

Risk Factors for Isolated Left Main Coronary Artery Disease

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ABSTRACT

Background & objective: Left main coronary artery (LMCA) stenosis (defined as 50 or > 50 percent narrowing of luminal diameter) usually has a bad prognosis unless revascularization done. Isolated left main coronary artery (ILMCA) disease is a rare clinical entity. Although it carries a grave prognosis, its etiology is not well-understood. Determining risk factors for ILMCA disease might be promising in the preventive strategy of ischemic heart diseases. The aim of this study was to determine the demographic and traditional risk factors for left main coronary artery disease.

Methods: This cross-sectional study was done on patients who underwent coronary angiogram (CAG) at Ibrahim Cardiac Hospital & Research Institute from February 2005 to June 2009. Total number of procedures done in Cath Lab was 7103. Of them 6708(94%) cases underwent CAG. Only 18 of them (0.27%) had isolated left main lesion and were included as cases. Patients who did not have ILMCA were taken as controls. The number of controls selected was 8 times the number of cases (n = 144). Of them 3 were excluded because of incomplete data leaving 141 controls finally. Fifty or > 50% stenosis in the left main was considered as significant stenosis. Major demographic and clinical information of patients were collected from the database of the Institute and were compared between the case and control groups.

Results: Of the 18 subjects who had ILMCA disease 44.4% exhibited stable angina, 27.8% had ACS. One third of these patients had normal ECG, ST-T changes in another one third of the patients and 11% had previous MI. 16.7% patients had wall motion abnormality in echocardiogram. Only 4 out of these 18 patients had ETT done before CAG and all were found positive. Patients with ILMCA disease were comparatively old (> 50 years) than the patients without ILMCA disease (p = 0.448). Females were more prevalent in the case group (27.8%) than that in the control group (22.2%) (p = 0.854). There was no significant difference between patients with or without ILMCA disease in terms of traditional risk factors for ischemic heart diseases like hypertension, diabetes, smoking habit, dyslipidemia and family history of ischemic heart diseases (p > 0.05).

Conclusion: Isolated and significant LMCA disease is an unusual angiographic finding and presents most commonly as stable angina. A female preponderance is usually observed. The prevalence of atherosclerotic risk factors of these patients is similar to that of the general population undergoing coronary angiogram.

Key words: Isolated left main disease, risk factors, coronary angiogram and significant lesion.

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Introduction

Left main coronary artery (LMCA) disease was first described in 1912 by James Herrick in a patient with acute myocardial infarction.¹ Angiographically significant LMCA stenosis is defined as percent diameter stenosis of 50% or more of luminal diameter of the left main

coronary artery. It accounts for 3-5% of patients undergoing cardiac catheterization for ischemic chest pain, congestive heart failure, or cardiogenic shock,² and is frequently accompanied by concomitant involvement of 1 or more of other epicardial vessels.^{3,4} Isolated and significant involvement of LMCA (ILMCA) in the

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absence of angiographically visible lesions in other epicardial vessels constitutes an unusual clinical entity. The etiology of ILMCA disease is poorly understood owing to its rare occurrence. This paper intends to find the demographic and clinical characteristics of patients to be associated with ILMCA stenosis.

Methods

This cross-sectional study was done on patients who underwent CAG at Ibrahim Cardiac Hospital & Research Institute from February 2005 to June 2009. Major demographic and clinical information of patients who underwent CAG (n = 6708) were kept along with angiographic findings in the database. Total number of procedures done in Cath Lab was 7103. Of them 6708(94%) cases underwent coronary CAG. Selective coronary arteriography was performed in almost all cases via the femoral route through Judkins catheter.⁵ Multiple views projection were recorded for each patient. The angiograms of 6708 patients selected from our angiography database were reviewed independently and only those cases were retained as ILMCA disease when there was a consensus that significant LMCA disease was present in the absence of angiographically significant lesions in other coronary vessels. Out of 6708 subjects, 321(4.8%) had significant left main artery lesion (obliteration of 50 or > 50% of the luminal diameter). However majority (n = 303) of them had concomitant significant lesions in other coronary arteries. Only 18 patients had isolated left main coronary lesions and were included as cases. Patients who underwent coronary angiogram but who did not have significant left main lesion were taken as controls. The number of controls selected was 8 times the number of cases (n = 144). Of them 3 were excluded for incomplete data leaving 141 finally to form control group. Statistical analyses were conducted using SPSS, version 11.5. Differences among groups were assessed by Chi-squared (χ^2) Test for categorical variables. Level of significance was set at 0.05 and p value < 0.05 was considered significant.

Results

Of the 18 subjects who had ILMCA disease, 8(44.4%) exhibited stable angina, 5(27.8%) had ACS (table I). One-third of these patients had normal ECG, ST-changes in another one third and previous MI in 11% cases. Only 4 out of these 18 patients had ETT done before CAG and all were found positive. The demographic characteristics and atherosclerotic risk factor profiles of patients of case and control groups are illustrated in table II & table III. Patients with isolated left main lesion were comparatively old (> 50 years) than the patients without isolated left main lesion (p = 0.448). Females were more

prevalent in the case group (27.8%) than that in the control group (22.2%) (p = 0.854). There was no significant difference between patients with or without

Table I. Distribution of patients with ILMCA disease by their presentation

Presentation	Frequency	Percent
Stable Angina	08	44.4
ACS (UA & AMI)	05	27.8
Old MI	02	11.1
Other	03	16.7

Table II. Demographic characteristics of the patients with ILMCA lesion

Demographic characteristics	ILMCA lesion		p-value
	Present(n = 18)	Absent(n = 141)	
Age (yrs.)			
50	5(27.8)	52(36.9)	
> 50	13(72.2)	89(63.1)	0.448
Mean \pm SD	54.8 \pm 9.0	54.8 \pm 9.0	
Sex			
Male	13(72.2)	109(77.3)	
Female	5(27.8)	32(22.7)	0.854
BMI (kg/m²)*			
25 (overweight & obese)	7(38.9)	65(46.1)	
< 25 (normal)	11(61.1)	76(53.9)	0.563

Figures in the parentheses denote corresponding percentage.

* Data were analysed using Chi-square (χ^2) Test.

Table III. Association between risk factors and ILMCA lesion

Risk factors	ILMCA		p-value
	Present(n=18)	Absent(n=141)	
Dyslipidaemia*			
Present	8(44.4)	56(39.7)	
Absent	10(55.6)	85(60.3)	0.700
Diabetes mellitus*			
Present	12(66.7)	78(55.3)	
Absent	6(33.3)	63(44.7)	0.360
Hypertension*			
Present	13(72.2)	97(68.8)	
Absent	5(27.8)	44(31.2)	0.767
Smoking habit*			
Present	2(11.1)	11(7.8)	
Absent	16(92.5)	130(92.2)	0.629
Family history of IHD#			
Present	1(5.6)	11(7.8)	
Absent	17(94.4)	130(92.2)	0.494

Figures in the parentheses denote corresponding percentage.

* Data were analysed using χ^2 Test. # Data were analysed using Fisher's Exact Test.

LMCA disease in terms of traditional risk factors for ischemic heart diseases like hypertension, diabetes, smoking habit, dyslipidemia and family history of ischemic heart diseases ($p > 0.05$).

Discussion

Before discussing the risk factors of isolated left main lesion, it would be convenient to highlight some of the salient anatomical and histological features of LM which are intimately related with LM lesion. LMCA arises from the midportion of the superior margin of the left aortic sinus of Valsalva. Typically, it runs leftward, superior, and anterior through the aortic wall in the left atrioventricular groove. It consists of 3 portions: the ostium or the portion of the left main arising from the aorta, the trunk or the midportion, and the distal portion. It ends by bifurcating into the left anterior descending and circumflex artery. In 30% of cases, it may also give rise to a ramus intermedius vessel.⁶ The maximum length of the LMCA is usually 4-6 cm.^{6,7} The caliber of the left main artery varies according to the gender and the size of the individual (small women have smaller arteries).⁸ In men, the diameter of a non-diseased left main artery is 4.5 ± 0.5 mm, while in women it is slightly smaller at 3.9 ± 0.4 mm.⁸ Regardless of body surface area, the LMCA is smaller in women than in men.⁸ The aortic wall at the origin of the left main artery is 2-4 mm in thickness. The ostium and proximal portion (first 2-4 mm) of the LMCA are within the aortic wall, and are subject to conditions that affect the aorta.⁶ Histologically, the LMCA ostium lacks adventitia and has considerable smooth muscle and elastic tissue, with aortic smooth muscle arranged perpendicular to and surrounding the ostium. The LMCA has the most elastic tissue of all the coronary vessels.⁹ These histologic properties make the LMCA unique among all coronary arteries. The most common site of LMCA stenosis is the midportion or at the bifurcation of the left main artery.⁹⁻¹¹ The majority of patients with significant LMCA stenosis have, in addition, significant narrowing of at least 1 of the other major coronary vessels.⁴ Isolated LMCA disease is an unusual clinical entity, and is seen predominantly at the ostium.¹⁰⁻¹² Isolated LMCA disease appears to be more common among women.¹³⁻¹⁵ Diabetes mellitus is seen more commonly in distal LMCA disease. There is a trend toward higher incidence of ostial left main stenosis in women and smokers. Patients with ostial LMCA lesion are more likely to be free of disease in other coronary arteries.^{10,12}

The etiology of significant LMCA disease is not well understood. The few studies that have involved histologic examination of coronary vessels have reported atherosclerosis as the primary cause of LMCA stenosis.^{11, 13}

Yamanaka *et al*¹³ found evidence of atherosclerotic changes in the left main artery at autopsy in 5 of 6 patients in their study group. Nonatherosclerotic causes of ostial stenosis reported in literature include syphilitic aortitis,¹⁶ giant cell arteritis,¹⁷ Takayasu disease,¹⁸ calcific diseases of the aortic valve and aortic valve replacement,¹⁹ coronary angiography,²⁰ mediastinal irradiation,²¹ and a high takeoff of the left main artery.¹⁰ Several case reports in literature have described severe intimal thickening consisting predominantly of fibrous tissue without extracellular deposits.^{22,23} Nonatherosclerotic causes for nonostial stenosis reported in literatures include extrinsic compression of the left main artery by tumor, aneurysm, patent ductus arteriosus,²⁴ spasm,²⁵ iatrogenic,²⁶ and type II hyperlipoproteinemia.⁴ This study observed that the prevalence of atherosclerotic risk factor profile in patients with LMCA disease was similar to that in the general population undergoing angiogram. The nonatherosclerotic causes of LMCA disease were not looked for in our study population. As coronary atherosclerosis is the predominant etiology of LMCA disease, it is expected that efforts aimed at reducing the prevalence of atherosclerotic risk factors in the general population will also reduce the prevalence of LMCA disease.

The present study indicates that significant LMCA disease can be seen in nearly 5% of patients who undergo catheterization every year (lower to the reported incidence in the studies of Miller *et al*¹⁴ and Topaz *et al*.¹²) Of them around 5% (18 out of 321) might have isolated LM lesion. Salem *et al*²⁷ reported a much lower incidence of LM lesion (0.88%, 1 patient with isolated left main lesion among 114 patients with significant left main stenosis). An even lower incidence of isolated left main lesion was reported by Tommaso *et al*²⁸ (0.15%), Proudfit *et al*²⁹ (0.30%). Isolated LMCA disease is more common among women¹³⁻¹⁵ In the present study as well a female predominance was observed among patients with LMCA disease, though the difference was not statistically significant. Miller *et al*¹⁴ found 5(0.12%) women with isolated LMCA disease among 4,000 patients with coronary artery disease, and Welch *et al*³⁰ reported 10(0.01%) women with isolated left main lesion among 1,000 women in their studies, although they did not mention any reason for female predominance. However, it is believed that a decline in estrogen resulting from menopause may have a role to play in its pathogenesis. Yamanaka *et al*¹³ have reported that all the women in their study had "primary" ostial left main stenosis, while other coronary vessels were normal. And 60% of them with atherosclerotic stenosis had surgical menopause.

The spectrum of clinical presentation with LMCA disease may vary from asymptomatic to sudden death.³¹ LMCA disease has been found to be associated with a higher prevalence of angina (43%),¹⁴ which is supported by the findings of the present study. The most common presentation of patients with isolated LMCA disease in the present study was stable angina (44.4%). Ostial stenosis of the coronary arteries involves the right coronary artery more frequently than the left coronary artery. It rarely involves both ostia.³² LMCA disease involves the left main ostium more frequently than other sites.¹⁵⁻¹⁶

These patients were selected purely on the basis of angiography. The visual estimation of the left main lesion by angiography has limited accuracy and considerable inter-observer and intra-observer variability.³³⁻³⁴ It has been reported that the angiographic determination of the degree of narrowing of the left main may be underestimated in as many as 71% of cases.^{4,30} Iner *et al*³³ compared angiograms of left main stenosis (done within 40 days of death) of 28 patients reviewed by 3 experienced angiographers with necropsy findings. They found that out of 84 judgments, 64% were wrong: 39% were underestimates and 25% were overestimates. This limitation has been confirmed by studies documenting the presence of significant left main atherosclerosis by intravascular ultrasound despite a minimal or insignificant angiographic appearance.³⁵ Although the angiographic technique and the quality of angiographic projections have improved with time, it remains subject to considerable error. In clinical practice intravascular ultrasound is finding greater acceptance as an accessory to diagnostic angiography to evaluate lesions of uncertain severity, especially in the left main coronary artery.

Significant LMCA disease in the absence of lesions in other coronary vessels is an unusual angiographic finding. It presents most commonly as stable angina. A female preponderance is observed in these patients. The prevalence of atherosclerotic risk factors of these patients is similar to that of the general population undergoing coronary angiogram. As the data on non-atherosclerotic causes of LMCA disease and the site of lesion are not available any further comment cannot be made on the probable association between the two variables. However, a predisposition toward ostial lesions in patients with LMCA disease has been reported by other studies. As coronary atherosclerosis is the predominant etiology of LMCA disease, it is expected that efforts aimed at reducing the prevalence of atherosclerotic risk factors in the general population will also reduce the prevalence of LMCA disease. However, if the lesion is isolated and located in the ostium a search for a non-atherosclerotic cause is recommended.

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