ORIGINAL ARTICLE

Coronary Artery Ectasia: Clinical and Angiographic Features

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Abstract

Objective: To investigate the clinical and angiographic characteristics of coronary artery ectasia (CAE) and its relation with the inflammatory marker, HsCRP.

Study Design: An observational study.

Place and Duration of Study: Rawalpindi Institute of Cardiology, Rawalpindi, from April 2015 till November 2016.

Methodology: Eighty-one patients with CAE and 57 age matched patients with stenotic coronary artery disease (CAD), but without CAE, were included in the study. Clinical, angiographic, and laboratory data were documented. Chi-square test was used to compare coronary risk factors between two groups. T test was used to compare means between the groups. Analysis of variance was used to analyse HsCRP levels among various types of ectasia. Correlation analysis was used to study association of ectasia with different risk factors.

Results: Males were predominant in both with & without CAE. 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%). HsCRP was higher in patients with CAE than those without and was significantly higher in patients with more extensive ectasia. Majority (65.4%) of CAE patients had significant CAD; whereas, only 7.4% had isolated CAE. Most common artery involved was RCA (70.4% of total) and most common pattern was single ectatic vessel.

Conclusion: Obesity and smoking predispose to CAE, along with male sex and hypertension. While diabetes is negatively associated with CAE. HsCRP levels tend to be higher in ectasia patients, especially those with severe forms. Finally, CAE has a predilection for RCA.

Key Words: *Coronary artery ectasia, Atherosclerosis, Inflammation, Coronary artery disease, Angiographic, Risk factors.*

INTRODUCTION

Coronary artery ectasia is a rare entity which can be congenital or acquired.[1-3] Coronary artery ectasia (CAE) is defined as abnormal dilation of coronary artery to at least 1.5 times of the adjacent normal coronary.[1,4] The incidence of CAE, according to CASS registry is 0.3 - 4.9%.[2] CAE has been attributed in most cases to atherosclerosis; being considered a variant of stenotic coronary artery disease (CAD).[5,6] Connective tissue diseases, congenital, inflammatory diseases and prior coronary intervention are among other etiologies.[6] Mostly, young patients have causes other than atherosclerosis; whereas, elderly have later as the pathogenesis.[1]

CAE has been associated with increased morbidity and mortality.[2,7] The most common presentation is angina.[1,4] Some patients present with myocardial ischemic symptoms; whereas, others present with symptoms of systemic disease.[8]

The pathogenesis of CAE is inflammation in the arterial wall and positive remodelling response brought about by degradation of extra cellular matrix by metalloproteinases.[1,6,4] The result is thinned out media and ectatic vessel. CAE is associated with sluggish flow, spasm, thrombosis, distal embolisation, dissection and poor collateral development.[7,9,10]

On angiogram, presence of abnormal dilated coronary and signs of delayed or stagnant flow diagnose coronary ectasia.[1,6,11] The management of coronary ectasia relies mainly on antiplatelets; antithrombotics have been supported by some evidence as well.[11] Nitrates probably worsen the outcome.[1,6] CAE when presenting as acute coronary syndrome (ACS) is often associated with high thrombus burden and lower rate of successful revascularisation. This may be translated into poor outcome.

Since inflammation is believed to play part in its pathogenesis, its serum markers will be raised in ectasia like in obstructive CAD. Inflammatory markers have been associated with CAE. Inflammatory markers may have a prognostic role in CAE as well. Higher levels of some markers, like HsCRP or Matrix metallo-proteinases, have been found in CAE than in patients with obstructive CAD or normal coronary arteries.[12]

The etiology, management, and prognostic implication of coronary ectasia is controversial and needs to be investigated further.[1,9]

The rational of the current study is to provide insight into the clinical features and prognosis of CAE. The objective of the study was to investigate the clinical and angiographic characteristics of coronary artery ectasia and its relation with the inflammatory marker, HsCRP.

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METHODOLOGY

Patients undergoing invasive angiogram from April 2015 till November 2016 at Rawalpindi Institute of Cardiology, Rawalpindi, were retrospectively evaluated. The study included patients with CAE and a group of age, gender and geographical region matched individuals with stenotic CAD, but without CAE to serve as control group. Exclusion criteria included patients who failed to give consent, had valvular heart disease or cardiomyopathy or a history of prior CABG or PCI. Also excluded were patients whose angiogram quality were suboptimal and patients having fever, sepsis, recent (three months) surgery or trauma, hematological malignancy or patients on current or recent (three months) steroid therapy and patients at extremes of ages (less than 20 years of age or more than 75 years).

Clinical data was obtained by interviewing the patient and, in addition, by reviewing hospital medical records. Angiogram films were reviewed by two cardiologists to diagnose CAE, classify it, and assess for associated coronary artery disease. Data about reason for presentation to hospital and reason for angiogram was collected on hospital admission for angiographic procedure and detailed clinical examination was performed. Most patients had angiogram done as an elective procedure after discharge for acute coronary syndrome admission, only few (10%) had angiogram done during the same admission. Samples for serum HsCRP levels were drawn from all the patients and analysed in Beckman Coulter AU48.

The research protocol was approved by the Ethical Review Board. Written informed consent was taken from all patients. The cardiologist who reported the angiogram was blinded to the clinical characteristics. Coronary angiography was performed through either radial or femoral approach using Terumo or Cordis sheaths and Terumo or Cordis diagnostic catheters of six or five French size. Coronaries were opacified with the standard iodinated contrast Ultravist (iopromide) in 370 mg I/mL concentration. Orthogonal views were taken for both the right and left coronary systems. Coronary artery (CA) ectasia and stenosis were evaluated by visual analysis and counterchecked, if needed, by quantitative analysis. Significant coronary artery disease was defined as $\geq$50% stenosis for left mainstem and $\geq$70% stenosis for other coronaries. A narrowing of coronary lumen of $\geq$50%, but less than 70% was defined as subcritical coronary artery disease; while stenosis of less than 50% was taken as minor CAD.

Hypertension was defined as the pressure of more than 140/90 mmHg on at least two consecutive measurements or treatment with antihypertensive agent. Hyperlipidemia was defined as fasting low density lipoprotein cholesterol >4.14 mmol/L or triglyceride >1.7 mmol/L. Obesity was defined as body mass index $\geq$30 Kg/m^2; whereas, overweight was defined as body mass index (BMI) of >25 Kg/m^2 but less than 30 Kg/m^2.

CAE was classified according to its extent and number of vessels involved as proposed by Markis.[1] Four types were listed as type 1 = diffuse ectasia of two or three vessels, type 2 = diffuse ectasia of one vessel and localised in another, type 3 = diffuse ectasia in one vessel only, and type 4 = localized or segmental involvement.

Data was analysed with SPSS 19 for Windows statistical package. Parametric variables were expressed as means and standard deviation; means (SD) and categorical variables were expressed as percentages. Variables which did not follow normal distribution were given as median (IQR). Chi-square test was applied for categorical data while Mann-Whitney test was used in nonparametric as appropriate. Analysis of variance was used to analyse HsCRP levels among various types of ectasia. Correlation analysis was used to study association of ectasia with different risk factors. A p-value of <0.05 was accepted as significant.

RESULTS

A total of 138 patients including 81 with CAE and 57 controls, *i.e.* with stenotic CAD but without CAE, entered the study.

Two groups were matched with respect to age. CAE group had mean age of 56.09 $\pm$8.684 years and non-CAE group had a mean age of 56.07 $\pm$9.096 years. They were also matched with respect to their geographical origin. Table I summarises the clinical characteristics and coronary risk factors of the patients. The two groups, *i.e.* with and without ectasia, did not differ significantly (p=0.353) with respect to gender, 93.8% (n=76) of former were males, and 89.5% (n=51) of later were males. Thus, it can be stated that CAE is a male prevalent disease like stenotic CAD. Hypertension, smoking, and obesity were significantly more common among patients with ectasia than without CAE (p <0.001, p <0.001 and p <0.001, respectively). Whereas, dyslipidemia was more prevalent in patients without CAE as compared to those with CAE. Diabetes was less frequent in CAE patients as compared to patients without CAE, but with CAD (p <0.001).

The incidence of CAE was found to be 2.54%. Considering presentation to hospital for coronary angiography, the two groups had the following distribution. Twenty-two CAE patients and 17 non-CAE patients presented with non-ST elevation MI (27.2% and 29.8%), while 4 patients with CAE and 3 without it suffered unstable angina (4.9% and 5.2%). ST elevation MI was the reason for admission in 37 CAE patients and 27 non-CAE patients (45.7% vs. 47.4%). However, stable angina brought 18 CAE patients to cath lab compared to 10 patients without CAE (22.2% vs. 17.5%, p<0.001).

Total number of ectatic vessels were 134. Ectasia involved one vessel in 50.6% (n=41) of patients, whereas two coronaries were ectatic in 33.3% (n=27); and all three coronaries were involved in 16% (n=13) of patients. The most common vessel involved by ectasia was right coronary artery (RCA) in 70.4% (57), left anterior descending (LAD) in 54.3% (43), and left circumflex was involved in 38.3% (30) of patients. Table II presents the distribution of patients according the four types of ectasia according to Markis. Thus the most prevalent type was type 1, which included diffuse and multivessel involvement. According to the anatomical type, more patients had fusiform ectasia (n=30) than sacular ectasia (n=20) 37% *versus* 24.7%. The anatomical classification was not applicable on 31 (38.3%) CAE patients.

A total of 53 (65.4%) patients with CAE had associated significant obstructive CAD. Out of them, 20 had triple-vessel coronary artery disease (TVCAD), 19 had double vessel coronary artery disease (DVCAD) and 13 had single vessel CAD, while only one had TVCAD with critical left main stenosis. 14.8% (12) had subcritical CAD, while minor CAD was found in 12.3% (10). Only 7.4% (6) had no associated obstructive coronary artery disease. In patients with non-significant coronary artery disease, the ectatic vessel distribution was similar. Similarly, in patients without CAD, *i.e.* isolated CAE, the pattern of vessel involvement was similar with RCA being the most commonly involved vessel.

Table I: Coronary risk factors in patients with and without ectasia.

Coronary risk factors	Patients with coronary artery ectasia (n*=81)	Patients with CAD without CAE (n*=57)
Hypertension (n*)%	(49)60.5%	(30) 52.6%p<0.001
Diabetes mellitus	(26) 32.1%	(24) 42.1%p<0.001
Smoking**	(46) 56.8%	(25) 43.9%p<0.001
Dyslipidemia	(24) 29.6%	(25) 43.9%p<0.001
Obesity	(65) 80.2%	(8) 14%p<0.001

**n = number of patients; **includes both current and ex-smokers.*

Table II: Distribution of patients* according to Markis classification.

Markis ectasia type	Number of patients (percentage)
Type 1	26 (32.1%)
Type 2	12 (14.8%)
Type 3	19 (23.5%)
Type 4	24 (29.6%)

**Total number (of patients with CAE)=81*

Table III: Regression analysis results.

Coronary risk factors	Odds ratio	95% confidence interval
Hypertension	1.45	0.55-3.79
Diabetes mellitus	0.78	0.30-2.03
Smoking	1.399	0.47-4.11
Dyslipidemia	0.64	0.24-1.71
Obesity	22.46	8.64-58.37
Male gender	1.59	0.27-9.15

Table Iv: Mean HsCRP levels in four types of ectasia.

Markis ectasia type	HsCRP level* median (IQR)
Type 1	3.80 (25.54)
Type 2	3.35 (13.30)
Type 3	2.94 (5.51)
Type 4	3.09 (7.53)

**mg/dl*

The median (IQR) value of serum HsCRP level was 3.40 (9.15) in the group with CAE; whereas, it was 3.16 (5.10) in patients without CAE. However, the difference came out to be statistically non-significant for median (p=0.839) even though it was significant for distribution (0.045). The mean body mass index (BMI) in patients with CAE was 26.37 (5.11 Kg/m^2), and it was 25.43 (4.21 Kg/m^2) in patients without CAE. Table III shows the median (IQR) value of serum HsCRP level in the four types of ectasias. In general, the HsCRP level was higher in patients with more diffuse ectasia and greater number of vessels involved. Univariate analysis of variance showed that the HsCRP level was significantly high in patients with diffuse ectasia and greater number of vessels involved as compared to those with localised or segmental involvement (p = 0.032, R squared = 0.078 and adjusted R squared = 0.050). A higher HsCRP was independently associated with diffuse and multivessel ectasia.

Correlation analysis, using logistic regression, showed that the presence of CAE was positively associated with smoking, obesity, male gender, hypertension and HsCRP levels, but inversely with diabetes. Although the association was significant only for obesity, being statistically non-significant for rest. Whereas, diabetes and dyslipidemia were negatively associated with CAE. Table IV shows the results of regression analysis.

DISCUSSION

The current study presents the clinical features of CAE, its angiographic characteristics and association with the inflammatory marker HsCRP. Thus, the current study adds to the understanding of CAE and may be helpful in making important decisions.

The prevalence of CAE varies according to the study population. In our study, it was found to be 2.54%. Amirzedagan reported a prevalence of 2.3%, Pinar *et al*. reported it around 3.39%, Lam presented it around 1.2%, while Giannoglou *et al*. presented it around 2.7% and Sharma found it around 12%.[3,13]

The most common cause is atherosclerosis.[6] Thus patients having atherosclerotic risk factors have atherosclerosis as the cause of CAE.[6] Abid *et al*. found CAE was associated with all the classic atherosclerotic risk factors except diabetes mellitus (DM) and Dogan *et al*. concluded inverse association with DM.[8,14] Amirzedagan found CAE patients were more likely to be obese and less likely to be diabetic. However, no traditional risk factor was correlated to CAE.[13] Aksu

stated that CAD risk factors were found to similar to some extent in CAE as in CAD in his study.[15] 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. Swaye *et al*. found no difference with respect to smoking among patients with and without CAE.[9] Fariba *et al*. found increased prevalence of hypercholesterolemia in patients with CAE; opposite to what the present authors found.[5]

Age was found to be inversely related to CAE by some previous researchers and to have no independent influence by others.[12,16] This opposes that CAE might be just an atherosclerotic variant. This study, however, involved age-matched patients with and without CAE so we cannot comment on it. Male predominance was found in CAE patients in previous studies and this was supported by the results of the current study.[9,13,17,18]

Obesity is a known atherosclerotic risk factor. Previous studies by Waly *et al*. and Cetin *et al*. concluded obesity was more prevalent in patients with coronary ectasia.[8,19] This was replicated in this study since obesity was significantly higher among patients with ectasia compared to stenotic CAD. Obesity may have role in the pathogenesis *via* inducing an inflammatory and prothrombotic state.

Coexisting CAD was found in 90.8% patients in CASS registry, 85% in a study by Abid and 84.7% in study by Demopoulos *et al*.[8,13] Similarly, a high proportion (65.4%) of CAE patients had coexisting CAD in this study. This observation supports atherosclerosis as the mechanism for CAE in majority of patients. Sanad showed that 57% had CAD with CAE while 42% were isolated CAE.[18]

Lam, Giannoglou and Shi-Min found predilection of ectasia to involve RCA, this was replicated in the current study.[3,20] One study found LAD to be most commonly involved vessel.[19] Single vessel involvement was most common according to CS Lam and the current study also showed single ectatic vessel to be more prevalent as compared to two or three vessels involvement.[3]

Inflammation is believed to be involved in the pathogenesis of CAE. Inflammatory markers, therefore, will be higher in CAE. It was found higher HsCRP level in CAE (median 3.40) than those without CAE (median 3.16), although difference was non-significant. Previous studies have found higher HsCRP levels in patients with CAE than those without it.[12,18,21,22] Turhan and Huang found that extensive and severe ectasia was associated with severe inflammation as proposed by various markers.[23] This study also found that higher HsCRP level was found in those with extensive and diffuse ectasia than those with limited involvement. HsCRP value correlated to the severity of CAE in previous studies as well.[12,19]

This study had several limitations like being single center based, small sample size, retrospective analysis and follow-up loss. In addition, etiology other than atherosclerosis was not studied and inflammatory markers other than HsCRP were not studied. Furthermore, most patients had associated CAD so patients with isolated CAE were under-represented. However, since CAE is commonly accompanied by CAD so conducting large scale studies of isolated CAE might be difficult. This study provides an insight into the predisposing factors of CAE and its angiographic characteristics as well as points towards its association with inflammation.

CONCLUSION

Obesity and smoking predispose to CAE, along with male sex and hypertension. While diabetes is negatively associated with CAE, HsCRP levels tend to be higher in ectasia patients, especially those with severe forms. Finally, CAE has a predilection for RCA.

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