

A Prospective Study on Clinical Profile and Angiographic Pattern of Coronary Artery Ectasia in Coronary Artery Disease Patients

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Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Coronary artery Ectasia (CAE) has been defined as an abnormal dilatation of coronary artery, with luminal diameter exceeding 1.5 times the adjacent normal reference segment. According to the extent of involvement ectasia may be labelled as focal or diffuse. Prevalence of CAE varies from 0.3% to 6% .The highest prevalence reported from India and Pakistan (10-12% &12.5% respectively). CAE may occur as an isolated form but most commonly seen in association with obstructive CAD . Ectasia is often viewed as a variant form of obstructive Coronary Artery Disease (CAD) and atherosclerosis is considered as a contributing factor in more than half of the cases. Although the association with atherosclerotic CAD is well evident, the relationship between traditional atherosclerotic risk factors and Ectasia remains controversial. Especially its poor correlation with Diabetes mellitus suggested Ectasia is a distinctive form of atherosclerosis characterized by positive remodeling– (Glagovian phenomenon) in contrast to obstructive disease (Negative Remodeling) .Hemodynamic factors like flow, stretch, shear stress along with inflammatory signals were proposed as the triggers for this abnormal

vascular remodeling and postulated as the link between atherosclerosis and CAE in susceptible individuals.

Aims & Objectives

1. To assess the prevalence of Coronary Artery ectasia in patients with CAD
2. To Analysis of Risk factors and clinical presentation of CAE and to compare it with patients having only obstructive CAD.
3. To describe the angiographic characteristics of CAE.
4. To study the influence of CAE on outcome of CAD.

Materials and Methods

Study Population

Adult patients >18 yrs. of age with the diagnosis of CAD, undergoing Angiography in Department of Cardiology Azeezia Medical College & Hospital, Meeyannoor, Kollam.

Cases

Inclusion criteria

1. Age \geq 18 years with diagnosis of CAD (both Stable Ischemic Heart disease and Acute Coronary Syndrome)
2. Patients having Coronary artery Ectasia and/or Coronary artery aneurysm in Coronary angiography.

Exclusion criteria

- 1) Age <18yrs
- 2) Patients already undergone PTCA ,CABG
- 3) Preexisting valvular heart diseases.
- 4) Preexisting cardiomyopathies
- 5) Preexisting Arrhythmias
- 7) Concomitant acute or chronic kidney disease
- 8) Vasculitis (Kawasaki disease ,Takayasu arteritis)

Results

Totally 2434 patients undergone angiogram during the study period with the suspicion of Coronary Artery Disease (Chronic Stable Angina or Prior MI, ACS).Of those 1966 patients was eligible for our study . Coronary ectasia was found in 136 (5.6%) patients of whom 24 (1.0%) patients were diagnosed to have isolated ectasia (isolated ectasia group) without evidence obstructive coronary disease and 112 (4.6%) (CAE+CAD group) patients with ectasia were having associated with obstructive CAD . Remaining 1830 patients were having pure obstructive CAD (CAD group)(75.2%).Baseline characters have been tabulated in Table 1. Isolated ectasia (dilated coronaropathy) was observed in 17.6%(n=24) ,remaining 82.4% had associated obstructive CAD (n=112) .

Conclusion

Isolated ectasia is a unique phenomenon, seen in relatively younger population, having inverse association (less frequent) with Diabetes mellitus , neutrophil mediated active inflammation and this has nil effect on mortality . But Coronary artery ectasia if associated obstructive CAD has evidence of high inflammatory activity than pure CAD ,but does not worsen the prognosis of coexisting CAD except for increased frequency of unstable angina.

Introduction

Coronary artery Ectasia (CAE) has been defined as an abnormal dilatation of coronary artery, with luminal diameter exceeding 1.5 times the adjacent normal reference segment. According to the extent of involvement ectasia may be labelled as focal or diffuse. Prevalence of CAE varies from 0.3% to 6 % .The highest prevalence reported from India and Pakistan (10-12% &12.5% respectively)¹⁻³.

CAE may occur as an isolated form but most commonly seen in association with obstructive CAD . Ectasia is often viewed as a variant form of obstructive Coronary Artery Disease (CAD) and atherosclerosis is considered as a contributing factor in more than half of the cases⁴. Although the association with atherosclerotic CAD is well evident, the relationship between traditional atherosclerotic risk factors and Ectasia remains controversial. Especially its poor correlation with Diabetes mellitus suggested Ectasia is a distinctive form of atherosclerosis characterized by positive remodeling– (Glagovian phenomenon) in contrast to obstructive disease (Negative Remodeling).⁵Hemodynamic factors like flow, stretch, shear stress along with inflammatory signals were proposed as the triggers for this abnormal vascular remodeling and postulated as the link between atherosclerosis and CAE in susceptible individual. Multiple studies in this area were showing conflicting evidence, hence the exact pathogenetic mechanism still not conclusively defined and in hypothetical stage.⁶

Thrombus formation, vasospasm ,slow flow, dissection were proposed as the pathophysiological mechanisms of clinical events related with CAE . Clinically the most common manifestation of CAE is angina, unstable angina myocardial infarction also occur in 30% of individuals, very rarely caused sudden cardiac death⁷⁻⁹ .Long term

prognosis remains unclear. Even isolated ectasia is not a benign entity can present with myocardial infarction during follow up. No consensus or guidelines available for the management of Coronary Artery Ectasia. In acute settings heparin infusion, if necessary thrombolysis considered mandatory. Medical management with Antiplatelet drugs is universally accepted, but role of anticoagulation remain controversial in long term. In view of prothrombotic milieu, complexities related with Percutaneous Intervention Coronary Artery in ectatic segment Bypass Grafting (CABG) is the preferred revascularization approach.^{10,11}

The etiopathogenesis of this entity puzzled the clinician since its discovery, but still there are some unclear undefined areas clinical significance remains uncertain and there is no consensus opinion regarding management¹². Hence further research is essential to solve these enigmas. Being in the country with highest prevalence of CAE, we planned this study to analyze the risk factors, clinical presentation and angiographic characteristics of patients with Coronary Artery Ectasia, also to assess the prognosis during the index hospitalization as well as during follow up¹³⁻¹⁴.

Materials and Methods:

Study Population: Adult patients >18 yrs. of age with the diagnosis of CAD, undergoing Angiography in Department of Cardiology, Azeezia Medical College, Meeyannoor, Kollam.

CASES:

Inclusion criteria

1. Age ≥ 18 years with diagnosis of CAD (both Stable Ischemic Heart disease and Acute Coronary Syndrome)
2. Patients having Coronary artery Ectasia and/or Coronary artery aneurysm in Coronary angiography

Exclusion criteria

1. Age <18yrs
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3. Preexisting valvular heart disease
4. Preexisting cardiomyopathies
5. Preexisting Arrhythmias
6. Concomitant acute or chronic kidney disease
7. Vasculitis (Kawasaki disease, Takayasu arteritis)

Methods

From the study population after obtaining informed written consent detailed history were taken Demographic and personal and health information were collected from the patient. Blood samples were collected for laboratory investigations.

Laboratory Investigations

- 1) Fasting Blood Sugar
- 2) Post prandial blood sugar
- 3) Serum creatinine
- 4) Blood urea
- 5) Lipid profile
- 6) HIV ELISA
- 7) Echocardiography
- 8) Coronary angiography

Definition of risk factors

Diabetes Mellitus:

Diabetes Mellitus was diagnosed

1. If a patient is already on oral hypoglycemic drugs or on Insulin therapy
 2. If a patient has symptoms of DM Plus Random Blood sugar of > 200 mg/dl or Fasting blood sugar >126mg %
- Systemic Hypertension: A patient was diagnosed to have hypertension

1. If he is on antihypertensive therapy
2. If his BP is >140/90 mm of Hg on presentation and on repeat recording

(>2 occasions)

Lipid abnormality : If a patient has

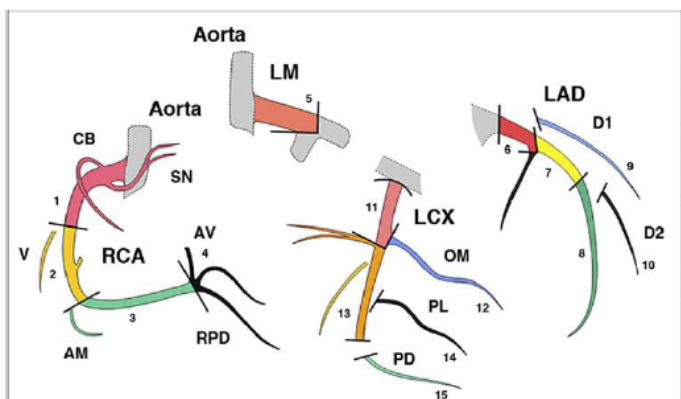
1. Elevated LDL cholesterol >100 mg%
2. High TGL >150 mg%
3. HDL cholesterol < 35 mg /dl

Any patient with Body Mass Index > 30 kg/m² was labelled as obese

Definition of Acute Coronary Syndrome:

Myocardial infarction was defined as per Universal definition of MI.

Definition of myocardial infarction
Criteria for acute myocardial infarction
The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischaemia. Under these conditions any one of the following criteria meets the diagnosis for MI:
<ul style="list-style-type: none"> • Detection of a rise and/or fall of cardiac biomarker values [preferably cardiac troponin (cTn)] with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following: <ul style="list-style-type: none"> • Symptoms of ischaemia. • New or presumed new significant ST-segment-T wave (ST-T) changes or new left bundle branch block (LBBB). • Development of pathological Q waves in the ECG. • Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. • Identification of an intracoronary thrombus by angiography or autopsy. • Cardiac death with symptoms suggestive of myocardial ischaemia and presumed new ischaemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased. • Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (>5 x 99th percentile URL) in patients with normal baseline values (<99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (i) symptoms suggestive of myocardial ischaemia or (ii) new ischaemic ECG changes or (iii) angiographic findings consistent with a procedural complication or (iv) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required. • Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischaemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL. • Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (>10 x 99th percentile URL) in patients with normal baseline cTn values (<99th percentile URL). In addition, either (i) new pathological Q waves or new LBBB, or (ii) angiographic: documented new graft or new native coronary artery occlusion, or (iii) imaging: evidence of new loss of viable myocardium or new regional wall motion abnormality.



LAD left anterior descending coronary artery;	LCX left circumflex coronary artery;
LM left main coronary artery;	RCA right coronary
D1 first diagonal branch;	D2 second diagonal branch;
OM obtuse marginal branch	PD posterior descending branch;
PL posterolateral branch	RPD right posterior descending branch

Definition of Ectasia

In our study we followed the definition used in CASS registry abnormal dilatation of coronary artery, with luminal diameter exceeding 1.5 times the adjacent normal reference segment. If no adjacent normal segment could

be identified, the mean diameters of the coronary segments in a control group without heart disease served as normal values.¹⁵⁻¹⁶

Types of Ectasia

1. Localized: If ectasia confined to a discrete portion of artery with an adjacent normal vessel within that segment
2. Diffuse: if the Ectasia involves the entire coronary aretery segment with no normal vessel in that segment

Coronary Ectasia have been classified according to Markis et al & Harikrishnan et al classification

Definition of obstructive CAD in angiogram

Obstructive CAD was diagnosed if a patient had > 50% loss of luminal diameter compared to the reference normal segment¹⁷.

Definition of Groups

Different types of ectasia in relation the segment of particular vessels as defined above were recorded . According to the angiography patients were categorized into three groups Group A = Isolated Ectasia patients having Ectasia without any evidence of significant obstruction in coronary artery (>50%), Group B Mixed CAE + CAD group Patients with Ectasia and also having significant obstruction in any of the coronaries .Group C= Pure CAD group patients having only CAD without evidence of CAE.

Patients were treated according to the guideline given by American College of Cardiology /American Heart association. Left ventricular systolic function was recorded with Philips IE 33 echocardiography machine. Clinical events LVF, in hospital mortality were recorded . Outcome data during follow up were collected specifically regarding the unstable angina, MI mortality and recoded for analysis.

Stastical Analysis

Continuous variables were analyzed with Mean ± SD (BMI, Lipid parameters, age) . Categorical variables sex, DM hypertension ,vessel involved outcome) were described with number & percentage .Chi Square test used to assess the significance P value < 0.05 were considered as stastically significant.

Results

Prevalence: Totally 2434 patients undergone angiogram during the study period with the suspicion of Coronary Artery Disease (Chronic Stable Angina or Prior MI, ACS).Of those 1966 patients was eligible for our study . Coronary ectasia was found in 136 (5.6%) patients of whom 24 (1.0%) patients were diagnosed to have isolated ectasia (isolated ectasia group) without evidence obstructive coronary disease and 112 (4.6%) (CAE+CAD group) patients with ectasia were having associated with obstructive CAD . Remaining1830 patients were having pure obstructive CAD (CAD group) (75.2%).Baseline characters have been tabulated in Table 1. Isolated ectasia (dilated coronaropathy) was observed in 17.6%(n=24) ,remaining 82.4% had associated obstructive CAD (n=112) .

Age & Sex

Mean age of the population in isolated ectasia is significantly lower (44±8.6 Vs 54.32±8.72 Vs 56±7.8 P<0.001) compared to mixed CAE +CAD group and isolated CAD . Sex distribution showed male predominance in all the groups .the proportion among total ectatic population is M:F 3.1:1.Significant male dominance was noted in Isolated ectasia group (7:1 p value <0.001). But when comparing total ectasia group (n=136) to isolated CAD the male dominance nullified indicated that male sex is a significant risk factor for Dilated coronaropathy(Isolated

ectasia). But male sex is not a significant risk factor mixed ectasia group (CAE+CAD) when comparing with isolated CAD group the male(2.7:1 Vs 2.5:1 P value NS) dominance is due to high incidence of CAD among males
Smoking : Among the isolated ectasia group 62.5% (n=15) patients were smokers whereas in mixed and isolated CAD group smokers were 53.6% (n=60),51.6% (n=944/1830) respectively.

Fig :1a

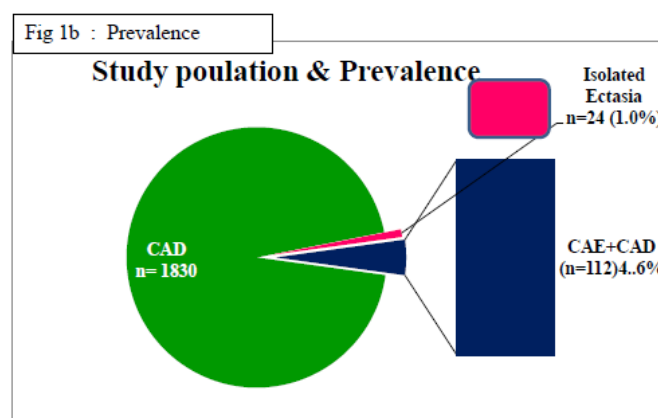
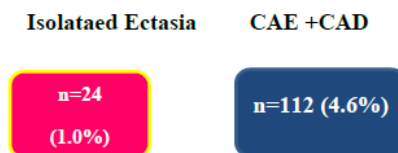
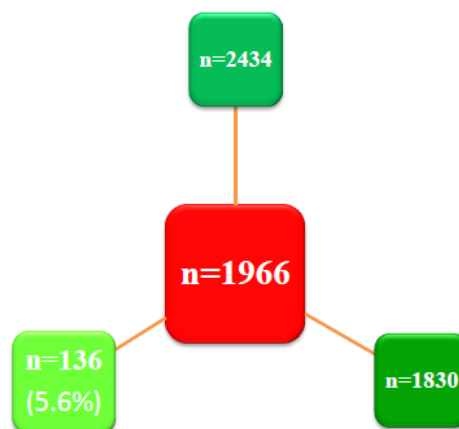


Table 1: Baseline Characters

	Isolated Ectasia n=24 (A)	CAE+CAD n=112 (B)	CAD n=1830 (C)	p value
Age (yrs)	44±8.6	54.32±8.72	56±7.8	<0.001
Sex Male	21 (87.5%)	82(73.2%)	1318(72%)	
Female	3(12.5%)	30(26.8%)	512(28%)	
Smoker	15(62.5%)	60(53.6%)	944 (51.6%)	0.813 NS
Diabetes	6(25%)	48(42.9%)	868(47.4%)	<0.05
SHT	8(33.3%)	53(47.3%)	904(49.4%)	0.55 NS
BMI (>30 mg /dl)	5(20.8%)	26(23.2%)	413(22.6%)	NS
LDL (>100 mg/dl)	7(29.2%)	41(36.6%)	679(37.1%)	NS
HDL(<35mg/dl)	13(54.1%)	51(45.5%)	866(47.3%)	NS
TGL (>150mg/dl)	5(20.8%)	43(38.3%)	763(41.7%)	NS

Table : 2 Gender distribution

	Total	Male n (%)	Female n (%)	M:F
All patients	1966	1421(72.3%)	545(27.7%)	2.6
Isolated Ecatsia	24	21 (87.5%)	3(12.5%)	7
CAE+CAD	112	82(73.2%)	30 (26.8%)	2.7
Total No CAE patients	136	103 (75.7%)	33(24.3%)	3.1
Isolated CAD	1830	1318 (72%)	512 (28%)	2.52

TABLE 3 Traditional Risk factors

	Isolated Ectasia n=24	CAE+CAD n=112	CAD n=1830	p value
Age (yrs)	44±8.6	54.32±8.72	56±7.8	<0.001
Sex Male	21 (87.5%)	82(73.2%)	1318(72%)	
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Diabetes	6(25%)	48(42.9%)	868(47.4%)	<0.05
SHT	8(33.3%)	53(47.3%)	904(49.4%)	0.55 NS
BMI (>30)	25.57±3.41	27.43 ± 3.19	28.15±3.56	<0.001
LDL (>100 mg/dl)	105± 22.68	104.9±19.8	108±16.7	0.12 NS
HDL(<35mg/dl)	37.9±8	36.19±7.13	37.52±6.9	0.136 NS
TGL (>150mg/dl)	155.9±31.9	167.17±42.99	163.34±37.15	0.35 NS

Table 4 : Novel Risk Markers

	Isolated Ectasia Mean±SD	CAE+CAD Mean±SD	Pure CAD Mean±SD	p value
Neutrophil (cells /mm ³)	5.986±1.497	6.019±1030	4.480±1.230	<0.001
Lymphocyte	1.520±0.268	1.700±0.275	1.680±0.268	0.011
NLR	3.98±0.89	3.58±0.56	2.82±0.60	<0.001
Mean Platelet voume (MPV)	9.94±1.56	9.56±1.06	9.70±1.36	0.379 NS
Red Cell Distribution Width (RDW)	12.59±0.60	12.09±0.85	12.12±0.70	<0.005

Outcome

Follow up data was available for all 24 isolated ectasia patients and for 103 patients in mixed group 1625 pure CAD patients .Duringfollow up UA angina is most frequently seen among Isolated ectasia and mixed group compared to pure CAD, 9(37.5%) vs vs 32 (31.2) vs 278(17.1). No ne of the isolated ectasaia patient had STEMI or mortality during follow up .But in mixed group Approximately similar incidence of STEMI in mixed 5 (4.9%) and pure CAD group 83(5.1%).Morality during follow up also same in both mixed and pure CAD 6 (5.8%) and 99 (6.1%) vs 0 in isolated ectasia group.

In our study conducted in South India ,totally 136 among 2434 patients with clinical suspicion CAD had coronary ectasia .So the prevalence of ectasia was 5.6% Prevalence of isolated ectasia was 1% (n=24) . In the literature prevalence of ectasia varies from 0.3% - 12.5%. the highest prevalence reported in Indian subcontinent (India - 10-12%, Pakistan 12.5%) .

Except few studies

majority reported prevalence < 5% (CASS registry- 4.9% Spain- 3.39% , Greek 2.7%) Similarly Harikrishnan et al from Kerala –South India reported 4.5% among 3200 angiogram The prevalence isolated ectasia without significant coronary stenosis (dilated coronaropathy) in our study was 1%(n=24) . Harikrishnan et al reported prevalence of 0.6 % Nyamu et al in their

dedicated study on isolated ectasia reported a prevalence of 1.9% among 6938 angiograms.

Conclusion

Isolated ectasia is a unique phenomenon, seen in relatively younger population, having inverse association (less frequent) with Diabetes mellitus, neutrophil mediated active inflammation and this has nil effect on mortality. But Coronary artery ectasia if associated obstructive CAD has evidence of high inflammatory activity than pure CAD, but does not worsen the prognosis of coexisting CAD except for increased frequency of unstable angina.

Limitations

1. The number of population in isolated group is very less.
2. Other inflammatory markers hs-CRP were not assessed.
3. Healthy controls were not selected for comparison.
4. Diastolic function was not assessed.

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List of Figures

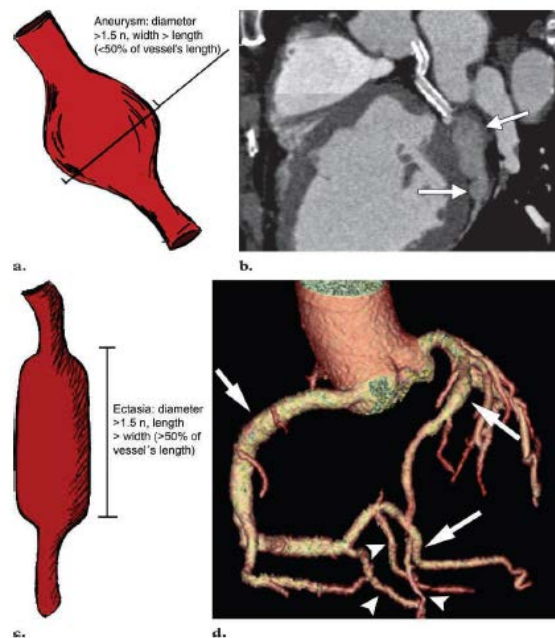


Fig 3 Saccular & Fusiform ectasia

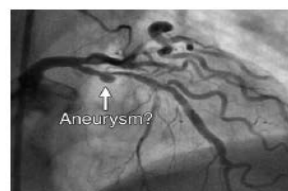


Fig 4 Saccular (discrete or focal ectasia) Ectasia

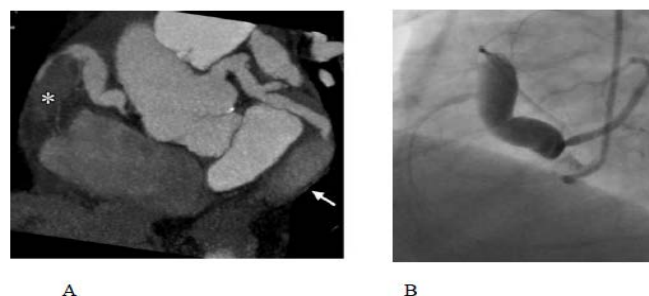


Fig 5 :Coronary CT angiogram (A) corresponding Conventional Angiogram (B) thrombus can be seen as attenuation of contrast (*) but in conventional angio it was seen as complete occlusion.