

The evaluation of predictive values of routine blood parameters for carotid artery disease in patients undergoing coronary artery bypass grafting

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ABSTRACT

Objectives: In this study, we aimed to investigate the value of inflammatory biomarkers and atherogenicity index in predicting concomitant carotid artery stenosis (CAS) in patients undergoing coronary artery bypass grafting (CABG).

Patients and methods: A total of 257 patients (163 males, 94 females; mean age 59.2±8 years; range, 33 to 75 years) admitted to our clinic and scheduled for isolated CABG between January 2016 and January 2019 were retrospectively analyzed. The patients were divided into two groups according to preoperative evaluation as those without significant CAS (Group 1, n=218) and those with CAS (≥50%) (Group 2, n=39).

Results: The mean age was 55.9±7.9 in Group 1 and 65.7±9.4 in Group 2 (p<0.001). The mean platelet volume, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio were significantly higher in Group 2 (p=0.021, p=0.016, p=0.038, and p<0.001, respectively). In the multivariate analysis, age (odds ratio [OR]: 1.645, 95% confidence interval [CI]: 1.174-3.432, p=0.005), three-vessel/left main coronary artery disease (OR: 0.779, CI 95%: 0.576-0.912, p=0.021), and TG/HDL-C ratio (OR: 1.334, CI 95%: 1.190-2.785, p=0.015) were found to be independent predictors of concomitant significant CAS.

Conclusion: Based on our study results, TG/HDL-C ratio, which can be measured from routine blood parameters, may be a useful predictor in predicting concomitant significant CAS in patients undergoing CABG.

Keywords: Carotid artery disease, coronary artery disease, inflammation, triglyceride.

Coronary artery bypass grafting (CABG) is one of the most valuable options in the treatment of atherosclerotic coronary artery disease (CAD).^[1] Although the surgical technique is the most important determinant of the success in these operations, systemic evaluation of the patients in the preoperative period is also very important. The preoperative diagnosis of possible comorbidities such as chronic obstructive pulmonary disease, cerebrovascular events, and other system arterial diseases which may affect the surgical strategy are of utmost importance. One of the most important parameters is the presence of carotid artery stenosis (CAS). Preoperative Doppler ultrasound (DUS) is still controversial for all patients undergoing CABG. However, preoperative recognition of CAS may lead to changes in the surgical strategy.^[2]

Atherosclerosis is a systemic disease which affects different arterial beds such as carotid, coronary, and peripheral arteries.^[3] Inflammation plays an important role in this process. Therefore, the relationship between inflammatory parameters and atherosclerotic diseases has been widely investigated in the literature. Among these parameters, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) are the most valuable ones. These parameters are practical as well, as they can be easily obtained from routine blood tests. Several studies have shown that these parameters can be used in the diagnosis and prognosis of cardiovascular diseases.^[4-6] Triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio, also known as the atherogenicity index, obtained from blood lipid

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parameters, has been also shown to be associated with the presence and burden of atherosclerosis.^[7]

In this study, we aimed to investigate the value of inflammatory biomarkers and atherogenicity index in predicting the presence of concomitant CAS in patients scheduled for CABG.

PATIENTS AND METHODS

This retrospective study included patients who were admitted to our clinic and scheduled for isolated CABG between January 2016 and January 2019. The medical data of the patients were obtained from the hospital registry system and patient files. Emergency operations, those with known systemic inflammatory disease, myocardial infarction within the previous month, those with additional cardiac disease (e.g., aneurysms or valvular heart diseases), those who received renal replacement therapy, those diagnosed with familial hyperlipidemia, and those who received steroid therapy were excluded from the study. Finally, a total of 257 consecutive patients (163 males, 94 females; mean age 59.2±8 years; range, 33 to 75 years) were included in the study. According to the preoperative evaluation, the patients were divided into two groups as follows: Group 1 (n=218) without significant CAS stenosis and Group 2 (n=39) with significant CAS (≥50%). Baseline demographic and clinical characteristics of the patients and blood test results including complete blood count, urea, creatinine, C-reactive protein (CRP), and lipids of all patients were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Harran University Faculty

of Medicine Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Blood parameters of the patients were measured from blood samples taken from antecubital veins during the hospital admission. Complete blood counts were measured using an automated whole blood analyzer. Hemoglobin, hematocrit, neutrophil, lymphocyte, and platelet counts, MPV, and white blood cell values were recorded. Then, the NLR and PLR were calculated. Biochemical values were measured using an automated device. Among the biochemical values, blood urea nitrogen, creatinine, triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and CRP values were analyzed. The TG/HDL-C ratio was, then, calculated.

Carotid artery DUS was performed in all patients included in the study during the preoperative period. Significant CAS was defined as an internal carotid artery (ICA) peak systolic flow rate (PSV) of 125 cm/s and above (≥50% stenosis) or ICA PSV/common carotid artery PSV of ≥2.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ±standard deviation (SD), median (min-max) or number and frequency. The Kolmogorov-Smirnov test and Shapiro-Wilk test were used to check the normal distribution of variables. The Student's t-test was used for the data with normal distribution and

Table 1. Demographic and clinical data of the patients

	Group 1 (n=218)					Group 2 (n=39)					p
	n	%	Mean±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	
Age (year)			55.9±7.9			65.7±9.4					<0.001*
Gender											0.294#
Male	134	61.4				29	74.3				
Hypertension	140	64.2				32	82				0.146#
Diabetes mellitus	42	19.2				13	33.3				0.313#
Tobacco use	83	38				20	51.2				0.374#
COPD	41	18.8				10	25.6				0.686#
Previous PCI	81	37.1				18	46.1				0.591#
Three-vessel disease/left main disease	105	48.1				33	84.6				<0.001#
History of CVA	18	8.2				8	20.5				0.019#
Ejection fraction				50	35-65				55	35-65	0.294**
Body mass index (kg/m ²)				29.2	19.9-38.6				28.6	21-41.2	0.412**
Statin use	77	35.3				16	41				0.778#

SD: Standard deviation; Min: Minimum; Max: Maximum; COPD: Chronic obstructive pulmonary disease; PCI: Percutaneous coronary intervention; CVA: Cerebrovascular accident; * Student's t test; ** Mann-Whitney U test; # Chi-square test.

Table 2. Laboratory data of the patients

	Group 1 (n=218)		Group 2 (n=39)		p*
	Median	Min-Max	Median	Min-Max	
White blood cell (10 ³ /μL)	8.7	3.6-12.1	9.1	4.1-11.8	0.230
Hematocrit (%)	40.4	32.4-49.1	41.3	33-51	0.456
Platelet (10 ³ /μL)	288	166-456	299	78-478	0.114
Neutrophil (10 ³ /μL)	4.9	2-9.2	5.2	2.1-9.9	0.094
Lymphocyte (10 ³ /μL)	2.1	0.8-4.9	1.9	1-4.6	0.114
Mean platelet volume (fl)	8.8	6.6-11	9.3	7-12	0.021
Neutrophil-to-lymphocyte ratio	2.8	0.9-8.2	3.2	1.1-9.1	0.016
Platelet-to-lymphocyte ratio	136.8	84.2-197.4	143.2	86-199	0.038
Urea (mg/dL)	24	14-52	26	12-58	0.318
Creatinine (mg/dL)	1.1	0.7-1.8	1.2	0.6-2	0.294
C-reactive protein (mg/L)	0.62	0.18-5.1	0.7	0.2-5	0.196
Total cholesterol (mmol/L)	5	4-6.1	5.3	4.8-6.3	0.109
LDL-C (mmol/L)	3.2	2.8-4.4	3.5	3.2-4.3	0.156
HDL-C (mmol/L)	1.3	0.8-1.5	1	0.7-1.2	0.061
TG (mmol/L)	1.4	1.1-1.8	1.6	1.2-2.4	0.107
TG/HDL-C	1.1	0.7-1.5	1.6	1.1-2.3	<0.001

* Mann-Whitney U test; LDL-C: low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; TG: Triglyceride; TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol.

the Mann-Whitney U test was used for the data without normal distribution. The chi-square test was performed to compare these data. A multivariate binary logistic regression analysis was used to analyze the predictors of additional CAS. The receiver operating characteristic (ROC) curve analysis was carried out to evaluate the predictive value of TG/HDL-C ratio in concomitant significant CAS and the area under the curve (AUC) values were calculated. A *p* value <0.05 was considered statistically significant.

RESULTS

The mean age was 55.9±7.9 in Group 1 and 65.7±9.4 in Group 2 (*p*<0.001). There was no significant

difference between the groups in terms of sex, body mass index, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, and tobacco use. However, the left main coronary involvement or three-vessel disease and cerebrovascular history rates were significantly higher in Group 2 (*p*=0.027 and *p*=0.019, respectively). Baseline demographic and clinical characteristics of the patients are shown in Table 1.

Laboratory parameters of the patients are presented in Table 2. Among the hemogram parameters, only MPV value was significantly higher in Group 2 (*p*=0.021). There was no significant difference in the biochemical blood parameters between the groups.

Table 3. Multivariate analysis results

Variables	Exp(B)	95% CI	p
	Odds ratio	Lower-Upper	
Age	1.645	1.174-3.432	0.005
Three-vessel disease/left main disease	0.779	0.576-0.912	0.021
History of CVA	1.679	0.756-2.797	0.216
Mean platelet volume	0.678	0.544-1.090	0.414
Neutrophil-to-lymphocyte ratio	1.119	0.984-3.214	0.055
Platelet-to-lymphocyte ratio	0.889	0.594-1.518	0.238
TG/HDL-C	1.334	1.190-2.785	0.015

CI: Confidence interval; CVA: Cerebrovascular accident; TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol; This model was verified by the Hosmer-Lemeshow test (*p*=0.745).

However, the mean NLR, PLR, and TG/HDL-C ratios of the patients were significantly higher in Group 2 ($p=0.021$, $p=0.016$, $p=0.038$, and $p<0.001$, respectively).

The multivariate logistic regression analysis results are shown in Table 3. Accordingly, age (odds ratio [OR]: 1.645, 95% confidence interval [CI]: 1.174-3.432, $p=0.005$), three-vessel/left main coronary artery disease (OR: 0.779, CI 95%: 0.576-0.912, $p=0.021$), and TG/HDL-C ratio (OR: 1.334, CI 95%: 1.190-2.785, $p=0.015$) were found to be independent predictors of concomitant significant CAS.

In the ROC curve analysis, the cut-off value for TG/HDL-C ratio was calculated as 1.28 with 75.4% sensitivity and 61.2% specificity (Figure 1).

DISCUSSION

In this current study, we showed that the presence of concomitant significant CAS in patients scheduled for CABG might be significantly associated with PLR, NLR, TG/HDL-C ratio, and MPV based on preoperative routine blood values. In the multivariate analysis, we found that the TG/HDL-C ratio, age, and three-vessel disease or left main coronary artery disease were independent predictors of presence of significant CAS in this patient population.

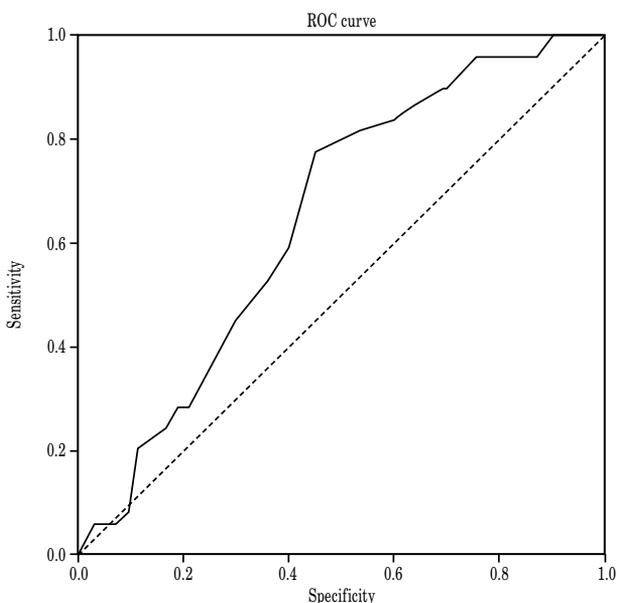


Figure 1. Receiver operation characteristic curve and AUC for TG/HDL-C ratio (cut-off= 1.28, AUC: 0.648, 95% CI: 0.568 - 0.724, $p=0.002$).

ROC: Receiver operation characteristic; UC: Area under the curve; TG/HDL-C: Triglyceride-to-high-density lipoprotein cholesterol; CI: Confidence interval.

Atherosclerosis is a systemic inflammatory disease which can affect multiple vascular beds simultaneously. The occurrence of atherosclerotic disease in more than one system is a condition that increases all-cause mortality and morbidity.^[8] Carotid artery stenosis alone is an important disease which may lead to serious morbidity and fatal results.^[9,10] It is, therefore, of utmost importance to reveal concomitant significant CAS in patients undergoing open heart surgery. The presence of significant preoperative CAS may lead to postoperative neurological complications.^[11]

Previous studies have shown that MPV, NLR and PLR values, which can be easily obtained from routine blood parameters, can be used in the diagnosis and prognosis of cardiovascular diseases. Platelets play an important role in atherosclerotic cardiovascular diseases. An increased platelet size is also associated with an increased enzymatic and metabolic activity. Therefore, several studies have demonstrated that high MPV and PLT values may play a role in the pathogenesis and progression of cardiovascular diseases.^[5,12,13] Increased neutrophil values in the blood indicate cellular immune system activation. The induction of the cellular immune system takes place through lymphocytes. Therefore, in atherosclerosis, which is an inflammatory process, the neutrophil count increases, while the lymphocyte count decreases and NLR increases.^[14] As a result, the PLR increases due to possible high platelet values and low lymphocyte counts. Currently, increased NLR and PLR values are widely used in the diagnosis and prognosis of cardiovascular diseases.^[6,15]

In a study, Yüksel et al.^[12] investigated the relationship between CAD severity and PLR in 388 patients undergoing coronary angiography. The patients were divided into three groups as normal, moderate, and severe disease according to coronary angiography results, and the PLR values were found to be significantly higher in the severe disease group. In addition, a positive correlation was found between the PLR and Gensini scores in patients with CAD ($r=0.268$, $p<0.001$). In another study by Aykan et al.,^[16] the severity of peripheral arterial disease could be predicted by the NLR. Another study by Ekici et al.^[17] investigated the burden of CAD and its possible relationship with MPV. At the end of the study, the authors reported that the severity of atherosclerotic disease was associated with high MPV in patients with CAD. In our study, similarly, the presence of concomitant CAS was found to be correlated with

higher MPV, PLR, and NLR values in patients scheduled for CABG.

Blood lipid parameters play an important role in the pathogenesis and progression of atherosclerosis. Hyperlipidemia plays a role in atherosclerotic process by leading to leukocyte adhesion in the vascular endothelium. Lipid structures also contribute to inflammation in the vascular endothelium, progressing to the vascular endothelium.^[18] Low HDL-C values are known to increase the cardiovascular risk.^[19] In addition, increased TG values were shown to be associated with the burden of atherosclerosis.^[20] In the light of these data, the TG/HDL-C ratio, also known as the atherogenicity index, is associated with the burden of atherosclerosis. In the literature, there are many studies investigating the relationship between TG/HDL-C ratio and presence and severity of atherosclerotic disease. In a study including 1,008 patients who underwent coronary angiography, increased TG/HDL-C values were associated with CAD presence.^[7] In another study by da Luz et al.,^[21] the relationship between CAD severity and lipid parameters was investigated in 374 patients and the authors found the strongest relationship between the CAD severity and TG/HDL-C ratio. Similarly, in this study, we found the TG/HDL-C to be an independent predictor of concomitant significant CAS in patients scheduled for CABG.

In a study conducted by Kazum et al.,^[22] the prevalence of CAS was investigated in 325 patients with CAD. The mean age of the patients was 68.8±9.9 years. In the multivariate analysis, peripheral arterial disease (OR: 3.186, 95% CI: 1.403-7.236, p=0.006), burden of CAD (OR: 1.543, 95% CI: 1.136-2.095, p=0.005), and age (OR: 1.028, 95% CI: 1.002-1.054, p=0.003) were found to be independent predictors of concomitant CAS in patients with CAD. In our study, age and three-vessel disease/presence of left main coronary artery disease were the independent predictors for CAS. Similar to our study, Avci et al.^[23] evaluated relationship between the degree of CAD and significant CAS in patients undergoing CABG. The Gensini score (OR=1.030, p=0.004), carotid bruit (OR=0.068, p<0.001), and male sex (OR=0.190, p=0.003) were found to be independent predictors of concomitant CAS. The multivariate model used in our study including inflammatory parameters was different from the aforementioned study. However, in our study, the burden of CAD was an independent predictor of concomitant CAS, consistent with the study of Avci et al.^[23]

It is critical to identify the presence of preoperative CAS in patients undergoing CABG. This situation can lead to changes in the surgical strategy in the preoperative period. Among the options, staged carotid endarterectomy (CEA)+CABG (CEA first), reversed staged CEA+CABG (CABG first), simultaneous CEA+CABG surgery, staged carotid stenting + CABG (CAS first) or same-day CEA with CABG surgery can be offered.^[2] In addition, recognizing the presence of preoperative CAS in patients scheduled for CABG may be a warning to the anesthesia team in terms of preventing puncture to the carotid artery in the neck region of the related part, while inserting the central venous catheter. In addition, it may be considered to keep the mean arterial pressure somewhat high during cardiopulmonary bypass in patients with concomitant significant CAS. The results of simultaneous CEA were investigated in patients scheduled for CABG by Vural et al.^[24] who reported that concurrent CEA could reduce stroke by 12%. However, the sequence of operations is still controversial.^[2] Nonetheless, the possible CAS should be established before the operation.

The main limitations of the present study include its single-center and retrospective design with small sample size. In addition, the use of DUS, which is an operator-dependent tool, is another limitation.

In conclusion, we can predict important CAS status from routine blood parameters in patients scheduled to undergo CABG. Although DUS is a valuable tool in the diagnosis of CAS, its use in all CABG-planned patients may increase treatment costs. Based on our study results, the TG/HDL-C value, which can be obtained easily from blood lipid parameters and is cost-effective, is an independent predictor of significant CAS in patients scheduled for CABG. We believe that this value can guide us in the preoperative evaluation of these patients.

Declaration of conflicting interests

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