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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Assessment of neutrophil / lymphocyte ratio in patients with myocardial bridge

Miyokardiyal kas bandı olan hastalarda nötrofil / lenfosit oranının değerlendirilmesi

Abdulkadir Yıldız, Mehmet Ata Akil, Fethullah Kayan, Murat Yüksel, Mehmet Zihni Bilik, Mustafa Oylumlu, Nihat Polat, Mesut Aydın, Halit Acet, Sait Alan

ABSTRACT

Objective: Myocardial bridge (MB) is a congenital anomaly characterized by systolic narrowing of the epicardial coronary arterial segment while traveling in the myocardium. It is a benign entity but previous studies showed that the proximal portion is prone to an enhanced atherosclerosis. Neutrophil/lymphocyte ratio (NLR) is a sensitive marker of systemic inflammation used as a predictor for adverse cardiovascular outcomes in atherosclerotic heart disease. So in this study, we sought to evaluate the association between NLR and myocardial bridging.

Methods: A total of 172 patients (mean age: 50.8 ± 11.5 years, 77.3% men) with either angiographically proven MB or normal coronary arteries were included in the study. For the entire study population, hematologic parameters were measured using an automatic blood counter.

Results: The study population consisted of 71 patients with MB (mean age: 51.4 ± 11.9 years, 80.3% male) and 101 patients with normal coronary arteries (mean age: 50.5 ± 11.3 years, 75.2% male). There were no significant differences between groups regarding hemoglobin level, platelet count, glucose and creatinine. Compared to the control group, NLR was significantly higher in patients with MB (2.45 ± 1.19 vs. 1.72 ± 0.48; p< 0.001). In ROC analysis, NLR > 1.82 predicted myocardial bridge presence with 70% sensitivity and 71% specificity (ROC area under curve: 0.733, 95% CI: 0.654-0.811, p < 0.001).

Conclusion: Our study findings demonstrated that MB is associated with elevated NLR, which is used to assess inflammatory status of the body. *J Clin Exp Invest 2014; 5 (1): 24-28*

Key words: Inflammation, neutrophil/lymphocyte ratio, and myocardial bridge

ÖZET

Amaç: Miyokardiyal kas bandı miyokart içinde seyreden epikardiyal koroner arterlerin sistolde daralması ile seyreden konjenital bir anomalidir. İyi huylu olmasına rağmen önceki çalışmalarda proksimal kesimlerin artmış ateroskleroza eğilimli olduğu gösterilmiştir. Nötrofil/lenfosit oranı (NLO) aterosklerotik kalp hastalıklarında kötü prognozu öngören sistemik enflamasyonun duyarlı bir belirtecidir. Biz bu çalışmada NLO ile miyokardiyal kas bandı arasında bir ilişki var olup olmadığını araştırmayı amaçladık.

Yöntemler: Anjiyografik olarak tespit edilmiş miyokardiyal kas bandı veya normal koroner arterleri olan 172 hasta (ortalama yaş: 50.8 ± 11.5 yıl, %77.3 erkek) çalışmaya dahil edildi. Otomatik kan sayacı kullanılarak tüm hastaların hematolojik parametreleri ölçüldü.

Bulgular: Çalışma 71 miyokardiyal kas bandı (ortalama yaş: 51,4 ± 11,9 yıl, %80,3 erkek) ve 101 normal koroner arterleri (ortalama yaş: 50,5 ± 11,3 yıl, %75.2 erkek) olan hastadan oluşmaktaydı. Hemoglobin, trombosit sayısı, glukoz ve kreatinin açısından gruplar arasında fark saptanmadı. Kontrol grubuna göre miyokardiyal kas bandı grubunda NLO anlamlı olarak daha yüksekti (2,45 ± 1,19 vs. 1,72 ± 0,48; p< 0,001). ROC analizinde, NLO > 1,82 miyokardiyal kas bandı varlığını %70 duyarlılık ve %71 özgüllükle öngörmüştür (ROC eğri altında kalan alan: 0.733, 95% güvenlik aralığı: 0.654-0.811, p < 0.001).

Sonuç: Çalışmamız miyokardiyal kas bandının vücutta enflamatuar düzeyi gösteren yüksek NLO seviyeleri ile ilişkili olduğunu göstermiştir.

Anahtar kelimeler: İnflamasyon, nötrofil/lenfosit oranı, miyokardiyal kas bandı

INTRODUCTION

Myocardial bridge (MB) is a congenital, usually benign coronary anomaly, in which a segment of major epicardial coronary artery courses through myocardium [1,2]. Angiographic frequency of MB in adults varies substantially in different populations, reported to range from 0.83% to 7.5% [3-5]. Myocardial bridges are prone to be localized in the mid-distal segment of the left anterior descending (LAD) artery [3-6]. Although MBs are not usually clinically significant, some longer and thicker ones can cause myocardial ischemia, life-threatening rhythm distur-

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

Correspondence: Abdulkadir Yıldız,
Dicle University School of Medicine, Department of Cardiology, Diyarbakir, Turkey Email: drakadiryildiz@gmail.com

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bances, acute coronary syndromes, or even sudden cardiac death [7-11].

Neutrophil/lymphocyte ratio (NLR) has recently proposed as a new prognostic marker [12-14]. The relationship between the NLR and a wide range of cardiovascular disorders has been shown in several studies [15]. Although intramural and distal portions of a bridged artery usually remain free from atherosclerosis, the proximal portion is prone to an enhanced atherosclerosis [16-18]. In the present study, we hypothesized that enhanced atherosclerosis proximal to bridged artery may be related with increased NLR. Therefore, we sought to measure NLR levels in patients with MB to assess the inflammatory status of the body.

METHODS

Study Population

Seventy-one patients with angiographically proven MB and 101 age- and gender-matched participants with normal coronary arteries were included in the study. Patients with acute coronary syndrome, previous cardiac surgery, known coronary artery disease, concomitant valvular disease, cardiomyopathy, heart failure, atrial fibrillation, congenital heart defects, renal or hepatic disease, malignancy, hematological disorders, and acute or chronic inflammatory disorders were excluded from this study.

Angiographic analysis

The diagnostic coronary angiograms of the patients were evaluated by the same cardiologist. Myocardial bridging was defined as systolic compression or milking of a segment of an epicardial coronary artery that courses intramurally on coronary angiography.

Laboratory measurements

Venous blood samples were obtained from all participants following a fasting period of 12 hours. Biochemical parameters were determined by standard methods. Hematological parameters were analyzed by an automatic blood counter (Abbott Cell-Dyn 3700; Abbott Laboratory, Abbott Park, Illinois). The local ethics committee approved the study.

Statistical analysis

Data were analyzed with the Statistical Package for the Social Sciences (SPSS) software version 16.0 for Windows (SPSS Inc, Chicago, IL). The Kolmogorov- Smirnov test was used to verify the normality of distribution of continuous variables. Continuous variables were defined as means ± standard deviation; categorical variables were given as percentages. The independent sample t test or the Mann- Whitney U test was used for the continuous variables and the chi-square test for categorical variables. Statistical significance was defined as $p<0.05$. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cutoff levels of N/L ratio in association with MB.

RESULTS

The study population consisted of 71 MB (mean age: 51.4 ± 11.9 years, 80.3% male) and 101 age- and gender-matched control participants with normal coronary arteries (mean age: 50.5 ± 11.3 years, 75.2% male). There were no significant differences between the groups with respect to age, gender, diabetes mellitus, hypertension, and smoking habits. The basal characteristics of the study population are listed in Table 1.

Table 1. Characteristics of the study population

Variables	Control (n=101)	Myocardial bridge (n=71)	P
Age, years	50.5 ± 11.3	51.4 ± 11.9	0.596
Male gender, n (%)	76 (75.2)	57 (80.3)	0.438
Hypertension, n (%)	24 (23.8)	14 (19.7)	0.529
Diabetes Mellitus, n (%)	13 (12.9)	4 (5.6)	0.130
Smoking, n (%)	30 (29.7)	15 (21.1)	0.208
Glucose, mg/dl	102 ± 20	98 ± 12	0.232
Creatinine, mg/dl	0.85 ± 0.16	0.88 ± 0.15	0.236
Hemoglobin, gr/dl	14.2 ± 1.4	14.1 ± 1.7	0.712
White blood cell count, x 10^3/L	7.70 ± 1.81	8.13 ± 1.95	0.141
Neutrophil count, x 10^3/L	4.34 ± 1.14	5.05 ± 1.64	0.002
Lymphocyte count, x 10^3/L	2.61 ± 0.65	2.23 ± 0.63	<0.001
Neutrophil/lymphocyte ratio	1.72 ± 0.48	2.45 ± 1.19	<0.001
Platelet count, x 10^3/L	253 ± 57	251 ± 67	0.850

In addition, there were no significant differences between groups regarding the hemoglobin levels, platelet counts, fasting blood glucose, and creatinine levels. Compared to the control group, the NLR value was significantly higher in patients with MB (2.45 ± 1.19 vs. 1.72 ± 0.48; p< 0.001; Figure 1). In ROC analysis, optimum cutoff level of the NLR in association with MB presence was 1.82 with 70% sensitivity and 71% specificity (ROC area under curve: 0.733, 95% CI: 0.654-0.811, p < 0.001; Figure 2).

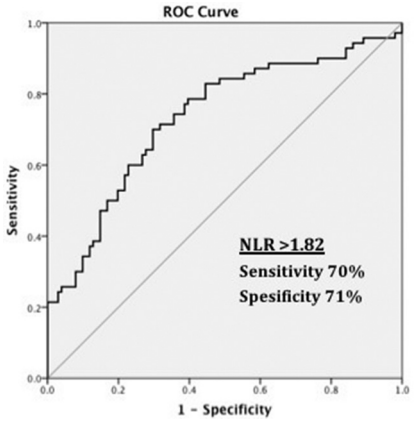

Figure 1. Box plot graphics of the neutrophil/lymphocyte ratios between myocardial bridge and control groups

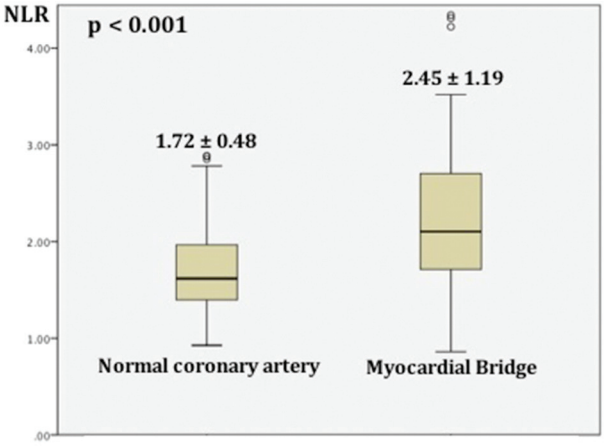

Figure 2. The receiver operating characteristic curve analysis of neutrophil/lymphocyte ratio for predicting the presence of myocardial bridge

DISCUSSION

To our knowledge, our study is the first to examine the NLR values in patients with coronary MB. We have found that patients with MB have significantly higher NLR values compared to control participants. Our results indicate that patients with MB tend to have increased inflammatory status.

Several studies have shown increased atherosclerotic plaque formation in the arterial segment proximal to MB [17-20]. As blood flow hemodynamics and atherosclerotic progression are closely related, low shear stress blood flow proximal to myocardial bridging enhances atherosclerosis by increased transfer of lipids into the intimal part of the coronary arteries [21]. However, higher shear stress within the MB causes decreased monocyte adhesion to the endothelium and a decreased lipid transfer through the artery wall resulting in the endothelium free from atherosclerosis [22-24]. Controversially, endothelial dysfunction was also demonstrated in the segments of coronary arteries beneath MB in another study [25]. This may be due to the systolic compression of the arteries causing damage to the endothelium and intima.

Neutrophil/lymphocyte ratio is a sensitive marker of systemic inflammation used as a predictor for adverse cardiovascular outcomes in atherosclerotic heart disease. In recent years, the NLR has been studied tremendously in various cardiovascular disorders. Its association with the severity of coronary artery disease, pulmonary arterial hypertension, coronary ecstasy, arrhythmias and acute coronary syndromes were demonstrated [12,14,26-30]. Increased NLR in our patients might be due to several different mechanisms. One of them might be endothelial damage caused by systolic kinking of the artery. The independent association between endothelial dysfunction and increased NLR was shown in various disorders of the body31-33. Another mechanism may be the important changes in coronary flow hemodynamics caused by MB. Blood flow-related shear stress has been asserted as a significant effect on endothelial function [34]. As atherosclerosis begins as local inflammation of arteries at sites of low shear stress, this may lead to enhanced plaque formation and progression of the coronary artery segment proximal to the MB. Ge et al. documented atherosclerotic plaque formation in the proximal to the bridged segments in 88% of the patients with MB by intravascular ultrasonography (IVUS) [20].

The main limitations of this study are relatively small sample size and cross-sectional study design. The lack of characteristics of the bridged segment is another limitation. It provides no information regarding cause or effect association between NLR and MB. The lack of IVUS use and assessment of endothelial dysfunction are other limitations.

In conclusion, our study findings demonstrated that MB is associated with elevated NLR levels. The mechanisms may be due to endothelial dysfunction

in the MB region or enhanced atherosclerosis in the segment proximal to MB due to low shear stress. Although NLR was different between patients with MB and controls, there is still no standardized cut-off level for the NLR. Further large-scale multicenter studies are needed to confirm the clinical significance of increased NLR in patients with MB.

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