN experienced a more complicated in-hospital clinical course(Table II) (Figure 3) and weight and MHRwere detected as independent risk factors of CIN in logistic regression analysis (Table III).

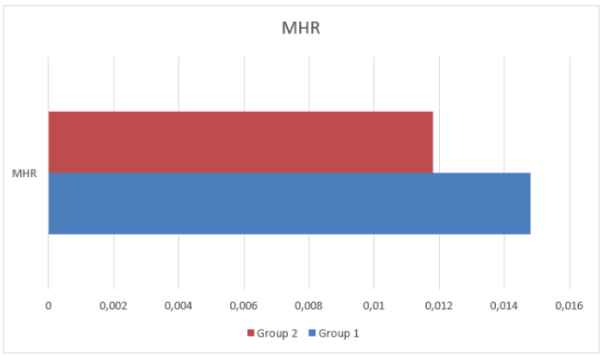

Figure 1: MHR: Monocyte to high-density lipoprotein ratio, NLR: , Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, Group 1 : Patients with CIN, Group 2: Patients without CIN. P < 0,05.

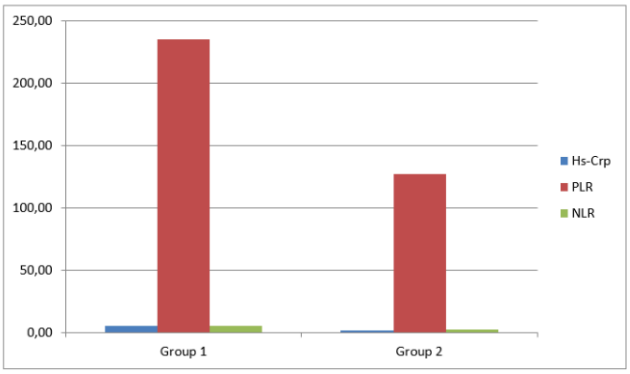

Figure 2: Group 1 experienced a more complicated in-hospital clinical course (Group 1: In patients with CIN, Group 2 : In patients without CIN ,p<0.05)

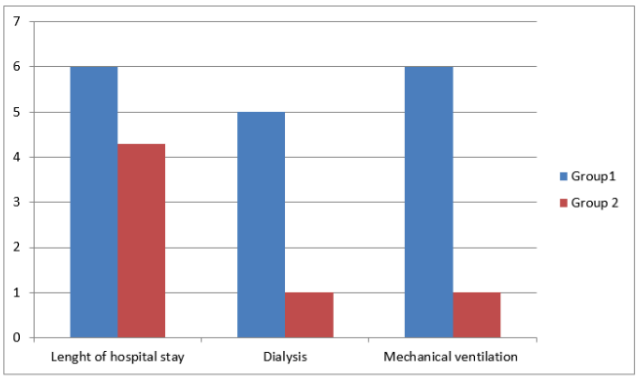

Figure 3: Group 1 experienced a more complicated in-hospital clinical course (Group 1: in patients with CIN, Group 2: In patients without CIN, p <0.005)

Table 1. Main Characteristics of Patients

	Patients with CIN N: 25	Patients with-out CIN N:345	P
Age (year)	57.4± 11.8	56.8± 10.8	NS
Men (n%)	14 (56%)	186(53.9%)	NS
Weigth (kg)	75.4±3.9	75.7±5.6	NS
HT (n%)	17(60%)	207 (68%)	NS
HL (n%)	14 (56 %)	110 (31.9%)	0.014
DM (n%)	11 (44 %)	93 (27 %)	NS
Smoker (n%)	5 (20%)	104(30.1%)	NS
Previous Miyocardial Infarction(n%)	9(36%)	91 (26.4%)	NS
Previous CABG(n%)	2 (8%)	103(29%)	0.019
Creatinine before PCI (mg/dl)	1.09±0.09	1.02±0.07	NS
EF(n%)	51.8±8.6	53.5±8.0	NS
eGFR (ml /min 1,73^2)	94.4± 16.5	89.2± 14.9	0.048

NS: Non significant, HT: Hypertension, DM: Diabetes Mellitus, HL: Hyperlipidemia, EF: Ejection fraction, CABG: Coronary artery bypass grefting,

Table 2. In-hospital clinical course of Patients

	Patients with CIN N: 25	Patients without CIN N:345	P
MHR	0.0148± 0.004	0.0118± 0.006	0.017
PLR	235,18±150,66	127,54±53,44	<0,001
NLR	5,47±3,64	2,59±1,82	<0,001
WBC	8.1±1.8	7.7±2.2	NS
HGB	13.7±1.8	13.5±1.5	NS
PLT	254.5±85.1	249.4±62.4	NS
NEU	5.2±1.5	4.7±1.8	NS
LYM	1.9±0.9	2.1±0.7	NS
MON	0.63±0.15	0.57±0.32	NS
HDL	44. 0±7.3	50.9±11.3	0.003
LDL	127.5±37.9	122.7±38.2	NS
TG	196.7±120.3	167.9±100	NS
NON HDL	157.9±39.0	156.7±42.8	NS
Glucose (mg/dl)	125.8±50.4	121.9±56.8	NS
HBA1C (%)	5.7±0.6	5.5±0.6	NS
HsCRP	5,76±4,9	2.1±3.3	<0,001
Uric Acid	5.7±1.7	5.5±1.6	NS
GRACE score	120.9±11.7	121.3±16.5	NS
Contrast volume ml	224.8± 16.3	228.2± 16.7	NS
Time to reperfusion h	4.2± 2.0	5.0± 2.2	0.029
Troponin peak (ng/dl)	2.1± 0.9	2.2± 0.8	NS
Length of hospital stay (days)	6.0± 2.6	4.3± 0.6	<0,001
Dialysis (n%)	5 (20%)	1 (0.3 %)	<0.001
Mechanical ventilation (n%)	6 (6&)	1 (0.3%)	<0.001
In-hospital mortality(n%)	2 (8%)	15 (4.3%)	NS
Medical treatment (n%)	4(16%)	36 (10.4 %)	NS
PCI (n %)	18 (72 %)	227 (80.3%)	NS
CABG (n%)	3 (12%)	31 (9 %)	NS

NS: Non significant, CABG: Coronary artery bypass grefting, PCI: Percutaneous coronary intervention, MHR: Monocyte to high-density lipoprotein ratio, NLR: , Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio

Table 3. Independent risk factors of CIN in logistic regression analysis

Variables	OR (95% C.I)	P
Weigth	0,8(0,7-0,9)	0,002
Age	1,1(1,0-1,2)	0,001
MHR	0,6(0,3-0,9)	0,048
eGFR	1,1(1,0-1,2)	<0,001
HT	1,5 (0,5-4,3)	0,38
DM	1,9 (0,7-4,9)	0,14

HT: Hypertension, DM: Diabetes Mellitus, EF: Ejection fraction, MHR: Monocyte to high-density lipoprotein ratio

Discussion

Our study showed that preprocedural MHR was an independent predictor of the development of CIN in the patients with NSTEMI undergoing PCI. Weight was also independent predictor for CIN in such patients.

Contrast-induced nephropathy during the course of NSTEMI is associated with increased morbidity and mortality(18). Inflammation may also play an important role in the initiation and extension phases of CIN (19). Early identification of patients with a high CIN risk plays critical role to allow the necessary interventions. Many of these biomarkers cannot be done in several centers at the time of admission. Therefore markers that can be used before the procedure and are widely available in many centers are needed. Monocytes account for the major source of pro-inflammatory and prooxidant factors, and they interact with endothelial cells and platelets leading to inflammation, thrombosis, and endothelial dysfunction (20,21). On the other hand, HDL-C has anti-inflammatory, antioxidant, and antithrombotic effects (22). So increased the MHR reflects the inflammatory process. MHR is also an important marker that reflect the inflammatory status in patients with atherosclerosis and has been demonstrated to predict the cardiovascular events in patients with ACS (14). As an inflammatory marker, the MHR has many advantages of being obtainable before the procedure. We observed that admission MHR was an independent predictor for CIN development. A recent study also revealed admission MHR as a risk factor for CIN in patients with STEMI and ACS (19). Preprocedural MHR measurement may help to identify patients with high risk of CIN and to take protective preventions such as reducing contrast volume and increasing fluid administration.

Contrast volume is an important risk factor for CINand dose minimization, on the background of a known baseline reduced renal function, may serve as an important strategy to limit the incidence of CIN (8).However, we used a relatively small amount of contrast, and we did not find significant difference in terms of dose of contrast used in all patients with and without CIN. We suggested that other factors, such as impaired renal function and DM, age and weight might contribute more to the development of CIN than contrast volume.

Also in our study; PLR, NLR and Hs-CRP were significantly higher in patients with CIN which were concordant with the previous studies(18,23-25). We also found that CIN was associated with increased incidence of adverse events during hospitalization.

This study has some limitations. First, it is a single-center

study. Second, the number of patients studied with CIN was relatively small, which could limit the number of independent predictors identified. However, we found some important results, consistent with the literature. Also, we only calculated MHR before the procedure. Serum HDL-C level and monocyte count may change with time; thus, single measurements of these parameters may not reflect any trend.

Conclusion

MHR is a risk factor for the development of CIN in patients with NSTEMI. The MHR is a simple marker of inflammation that can easily be obtained on admission and can be used to predict CIN risk.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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