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Impact of high triglyceride/high-density lipoprotein cholesterol ratio in non-st segment elevation myocardial infarction

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Abstract

Introductıon: Globally, cardiovascular disease (CVD) is the leading cause of death. Among these risk factors, dyslipidemia, hypertension, and diabetes mellitus (DM) are significant pathological disorders that lead to this illness. In addition to being a risk factor for cardiovascular disease, insulin resistance is a prevalent characteristic of metabolic syndrome, obesity, and diabetes mellitus. It has been demonstrated that the triglyceride/HDL ratio is a valid indicator of insulin resistance.

In this study, we tried to emphasize the criticality of early intervention in NSTEMI patients by revealing whether the TG/HDL ratio indicating insulin resistance is different between NSTEMI and ST elevation myocardial infarction (STEMI) patients.

Methods: Patients admitted to a training and research hospital with a prediagnosis of acute coronary syndrome and diagnosed as having NSTEMI or STEMI were included in the study. Our study included 113 NSTEMI and 166 STEMI patients.

Results: In NSTEMI patients, the mean HDL value was 39 (25-65) mg/dl, the mean LDL value was 105 (29-244) mg/dl, the mean T. cholesterol value was 180 (78-356) mg/dl, and the mean triglyceride value was 136 (37-360) mg/dl. When NSTEMI patients were compared with STEMI patients in terms of TG/HDL ratio, NSTEMI patients were significantly higher. (p:0.027; p<0.005).

Conclusıon: Increased TG/HDL ratios are one measure of insulin resistance. The TG/HDL ratio is elevated in NSTEMI patients, according to our research. Therefore, we can help reduce morbidity and mortality by planning early intervention in NSTEMI patients with high TG/HDL ratios.

Keywords: acute coronary syndrome, Non-ST segment elevation myocardial infarction, ST elevation myocardial infarction, Triglyceride, high density lipoprotein

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Yüksek trigliserit/yüksek yoğunluklu lipoprotein kolesterol oranının non-st segment yükselmeli mıyokard enfarktüsünde etkisi

Öz

Giriş: Kardiyovasküler hastalıklar (KVH) dünya çapında en yaygın ölüm nedenidir. Bu risk faktörleri arasında diabetes mellitus (DM), hipertansiyon ve dislipidemi bu hastalığa neden olan önemli patolojik durumlardır. İnsülin direnci metabolik sendrom, obezite ve DM'nin ortak bir özelliğidir ve aynı zamanda kardiyovasküler hastalık için bir risk faktörüdür. Trigliserit/HDL oranının insülin direncinin güvenilir bir belirteci olduğu gösterilmiştir. Bu çalışmada, insülin direncini gösteren TG/HDL oranının NSTEMI ve ST yükselmeli miyokard enfarktüsü (STEMI) hastaları arasında farklı olup olmadığını ortaya koyarak NSTEMI hastalarında erken müdahalenin kritikliğini vurgulamaya çalıştık.

Yöntemler: Bir Eğitim ve Araştırma Hastanesi'ne akut koroner sendrom ön tanısı ile başvuran ve NSTEMI ve STEMI tanısı alan hastalar çalışmaya dahil edildi. Çalışmamıza 113 NSTEMI ve 166 STEMI hastası dâhil edilmiştir.

Bulgular: NSTEMI hastalarında ortalama HDL değeri 39 (25-65) mg/dl, ortalama LDL değeri 105 (29-244) mg/dl, ortalama T. Kolesterol değeri 180 (78-356) mg/dl ve ortalama Trigliserid değeri 136 (37-360) mg/dl idi. NSTEMI hastaları ile STEMI hastaları TG/HDL oranı açısından karşılaştırıldığında, NSTEMI hastalarının TG/HDL oranı anlamlı olarak daha yüksekti (p:0.027; p<0.005).

Sonuç: Yüksek TG/HDL oranı insülin direncini gösteren bir parametredir. Çalışmamız NSTEMI hastalarında TG/HDL oranının yüksek olduğunu ortaya koymuştur. Bu nedenle, TG/HDL oranı yüksek olan NSTEMI hastalarında erken müdahale planlayarak morbidite ve mortalitenin azaltılmasına yardımcı olabiliriz.

Anahtar kelimeler: Akut koroner sendrom, ST segment yükselmesiz miyokard enfarktüsü, ST yükselmeli miyokard enfarktüsü, Trigliserid, Yüksek yoğunluklu lipoprotein.

INTRODUCTION

Globally, cardiovascular disease (CVD) is the leading cause of death. Over 15 million people died globally in 2019 from acute coronary syndrome (ACS), with patients under 70 years old accounting for 40% of these untimely deaths[1]. Atherosclerosis is the primary cause of coronary artery disease. The beginning of atherosclerosis is atherosclerotic plaques. There are many risk factors that cause the progression of atherosclerosis plaques. Among these risk factors, diabetes mellitus (DM), hypertension, and dyslipidemia are important pathological conditions that cause this disease. ACS is an urgent disease condition among atherosclerotic diseases. Research indicates that DM affects around 37% of ACS patients[2]. Patients with DM are more likely to experience worse cardiovascular events than ACS patients without DM[3,4]. Non-ST segment elevation myocardial infarction (NSTEMI) is the most common subtype of ACS. In patients with NSTEMI, the presence of DM doubles mortality rates. Therefore, the presence of DM should be considered as a mortality-increasing factor for NSTEMI patients[5].

One of the most important factors leading to the onset and progression of atherosclerotic events is insulin resistance. Insulin resistance is defined as a weaker sensitivity to insulin against insulin-induced effects during the action of insulin in target tissues. Research indicates that DM 2 affects around 37% of ACS patients. Patients with DM are more likely to experience worse cardiovascular events than ACS patients without DM[6]. There is increasing evidence that insulin resistance plays an important role in the development and pathogenesis of cardiovascular diseases[7]. Therefore, early detection of insulin resistance will prevent the development of cardiovascular diseases. Some indices that can reveal insulin resistance will be important for early diagnosis in the community. The triglyceride/HDL ratio has been shown to be a reliable marker of insulin resistance[8]. In people who develop insulin resistance, high

triglyceride and low HDL ratios will be important[9]. The TG/HDL-C ratio is important in terms of early diagnosis of the atherosclerosis process because it is easily obtainable and predictive of insulin resistance. In this study, we tried to emphasize the criticality of early intervention in NSTEMI patients by revealing whether the TG/HDL ratio indicating insulin resistance is different between NSTEMI and ST elevation myocardial infarction (STEMI) patients.

METHODS

Patients admitted to a training and research hospital with a prediagnosis of acute coronary syndrome and diagnosed as NSTEMI and STEMI were included in the study. Our study included 113 NSTEMI and 166 STEMI patients. This study was conducted by including all patients admitted to our hospital in 2020 and diagnosed with NSTEMI and STEMI. Patients admitted to our hospital with a diagnosis of NSTEMI and STEMI during the last year were included in the study. However, patients under the age of 18 years, pregnant women, patients with malignancy, and patients with missing follow-up data were excluded. Demographic characteristics of the patients were recorded. Laboratory records of NSTEMI and STEMI patients at the time of hospital admission were determined and recorded. The blood parameters obtained from the patients were from the time of their first hospitalization when they were diagnosed with NSTEMI and STEMI. Coronary angiographic imaging and the resulting interventional treatment decisions were recorded.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) for windows, Version 23.0 (SPSS, Inc., Chicago, IL, USA). The distribution of variables was measured by kolmogorov simirnov. Normal distribution variables are expressed as mean±standard deviation, while non-normally distributed variables are expressed as median (minimum-maximum). The p-values obtained from the Mann-Whitney U-test for non-normally distributed numerical variables and the t-test for regularly distributed numerical variables for independent samples are shown. By displaying the percentages of the categorical variables and accounting for the expected value, the chi-square test p result is obtained. The statistical significance level was assumed to be $p<0.05$. This study was approved by the Scientific Research Ethics Committee of a Provincial Health Directorate Training and Research Hospital with the decision numbered 364 dated 03.03.2023.

RESULTS

The study included patients admitted to the hospital with a prediagnosis of ACS and treated with a diagnosis of NSTEMI and STEMI. 113 patients with NSTEMI and 166 patients with STEMI were hospitalized and treated. The mean age of NSTEMI patients was 59.6±12.3 years and the mean age of STEMI patients was 57.7±11.7 years. Among 113 NSTEMI patients, 75.2% were male and 24.8% were female, and among 166 STEMI patients, 22.9% were female and 77.1% were male. 34 (30.1%) of 113 NSTEMI patients had DM, while 43 (25.9%) of 166 STEMI patients had DM. HT disease was present in 31% (35 patients) of NSTEMI patients and 23.5% (39 patients) of STEMI patients.(Table-1) 11.5% (13/100) of NSTEMI patients and 9.6% (16/150) of STEMI patients had previously received statin therapy. 12.4% (14/99) of NSTEMI patients and 7.2% (12/154) of STEMI patients were using the calcium channel blocker dihydropride. B-blockers were used by 18.6% (21/92) of NSTEMI patients and 12.7% (21/155) of STEMI patients. Angiotensin-conventing enzyme (ACE-inh) inhibitors were used by 15.9% (18/95) of NSTEMI patients and 10.2% (17/149) of STEMI patients. Angiotensin-conventing enzyme receptor blockers (ARB) were used by 10.6%

(12/101) of NSTEMI patients and 12% (20/146) of STEMI patients (Table I).

Table I: Demographic characteristics of the patients

	NSTEMI (n=113)	STEMI (n=166)	P
Age	59.6±12.3	57.7±11.7	0.192
Gender, f/m (%f)	28/85 (24.8%)	38/128 (22.9%)	0.716
DM, y/n (%y)	34/79 (30.1%)	43/123 (25.9%)	0.443
HT, y/n (%e)	35/78 (31%)	39/127 (23.5%)	0.165
DHD CaKb, y/n (%y)	14/99 (12.4%)	12/154 (7.2%)	0.146
NDHD CaKb, y/n (%y)	0/113 (0%)	2/164 (1.2%)	0.516
B-Blokör, y/n (%y)	21/92 (18.6%)	21/155 (12.7%)	0.174
ACE inh, y/n (%y)	18/95 (15.9%)	17/149 (10.2%)	0.159
ARB, y/n (%y)	12/101 (10.6%)	20/146 (12%)	0.713
Antiaggregants, y/n (%y)	29/84 (25.7%)	29/137 (17.5%)	0.098
Statin, y/n (%y)	13/100 (11.5%)	16/150 (9.6%)	0.616

Abbreviations: DM; Diabetes Mellitus, HT: Hypertension, DHD CaKb: Dihydropyridine calcium channel blocker, NDHD CaKb: Nondihydropyridine calcium channel blocker, ACE inh: Angiotensin Conventing enzyme inhibitor, ARB: Angiotensin Conventing enzyme receptor blocker. f:Female, m: male, y:yes,n: no. aIndependent sample-t test bPearson chi square test cContiunity correction test

113 NSTEMI and 166 STEMI patients underwent coronary angiographic imaging (CAG). After CAG, patients were classified according to the presence of atherosclerotic lesions in the coronary arteries. Critical atherosclerotic stenosis was present in one coronary artery in 12.5% of NSTEMI patients, in 16.3% of STEMI patients, in 32.1% of NSTEMI patients, in two coronary arteries in 40.4% of STEMI patients, in 55.4% of NSTEMI patients, and in three coronary arteries in 43.4% of STEMI patients. Lesions in the left main coronary artery (LMCA) were present in 8% of NSTEMI patients and 7.2% of STEMI patients. On coronary angiographic imaging, 92.9% (105/8) of NSTEMI patients had atherosclerotic stenosis in the LAD, 68.1% (77/36) in the RCA, 79.6% (90/23) in the CX, and 8% (9/104) in the LMCA. In STEMI patients (153/13) 92.2% had atherosclerotic lesions in LAD, (124/42) 74.7% in RCA, (100/66) 60.2% in CX, (12/154) 7.2% in LMCA (Table II).

Table II: Coronary angiographic imaging results of the patients

	NSTEMI (n=113)	STEMI (n=166)	P
LAD, y/n (%e)	105/8 (92.9%)	153/13 (92.2%)	0.815
RCA, y/n (%e)	77/36 (68.1%)	124/42 (74.7%)	0.231
LCx, y/n (%e)	90/23 (79.6%)	100/66 (60.2%)	**0.001**
LMCA, y/n (%e)	9/104 (8%)	12/154 (7.2%)	0.819
Coronary Artery			
1 Coronary Artery	14 (12.5%)	27 (16.3%)	
2 Coronary Artery	36 (32.1%)	67 (40.4%)	
3 Coronary Artery	62 (55.4%)	72 (43.4%)	0.146
Critical LMCA, y/n (%y)	1/8 (11.1%)	1/11 (8.3%)	0.989
Critical LAD, y/n (%y)	88/25 (77.9%)	116/50 (69.9%)	0.139
Critical RCA, y/n (%y)	53/60 (46.9%)	91/75 (54.8%)	0.194
Critical LCx, y/n (%y)	64/49 (56.6%)	63/103 (38%)	**0.002**
Critical stenosis, y/n (%y)	110/3 (97.3%)	162/4 (97.6%)	0.988
CABG, y/n (%y)	5/108 (4.4%)	4/162 (2.4%)	0.493
Medical/Interventional (%med)	5/108 (4.4%)	0/166 (0%)	**0.010**
Mortality, y/n (%y)	4/109 (3.5%)	3/163 (1.8%)	0.446

Abbreviations: LAD: Left coronary artery, RCA: Right coronary artery, LCx: circumflex coronary artery, LMCA: Left main coronary artery, CABG: coronary artery bypass grafting, y: yes, n: no. a Contiunity correction test bPearson chi square test

The laboratory tests performed at the time of admission in patients hospitalized with NSTEMI and STEMI are summarized in Table-3. As a result of the analysis, a significant difference was observed in the Neu/Lymp ratio when NSTEMI patients were compared with STEMI patients. ($p<0.001$) (Table-3) In NSTEMI patients, the mean HDL value was 39 (25-65) mg/dl, the mean LDL value was 105 (29-244) mg/dl, the mean T. Cholesterol value was 180 (78-356) mg/dl, and the mean Triglyceride value was 136 (37-360) mg/dl. When NSTEMI patients were compared with STEMI patients in terms of TG/HDL ratio, NSTEMI patients were

significantly higher. (p:0.027; p<0.005) (Table III).

Table III: Laboratory results of the patients

	NSTEMI (n=113)	STEMI (n=166)	P
WBCX10^3	10.5 (2.9-29.6)	12 (5.2-26.7)	**<0.001**
Hb	14±1.7	14.2±1.7	0.345
Htc	43±4.6	43.3±4.8	0.493
Neu X10^3	7.7 (1.7-26.8)	9.3 (3.1-24.3)	**<0.001**
Lym X10^3	2.13 (0-5)	1.91 (1-5)	0.066
Plt X10^3	264 (87-611)	259 (32-715)	0.937
Neu/Lymp	3.47 (1.01-20)	5.2 (0.9-27.7)	**<0.001**
Plt/Lymp	127 (50-490)	135 (15.7-643)	0.109
Creatinin, mg/dl	0.92 (0.61-2.27)	0.91 (0.53-1.68)	0.511
GFR	84 (19-121)	83 (45-128)	0.619
TSH	1.13 (0.22-7.37)	1.1 (0.02-4.47)	0.515
HDL	39 (25-65)	39 (18-96)	0.387
LDL	105 (29-244)	108 (26-241)	0.989
T. Cholesterol	180 (78-356)	179 (54-364)	0.816
Triglyceride	136 (37-670)	123 (30-549)	**0.027**
Tg/HDL	3.68 (1.1-19.4)	3.2 (0.74-24.3)	**0.027**
Troponin	17.3 (0.10-6630)	106 (0.10-10000)	**0.007**
Uric acid	4.9 (2.4-11.1)	5.3 (2.6-8.5)	0.496
Hba1C	6 (4.6-13.6)	5.9 (4.9-13.9)	0.999
Procalcitonin	0.05 (0.02-0.1)	0.05 (0.02-0.1)	0.107
SII	964 (172-4764)	1284 (98-15655)	**0.001**
CRP	2 (2-92.9)	3.1 (2-187)	0.137
Albumin	41 (29-49)	41 (25-47)	0.640
CRP/Albumin	0.058 (0.04-2.32)	0.077 (0.04-6.69)	0.291

Abbreviations: Hb: hemoblobin, Htc: hematocrit, Neu: neutrophil, Lym: lymphocyte, Plt: Platalet, GFR: Glomerular filtration rate, TSH: Troit stimulating hormone,HDL: high density lipoprotein, LDL: low density lipoprotein, CRP: c reactive protein.aMan whitney-u test bIndependent sample-t test

DISCUSSION

Globally, ACS is a leading cause of illness and mortality[10]. NSTEMI is the most common subtype of ACS. With increasing life expectancy, the number of NSTEMI patients is increasing[11]. When ACS is compared among ACS, NSTEMI patients have a better short-term prognosis than STEMI patients, but have a worse long-term prognosis[12]. The diagnosis of NSTEMI is more difficult than the diagnosis of STEMI. Therefore, the prevalence of NSTEMI has been determined on the basis of multiple screening and registries[13]. In general, the data show that the annual incidence of NSTEMI is gradually increasing compared to the incidence of STEMI. The increase in the annual incidence of NSTEMI may be attributed to the increased prevention efforts related to CAD in recent years[14].

The most important factor in atherosclerosis, that is involved in the physiopathology of coronary artery disease, is dyslipidemia. Dyslipidemia is defined as an increase in triglycerides, total cholesterol and LDL and a decrease in HDL levels[15,16]. DM or insulin resistance are important pathological conditions both in terms of their effect on dyslipidemia and their direct effect on the atherosclerotic process. Glucose metabolism is closely related to lipid metabolism[17]. Many studies have found a relationship between high triglyceride levels, low HDL levels, and cardiovascular disease risk[18]. Therefore, many indices indicating dyslipidemia and insulin resistance have been used to determine the morbidity and mortality of cardiovascular disease. One of these indicators that is very predictive of atherosclerosis, insulin resistance, and the risk of cardiovascular disease is the TG/HDL-C ratio[17,19]. Since TG is hydrophobic, it must combine with associated proteins to form lipoprotein particles that are transported in the plasma[20]. TG is the main component of

chylomicrons, very low density lipoproteins (VLDL), and the triglyceride-rich lipoproteins formed as a result of their metabolism[20]. According to a study, circulating lipoproteins typically use transcytosis to enter and exit the artery wall, allowing lipoproteins to pass through the endothelium[21]. TG remnants carry more cholesterol per particle than LDL because they are bigger than LDL. The remains of TG are readily absorbed by macrophages and do not require oxidation to become atherogenic. Consequently, TG remnants have a higher atherogenic impact than LDL[22]. Given that TG and residual cholesterol levels are closely correlated, it follows that increased TG levels may contribute to CVD. A more significant role for non-HDLC and TG lowering in coronary artery disease was supported by Puri R et al.'s[23] findings, which demonstrated that changes in non-HDLC were more closely connected with changes in coronary atheroma progression than LDL-C and were only associated with TG levels above 200 mg/dL. In our study, the TG/HDL ratio was higher in NSTEMI patients than in STEMI patients. The fact that this ratio was higher in NSTEMI patients may be thought to be due to the fact that the identification of this patient group is later. Considering that there are more DM patients in this patient group, the fact that such ratios revealing insulin resistance are higher will make the relevant specialist more careful and the diagnosis of NSTEMI will be left more often. Insulin resistance is the stage before the diagnosis of DM is abandoned. Therefore, the stage of insulin resistance, also interpreted as Pre-DM, is important in terms of cardiovascular disease risk[8]. When we look at in-hospital mortality rates, mortality is higher in STEMI patients. When we look at longer-term mortality rates, mortality rates are higher in NSTEMI patients than in STEMI patients[25]. The reasons for the higher mortality rates in long-term NSTEMI patients are that this patient group is older and has more comorbid diseases such as DM[26]. The presence of DM in NSTEMI patients doubles the association rates with mortality. Therefore, the presence of DM should be considered as a mortality-increasing factor for NSTEMI patients[27]. In general, 20-30% of NSTEMI patients have DM and most of them have type 2 DM with insulin resistance[28].

In our study, 30.1% of NSTEMI patients and 25.49% of STEMI patients had DM disease. When these two groups of patients were compared, no significant difference was observed (p: 0.443, p>0.005). However, when a comparison was made in terms of TG/HDL ratio, which is considered important in showing insulin resistance, this ratio was significantly higher in NSTEMI patients. TG/HDL-C ratio is a strong predictor of insulin resistance as well as atherosclerosis and CVD risk[16]. Insulin resistance is the stage before the diagnosis of DM is abandoned[29] Therefore, it is important to reveal insulin resistance, which is also interpreted as pre-DM, in terms of cardiovascular disease risk[24]. In our study, although DM rates were similar in the two patient groups, the TG/HDL ratio was significantly different, which we can associate with pre-DM status[30]. The higher prevalence of pre-DM in NSTEMI patients is due to the fact that the diagnosis of NSTEMI is more difficult and less frequent. Therefore, since the diagnosis of NSTEMI is more difficult than the diagnosis of STEMI, we can increase the dropout rates of NSTEMI by requesting troponin more frequently from patients with suspected CVD. Because the diagnosis of NSTEMI patients is delayed, the incidence of comorbid disease will increase. With a higher TG/HDL ratio indicating insulin resistance, earlier intervention can be planned for NSTEMI patients, contributing to reduced mortality and morbidity. Lowering the TG/HDL-C ratio was linked to a positive impact on the advancement of coronary atherosclerosis in long-term care diabetic patients, according to research by Nicholls et al[31].Two thirds of patients with acute or chronic coronary artery

disease have been found to have impaired glucose metabolism[32]. Research indicates that in individuals with DM who have had NSTEMI, early interventional techniques should be chosen over conservative ones. Research has demonstrated a 22-27% decrease in the mortality and non-fatal MI rates among diabetes patients who were randomly assigned to an early interventional strategy as opposed to a conservative approach[28]. Many studies have demonstrated an association between insulin resistance and coronary artery disease. However, in this study, we compared the TG/HDL ratio, which is an indicator of insulin resistance, between patients with NSTEMI and STEMI, two emergencies of coronary artery disease. The results of the study showed that the TG/HDL ratio was higher in NSTEMI patients. This suggests that the diagnosis of NSTEMI should be retained more and that more troponin screening should be performed. By being able to leave more NSTEMI diagnoses, more patient groups with insulin resistance will be identified. By identifying patients with insulin resistance more quickly, the chance of early intervention will increase. In addition, the higher TG/HDL ratio in the NSTEMI patient group will reveal the need for more primary prevention plans for this patient group. Earlier treatment of dyslipidemia in the NSTEMI patient group with a higher TG/HDL ratio will have positive effects on morbidity by stabilizing atherosclerotic plaques. In addition, although DM disease was similar in both groups in our study, the TG/HDL ratio was higher in the NSTEMI group, which we think is due to the fact that the diagnosis of this disease was discontinued later than the diagnosis of STEMI.

Our study's limitations include that it is a single-center investigation with a limited sample size. To verify these results, additional multicenter studies with larger sample sizes are required, as there is a certain selection bias. Secondly, no comparative analysis between the TG/HDL index and conventional markers of insulin resistance was done in this study. Third, even though the research analysis took into account a large number of confounding factors, certain known factors (such nutritional status) or unknown factors that were left out of the analysis could still have an impact on the findings.

CONCLUSION

A high TG/HDL ratio is a parameter indicating insulin resistance. Our study revealed that the TG/HDL ratio is high in NSTEMI patients. Therefore, we can help reduce morbidity and mortality by planning early intervention in NSTEMI patients with high TG/HDL ratios.

Ethics Committee Approval: The statistical significance level was assumed to be $p<0.05$. This study was approved by the Scientific Research Ethics Committee of a Provincial Health Directorate Training and Research Hospital with the decision numbered 364 dated 03.03.2023.

Conflict of Interest: The authors declared noconflicts of interest.

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