Original Article

Relationship between Modifiable Atherosclerotic Cardiovascular Risk Factors and Coronary Artery Bifurcation Lesion

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Abstract

Background: Modifiable atherosclerotic cardiovascular disease risk factors are hypertension, diabetes mellitus, dyslipidemia, cigarette smoking, and obesity; the term coronary artery bifurcation is used when a coronary artery divides into two hemodynamically important branches or when the main branch has a hemodynamic significant side branch, bifurcation lesion represent 20% or more of coronary artery stenoses undergoing angiography. **Objectives:** To evaluate the relationship of hypertension, diabetes, dyslipidemia, cigarette smoking, and obesity to coronary bifurcation disease. **Materials and Methods:** In a cross-sectional study conducted in the Iraqi Center for Heart Diseases from May 2020 to May 2021, a total of 140 adult patients (70 cases with coronary bifurcation lesions and 70 control cases with non-bifurcation lesions) with angiography-documented stenotic coronary artery disease (CAD) were defined. Case demographics and modifiable CAD risk factors were addressed. **Results:** In the bifurcation group, the non-bifurcation lesion was mostly an associated angiographic finding (82%). The most significantly correlated atherosclerotic risk factor with bifurcation lesion compared to non-bifurcation lesion was diabetes, followed by systemic hypertension. Dyslipidemia was the most common prevalent risk factor, equally distributed in both groups. Smoking and obesity were distributed nearly equally in both groups. **Conclusion:** There is a significant relationship between diabetes and hypertension with coronary bifurcation lesions compared to non-bifurcation lesions.

Keywords: Bifurcation lesion, coronary artery disease, risk factors

Introduction

Coronary artery disease is widely prevalent both in developed and developing countries and continues to be a major leading cause of morbidity and mortality despite recent advances in diagnostic facilities and treatment modalities.[1]

Cardiovascular diseases account for most of noncommunicable disease deaths. It numbers at 17.7 million annually all over the world, particularly in low and middle-income countries.[2]

Cardiovascular disease ranks first as a cause of noncommunicable disease-related death in Iraq.[3]

While globalization often improves healthcare systems, the adoption of Western lifestyles can lead to a higher prevalence of modifiable cardiovascular risk factors, particularly high BMI, diabetes mellitus, hypertension, and high cholesterol. Tobacco consumption is supposed to be decreasing but could easily become the leading risk factor for years of life lost according to the worst health scenarios.[4]

Smoking proved an important predictive factor for coronary artery disease (CAD), followed by hypertension, diabetes, dyslipidemia, and family history of premature CAD (males <55 years, females <60 years) in descending order of significance. Obesity is a known risk factor for DM, hypertension, dyslipidemia, and CAD. Smoking,

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dyslipidemia, and diabetes were positively associated with atherosclerotic involvement of all three major coronary arteries, whereas hypertension was related to significant stenosis of the left anterior descending and left circumflex arteries. Diabetes and age were strong CAD risk factors correlated to left main CAD.[5]

The term coronary bifurcation is generally used when a coronary artery divides into two equally important branches or when the main branch has a side branch (SB) that is large enough to be of hemodynamic significance.[6]

The European Bifurcation Club defines a bifurcation lesion as a coronary artery narrowing occurring adjacent to and/or involving the origin of a significant SB, for which acute closure would be substantially detrimental (e.g., symptoms, location of ischemia, viability, collateralization, vessel, left ventricular function).[7] The Medina classification is a simplified and universal classification of bifurcation lesions validated by the European Bifurcation Club.[8]

It consists of recording any narrowing in excess of 50% in each of the three arterial segments of the bifurcation in the following order: proximal main vessel, distal branch, and SB; 1 is used to indicate the presence of significant stenosis, and 0 represents the absence of stenosis. Simple bifurcations are those that have SB origins without significant stenosis ([1,1,0], [1,0,0], and [0,1,0]). Complex (true) bifurcations, in which, in addition to SB significant stenosis, the proximal [1,0,1], distal [0,1,1], or both [1,1,1] components of the main vessel are involved.[9]

Coronary artery bifurcations are susceptible to atherosclerotic plagues as a result of the unique local flow patterns and the subsequent endothelial shear stress (ESS) environment that are conducive to the development of plaques along the lateral walls of the main vessel and SBs, a distinct flow pattern is observed with local low and oscillatory ESS, while moderate/high ESS develops at the flow divider (carina) which is generally protected, histopathologic studies have shown that the distribution of plaque at bifurcation regions is related to the local ESS patterns. The local ESS profile also influences the outcome of percutaneous intervention in bifurcation lesions.[10]

The aim of the study was to evaluate the predominant association between modifiable cardiovascular disease risk factors like DM, Hypertension, Smoking dyslipidemia, and obesity with coronary artery bifurcation lesions compared to non-bifurcation lesions.

Materials and Methods

Study design

A cross-sectional study was performed at the Iraqi Center for Heart Diseases between May 2020 and May 2021.

Direct interview with a predesigned questionnaire to collect demographic and cardiovascular risk factors. The main clinical and demographic characteristics of the patients were recorded; the age, weight, height, body mass index (BMI), and gender of the cases were defined. Obesity was defined as a BMI of over 30 kg/m^2. BMI = (body weight—kg]/[length—m^2].

Patients were classified as current cigarette smokers (pack-years), nonsmokers, and ex-smokers; the patient who quit smoking less than 2 years period was included in the smoker category. The presence of diabetes was defined as at least two fasting blood glucose levels of over 126 mg/dl, or two hours postprandial venous glucose level of >200 mg/dl, or glycated hemoglobin of > 6.5%, or use of antidiabetic medication.

Hypertension was defined as at least two blood pressure levels of over 140/90 mm Hg or on antihypertensive medication.

In these high to very high-risk patient groups (with established CAD), hypercholesterolemia was defined as a low-density lipoprotein level > 100 mg/dl.

Most selected patients have had prior diagnostic coronary angiography and were referred for elective PCI; others were referred for first diagnostic coronary angiography and/or *ad hoc* PCI. Almost all patients are admitted to a precath facility with stable CAD.

Selective coronary angiography was performed using standard techniques (mostly femoral and occasionally radial approaches); atherosclerotic significant stenotic lesions of the main epicardial coronary vessels and/or SBs were assessed visually by an independent expert interventional cardiologist with the comparison of the stenotic areas with the adjacent normal segments.

Patients with nonsignificant coronary artery lesions were excluded from the study.

Inclusion criteria

1. In both groups, atherosclerotic lesions creating stenosis >70% in LAD, LCx, or RCA and > 50% stenosis in LMCA were candidates for our study.
2. In addition to the above, in the bifurcation lesion group true bifurcation lesion (Medina classification), SB more than 2.0–2.5 mm diameter with more than 5 mm significant proximal stenosis considered hemodynamically significant (supplying more than 10% of the myocardium) and enrolled in inclusion criteria.

Exclusion criteria

1. In both groups, atherosclerotic lesions creating stenosis <70% in LAD, LCx, and RCA and <50% stenosis in LMCA were excluded from the study.
2. In bifurcation lesion group SB ostial lesion, less than 5 mm. Length or less than 2.0–2.5 mm diameter excluded from the study.

Table 1: Age distribution according to studied groups

	Group	No.	Mean age	Std. deviation	*P* value
Age (years)	BL (38–85) years	70 (50%)	57.67	9.237	0.934
	NBL (36–83) years	70 (50%)	57.80	9.193	

Significant age difference between the two groups is $P < 0.05$

3. Detailed bifurcation lesion treatment and procedure technique beyond the scope of this study.

Statistical analysis

Collected data were categorized into Microsoft Office Excel sheet 2016, the Statistical Package V.24 for Social Science (SPSS, Inc., Chicago) program, and independent two samples *t*-test utilized to define significant differences between numerical variables and expressed as percentages. The Chi-square test was used for intergroup analysis of related categorized variables. A *P*-value of less than 0.05 is considered a statistically significant discrimination point. Descriptive statistics are presented as tables and grafts.

Ethical approval

The study was approved by the Internal Medicine Department Ethical Committee, College of Medicine, University of Babylon. Patients were informed about enrollment in the study, and verbal consent was obtained. According to document number 315, a local ethics commission reviewed and gave its approval to the study protocol, subject information, and permission form on April 18, 2020.

Results

This study included 140 patients with coronary angiography-documented CAD divided into two groups: Group 1 (cases) included 70 patients with bifurcation lesions (according to bifurcation lesion definition), and Group 2 (control) and included 70 patients with non-bifurcation coronary lesion.

Table 1 shows that the mean age of the bifurcation group was 57.67 ± 9.24 years, which is not significantly different than the mean age of the non-bifurcation group (57.8 ± 9.19 years), *P* value = 0.934 according to independent 2 samples *t*-test.

Figure 1 shows that males constitute 98 (70%) and females constitute 42 (30%) cases of the total studied sample; the same gender percentages are represented in the two groups with no significant differences, *P* value = 1.

Figure 2 illustrates that of the total sample, 36.6% were obese, 44.2% were smokers, 82.1% were hypercholesterolemic, 50.7% were hypertensives, and 61.4% were diabetics. On the other hand, of the total study sample, 61.4% had normal BMI, 55.8% were nonsmokers, 17.9% had normal LDL-cholesterol, 49.3% were normotensives, and 38.6% were nondiabetics.

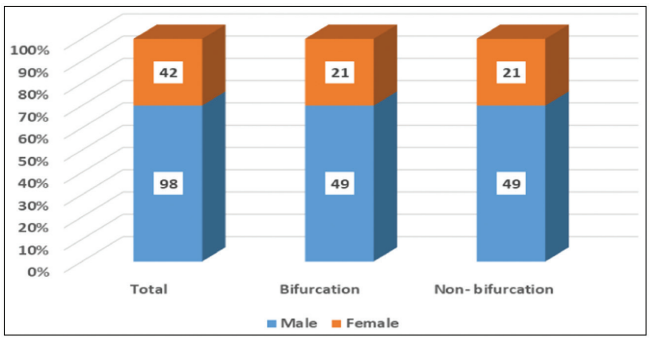

Figure 1: Gender distribution in studied groups

Table 2 shows that 61.4% of the total sample had diabetes; the rate of diabetes in the bifurcation group (71.4%) was significantly higher than that in the non-bifurcation group (51.45%), *P* value = 0.015.

About 50.7% of the total studied sample had hypertension; the rate of hypertension in the bifurcation lesion group (60%) was significantly higher than that in the non-bifurcation lesion group (41.4%), *P* value = 0.028.

A percentage of 82.1% of the total sample had increased LDL-cholesterol (dyslipidemia); the rate of elevated LDL in the bifurcation lesion group (80%) was not significantly different than that in non-bifurcation lesion group (84.2%), *P* value = 0.508.

About 44.2% of the total sample were smokers; the rate of smoking in the bifurcation lesion group (51.4%) was not significantly different than that in the non-bifurcation lesion group (36.2%), *P* value = 0.071.

About 38.5% of the total sample were obese; the rate of obesity in the bifurcation lesion group (44.2%) was not significantly different than that in the non-bifurcation lesion group (32.8%), *P* value = 0.165.

For every cardiovascular risk factor with $P < 0.05$, significant differences were derived from comparisons between specific angiographic groups (bifurcation and non-bifurcation).

Table 3 shows that LAD lesions formed 47.1% of the total lesion; the rate of LAD lesions in the bifurcation group was significantly higher than that of the non-bifurcation group, *P* value = 0.001.

LCx lesions formed 12.5% of total lesions; the rate of LCx lesions in the bifurcation group was significantly higher than that of the non-bifurcation group *P* value = 0.001.

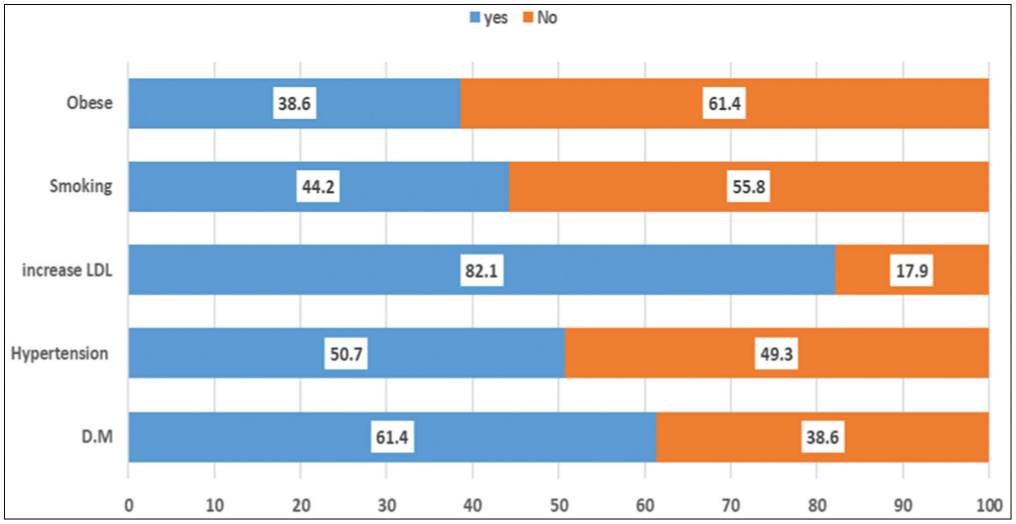

Figure 2: Distribution percentages of studied cases according to studied variables (yes = have a risk factor, no = no risk factor)

Table 2: Association between studied variables and group of study

		Total		Bifurcation		Non bifurcation		*P* value
		N	%	*N*	%	*N*	%	
DM	Yes	86	61.4	50	71.4	36	51.4	0.015
	No	54	38.6	20	28.6	34	48.6	
Hypertension	Yes	71	50.7	42	60.0	29	41.4	0.028
	No	69	49.2	28	40.0	41	58.5	
LDL	Yes	115	82.1	56	80.0	59	84.2	0.508
	No	25	17.8	14	20.0	11	15.7	
Smoking	Yes	62	44.2	36	51.4	25	36.2	0.071
	No	78	55.8	34	48.6	44	63.8	
Obese (BMI)	Yes	54	38.5	31	44.2	23	32.8	0.165
	No	86	61.4	39	55.7	47	67.1	

Table 3: Distribution of studied cases according to number of lesions in epicardial coronary vessel and group of study

Vessel	Total		Bifurcation		Non bifurcation		*P* value
	N	%	*N*	%	*N*	%	*P*
LAD	66	47.1	43	61.4	23	32.9	0.001
LCX	18	12.9	17	24.3	1	1.4	0.001
RCA	8	5.7	1	1.4	7	10.0	0.029
LMCA	13	9.2	5	7.1	8	11.4	0.001
Single	92	65.7	61	87.1	31	44.3	0.001
Double	30	21.4	8	11.4	22	31.4	0.004
Triple	18	12.9	1	1.4	17	24.3	0.001

Table 4: Distribution of total occlusion cases in epicardial coronary vessel and group of study

Vessel	Total no.		Bifurcation		Non-bifurcation		*P* value
	N	%	*N*	%	*N*	%	*P*
LAD	9	6.4	4	5.7	5	7.1	0.063
LCX	8	5.7	6	8.5	2	2.8	0.012
RCA	13	9.2	6	8.5	7	0.10	0.51
Total	30	21.4	16	22.8	26	37.14	0.001

RCA lesions formed 5.7% of total lesions; the rate of RCA lesions in the bifurcation group was significantly lower than that of the non-bifurcation group, *P* value = 0.029.

LMCA lesions constitute 9.1% of total lesions; its rate in the bifurcation group was significantly lower than that of the non-bifurcation group, *P* value = 0.001.

Single lesions formed 65.7% of total lesions, and its rate in the bifurcation group was significantly higher than that of the non-bifurcation group, *P* value = 0.001.

Double lesions formed 21.4% of total lesions, and its rate in the bifurcation group was significantly lower than that of the non-bifurcation group, *P* value = 0.004.

Triple lesions formed 12.9% of total lesions, and its rate in the bifurcation group was significantly lower in bifurcation than that of the non-bifurcation group, *P* value = 0.001.

For every CAD with $P < 0.05$, the significant differences were derived from comparisons between specific angiographic groups (bifurcation and non-bifurcation).

Table 4 illustrates the prevalence of total occlusion in the right and left coronary circulation, which approaches 21.4% of the total sample, and RCA was the commonest vessel involved in total occlusive disease at 13%, with no significant difference between the two groups, *P* value = 0.51.

LAD CTO lesions formed 6.4% of total lesions, with no significant difference between the two groups, *P* value = 0.063. Of total occlusive lesions, LCx CTO lesions formed 5.7%, which is significantly higher in the bifurcation group relative to the non-bifurcation group *P* value = 0.012.

For every CAD with $P < 0.05$, the significant differences were derived from comparisons between specific angiographic groups (bifurcation and non-bifurcation).

Compared to multiple lesions, Table 5 shows that significant associations were noticed between single lesions and DM, HTN, and non-hypertensives in bifurcation lesions, *P* value = 0.001, and non-DM and single lesions, *P* value = 0.045.

For every cardiovascular risk factor (present or absent) with $P < 0.05$, the significant differences were derived from comparisons between specific angiographic groups (single and Multiple vessel disease groups).

Table 5 shows stenotic LAD disease, compared to LCx or RCA disease, has no significant correlation with DM nor HTN in the bifurcation group, with a *P* value of more than 0.05 [Table 6].

The same results were obtained in the non-bifurcation group.

In BL and NBL angiographic groups, LAD disease vs. other vessel disease in DM and HTN, significant differences were derived from $P < 0.05$.

Discussion

SVD constitutes 65.7% of total lesion number, which was significantly higher in the bifurcation group 87.1% versus the non-bifurcation group 44.3%, and LAD lesion forms 47.4% from total coronary lesions, and the least common vessel affected is the RCA lesion, 5.7%.

LMCA lesion constitutes 9.2% of the total sample, which was more prevalent in NBL group as an SVD or part of MVD.

Total occlusive (CTO) lesions approach 21.4% of the total sample, mostly prevalent in diabetic, elderly males. RCA was the commonest vessel involved in total occlusive disease.

DVD constitutes 21.4% of the total studied sample, with a significantly higher percentage of 31.4% in the non-bifurcation group versus 11.4% in the bifurcation group.

Triple vessel disease (TVD) constitutes 12.9% of the total studied sample, with a significantly higher percentage in the non-bifurcation 24.3% versus 1.4% bifurcation arm of the study.

These study results sequence from highest to lowest (SVD, DVD, TVD) in the two groups are comparable to results achieved by Mohammed *et al.*[11] Iraq who found that SVD accounts 35%, followed by DVD and TVD, around 23% for each, and Deora *et al.*,[12] who found that SVD, DVD, and TVD constitute (30.6%, 15.3%, and 10.5%), respectively.

Contrary to our study findings, Shah *et al.*,[13] found that TVD constituted the highest percentage, 45%, followed by DVD (18.6%) and SVD (14.6%), and Akanda *et al.*[14] who found that TVD, DVD. And SVD constitutes (40.6%, 18.6%, and 14.5%) respectively.

DM is a known risk factor for CAD; in addition, other independent CAD risk factors like hypertension and dyslipidemia are higher in DM. However, a comprehensive clinical and statistical analysis for complex bifurcation lesion or CTO are lacking.[15-17]

In this study, diabetes was approximately 61.4% of the total sample, with a significantly higher percentage (71.4%) in the bifurcation arm of the study compared with the non-bifurcation (51.45%); this result concurs with studies conducted by Mustafa *et al.*[15] who found that 31% of diabetics have complex bifurcation lesions and only 14% of nondiabetics have coronary bifurcation lesions, and Baris *et al.*[18] who found significantly higher bifurcation and ostial lesions over non-bifurcation lesions in diabetics, and Myrto *et al.*[19] who found that diabetes was the only risk factor significantly associated with LAD-diagonal bifurcation sites.

Diabetic patients are known to have increased atherosclerotic burden, MVD, and a high number of

Table 5: Distribution of cases according to studied variables with group of study and number of lesions

Variable		Group	Single lesion		Multilesions		*P* value
			No.	%	No.	%	
DM	DM	BL	44	88.0	6	12.0	0.001
		NBL	14	38.9	22	61.1	
	No DM	BL	15	75.0	5	25.0	0.045
		NBL	16	47.1	18	52.9	
HTN	Hypertens	BL	33	78.6	9	21.4	0.001
		NBL	10	34.5	19	65.5	
	Normal	BL	26	92.9	2	7.1	0.001
		NBL	20	48.8	21	51.2	
LDL	Increase	BL	49	87.5	7	12.5	0.001
		NBL	26	44.1	33	55.9	
	Normal	BL	10	71.4	4	28.6	0.080
		NBL	4	36.4	7	63.6	
Smoking	Smoker	BL	29	80.6	7	19.4	0.078
		NBL	15	60.0	10	40.0	
	Nonsmoking	BL	30	88.2	4	11.8	0.001
		NBL	15	34.1	29	65.9	
BMI	Obese	BL	25	80.6	6	19.4	0.002
		NBL	9	39.1	14	60.9	
	Normal	BL	34	87.2	5	12.8	0.001
		NBL	21	44.7	26	55.3	

Table 6: Association between LAD lesions in DM and hypertension according to lesion type

		DM				HTN			
		DM		No DM		HTN		Non-HTN	
		No	%	No	%	No	%	No	%
Bifurcation	LAD	36	70.6%	15	29.4%	28	54.9%	23	45.1%
	Other	14	73.7%	5	26.3%	14	73.7%	5	26.3%
P value			0.799				0.154		
Non-bifurcation	LAD	30	55.6%	24	44.4%	23	42.6%	31	57.4%
	Other	6	37.5%	10	62.5%	6	37.5%	10	62.5%
P value			0.204				0.719		

complex lesions, such as long lesions and diffuse small vessel disease.[20,21] Some of these results contradict the results of this study, which show that SVD in bifurcation and non-bifurcation groups was more significantly associated with DM than MVD.

LAD is the commonest site of differential epicardial coronary vessel afflicted by atherosclerotic pathology and has been reported more frequently in DM.[22] In this study, LAD lesion was significantly higher in the bifurcation group (61.4%) compared to that of the non-bifurcation group (32.9%); nevertheless, no significant association was appreciated between diabetes and LAD lesion in either group.

Hypertension is the second most common preventable CAD risk factor in several studies.[23-25] In this study, 50.7% of the total studied sample were hypertensive patients with a statistically significant correlation between hypertension and bifurcation lesion (60%) compared to non-bifurcation lesion (41.4%).

There was no significant difference in differential epicardial vessel lesions between the two studied groups in association with hypertension.

Dyslipidemia constitutes the highest ranked percent in this study, mounted to 82.1% of the total sample; this result was higher than previous studies conducted by Ameen *et al.* Sanghvi *et al.*[25] and Myrto *et al.* where hypercholesterolemia affects 23%–42% of the total studied sample, this wide discrepancy in results probably resulted from sample selection in our study involves only angiography documented significant CAD cases (established CAD), with the exclusion of normal cases, diabetes and obesity (with their associated dyslipidemia) are highly prevalent in our study, in addition, noncompliance or using cheap generic tablets, suboptimal statin dose, and avoidance of high-intensity statin regimen use which indicated in high percent of established CAD patients.

There was no considerable relation between high LDL cholesterol and BL compared to NBL. Smoking is a common preventable CAD risk factor; there is a wide difference in the prevalence of smoking habit in different societies in the range (10%–52%)[18,19] worldwide, 42.2% of the total study sample are smokers with no significant difference in CAD prevalence between the two groups.

Conclusions

There is a significant relationship between DM and bifurcation lesions, and there is also a significant relationship between hypertension and bifurcation lesions. The most common epicardial coronary vessel involved in significant atherosclerotic disease is LAD, which is affected nearly equally in bifurcating and non-bifurcating vessels. The researchers found a single vessel disease compared to multivessel disease in both bifurcating and non-bifurcating vessels is significantly correlated with DM, HTN, high LDL cholesterol, high BMI, and smoking; also, the researchers found LMCA and CTO lesions were common CAD lesions.

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Conflicts of interest

There are no conflicts of interest.

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