

## Research Article

# The relationship between neutrophil to lymphocyte ratio and myocardial bridge

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### ABSTRACT

**Background:** Although myocardial bridge (MB) is a benign congenital anomaly, clinical trials have shown it to cause increased risk of atherosclerosis, which is a low-grade chronic inflammatory disease. The neutrophil-lymphocyte ratio (NLR) is an inflammatory indicator for mortality and morbidity in atherosclerotic heart disease. In this study, NLR was investigated in patients with MB.

**Methods:** A retrospective evaluation was made of patients admitted to our clinic for coronary angiography from 01<sup>st</sup> January 2014 to 31<sup>st</sup> December 2015. Patients included in the study were those diagnosed with MB and no evidence of atherosclerosis after coronary angiography and patients diagnosed with normal coronary vascularity. The NLR was calculated from the biochemical and hematological parameters based on the results of pre-angiographic values.

**Results:** Evaluation was made of 53 patients with MB (mean age: 56.70±11.45 years, 73.6% male), and 59 patients with normal coronary vascularity (mean age: 52.25±12.42 years, 39% male). No significant difference was determined between the groups in respect of biochemical or hematological parameters or in NLR values (2.34±0.88 versus 2.56±1.66; p=0.384).

**Conclusions:** The results of this study showed no relationship between MB and the inflammatory indicator of NLR.

**Keywords:** Atherosclerosis, Inflammation, MB, Neutrophil-lymphocyte ratio

## INTRODUCTION

Myocardial bridge (MB) is a congenital anomaly in which a segment of epicardial coronary artery lies below the myocardial muscle and narrows with systole.<sup>1</sup>

Prevalence has been reported to vary between 0.5 % and 16.0 % in coronary angiography studies.<sup>2</sup>

In autopsy studies, prevalence has been reported as between 15 % and 85 %. The wide range of values is believed to be due to the low sensitivity of coronary angiography in congenital anomaly diagnosis.<sup>2,3</sup> MB is generally benign in character but in some cases may cause complications such as unstable angina pectoris,

fatal ventricular arrhythmias, acute myocardial infarct, syncope, atrioventricular block and sudden cardiac death.<sup>4,5</sup>

Myocardial bridge plays a role in the predisposition for atherosclerosis development.

Inflammation is known to be an important mechanism in the development and progress of coronary vascular disease, but in cases of MB, the role of inflammation in the atherosclerotic process is not clear. The neutrophil/lymphocyte ratio (NLR) has been accepted as a new inflammatory indicator for cardiovascular risk and mortality. The aim of this study was to evaluate the relationship between MB and NLR.

## METHODS

This retrospective study included patients with stable angina pectoris who were diagnosed with MB in coronary angiography at Kahramanmaraş Necip Fazıl City Hospital from 01<sup>st</sup> January 2014 to 31<sup>st</sup> December 2015. As a control group, patients with normal coronary vascular findings in the same date range were included.

### *Biochemical parameters*

From samples taken prior to angiography, the lipid profile, urea, creatinine, sodium, and potassium levels and complete blood count were recorded. After waiting 20 minutes, the samples in biochemistry tubes were centrifuged at 3500 rpm for 5 minutes to separate the serum. Biochemical parameters were assayed with a Roche, Cobas 501 analyzer. Complete blood count parameters were assayed within tubes containing K2EDTA using a Sysmax XE-5000 hematology analyzer.

### *Application and evaluation of angiography*

The coronary angiography procedure was performed with a Toshiba Infinix CS-I angiography system. With the patient in a supine position, local anesthesia was administered, then femoral catheterization was applied using the Seldinger technique with a 6F catheter sheath, and right and left 6F Judkins catheters. To ensure good angiographic evaluation, images were taken at four standard projections (left caudal, right caudal, left cranial, straight cranial).

For right coronary artery evaluation, two standard image projections were taken at right and left cranial. Additional images were taken if necessary. Lohexol (Omnipaque-350) was used as the contrast agent and was manually injected at a dose of 6 - 8 ml for each projection. The images for each projection were evaluated by an experienced researcher and patients were grouped as normal vascularity and MB.

### *Exclusion criteria*

Patients with previous myocardial infarct, atherosclerotic coronary artery disease, hypertension, diabetes, acute coronary syndromes including unstable angina pectoris, non-ST/ST segment elevated myocardial infarct, myocarditis, acute or chronic systemic inflammatory disease, congestive heart failure with reduced or preserved ejection fraction, or chronic renal failure were excluded from the study.

### *Statistical analysis*

Normality of data was tested with the Kolmogorov Smirnov test. Continuous variables with normal distribution were compared by parametric tests e.g. Independent samples t test, while those variables without normal distribution were compared by non-parametric

tests. The distribution of categorical variables was analyzed using the Chi-Square test. Correlation analysis of continuous and categorical variables was applied using Pearson and Spearman tests, respectively. A value of  $p < 0.05$  was accepted as statistically significant. Statistical analysis was applied using IBM SPSS 15.0 software (IL, USA).

## RESULTS

The patients included in the study were divided into two groups as Group I with no positive findings for MB and Group II, diagnosed with MB. The mean age for Group I and Group II was  $52.25 \pm 12.42$  years and  $56.70 \pm 11.45$  years respectively. There was no significant difference between the groups in respect of age ( $p = 0.052$ ). The male/female ratio was 23/36 in Group 1 and 29/14 in Group 2, which was a statistically significant difference ( $p < 0.001$ ) (Table 1).

There was no significant difference between the groups in respect of white blood cell, neutrophil, lymphocyte and platelet counts, hematocrit, total cholesterol, blood urea nitrogen, serum creatinine, aspartate amino transferase and alanine amino transferase values (Table 1).

The neutrophil/lymphocyte ratio, the main parameter for the study was determined as  $2.34 \pm 0.88$  in Group 1 and  $2.56 \pm 1.66$  in Group 2. There was no statistically significant difference between the two groups in respect of the NLR values ( $p = 0.384$ ) (Table 1).

## DISCUSSION

Myocardial bridge is usually believed to be a clinically benign, congenital anomaly. Nevertheless, it requires clinical attention, because although rare, it can cause ischemic heart diseases through different mechanisms and result in unexpected clinical outcomes. One of these mechanisms is the effect of shear stress producing a state which is prone to atherosclerosis prior to MB segment.<sup>7, 8</sup>

The hemodynamics of blood flow at the proximal of the MB segment are closely related to atherosclerosis. The low level shear stress produced by blood flow increases lipid transmigration to the intimal layer of coronary arteries and thereby contributes to the development of atherosclerosis.<sup>9</sup> In addition, the higher shear stress in the MB segment lowers lipid transmigration and monocyte invasion to endothelia and therefore results in purged endothelia.<sup>10-12</sup>

Ge et al reported the presence of atherosclerotic plaque on intracoronary ultrasound in 90% of MB patients prior to MB segment.<sup>7</sup> An autopsy series proved that there is more endothelial damage in the segment prior to myocardial bridge compared to other arterial endothelial surfaces.<sup>13</sup> Zoghi et al reported that endothelial dysfunction is an important pathophysiological abnormality in MB patients.<sup>14</sup> Another study showed that

there is endothelial dysfunction in MB segments of coronary arteries.<sup>15</sup> Consequently, several studies have shown that the atherosclerotic state increases in the segment prior to MB.<sup>7,8,16,17</sup>

Atherosclerosis is a low-grade chronic, inflammatory disease.<sup>18,19</sup> It is accepted that the inflammatory process plays an important role at all levels of atherosclerosis.<sup>19</sup> White blood cell, neutrophil and lymphocyte counts and NLR are accepted as indicators for systemic inflammation.<sup>20-22</sup>

Many studies have shown that white blood cell and sub-group counts are important inflammatory markers in the prediction of cardiovascular results.<sup>21,23</sup> Neutrophil/lymphocyte ratio has recently started to be used as an inflammatory marker to predict the mortality of patients with coronary vascular disease.<sup>24-27</sup> Kalay et al reported that NLR is a marker for progression of atherosclerosis in coronary artery disease.<sup>28</sup> It has also been shown that NLR is a marker for possible cardiac events and mortality in patients with stable coronary artery disease.<sup>27</sup>

**Table 1: Baseline characteristics of the groups (MB negative and MB positive).**

Continuous variables	Total	Groups		p
		Myocardial bridge negative	Myocardial bridge positive	
Age (years)*	54.36±12.12	52.25±12.42	56.70± 11.45	p=0.052
Gender M/F % (n)	50.98/49.02 (n=52/50)	39/61(n=23/36)	73.6/26.4(n=29/14)	p<0.001
WBC (1/uL) <sup>#</sup>	7575.0(6692.5-9030.0)	7430 (6600-9290)	7800 (7005-8930)	p=0.562
Neutrophil (1/uL) <sup>#</sup>	4355(3802.5-5587.5)	4440.0 (3810.0-5860.0)	4300.0 (3800.0-5530.0)	p=0.716
Lymphocytes (1/uL)*	2184.82±661.87	2247.8±674.27	2114.72±646.91	p=0.290
Hemotocrit*	41.60±4.27	41.01±3.65	42.24±4.82	p=0.128
Platelets (1/uL)*	235160.71±58187.42	239016.95±63193.87	230867.92±52320.40	p=0.462
Glucose (mg/dl) <sup>#</sup>	95 (87.0-102.8)	95 (88-107)	93 (85.5-100.5)	p=0.093
BUN (mg/dl)*	28.15±6.50	27.740±6.69	28.61 (25.0-32.0)	p=0.483
Cr (mg/dl)*	0.81±0.15	0.8 (0.7-0.9)	0.82±0.14	p=0.280
AST (U/L)*	23.27±6.50	22.64±6.24	23.96±6.78	p=0.286
ALT (U/L)*	23.11±9.03	22.90±9.97	23.34±7.96	p=0.798
T. Chol. (mg/dl)*	182.86±43.38	186.24±43.79	179.09±43.03	p=0.387
LDL (mg/dl)*	116.82±38.24	118.42±36.56	115.04±40.30	p=0.642
NLR*	2.44±1.31	2.34±0.88	2.56±1.66	p=0.384

\*Parametric results were expressed as mean ± SD; #non-parametric results were expressed as median (25-75 percentiles); NLR: neutrophil/lymphocyte ratio, WBC: White Blood Cell, T. chol: Total cholesterol, BUN: Blood urea nitrogen, Cr: serum creatinin, AST: aspartate amino transferase, ALT: alanine amino transferase.

Another study demonstrated a relationship between NLR and severe coronary artery disease and claimed that it could be used to predict moderate-severe coronary artery disease.<sup>29</sup>

Duygu et al found the existence of low-grade inflammation in patients with MB and atherosclerotic disease and claimed that high sensitive C reactive protein could be used as a marker for atherosclerotic development in MB patients.<sup>30</sup>

In a study by Yıldız et al, the relationship between NLR and MB was investigated by comparing the hematological parameters of 71 patients with MB and 101 patients with normal coronary artery, obtained by automatized blood counter. No statistically significant difference was found between the groups in respect of hemoglobin, platelet count, glucose level and creatinine. The MB group showed statistically significantly higher

NLR values compared to the control group (2.45±1.19 vs 1.72±0.48; p<0.001). The results of that study claimed MB to be related with NLR levels, showing the inflammatory state of the body.<sup>31</sup>

In the current study, the NLR value was 2.34±0.88 in the control group and 2.56±1.66 in the MB patient group. There was no statistically significant difference between the two groups in respect of the NLR values. This research showed that there is no significant relationship between MB and NLR.

### Limitations

The major limitations of this study were its retrospective design and small number of patients. In addition, the male/female ratios were different in the groups and no comparison was made of NLR and other inflammatory markers.

## CONCLUSION

No significant relationship was found between MB, which can create a predisposition for atherosclerosis, and NLR, which is a strong inflammatory marker for atherosclerosis. However, there is a small-scale study in literature that has shown a relationship between MB and NLR. In the light of these results, there can be seen to be a need for larger prospective studies about this issue.

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