Sol Koroner Arter Bifurkasyon Açısı ve Sol Ana Koroner Arter Uzunluğunun Aterosklerotik Plak Yükü Üzerine Etkisi

Effect of Left Coronary Bifurcation Angle and Left Main Coronary Artery Length on Coronary Artherosclerotic Plaque Burden

Murat Ziyrek, **Zafer Büyükterzi**

Konya Eğitim ve Araştırma Hastanesi, Kardiyoloji Kliniği, Konya, Türkiye

ÖZ

GİRİŞ ve AMAÇ: *Koroner arter hastalığı (KAH) önemli bir halk sağlığı sorunudur. Gensini skorlama sistemi (GS) klinik pratikte ateroskleroz yükü, KAH yaygınlığı ve ciddiyetini belirlemede kullanılan en popüler skorlama yöntemlerinden birisidir. Daha önce yapılmış çalışmalarda geniş açılanma ile ciddi koroner arter darlığı arasında korelasyon olduğu gösterilmiştir. Bu çalışmada, koroner arter bifurkasyon açısı ve LMCA uzunluğunun koroner aterosklerotik yük ile ilişkini incelemeyi amaçladık.*

YÖNTEM ve GEREÇLER: *Koroner anjiografi yapılan hastalar incelendi. Akut koroner sendromu, normal koroner arterleri, LMCA osteal lezyonu, LAD osteal lezyonu, CX osteal lezyonu, bifurkasyon açısının ölçümü için yeterli görüntüleme yapılamamış olan hastalar dışlandı. 2 deneyimli kardiyolog tarafından "extreme pacs" yazılım sistemi kullanılarak çalışmaya dahil edilen hastaların LAD-CX bifurkasyon açısı ve LMCA uzunluğu ölçüldü. Dahil edilen hastaların aterosklerotik plak yükü GS kullanılarak hesaplandı.*

BULGULAR: *63 hasta (36 erkek, 27 kadın) çalışmaya dahil edildi. LAD-Cx bifurkasyon açısı ile gensini skoru arasında kuvvetli pozitif korelasyon mevcuttu (r= 0,854; p<0,001). LAD-CX bifurkasyon açısı ile LMCA uzunluğu arasında ise istatistiksel olarak anlamlı olmayan pozitif korelasyon mevcuttu (r= 0,228; p=0,11). Regresyon analizi ile LAD-CX bifurkasyon açısının aterosklerotik plak yükü için bağımsız bir risk faktörü olduğu gösterildi.*

TARTIŞMA ve SONUÇ: *Bu çalışma ile LAD-CX bifurkasyon açısı arttıkça aterosklerotik plak yükünün de arttığı gösterilmiştir. Bunun yanında bifurkasyon açısının aterosklerotik plak yükü için bağımsız bir risk faktörü olduğu söylenebilir.*

Anahtar Kelimeler: *Gensini skoru, bifurkasyon açısı, ateroskleroz*

ABSTRACT

INTRODUCTION: *Coronary artery disease (CAD) is an important public health problem. The Gensini score system (GS) is one of the most popular coronary scoring systems used in clinical practice to determine the atherosclerotic burden, extent and severity of CAD. Previous studies have showed the direct correlation between wide angulation and significant coronary stenosis. In this study we analysed the effect of coronary bifurcation angle and left main coronary artery (LMCA) length on the coronary atherosclerotic burden.*

METHODS: *Patients, who underwent coronary angiography were scanned. Patients having; acute coronary syndrome, normal coronary arteries, LMCA lesion, osteal left anterior descending (LAD) coronary artery lesion, osteal circumflex (CX) coronary artery lesion, inadequate visualisation for bifurcation angle measurement were excluded. LAD-CX coronary artery bifurcation angle and LMCA length of included patients were analysed by 2 experienced cardiologists by using "extreme pacs" software system. Atherosclerotic burden of included patients were determined by GS.*

RESULTS: *63 patients (36 male, 27 female) were included. There was a strong positive correlation between LAD-CX bifurcation angle and gensini score (r= 0,854; p<0,001). There was a statistically nonsignificant positive correlation between LAD-CX bifurcation angle and LMCA length (r= 0,228; p=0,11). Regression analysis showed that LAD-CX bifurcation angle is an independent risk factor for atherosclerotic burden*

DISCUSSION and CONCLUSION: *In this study, we concluded that as the LAD-CX bifurcation angle increases atherosclerotic burden significantly increases. It might also be said that LAD-CX bifurcation angle is an independent risk factor for atherosclerotic burden*

Keywords: *Gensini score, bifurcation angle, atherosclerosis*

INTRODUCTION

Atherosclerotic coronary artery disease (CAD) is the leading cause of death in both the developed and developing world (1). Atherosclerosis also causes a decrease in cognitive functions (2) and renovascular alterations (3). Furthermore, there is a direct correlation between atherosclerotic plaque burden and complications. Consequently, detection of the extent and severity of CAD by easily applicable and cost-effective methods is of great importance. The Gensini score system is one of the most popular coronary scoring systems used in clinical practice to determine the atherosclerotic plaque burden, extent and severity of CAD (4).

Effect of vascular geometry on the development of atherosclerosis is another challenging issue. Since the pioneering research of Caro et al. (1971), a substantial body of work has been carried out in order to analyze the relationship between vascular geometry and atherosclerosis (5). It is now accepted in multiple studies that flow disturbance caused by vascular geometry is the trigger for vascular endothelial dysfunction which enhances inflammation and atherosclerosis (6). For this reason, in this study, we aimed to analyze the effect of coronary bifurcation angle and left main coronary artery (LMCA) length on the coronary atherosclerotic plaque burden.

MATERIALS and METHODS

1. Study design and population

In this observational cross-sectional study, subjects were selected from the patients who underwent coronary angiography between 01.06.2018 - 31.12.2018. Patients having; acute coronary syndrome, normal coronary arteries, LMCA lesion, osteal left anterior descending (LAD) coronary artery lesion, osteal circumflex (CX) coronary artery lesion, inadequate visualization for bifurcation angle measurement were excluded. 63 patients (36 male, 27 female) were included.

2. Study protocol

Clinical and demographic features of all included patients were recorded. Venous blood samples for biochemical analysis were drawn from all subjects after overnight fasting. Complete blood count, triglyceride (TG), total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), blood urea nitrogen (BUN), creatinine, sodium, potassium, and plasma glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT) levels were analyzed. Subsequently, all patients' LAD-CX bifurcation angle, LMCA length and Gensini score (GS) were calculated.

3. Coronary angiographic evaluation

The coronary angiographies were performed and interpreted by interventional cardiologists who have more than five years of working experience. Angiographic data were analyzed by 2 experienced cardiologists. LAD-CX bifurcation angle and LMCA length were measured at LAO-500 caudal-300 view by using "extreme pacs" software system (Figure 1). Mean of 3 consecutive measurements were taken. Results were expressed in millimeters. GS is based on the percentage of luminal narrowing (25%:1 point; 50%:2 points; 75%:4 points; 90%:8 points; 99%:16 points, and total occlusion:32 points). Each coronary lesion score was calculated using the percentage of luminal narrowing multiplied by coefficient of coronary segment: the left main coronary artery (LMCA) x5; the proximal segment of the left anterior descending coronary artery (LAD) x 2.5; the proximal segment of the circumflex artery (CX) x 2.5; the mid-segment of the LAD x 1.5; the distal segment of the LAD, all segments of the right coronary artery (RCA) and the obtuse marginal artery x 1; and other segments x 0.5.
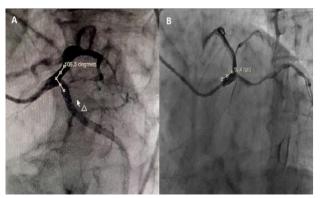

Figure 1. Measurement of A, LAD-CX bifurcation angle; B, left main coronary artery angle at the LAO-50 caudal-30 view.

The GS was calculated by the summation of individual coronary segment scores (7) (Figure 2).
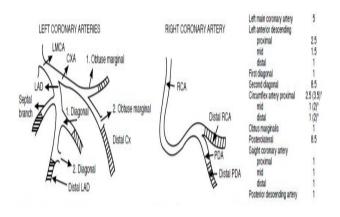

Figure2 . Position of the lesion in the coronary arterial tree. LMCA. Left main coronary artery; LAD, Left anterior descending artery; Cx, circumflex artery; RCA, right coronary artery; PDA, posterior descending artery

Statistical analysis

Statistical analyses were conducted with a commercially available software package (SPSS version 16.0, SPSS, Chicago, IL). In this study, data are expressed as mean±SD for continuous variables and as counts and percentage for categorical variables.

Differences were considered statistically significant at $p<0,05$. Fitness to the normal distribution was analyzed with the Kolmogorov-Smirnov test. Correlations of continuous variables were evaluated using Pearson correlation analysis or its nonparametric counterpart Spearman's correlation analysis.

Linear logistic regression analysis was performed to explore independent factors associated with GS.

RESULTS

63 patients (36 male, 27 female) were included. Of these 63 patients; 40 had hypertension, 38 had diabetes mellitus, 42 were smoking cigarette, 25 had a positive family history of CAD. Patients' demographic and biochemical data are given in table 1.

Table1. Demographic and biochemical characteristics of the study population	
Variable	**Mean value**
Age (years)	65,9±10,1
Male gender, n (%)	36 (%57,1)
Hypertension n(%)	40 (%63,4)
Diabetes mellitus n(%)	38 (%60,3
Smoking n(%)	42 (%66,6)
Family history n(%)	25 (%39,6)
Fasting blood glucose (mg/dl)	157,2±73,8
LDL (mg/dl)	109,3±42,7
HDL (mg/dl)	40,8±8,8
Triglyceride (mg/dl)	161,5±98,6
Total cholesterol (mg/dl)	185,0±46,9
Urea (mg/dl)	39,6±18,1
Creatinine (mg/dl)	1,02±0,35
AST (mg/dl)	28,4±11,6
ALT (mg/dl)	23,0±6,2
Hemoglobin (g/dl)	13,7±1,85
WBC (10^9/l)	8,46±1,59
PLT (10^9/l)	251,2±78,5
Sodium (mmol/l)	135,3±3,6
Potassium (mmol/l)	4,1±0,3

In the correlation analysis, we found that; there was a statistically significant strong positive correlation between LAD-CX bifurcation angle and GS ($r= 0,854$; $p<0,001$) (Figure 3). On the other hand, the correlation between LMCA length and GS was statistically nonsignificant ($r= 0,228$; $p=0,116$). Linear regression analysis showed that LAD-CX bifurcation angle is an independent risk factor for GS ($\beta=0,854$; $p=0,0001$)
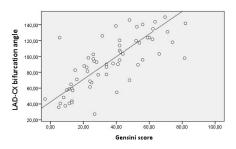

Figure 3. There is statistically significant strong positive correlation between Gensini score and LAD-CX bifurcation angle. (LAD: Left anterior descending artery; CX: Circumflex artery)

DISCUSSION

In this study, we found that there is a significant correlation between LAD-CX bifurcation angle and atherosclerotic plaque burden. Furthermore, LAD-CX bifurcation angle is an independent risk factor for atherosclerotic plaque burden.

Atherosclerosis is the underlying cause of life-threatening cardiovascular events such as myocardial infarction and stroke and represents the leading cause of morbidity and mortality (8). Shear stress, defined as a frictional force acting on vascular endothelial cells, is crucial for endothelial homeostasis under normal physiological conditions (9). Although laminar shear stress formed by endovascular laminar flow is atheroprotective, disturbed flow creates an atheroprone environment (10). Laminar flow is corrupted especially at the bifurcation sites of the vascular tree. Nonlaminar flow promotes changes in endothelial gene expression, cytoskeletal arrangement, leukocyte adhesion, and vasoreactive, oxidative, and inflammatory states of the artery which enhances atherosclerosis (11). Effect of bifurcation angle on the shear stress is previously studied in various localizations. The review by Chiu et al demonstrated that the majority of plaque formation cases occur close to bifurcations and, more specifically on the outer walls of those bifurcations where the shear stress is minimum (12). Lauric et al provided that, narrow angled symmetrical bifurcations are characterized by the protective effect on cerebral aneurysms (13). In another study, Tütüncü et al showed that widened bifurcation angle is associated with basilar bifurcation aneurysms (14). Thomas et al showed that localization of atherosclerotic plaque is associated with arterial geometries especially in or close to the coronary and carotid bifurcations (15). At the coronary anatomy, LAD-CX bifurcation is the first site on the left coronary system where laminar flow disturbs. In a study, Cui et al postulated that wider LAD-CX bifurcation angle is related to non-calcified lesions (16). Atherosclerotic plaque burden is the marker of extent and severity of CAD. It is of particular importance in the treatment and prognosis of diseases caused by atherosclerosis (17). In our study, we showed a strong positive correlation between LAD-CX bifurcation angle and gensini score. The other important point of this study was the LMCA length. Although the relationship between the coronary artery diameter and atherosclerosis is fairly well investigated (18), there is unsatisfactory data about the relationship between LMCA length and atherosclerosis. In a previous postmortem examination study, Gazetepoulos et al suggested that in patients with short LMCA the atherosclerotic lesions in the left coronary artery branches appear earlier, progress and lead more frequently to myocardial infarction, than in cases with a long left coronary artery trunk (19). Controversially, we couldn't find a significant correlation between LMCA length and GS.

LIMITATIONS OF THE STUDY

Major limitation of our study is the measurement technique of the bifurcation angle. Although the computerized tomography was the technique to measure bifurcation angle in most of the published studies, angiographic views were also used in various studies. Another limitation was the small sized study population. Further studies with larger cohorts of patients needed.

CONCLUSION

In this study, we concluded that as the LAD-CX bifurcation angle increases atherosclerotic burden significantly increases. However, LMCA length has no significant effect on the atherosclerotic burden. It might also be said that LAD-CX bifurcation angle is an independent risk factor for atherosclerotic burden.

Conflict of interest
None declared.

REFERENCES

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. The global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. TheLancet. 2006; 367(9524):1747-57.

2. Hansen T, Kilander L, Ahlström H, Lind L. Total atherosclerotic burden measured by magnetic resonance imaging is related to a five-year decline in cognitive function. Clin Physiol Funct Imaging. 2018 May;38(3):373-377.

3. Geraci G, Buccheri D, Zanoli L, Fatuzzo P, DiNatale K, Zammuto MM, Nardi E, Geraci C,

Mancia E, Zambelli G, Piraino D, Signorelli SS, Granata A, Cottone S, Mule G. Renal haemodynamics and coronary atherosclerotic burden area associated in patients with hypertension and mild coronary artery disease. Exp Ther Med. 2019 Apr;17(4):3255-3263.

4. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51:606.

5. Caro C G, Fitz-Gerald J. M and Schroter R. C (1971). Atheroma and arterial wall shear observation, correlation, and proposal of a shear-dependent mass transfer mechanism for atherogenesis. Proc. R. Soc. Lond. B Biol. Sci. 177, 109–133.

6. Stewart Dowding, Constantine Zakkaroff, Stephen Moore and Tim David. Coronary Smooth Muscle Cell Calcium Dynamics: Effects of Bifurcation angle on atheroprone conditions. Frontiers in physiology. 2018;9: 1-13. doi: 10.3389/fphys.2018.01528.

7. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 2012;51:606

8. Hackman DG, Anand SS. Emerging risk factors for atherosclerotic vascular disease: a critical review of the evidence. JAMA. 2003 Aug 20; 290(7):932-40

9. Cunningham KS, Gotlieb AI. The role of shear stress in the pathogenesis of atherosclerosis. Lab Invest. 2005 Jan;85(1):9-23.

10. Zhonghua Sun, Thanapong Chaichana. An investigation of the correlation between left coronary bifurcation angle and hemodynamic changes in coronary stenosis by coronary computed tomography angiography-derived computational Fluid Dynamics. Quant Imaging Med Surg 2017;7(5):537-548

11. A. Tedgui and Z. Mallat, "Cytokines in atherosclerosis: pathogenic and regulatory pathways," Physiological Reviews, vol. 86, no. 2, pp. 515–581, 2006

12. Chiu, J. J., and Chien, S. (2011). Effects of disturbed flow on vascular endothelium: pathophysiological basis and clinical perspectives.

Physiol. Rev. 91, 327–387. doi: 10.1152/physrev.00047.2009

13. Lauric A, Hippelheuser JE, Malek AM. Induction of aneurysmogenic high positive wall shear stress gradient by the wide angle at cerebral bifurcations, independent of flow rate. J Neurosurg. 2018 Aug 1:1-11. doi: 10.3171/2018.3.JNS173128

14. Tütüncü F, Schimansky S, Baharoglu MI, Gao B, Calnan D, Hippelheuser J, Safain MG, Lauric A, Malek AM. Widening of the basilar bifurcation angle: association with the presence of an intracranial aneurysm, age, and female sex. J Neurosurg. 2014 Dec;121(6):1401-10. doi: 10.3171/2014.8.JNS1447

15. Thomas, J. B., Antiga, L., Che, S. L., Milner, J. S., Steinman, D. A. H., Spence, J. D., et al. (2005). Variation in the carotid bifurcation geometry of young versus older adults: Implications for geometric risk of atherosclerosis. Stroke 36, 2450–2456. doi: 10.1161/01.STR.0000185679.62634.0a

16. Cui Y, Zeng W, Yu J, Lu J, Hu Y, Diao N, Liang B, Han P, Shi H. Quantification of left coronary bifurcation angles and plaques by coronary computed tomography angiography for prediction of significant coronary stenosis: A preliminary study with dual-source CT. PLoS One. 2017 Mar 27;12(3):e0174352. doi: 10.1371/journal.pone.0174352. collection 2017.

17. Neunteufl T, Katzenschlager R, Hassan A, Klaar U, Schwarzacher S, Glogar D, et al. Systemic endothelial dysfunction is related to the extent and severity of coronary artery disease. Atherosclerosis 1997;129:111-8.

18. Zhou F., Liu Y, Ge P C, Chen Z, Ding X, Liu J, Jia Q, An F, Li L, Wang L, Ma W, Yang Z, Jia E. Coronary Artery Diameter is Inversely Associated with the Severity of Coronary Lesions in Patients Undergoing Coronary Angiography. Cell Physiol Biochem 2017;43:1247–1257

19. N Gazetopoulos, PJ Ioannidis, C Karydis, C Lolas, K Kiriakou, and C Tountas. Short left coronary artery trunk as a risk factor in the development of coronary atherosclerosis. Pathological study. Br Heart J. 1976 Nov; 38(11): 1160–1165.