DOI:10.24938/kutfd.539647 Kırıkkale Üniversitesi Tıp Fakültesi Dergisi 2019;21(2):195-201
Original Article *Özgün Araştırma*

ASSOCIATION BETWEEN MYOCARDIAL BRIDGING AND CORONARY ARTERY DISEASE

Koroner Arter Hastalığı ile Myokardiyal Köprüleşme Arasındaki İlişki

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ABSTRACT

Objective: Myocardial bridging is a congenital variant of a coronary artery in which a portion of an epicardial coronary artery takes an intramuscular course. Although it is considered as benign, it may lead to complications such as myocardial ischemia, acute coronary syndromes, coronary spasm, exercise-induced dysrhythmias or even sudden death. SYNTAX score is the angiographic scoring system and is commonly used to evaluate the severity and complexity of coronary artery disease. This study was conducted with the aim to evaluate the association between myocardial bridging and SYNTAX score.

Material and Methods: The medical records of consecutive patients, who underwent coronary artery bypass graft surgery, were retrospectively reviewed. The study group consisted of 267 patients. The prevalence of myocardial bridging was found to be 13.4%. Biochemical, clinical, echocardiographic parameters and SYNTAX score were evaluated in all patients. The patients were divided into two groups according to the SYNTAX score (≥23: high, <23 low).

Results: The High SYNTAX score group was older and had higher prevalence of hyperlipidemia, smoking, and diabetes mellitus. On univariate analysis age, diabetes mellitus, smoking, and hyperlipidemia were associated with higher SYNTAX score. On multivariate analysis diabetes mellitus and hyperlipidemia were independent predictors of higher SYNTAX score (OR 2.957; 95% CI: 1.391–5.183; p<0.001, OR 3.267; 95% CI: 1.973-6.739; *p*<0.001; respectively).

Conclusion: In our study, we have found that diabetes mellitus and hyperlipidemia were independent predictors of high SS. There was no significant difference between both groups regarding the presence of myocardial bridging.

***Keywords**: Coronary artery disease, myocardial bridging, diabetes mellitus, hyperlipidemia.*

ÖZ

Amaç: Miyokardiyal köprüleşme, bir epikardiyal koroner arterin bir bölümünün intramüsküler bir seyir içine girdiği bir koroner arterin konjenital varyantıdır. İyi huylu olarak görülmesine rağmen, miyokard iskemisi, akut koroner sendromlar, koroner spazm, egzersize bağlı aritmiler ve hatta ani ölüm gibi komplikasyonlara yol açabilir. SYNTAX skoru anjiyografik skorlama sistemidir ve genellikle koroner arter hastalığının yaygınlık ve ciddiyetini değerlendirmek için kullanılır. Bu çalışma, myokard köprüleşmesi ve SYNTAX skoru arasındaki ilişkiyi değerlendirmek amacıyla yapıldı.

Gereç ve Yöntemler: Koroner arter bypass greft ameliyatı yapılan ardışık hastaların tıbbi kayıtları retrospektif olarak incelendi. Çalışma grubu 267 hastadan oluşuyordu. Myokardial köprüleşme prevalansı %13.4 saptandı. Tüm hastalarda biyokimyasal, klinik, ekokardiyografik parametreler ve SYNTAX skoru değerlendirildi. Hastalar SYNTAX skoruna göre iki gruba ayrıldı (≥23: yüksek, <23 düşük).

Bulgular: Yüksek SYNTAX skoru grubu daha yaşlıydı ve hiperlipidemi, sigara içme ve diabet prevalansı daha yüksekti. Tek değişkenli analizlerde yaş, diabet, sigara içme ve hiperlipidemi yüksek SS ile ilişkiliydi. Çok değişkenli analizlerde diabet ve hiperlipidemi yüksek SYNTAX skoru'nun bağımsız belirleyicileriydi (OR 2.957; 95% CI: 1.391–5.183; p<0.001, OR 3.267; 95% CI: 1.973-6.739; *p*<0.001; sırasıyla).

Sonuç: Çalışmamızda, diabet ve hiperlipideminin yüksek SYNTAX skoru'nun bağımsız belirleyicileri olduğunu bulduk. Her iki grup arasında myokardiyal köprüleşme varlığı yönünden anlamlı fark yoktu.

***Anahtar Kelimeler**: Koroner arter hastalığı, myokardiyal köprüleşme, diyabet, hiperlipidemi*

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KÜ Tıp Fak Derg 2019;21(2):195-201
Doi:10.24938/kutfd.539647

INTRODUCTION

Myocardial bridge (MB) is defined as an intramyocardial segment of an epicardial coronary artery, and described firstly by Geiringer in 1951 (1). It is the most common congenital anomaly of the coronary arteries, with a prevalence between 0.5 and 16% in routine coronary angiographies and up to 80% at autopsy (2,3). Although it is considered as benign, it may lead to myocardial ischemia, acute coronary syndromes, coronary spasm, left ventricular dysfunction, apical ballooning syndrome, syncope, and even sudden death (4-6). It's known that coronary arteries which are under an MB and distal segment of MB are free from atherosclerotic disease, but a proximal segment of the MB is very sensitive to atherosclerosis (7,8). On the other hand, age, MB, and diabetes mellitus were found independent predictors of severe stenosis in a left anterior descending artery (LAD) (9).

SYNTAX score (SS) is an angiographic grading tool to evaluate the extensity and complexity of coronary artery disease (CAD). SS is beneficial to chose for determining the optimal revascularization strategy in patients with CAD (10-13).

There are scarce data about the association between MB and SS in patients undergoing coronary artery bypass graft (CABG) surgery. In the light of this knowledge, we assessed the relationship between the MB and SS in patients who underwent CABG surgery.

MATERIALS AND METHODS

Two hundred and sixty-seven consecutive patients, who underwent on-pump CABG surgery were included in this study. Consecutive patients who underwent CABG surgery between from January 2014 to January 2019 were evaluated retrospectively.

Thirty-six patients with MB and 231 patients without MB were included in the study. We excluded patients with acute coronary syndromes, with absence of echocardiography report, and requirement of urgent surgery. The data of patients were retrospectively analysed for the demographic features, echocardiographic parameters, biochemical parameters, and SS. The study was approved by the local ethics committee (YDU, Date: 21.12.2017, Desicion No: /2017/53-506). All procedures have been applied in accordance with the principles of the Declaration of Helsinki.

Echocardiographic Examination

All patients underwent transthoracic echocardiography using Vivid E9 (GE healthcare) echocardiography device and Mass S5 probe. Standard two-dimensional and colour flow Doppler views were acquired according to the guidelines of the American Society of Echocardiography and European Society of Echocardiography (14). The ejection fraction was measured according to the Simpson's method.

Coronary Angiography

All patients underwent elective coronary angiography according to the Judkins technique. The LAD coronary artery, the left circumflex coronary artery and the right coronary artery were observed by various angulations. The presence of MB was defined as the following criteria: narrowing of coronary vessel lumen during systole and dilation during diastole; no evidence for occurrence of coronary vasospasm. All MBs were seen in LAD artery.

SYNTAX Score

All lesions causing ≥ 50% stenosis in a coronary artery with a diameter ≥1.5 mm were included in the SYNTAX score calculation. For calculation, website software (http://www. SYNTAXcore.com) was used. SYNTAX score was divided into two groups: ≥23: high, <23 low.

Patients with diabetes mellitus (DM) were identified on admission as those with documented DM using either oral hypoglycemic agents or insulin treatment.

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Hypertension (HT) was defined as blood pressure above 140/90 mmHg or using antihypertensive therapy on admission. Hyperlipidemia (HL) was defined as total cholesterol at least 200 mg/dL or using antihyperlipidemic therapy on admission. Body mass index (BMI) was calculated using weight and height (kg/m^2).

Statistical Analysis

Statistical analysis was performed using the SPSS (version 20.0, SPSS Inc., Chicago, Illinois) software package. Continuous variables were expressed as the mean±standard deviation (mean± SD), and categorical variables were expressed as a percentage (%). The Kolmogorov-Smirnov test was used to evaluate the distribution of variables. Student's t-test was used to evaluate continuous variables showing normal distribution, and Mann-Whitney U-test was used to evaluate variables that did not show normal distribution. A p-value <0.05 was considered statistically significant. To identify predictors of higher SS, the following variables were initially assessed in a univariate model: age, HL, smoking, and DM. Significant variables in univariate analysis were then entered into a multivariate logistic regression analysis using backwards stepwise selection.

RESULTS

Prevalence of MB was found 13.4% in this study group. MB and control group were composed of 36 and 231 patients respectively. The demographic characteristics of both groups are summarised in Table 1.

There was no significant difference between both groups regarding gender, HT, BMI, left ventricular ejection fraction, and MB (39.7% vs. 41.2% p=0.734, 29.4% vs. 28.5% p=0.623, 26.3±7.9 vs. 27.9±6.4 p=0.597; 62.7±5.9% vs 61.4±6.7 p=0.689, 14.1% vs 13.2% p=0.738; respectively) (Table 1).

There was significant difference between both groups regarding age, hyperlipidemia, smoking, and DM (51.4±12.9 vs. 64.1±10.7 p<0.001, 34.6% vs. 57.1% p<0.001, 24.3% vs. 38.6% p<0.001, 16.6% vs. 28.5% p<0.001; respectively) (Table1).

There was no significant difference between both groups regarding hemoglobin, white blood cell, creatinine, C-reactive protein (11.9±2.3 vs 12.3±2.6 p=0.583, 7.4±3.9 vs 7.7±3.4 p=0.716, 0.87±0.31 vs 0.89±0.43 p=0.879, 1.53±0.89 vs 1.86±1.03: respectively) (Table2). There was significant difference between both groups regarding fasting plasma glucose, total cholesterol, high density cholesterol, low density cholesterol, and trigyliceride (96.3±21.8 vs 124±46.3 p=0.01, 187.9±46.7 vs 227.6±58.9 p=0.02, 44.3±14.7 vs 33.1±16.2 p=0.01, 147.9±63.9 vs 183.5±79.2 p<0.001, 134.7±34.3 vs 184.6±62.5 p=0.01; respectively) (Table2).

The results of univariate analyses are presented in Table 3. On univariate analysis, age, hyperlipidemia, smoking, and DM were associated with higher SS (Table3).

On multivariate analysis DM and hyperlipidemia were independent predictors for higher SS (OR 2.957; 95% CI: 1.391–5.183; p<0.001, OR 3.267; 95% CI: 1.973-6.739; p<0.001; p<0.001 respectively) (Table 4).

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Table 1: Characteristics of patients in the study

Variables	**SYNTAX Score <23 (n=78)**	**SYNTAX Score ≥23 (n=189)**	**p**
Age (years)	51.4±12.9	64.1±10.7	<**0.001**
Male gender, n (%)	31 (39.7)	78(41.2)	0.734
Hyperlipidaemia, n (%)	24 (34.6)	108(57.1)	**<0.001**
Smoking, n (%)	19 (24.3)	73(38.6)	**<0.001**
Diabetes mellitus, n (%)	13 (16.6)	54(28.5)	**<0.001**
Hypertension, n (%)	23 (29.4)	63 (28.5)	0.623
Body mass index (kg/m^2)	26.3±7.9	27.9±6.4	0.597
Ejection fraction (%)	62.7±5.9	61.4±6.7	0,689
Myocardial bridging, n (%)	11 (14.1)	25 (13.2)	0.738

Table 2. Laboratory parameters of the study population

Laboratory parameters	**SYNTAX score <23 (n=78)**	**SYNTAX score ≥23 (n=189)**	**p**
Hemoglobin (g/dl)	11.9±2.3 (12.4)	12.3±2.6 (12.6)	0.583
White Blood Cell (10^3/ μL)	7.4±3.9 (8.3)	7.7±3.4 8.6)	0.716
Creatinine (mg/dl)	0.87±0.31 (0.79)	0.89±0.43 (0.81)	0.879
Fasting Plasma Glucose (mg/dl)	96.3±21.8 (98.7))	124±46.3 (134.9)	**0.01**
C Reactive Protein (mg/dl)	1.53±0.89 (1.37)	1.86±1.03 (1.1.54)	0.347
Total Cholesterol (mg/dl)	187.9± 46.7(194.2)	227.6±58.9 (248.3)	**0.02**
High Density Lipoprotein (mg/dl)	44.3±14.7 (48.9)	33.1±16.2 (37.1)	**0.01**
Low Density Lipoprotein (mg/dl)	147.9±63.9 (160.8)	183.5±79.2 (226.9)	**<0.001**
Trigyliceride (mg/dl)	134.7±34.3 (153.9)	184.6±62.5 (208.6)	**0.01**

TSH: Thyroid-stimulating hormone

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Table 3. Univariate Analysis of Predictors for higher SYNTAX Score

Predictor Variables	OR (95% C.I.)	p
Age (years)	2.392 (1.728–3.935)	**<0.001**
Hyperlipidemia, n (%)	1.376 (1.173-1.937)	**<0.001**
Smoking, n (%)	1.483 (1.257-2.056)	**<0.001**
Diabetes mellitus, n (%)	2.964 (2.186–4.518)	**<0.001**

Table 4. Multivariate analysis of predictors for higher SYNTAX Score

Predictor Variables	OR (95% C.I.)	p
Diabetes mellitus, n (%)	2.957 (1.391-5.183)	**<0.001**
Hyperlipidemia, n (%)	3.267 (1.973-6.739)	**<0.001**

DISCUSSION

Our study revealed that DM and HL were independently associated with higher SS. There was no significant difference between both groups regarding the presence of MB.

Hyperlipidemia has been a well-known risk factor for CAD. A recent studies have revealed that increased serum levels of triglyceride are associated with the development of CAD independent of other coronary risk factors (15-17). In our study, HL was found an independent predictor of higher SS.

DM is a major risk factor for the development of CAD and is associated with poor clinical outcomes. The association between the pathogeneses of DM and atherosclerosis is hyperinsulinemia resulting from insulin resistance (IR). IR is leading to decreased nitric oxide synthesis in coronary arteries. Changes in carbohydrate and lipid metabolism accompanying IR lead to increasing concentration of free fatty acids. Several studies found that DM is associated with extensity and complexity of CAD (18,19). Our study showed that DM is an independent predictor of higher SS consistently with previous studies.

MB is a common anatomic variant that predominantly involves the mid or distal coronary segments of the LAD artery. Reduced blood flow reserve and decreased blood perfusion derived from delayed arterial relaxation in diastole, the progression of atherosclerotic plaque frequently reported in the segment proximal to the MB. The milking effect may produce systolic retrograde flow and overall flow disruption with augmented shear stress. Especially, the distribution of wall shear stress about the tunnelled segment may play a key role because lower shear stress has been postulated to predispose patients to enhanced lipid transfer across the endothelium and to more atherosclerosis. Another possible mechanism for plaque formation includes abnormal flow profiles at this segment such as oscillatory flow reversal with or without significant collision with the antegrade coronary flow. MB has been associated with coronary endothelial dysfunction that is an early stage of atherosclerosis and is associated with spasm, symptoms and adverse events (20-22).

Interestingly, coronary artery segments with MBs are free of atherosclerotic plaque in several studies (23,24). Hemodynamic factors have been proposed to explain the absence of atherosclerosis in bridged coronary artery segments (25-27). Another possible mechanism is that bridged coronary arteries are protected from the influence of perivascular adipose tissue by the overlying myocardium.

There are scarce data about the association between extensity/severity of CAD and MB in literature. In our study, we found that there was no significant difference between both groups regarding the presence of MB.

As well as the protective effect of MB on tunnelled coronary artery segment, taking into account controversial results regarding the protective or predisposing role of MB on CAD further studies with a larger number of patients are needed on this topic.

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Our study has some limitations. First, the study design is retrospective. Second, the sample size is small.000

In our study, DM and HL were found independent predictors of higher SS. There was no significant difference between both groups regarding the presence of MB. Further studies with a larger number of patients are required for the evaluation of the association between MB and CAD.

Conflict of Interest: The author has no conflicts of interest to declare.

Financial Disclosure: The author declared that this study had received no financial support.

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