CLINICAL FEATURES OF PATIENTS WITH CORONARY ARTERY ECTASIA COMPARED WITH STENOTIC CORONARY ARTERY DISEASE

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ABSTRACT

Objective: To study the prevalence of coronary artery ectasia in the population of patients referred for coronary angiography. To describe clinical characteristics of patients with coronary artery ectasia, analyzing presentation and cardiovascular risk. To compare clinical and angiographic variables in patients with and without coronary artery ectasia.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Adult cardiology department in Armed Forces Institute of Cardiology/NIHD, Rawalpindi, 6 months duration after approval of synopsis i.e. Oct 2018 to May 2019.

Methodology: After meeting the inclusion criteria 300 patients were enrolled. Patients admitted in AFIC/NIHD with chest pain, ST-elevation MI, Non-ST-elevation myocardial infarction and unstable angina were enrolled. Coronary angiogram was done by cardiologist. Two distinct cardiologists or resident cardiologists reported the angiograms including the coronary artery anatomy and the presence of ectatic segments or any stenotic lesions in each vessel. All the collected data was entered and analyzed on SPSS version 23.

Results: The mean patients was 58.23 ± 11.73 years. The male to female ratio was 14:1. Coronary artery ectasia was detected in 53 (17.7%) patients of coronary angiography. Stenotic coronary artery disease was detected more commonly in patients having factors like diabetes, hypertension, and dyslipidemia but specifically among smokers, ectatic segments were detected higher.

Conclusion: Compared to coronary artery disease, coronary ectasia occurred more in smokers and less in diabetes.

Keywords: Angiography, Coronary artery ectasia, Diabetes, Hypertension, Stenotic coronary artery disease.

INTRODUCTION

The considerable cause of morbidity and mortality is coronary artery disease (CAD) around the globe. Every year, around 635,000 Americans have first cardiac event (definition is new onset hospitalized myocardial infarction (MI) or coronary artery disease related mortality) and an estimated 280,000 have multiple attacks[1]. Ectatic coronary arteries, also known as dilated coronopathy, is a comparatively uncommon angiographic finding. This condition is seen when comparing to normal artery segment the diameter of a dilated segment of an artery is 1.5 times greater[2].

However, many investigations have advocated that connective tissue, congenital, and inflammatory disorders are possible etiologies and that the process of atherosclerosis is the root cause in maximum number of cases. Moreover, the prognosis differs significantly between studies, with the yearly mortality rate having been reported between 2-15%. It is estimated that atherosclerosis is the cause of CAE in 50% of cases. Stenosis of coronary arteries usually coexists with CAE[3].

CAE can affect all the three coronary vessels, however almost 75% of patients have a single artery that is ectatic. The proximal and mid segment of the right coronary artery (RCA) is the most commonly affected in patients with concomitant coronary heart disease. For assessment of ectasia and anatomy of coronary arteries,

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coronary angiography is the gold standard test. Intravascular ultrasound (IVUS) can be used for assessment of pathologies of vessel wall and luminal extension. It can also be used for identification of the false aneurysms.

In CAE, washout and distortions in flow are common and are directly related with the severity of dilatation. Signs which can be seen on angiography are turbulent and stagnant flow including delayed antegrade filling of contrast, a segmental back flow and local stagnation of contrast in the dilated coronary segment (stasis)[4,5]. Younger male patients have more propensity towards the occurrence of ectasia. Patients with CAE presents with chest pain and angina and undergo extensive intervention thus proving its sinister nature. The layout of CAE among the LMS, LAD, LCX and RCA also varies to that in CAD[6].

Congenital cases of coronary ectasia are approximately 25%. Acquired cases are 75%. Of the acquired cases, half of them are linked with atherosclerosis while 10%-20% are linked with connective tissue diseases, inflammatory, syphilis, and bacterial infections[7,8].

The etiology, prognosis, morbidity, and mortality related to CAE are still a matter of debate and whether CAE is a distinctive clinical finding or a state resulting from other clinical entities is still unknown. Ectasia is observed in patients undergoing coronary angiography for assessment of coronary artery disease (CAD). It is not completely clear whether CAE is a variant of CAD or a distinct disease itself. Also there is little contemporary data available regarding CAE in our local population. This study will help to identify the patients who are at risk of infarction, thrombus formation and clogging of microcirculation as CAE is not a benign condition and there is 15% mortality rate after 7 years[9].

METHODOLOGY

It was a simple descriptive cross sectional study conducted at Adult cardiology department in AFIC/NIHD, Rawalpindi, study duration was 6 months after the proper approval of Institutional review board. Non-probability consecutive sampling was done, WHO calculator was used for sample size calculation i.e. a) confidence level at 95%, b) prevalence from the literature =23%, c) precision=5%; A sample of 300 patients was included in the study.

Patients age 30-70 years, of both genders, had chest pain suggestive of angina, STEMI, NSTEMI and Positive Stress Test undergoing coronary angiography was included in this study. Patients with completely normal vessels or <50% luminal stenosis, patients with extensive coronary artery disease (CAD), history of multi-vessel PCI or patients withcongenital or valvular heart diseases were excluded.

Permission was sought from hospital ethical committee. Written informed consent was taken from participants of study. Particulars of all the patients who meet the inclusion and exclusion criteria were recorded in the Proforma. Charges of the tests were borne by hospital administration and not by the patient.

Patients admitted in AFIC/NIHD with angina or positive ETT who are to undergo angiogram was enrolled in the study. Coronary angiogram was done by resident cardiologist. Two distinct cardiologists or resident cardiologists reported the angiograms including the coronary artery anatomy and the presence of ectatic segments or any stenotic lesions in each vessel.

Statistical analysis was performed using statistical software SPSS 23. For continuous variables i.e. age, mean and standard deviation was calculated. For categorical variables i.e. gender, CAD, CAE and angiographic profile, frequency and percentages were calculated.

By applying chi square test, clinical and angiographic profile of patients with and without CAE were observed compared in CAE and stenotic CAD group and *p*-values were calculated. A *p*-value ≤0.05 was taken as significant.

RESULTS

The mean age of the patients was 58.23 ± 11.73 years with minimum and maximum ages of 36 & 86 years respectively. In this study 280

(93.33%) patients were males whereas 20 (6.67%) patients were females. Male to female ratio was 14:1, fig-1.

In this study, 53 (17.7%) had CAE while 247 (82.3%) had stenotic CAD. Fig-2 shows the

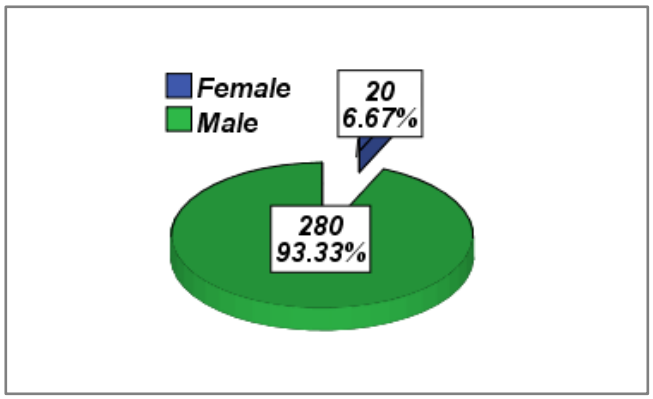

Figure-1: Frequency distribution of gender.

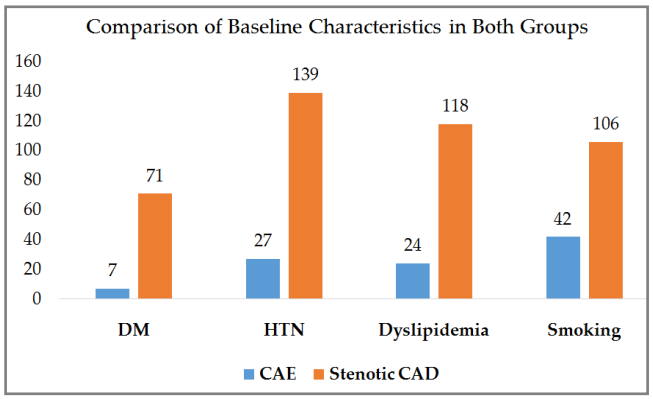

Figure -2: Comparison of baseline characteristics.

graphical presentation of baseline characteristics. Among diabetics, stenotic CAD (28.7%) was more common than CAE (13.2%). Among hypertensive, stenotic CAD (56.3%) was more common than CAE (50.9%). Among dyslipidemias, stenotic CAD (47.8%) was more common than CAE (45.3%). Among smokers, CAE was more common (79.2%) than stenotic CAD (42.9%). The difference was insignificant for hypertension and dyslipidemia (p>0.05) while significant for diabetes and smoking (p<0.05) as shown in table-I.

Data was stratified for effect modifiers. For RCA involvement, stenotic CAD was significantly more common whether age ≤50 years or >50 years. Stenotic CAD was significantly more common in males and its findings were significant (p=0.04). Stenotic CAD was insignificant for non-hypertensive patients but significant for non-hypertensive (p<0.05). But among smokers, CAE was more common than stenotic CAD, however, among non-smokers, stenotic CAD was more common (p>0.05). Similarly among diabetics, stenotic CAD was insignificant higher than CAE (p>0.05) and among dyslipidemia, stenotic CAD was significantly higher than CAE (p<0.05) as mentioned in table-II.

Table-I: Comparison of baseline characteristics in both groups.

		Study groups		*p*-value*
		CAE	Stenotic CAD	
Age (Years)	≤50	9 (16.9%)	76 (30.7%)	0.04
	>50	44 (80.3%)	171 (69.2%)	
Gender	Male	52 (98.1%)	228 (92.3%)	0.124
	Female	01 (1.8%)	19 (7.7%)	
Diabetes	Yes	7 (13.2%)	71 (28.7%)	0.02
	No	46 (86.8%)	176 (71.3%)	
Hypertension	Yes	27 (50.9%)	139 (56.3%)	0.479
	No	26 (49.1%)	108 (43.7%)	
Dyslipidemia	Yes	24 (45.3%)	118 (47.8%)	0.742
	No	29 (54.7%)	129 (52.2%)	
Smoking	Yes	42 (79.2%)	106 (42.9%)	<0.0001
	No	11 (20.8%)	141 (57.1%)	

**Pearson's chi-square test*

Table-III, shows that data was stratified for effect modifiers. For LCX involvement, both groups had insignificant difference (p>0.05) in age ≤50 years, but in stenotic CAD was more common in age >50 years (p<0.05). In males, ste-

notic CAD was more common than CAE (p<0.05) but insignificant in females. In hypertensive patients, stenotic CAD was more common than CAE (p<0.05) but insignificant in non-hypertensive (p>0.05). Among smokers, stenotic CAD was more common than CAE (p<0.05), however, in non-smokers, difference was insignificant (p>0.05). Among diabetics, stenotic CAD was higher than CAE (p>0.05) and among dyslipidemia, stenotic CAD was significantly higher than CAE (p<0.05).

Table-II: Comparison of RCA vessel involvement in both groups stratified for effect modifiers.

RCA		Study Groups		*p*-value
		CAE	Stenotic CAD	
Age (years)	≤ 50	2	47	0.047
	> 50	23	133	
Gender	Male	25	175	0.399
	Female	0	5	
Hypertension	Yes	20	110	0.06
	No	5	70	
Smoking	Yes	19	83	0.005
	No	6	97	
Diabetes	Yes	6	49	0.733
	No	19	131	
Dyslipidemia	Yes	9	84	0.315
	No	16	96	

Table-III: Comparison of LCX vessel involvement in both groups stratified for effect modifiers.

LCX		Study Groups		*p*-value
		CAE	Stenotic CAD	
Age (years)	≤ 50	2	32	0.577
	> 50	9	92	
Gender	Male	11	119	0.497
	Female	0	5	
Hypertension	Yes	7	86	0.695
	No	4	38	
Smoking	Yes	9	59	0.030
	No	2	65	
Diabetes	Yes	1	33	0.199
	No	10	91	
Dyslipidemia	Yes	6	64	0.852
	No	5	60	

Data was stratified for effect modifiers. For LMS involvement, stenotic CAD was more common whether age ≤50 years or >50 years. Stenotic CAD was also insignificant in males and females than CAE (p>0.05). Stenotic CAD was more common in hypertensive patients (p>0.05) but didn't find in non-hypertensives. Among smokers and non-smokers, CAE was more common than stenotic CAD, however, difference was insignificant (p>0.05). Similarly among diabetics, stenotic CAD was insignificant than CAE (p>0.05) and in dyslipidemia, stenotic CAD was insignificant than CAE (p>0.05) shown in table-IV.

Table-IV: Comparison of LMS vessel involvement in both groups for effect modifiers.

LMS		Study Groups		*p*-value
		CAE	Stenotic CAD	
Age (years)	≤ 50	1	4	0.311
	> 50	1	17	
Smoking	Yes	1	10	0.95
	No	1	11	
Diabetes	Yes	1	13	0.74
	No	1	8	
Dyslipidemia	Yes	0	4	0.497
	No	2	17	

Table-V: Comparison of LAD vessel involvement in both groups stratified for effect modifiers.

LAD		Study Groups		*p*-value
		CAE	Stenotic CAD	
Age (years)	≤ 50	0	49	0.017
	> 50	17	143	
Gender	Male	17	179	0.27
	Female	0	13	
Hypertension	Yes	10	112	0.97
	No	7	80	
Smoking	Yes	14	90	0.005
	No	3	102	
Diabetes	Yes	1	52	0.054
	No	16	140	
Dyslipidemia	Yes	8	92	0.95
	No	9	100	

Data was stratified for effect modifiers. For LAD involvement, stenotic CAD was significantly more common whether age ≤50 years or >50 years. Stenotic CAD was significantly more common in males but insignificant in females than CAE (p>0.05). Stenotic CAD was significantly more common in hypertensive patients and also in non-hypertensive (p<0.05). Among smokers and non-smokers, stenotic CAD more common than CAE. Among diabetics and non-diabetics, stenotic CAD was significantly higher than CAE

(p<0.05) and among dyslipidemia, stenotic CAD was significantly higher than CAE (p<0.05) mentioned in table-V.

DISCUSSION

This present cross sectional study was carried out at Adult cardiology department in AFIC/NIHD, Rawalpindi, to determine frequency of CAE and CAD among patients undergoing coro-nary angiography and to compare the clinical profile of patients having coronary artery ectasia (CAE) with those having stenotic coronary artery disease (CAD). Coronary artery ectasia is one of the uncommon cardiovascular disorders, its incidence ranges from 1.2%-4%. It likely represents an exaggerated form of expansive vascular remodeling in response to atherosclerotic plaque growth with atherosclerosis being the most common cause[10].

In this study, 53 (17.7%) had CAE while 247 (82.3%) had stenotic CAD. Among diabetics, stenotic CAD (28.7%) was more common than CAE (13.2%). Among hypertensive, stenotic CAD (56.3%) was more common than CAE (50.9%). Among dyslipidemias, stenotic CAD (47.8%) was more common than CAE (45.3%). Among smokers, CAE was more common (79.2%) than stenotic CAD (42.9%). The difference was insignificant for hypertension and dyslipidemia (p>0.05) while significant for diabetes and smoking (p<0.05). Thus showing strong relation of smoking with CAE.

Diabetes mellitus is a well-known risk factor for coronary atherosclerosis and its complications[11]. Several recent studies have compared and evaluated traditional cardiovascular risk factors in patients with CAE (13.2% in CAE vs 28.7% in stenotic CAD) and in those with stenotic CAD. As in our study, an interesting observation is the negative correlation with diabetes and CAE has also reported by others. The prevalence of diabetes in patients with ectasia was found to be less frequent than that in patients with stenotic CAD[12].

A study by Rashid *et al*, resulted in their study that males were predominant in both with & without CAE[13], Hypertension, smoking and obesity were significantly more common among CAE patients than those without (60.5% vs. 52.6%, 56.8% vs. 43.9% and 80.2% vs. 14%, respectively). Diabetes was much less in CAE group (32.1% vs. 42.1%).

Among the patients in our study the diameter of the artery was as much as twice that found in patients without CAE. Moreover, as in the series reported by Papadakis *et al*, coronary artery blood flow calculated with the TIMI Frame Count was slower in patients with CE. Although structural alterations (breakdown of the vessel wall, dilation of the artery) could explain the tendency to provoke thrombosis and vasospasm, this slower blood flow may be the cause of the symptoms of angina and might even be one of the factors involved in the alterations that cause myocardial infarct in some patients with CAE[14].

Given that the mechanism that causes CAE is not clearly understood, it is important we investigate the risk factors in these patients which could influence the appearance of this condition. In our study, after correction for other variables, male sex and the absence of diabetes were the only variables independently associated with CAE.

Patients with CAE are predominately men, and in our study they represent of all cases. Sudhir *et al*, found a higher prevalence of CAE in patients with a family history of high blood cholesterol[15]. In our study, percentages of hyperlipemia and hypertension were higher, but similar to those of patients with ischemic heart disease and without CAE, which is consistent with other findings. However, there were significantly more smokers among patients with CAE[16,17].

One significant finding, not previously reported, was the minimal prevalence of diabetes among patients with CAE. The percentage was especially low among those with CAE. Coronary artery ectasia seems to be a distinctive form of coronary artery atherosclerosis, caused by the action of different risk factors based on a genetic predisposition. This would lead to initial endo-

thelial damage activating a series of inflammatory mediators (macrophages, metalloproteins, etc) that cause degeneration of the medial layer of the vessel. These structural alterations, together with the action of nitric oxide and other vasodilators, lead to a dilation of the coronary artery: an extreme form of positive remodeling[18]. However, among diabetic patients we found more cases of coronary arteries with diffuse conditions and (negative remodeling), without large amounts of plaque, but with luminal reduction and a decrease in the size of the vessel. One explanation might lie in the association of diabetes with a reduction in endothelium-dependent vasodilation, caused by alterations in the synthesis and inhibition of nitric oxide, which seems to play a significant role in the genesis of CE. primarily affects the intimal, but not the medial layer of the vessel, thus causing (negative remodeling) It seems reasonable to hypothesize that positive remodeling appears in recently developed lesions, whereas negative remodeling occurs at a later stage, after structural changes. Perhaps diabetic patients tend to develop a more aggressive, evolved form of atherosclerosis, whereas alterations in lipoprotein metabolism are more closely associated with the phenomenon of positive remodeling. We can probably add to these risk factors the existence of a certain genetic predisposition, as men make up more than 90% of the patients with CAE. Studies that enable us to clarify this genetic factor and explain the exact mechanisms that cause CAE are needed.

One study showed that the smoking and hypertension were more common in patients with CAE, but dyslipidemia and diabetes were less frequent in patients with CAE. Smoking may predispose to CAE by inducing inflammation and thrombosis. However, there is a controversy regarding smoking as independent risk factor for CAE[19].

CONCLUSION

We have got the local evidence and found CAE in significant number of cases (17.7%) who underwent coronary angiography. Compared to CAD, coronary ectasia was more frequent in smokers and less in diabetics.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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