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Association between the bifurcation angle and the angle of the origin of the left anterior descending with the severity of coronary artery disease

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Abstract

BACKGROUND: This study aimed to evaluate the association between the bifurcation angle and the angle of the origin of the left anterior descending (LAD) coronary artery with the degree of proximal LAD (pLAD) stenosis.

METHODS: This study was cross-sectional and addressed 578 patients suspected of coronary artery disease (CAD) who underwent coronary computed tomography angiography (CCTA) because of angina pectoris symptoms at Shahid Chamran Hospital, Isfahan. PLAD stenosis as well as the left main (LM)-LAD and the LAD-left circumflex artery (LCX) (bifurcation) angles were assessed and recorded on CCTA images. Then, one-way analysis of variance (ANOVA) or chi-squared tests were used. ROC analysis was used to evaluate the diagnostic value of each of the two angles in identifying pLAD stenosis.

RESULTS: Using a cut-off value of 23° for the LM-LAD angle, the sensitivity and specificity for predicting pLAD stenosis <50% were 63.70% and 47.67%, respectively. In addition, using a cut-off value of 30° for the LM-LAD angle, the sensitivity and specificity for predicting pLAD stenosis ≥50% were 52.24% and 68.77%, respectively (P value<0.05). Moreover, for predicting pLAD stenosis <50%, a 49° cut-off for the LAD-LCX angle demonstrated a sensitivity and specificity of 61.64% and 56.99%, respectively. Furthermore, for predicting pLAD stenosis ≥50%, a 50° cut-off for the LAD-LCX angle yielded a sensitivity and specificity of 70.15% and 58.63%, respectively (P value<0.05).

CONCLUSION: The findings of this study showed that the LAD-LCX and LM-LAD angles had a direct and significant association with the severity of pLAD stenosis, such that wider angles were associated with greater pLAD stenosis.

Keywords: Bifurcation Angle; Stenosis; Left Main Coronary Artery; Left Circumflex Artery; Coronary Artery Disease; Left Anterior Descending

Introduction

Coronary artery disease (CAD) remains a global health burden, underscoring the need for innovative diagnostic approaches to improve risk stratification and preventive care[1]. Coronary computed tomography angiography (CCTA) represents a significant advancement in non-invasive cardiac imaging through its ability to precisely evaluate coronary lumen stenosis and atherosclerotic plaque characteristics, including composition and vulnerability[2,3]. This feature could be a key solution in predicting cardiac events and preventing CAD by improving the understanding of plaque vulnerability and the pathogenesis of coronary atherosclerosis[4,5].

Atherosclerotic stenosis often occurs in the arterial bifurcations and inner curvatures. Substantial research evidence indicates a direct association between hemodynamic parameters—including blood pressure, wall shear stress (WSS), and flow patterns—and atherosclerotic plaque progression[6]. Indeed, plaque accumulation and endothelial dysfunction are promoted by low WSS at coronary bifurcations that are worsened by turbulent flow patterns[7,8].

The proximal segment of the left anterior descending (pLAD) artery is a frequent site for atherosclerotic plaque formation in the coronary arteries, especially at the bifurcation where the left circumflex (LCX) and LAD arteries intersect[9].

In the past few years, much effort has been devoted worldwide to find the cause of stenosis using computational fluid dynamics (CFD) and multiple randomized clinical trials (RCTs) addressing the hemodynamic behavior of arteries[6]. Critical hemodynamic parameters, including wall pressure reduction, low WSS, and recirculation zones in blood flow, are challenging to be measured directly in patients with CADs[10].

According to findings from recent studies using CFD, the association between the LAD-LCX bifurcation angle and the occurrence of CAD is attributed to the change in WSS observed at bifurcation angles of varying sizes. Consequently, it seems that the LAD-LCX bifurcation angle may indicate the likelihood of a patient developing CAD and could be a useful tool to increase the accuracy of diagnostic reports[11,12]. In fact, it has been shown in simulated and real models that higher bifurcation angles and angles of origin of the LAD from the left main coronary artery (LMCA) may cause low WSS, which may lead to the development and progression of CAD[13].

As the quantitative diagnostic performance of left coronary bifurcation angles by CCTA has been less widely studied for predicting significant coronary artery stenosis, this study aimed to investigate the association of the bifurcation angle and LAD angle of origin with the severity of proximal LAD (pLAD) stenosis.

Materials and Methods

A cross-sectional study aimed at the diagnostic value of suspected CAD patients undergoing CCTA was conducted at Shahid Chamran Specialized Heart Center, Isfahan, Iran, in 2023.

The sample size was considered to be 610 patients at a confidence level of 95%, and considering the diagnostic sensitivity of the LM-LAD angle criterion in predicting severe LAD stenosis in previous studies equal to 73%, the matching ratio equal to 0.50[14], and the error level equal to 0.05.

The inclusion criteria comprised patients suspected of CAD with CCTA report and aged over 18 years. Patients with reports of ectatic, aneurysmal, and slow flow vessels on CCTA or patients with congenital coronary artery anomalies, previous history of coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), valvular heart diseases, or poor quality of CCTA images were excluded from the study.

Following approval by the Ethics Committee of Isfahan University of Medical Sciences (approval code: IR.MUI.MED.REC.1403.065), 610 patients were randomly selected using a random number table from the list of patients with CCTA reports. After assessing the inclusion criteria, permission was obtained via telephone call to use their information, and they were assured that their information would remain confidential. Then, in the data collection checklist, the patients' demographic information including age, gender, body mass index (BMI), weight, height, smoking status, and underlying diseases (including blood pressure, diabetes, dyslipidemia, etc.) were recorded.

CCTA was performed for all patients with a Siemens 256 multi-detector scanner and was assessed by an experienced radiologist and cardiologist for the severity of pLAD stenosis. Different plaques were assessed for the degree of artery stenosis, and the most severe stenotic plaque was considered as the severity of this artery stenosis.

Then, the LAD-LCX and the LM-LAD (bifurcation) angles were measured twice by a radiologist using 2D axial images (Figure 1).

Statistical analysis

SPSS (Ver. 26) software was used to analyze the collected data. Quantitative data were expressed as mean ± standard deviation (SD), and qualitative data as frequency (percentage). As the Kolmogorov-Smirnov test indicated the normality of the data distribution, quantitative variables among different degrees of pLAD stenosis were compared using one-way analysis of variance (ANOVA). Moreover, the frequency distribution of qualitative data was compared using the chi-square test. In addition, ROC analysis was used to evaluate the diagnostic value of the bifurcation angles and the LM-LAD angle in predicting pLAD stenosis. The specificity, sensitivity, area under the curve indices, and positive and negative predictive values were also reported. All analyses considered a significance level of less than 0.05.

Results

In this study, two patients with congenital coronary artery anomalies, ten patients with previous PCI and CABG, one patient with valvular heart disease, and nineteen patients with poor quality of CCTA images were excluded.

In patients with normal pLAD, 203 (55.6%) cases were female and 162 (44.4%) cases were male, with a mean age of 53.03±11.42 years. In patients with stenosis <50%, 61 (41.8%) cases were female and 85 (58.2%) cases were male, with a mean age of 60.41±11.52 years. Moreover, in patients with stenosis ≥50%, 28 (41.8%) cases were female and 39 (58.2%) cases were male, with a mean age of 65.39±9.51 years. Statistically, the frequency distribution of pLAD stenosis showed a significant difference in terms of factors such as gender, age, diabetes, dyslipidemia, and hypertension (P value<0.05) (Table 1).

The results of evaluating the LAD-LCX (bifurcation) and the LM-LAD angles with the degree of pLAD stenosis revealed that the LM-LAD angle in the normal group (without pLAD stenosis), with a mean of 24.42±11.27°, was significantly lower than the angle in the pLAD stenosis <50% group, with a mean of

Figure 1. Measurement of two angles LMCA-LAD and LAD-LCX, LMCA (red arrow), LAD (blue arrow) and LCX (green arrow)

Table 1. Patients' baseline and clinical characteristics by degree of pLAD stenosis

Characteristics		Normal	< 50% stenosis	≥ 50% stenosis	P value
Sex	Female	203(55.6%)	61(41.8%)	28(41.8%)	0.006
	Male	162(44.4%)	85(58.2%)	39(58.2%)	
Age; year		53.03±11.42	60.41±11.52	65.39±9.51	<0.001
Height; cm		167.34±9.53	168.53±9.89	166.01±8.29	0.178
Weight; kg		77.58±13.46	77.45±14.53	73.97±12.03	0.129
BMI; kg/m^2		27.74±4.58	27.49±6.92	26.87±4.29	0.447
DM		75(20.5%)	32(21.9%)	24(35.8%)	0.022
Dyslipidemia		164(44.9%)	82(56.2%)	41(61.2%)	0.010
HTN		145(39.7%)	78(53.4%)	39(58.2%)	0.002
Smoking		67(18.4%)	33(22.6%)	12(17.9%)	0.520

Data shown mean± SD or n(%)

Table 2. Determination and comparison of the mean LM-LAD (Bifurcation) and LAD-LCX angles based on the degree of pLAD stenosis

Angles	Normal	< 50% stenosis	≥ 50% stenosis	P value
LM–LAD angle; °	24.42±11.27	27.46±11.54	29.66±10.00	<0.001
LAD–LCX angle; °	50.09±18.75	57.47±21.73	59.45±19.38	<0.001

Data shown mean± SD

Table 3. Diagnostic value of LM-LAD and LAD-LCX angles in predicting pLAD stenosis

Angles	Cut off points	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV	AUC	P value
LM–LAD angle	>23 *	63.70(55.3 - 71.5)	47.67(42.4 - 52.9)	32.7	76.7	0.569	0.0158
	>30 **	52.24(39.7 - 64.6)	68.77(63.7 - 73.5)	23.5	88.7	0.638	0.0004
LAD–LCX angle	>49 *	61.64(53.2 - 69.6)	56.99(51.7 - 62.1)	36.4	78.8	0.603	0.0003
	>50 **	70.15(57.7 - 80.7)	58.63(53.4 - 63.7)	23.7	91.5	0.653	0.0001

*: Comparison of pLAD stenosis <50% with proximal LAD
**: Comparison of pLAD stenosis ≥50% with proximal LAD

27.46±11.54°, and the angle in the pLAD stenosis ≥50% group, with a mean of 29.66±10.00° (P value<0.001). Furthermore, the LAD-LCX angle in the normal group (without pLAD stenosis), with a mean of 50.09±18.75°, was significantly lower than the LAD-LCX angle in the pLAD stenosis <50% group, with a mean of 57.47±21.73°, and the angle in the pLAD stenosis ≥50% group, with a mean of 59.45±19.38° (P value<0.001) (Table 2).

Based on ROC analysis, the LM-LAD angle with a cut-off point >23° had a sensitivity of 63.70% and specificity of 47.67% in predicting pLAD stenosis <50% (P value<0.01). Moreover, the LM-LAD angle with a cut-off point >30° had a sensitivity of 52.24% and specificity of 68.77% in predicting pLAD stenosis ≥50% (P value<0.01). Furthermore, the LAD-LCX angle with a cut-off point >49° had a sensitivity of 61.64% and specificity of 56.99% in predicting pLAD stenosis <50% (P value<0.01). In addition, the LAD-LCX angle with a cut-off point >50° had a sensitivity of 70.15% and specificity of 58.63% in predicting pLAD stenosis ≥50% (P value<0.01) (Table 3, Figure 2).

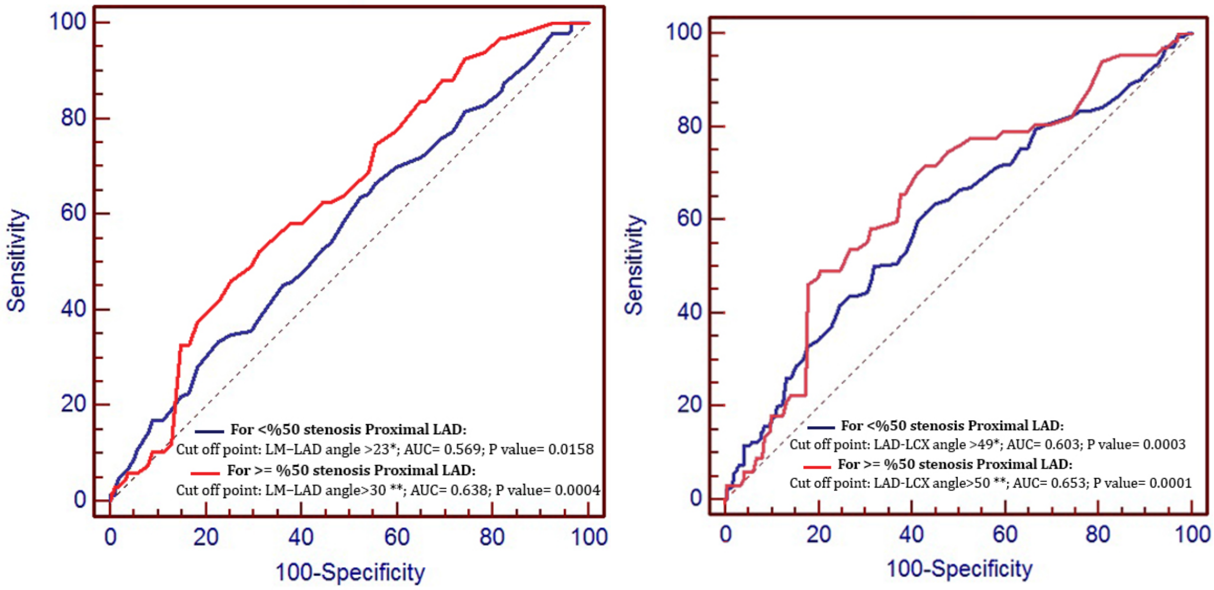

Figure 2. ROC plot of LM-LAD and LAD-LCX angles for predicting the degree of pLAD stenosis

Discussion

In the present study, the degree of stenosis of the pLAD and the relationship of demographic variables and comorbidities with the severity of stenosis (normal, <50%, and ≥50%) were investigated in 578 patients with CAD. While such a relationship was not observed for height, weight, BMI, and smoking status, comorbidities (diabetes, dyslipidemia, and hypertension) were associated with pLAD stenosis.

The results of the present study examining the degree of pLAD stenosis revealed that 25.3% and 11.6% of patients had stenosis <50% and ≥50%, respectively. The frequency distribution of pLAD stenosis showed significant differences in patients' baseline and clinical characteristics such as gender, age, diabetes, dyslipidemia, and hypertension.

In line with the findings of the present study, Yahia et al. showed that patients with significant pLAD stenosis, as compared to patients with non-significant pLAD stenosis, were older, had a higher frequency of diabetes, and had higher levels of serum creatinine and low-density lipoprotein (LDL-C)[14].

Many other studies have also reported age, DM, and DLP as risk factors associated with worsening vascular function and increased risk of CAD[15–17]. In this regard, it has been shown that statins and thiazolidinedione should be considered as a therapeutic approach in secondary prevention of heart diseases because it seems that their administration can significantly prevent the progression of coronary atherosclerotic plaques[18–20].

In addition, the findings of this study indicated that the LAD-LCX and LM-LAD angles were significantly associated with the severity of pLAD stenosis. In detail, wider angles were associated with the severity of pLAD. The cut-off value of 23° for the LM-LAD angle in predicting pLAD stenosis <50% had a sensitivity of 63.70% and specificity of 47.67%. Moreover, the cut-off value of 30° for the LM-LAD angle in predicting pLAD stenosis ≥50% had a sensitivity of 52.24% and specificity of 68.77%. Furthermore, the cut-off value of 49° for the LAD-LCX angle in predicting pLAD stenosis <50% had a sensitivity of 61.64% and specificity of 56.99%, while the cut-off value of 50° for the LAD-LCX angle in predicting pLAD stenosis ≥50% had a sensitivity of 70.15% and specificity of 58.63%.

Konishi et al. reported a cut-off value of 34° for the LM-LAD angle in predicting restenosis after pLAD stenting. Moreover, Girasis et al. and Temov et al. reported a cut-off value of 80° for the LAD-LCX angle for the presence of CAD or LAD stenosis[11,15,20]. Moon et al. also reported a cut-off value of 40º for the LM-LAD angle in predicting LAD stenosis with a sensitivity of 88.9% and specificity of 68.5%. Moreover, they reported a cut-off value of 60º for the LAD-LCX angle in determining LAD stenosis with a sensitivity of 73.2% and specificity of 53.1%[10].

Low WSS stress followed by LAD atherosclerosis progression is caused by wide LAD-LCX and LM-LAD angles. Blood turbulence increases in line with the increase in the bifurcation angle. Induction of endothelial dysfunction, enhancement of adhesion molecule expression, foam cell production, and proliferation of smooth muscle cells are caused by turbulence. The progression of coronary plaques around the bifurcation angle is contributed to by the mentioned mechanisms[21,22].

Nevertheless, there exists a difference in the ratio of the LM-LCX and the LM-LAD angles that constitute the LAD-LCX angle, even in spite of the same LAD-LCX angle. A region of low shear stress may be formed in the bifurcating region (LM-LAD) in the case of a large contribution of the LM-LAD angle. In other words, in the case of the same LAD-LCX angle, there may be a large or small LM-LAD angle, and when the LM-LAD angle is large, low shear stress may be applied[18,23].

Conclusion

According to the results of this study, the LM-LAD and LAD-LCX angles can predict the severity of proximal LAD stenosis. In detail, the widening of these angles is significantly associated with the severity of proximal LAD stenosis. Therefore, it seems that careful follow-up of these patients and preventive measures to avoid the occurrence or progression of coronary artery stenosis can affect the cardiovascular outcome.

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Conflict of interests

The authors declare no conflict of interest.

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Author's Contributions

Study Conception or Design: MM, FP
Data Acquisition: AMM, FP
Data Analysis or Interpretation: SZ, FP
Manuscript Drafting: MM, SZ, FP
Critical Manuscript Revision: MM, SZ, FP
All authors have approved the final manuscript and are responsible for all aspects of the work.

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