Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(4), 2111-2117 | ISSN:2251-6727

"Coronary Ectasia in Patients Undergoing Coronary Angiography at a Tertiary Care Center: Prevalence and Prognostic Implications"

Running Title: "Assessing Coronary Ectasia in Tertiary Care: Prevalence and Prognosis"

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(Received: 02 September 2023 Revised: 14 October Accepted: 07 November)

KEYWORDS
Coronary artery ectasia (CAE), Prevalence, Risk factors, Markis classification, Prognosis

ABSTRACT
Coronary artery ectasia (CAE) is characterized by abnormal expansion of coronary arteries, with variable clinical manifestations. This study investigates the prevalence, clinical profiles, risk factors, and angiographic features of CAE, as well as its impact on coronary blood flow and prognosis in patients with coronary artery disease.
A prospective, observational study was conducted in tertiary hospital over two years (April 2021 to April 2023). The study consisted of 60 consecutive patients undergoing coronary angiography, with a focus on age, gender, comorbidities, and risk factors. The Markis classification system was used to categorize CAE patterns. The study also examined the relationship between diabetes, inflammation, dyslipidemia, homocysteine levels, vitamin D deficiency, and CAE. Long-term outcomes and the impact of CAE on coronary blood flow were assessed.
Results: The study found a male predominance in the CAE population, with an average age of 56.62 years. Diabetes and smoking were identified as risk factors associated with CAE, and ST-segment elevation myocardial infarction was the most common presentation. The Markis type 4 pattern was most frequently observed, with the right coronary artery being the most affected. Diabetic patients with CAE had distinct ectatic segments. Inflammation, neutrophil : lymphocyte ratio, C-reactive protein, dyslipidemia, elevated LDL-C, serum homocysteine levels, and vitamin D deficiency were all linked to CAE. Slow blood flow and alterations in blood flow patterns were observed in patients with ectatic coronary arteries. Mortality rates in CAE patients were similar to those with coronary artery disease without ectasia.
Conclusion: CAE is associated with various clinical and biochemical factors, impacting coronary blood flow. A better understanding of these associations can guide clinical management decisions in patients with CAE.

INTRODUCTION

Coronary artery ectasia, or CAE, is a medical condition where one or more epicardial coronary arteries experience abnormal widening. This expansion can happen throughout the entire artery or in a particular localized region. For a diagnosis of CAE, the diameter of the affected artery needs to be at least 1.5 times greater than the adjacent segment deemed within the standard size range. Research has indicated that around 5% of individuals undergoing coronary angiography exhibit this condition. [1,2].

John E. Markis, a prominent researcher in the field, initially classified coronary ectasia, which is characterized by coronary artery dilation. His

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(4), 2111-2117 | ISSN:2251-6727

classification system divided coronary ectasia into four distinct groups. This classification system has since been widely adopted by researchers and clinicians to better understand and categorize this pathological condition. The vascular ectasia classification system includes four types: Type 1, involving diffuse ectasia in two or more vessels; Type 2, where one vessel exhibits diffuse ectasia, and another vessel shows focal disease; Type 3, characterized by diffuse ectasia in a single vessel; and Type 4, involving localized or segmental involvement. This system offers a framework for comprehending the various patterns of vascular ectasia [3].Atherosclerosis has been extensively documented as the primary underlying mechanism leading to the development of coronary ectasia. (PCI) [4, 5, 6].

Coronary artery ectasia (CAE) presents a wide range of clinical manifestations, including incidental discovery in asymptomatic individuals, exertional angina, exercise-induced ischemia observed during treadmill testing, and acute coronary syndrome (ACS) [5, 6]. The prognosis and management of CAE remain subjects of ongoing discussion within the academic and professional communities. Numerous studies have examined the occurrence of major adverse cardiovascular events (MACE) in individuals with dilated coronary arteries who have experienced myocardial infarction (MI) [8].

The management of patients diagnosed with coronary artery ectasia (CAE) poses a significant therapeutic challenge for interventional cardiologists. However, due to the limited availability of comprehensive data and guidelines regarding pharmacological and interventional treatments, clinicians often rely on their personal expertise in making treatment decisions.

In our ongoing study conducted within our hospital's specialized tertiary care facility, our principal objective was to evaluate the frequency of coronary artery ectasia in individuals who were undergoing coronary angiography. Our investigation also sought to explore potential associations between coronary artery ectasia and a range of demographic and biochemical variables. Furthermore, we delved into the effects of CAE on coronary blood flow and its impact on the prognosis of coronary artery disease (CAD). To accomplish this, we assessed the incidence of major adverse cardiovascular events (MACE) in patients with CAE, comparing their outcomes with those of individuals having obstructive CAD and those with unremarkable coronary arteries

AIM AND OBJECTIVES

AIM

To assess the prevalence of coronary ectasia in patients undergoing coronary angiography.

OBJECTIVES

To study the clinical profile, biochemical parameters and angiographic features of patients diagnosed with coronary ectasia.

To compare the biochemical parameters and angiographic features of coronary ectasia with obstructive coronary artery disease.

To study the influence of coronary ectasia on outcome in patients diagnosed with obstructive coronary artery disease by estimating the incidence of recurrence of acute coronary syndrome in patients with coronary ectasia.

MATERIAL AND METHODS

This prospective, observation, clinical study was conducted in patients undergoing angiography in Department of Cardiology Bharati Vidyapeeth (Deemed to Be University) and medical college hospital and research centre, Pune which included 122 consecutive patients satisfying the inclusion and exclusion criteria coming to our hospital for coronary angiography for 2years (April 2021 to April 2023) Patients of both gender with age of >18 years, undergoing coronary angiography, as per clinical condition and those willing to give written informed consent were included in the study and Patients who are not willing or not medically fit to undergo coronary angiography based on clinical and biochemical parameters were excluded from the study.

Methodology

All necessary investigations were done before the procedure and patient were managed as per protocol of department. A detailed history was elicited, and a physical examination was carried out. The enrolled patients underwent the investigations of Hemogram, lipid Profile, Glycated hemoglobin (HbA1c), C-reactive protein (CRP), Serum homocysteine , Electrocardiogram (ECG), Angiography According to the following criteria, they were classified as having either unstable angina (UA), non-ST segment elevation myocardial infarction

Journal of Chemical Health Risks
www.jchr.org
JCHR (2023) 13(4), 2111-2117 | ISSN:2251-6727

(NSTEMI), or ST segment elevation myocardial infarction (STEMI)

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www.jchr.org
JCHR (2023) 13(4), 2111-2117 | ISSN:2251-6727

STATISTICAL ANALYSIS AND METHODS

The data were meticulously scrutinized utilizing Microsoft Excel 2021. A 'p' value below 0.05 was deemed to be indicative of statistical significance. Descriptive statistics for categorical variables, namely age, gender, patient groups with and without comorbidities, as well as those with and without ectasia, were meticulously analyzed and presented as percentages. To compare these categorical variables, the Chi-squared test was employed.

For data categorized as continuous variables, we systematically evaluated and presented the data as the Mean in conjunction with its accompanying standard deviation. The ANOVA test was employed to appraise the relationship between the TIMI frame count and various subgroups within the study population, including patients with isolated coronary ectasia, patients with ectasia and obstructive coronary artery disease, patients with obstructive coronary artery disease but without ectasia, and those with normal coronary arteries. A similar application of the ANOVA test was undertaken for other continuous variables, encompassing the neutrophil-to-lymphocyte ratio, serum homocysteine levels, C-reactive protein levels, vitamin D levels, and lipid profile. The association between two continuous variables was explored utilizing the Spearman rank correlation coefficient test, with both the correlation coefficient (rho) and 'p' value being computed.

TABLE 2: Distribution of Gender and age in Study Population

	Isolated Coronary Ectasia	Coronary Ectasia with Coronary artery disease	Coronary artery disease without ectasia	Normal Coronary arteries	Chi-Square Statistic (X^2)	"P"
Male	17	79	85	79	5.94	>0.05
Female	5	21	37	43		
Age (Mean +_ SD) Years	60.3 ±9.7	55.81±10.7	56.5±10.6	57.01±10.1	-	>0.05

TABLE 3: Distribution of Comorbidities and risk factors in the study and control Population

Comorbidity and risk factor		Isolated Coronary Ectasia N (%)	Coronary artery ectasia with coronary artery disease N (%)	Coronary artery disease without coronary ectasia N (%)	Normal coronary arteries N (%)	Chi square statistic (X^2)	"p" value
Hypertension	Present	11 (50%)	37 (37%)	55 (45%)	58 (47%)	2.98	0.39
	Absent	11 (50%)	63 (63%)	67 (55%)	64 (53%)		
Total		22(100%)	100 (100%)	122 (100%)	122 (100%)		
Diabetes Mellitus	Present	10 (45%)	39 (39%)	58 (47%)	47 (38%)	2.6	0.45
	Absent	12 (55%)	61 (61%)	64 (53%)	75 (62%)		
Total		22 (100%)	100 (100%)	122 (100%)	122 (100%)		

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Smoking	Present	6 (27%)	47 (47%)	42 (34%)	45 (36%)	0.79	0.15
	Absent	16 (73%)	53 (53%)	80 (66%)	77 (64%)		
Total		22 (100%)	100 (100%)	122 (100%)	122 (100%)		

Table 4: Distribution of Ischemic heart disease amongst the study population.

Types of ischaemic heart disease	**N**	**Percentage (%)**
Unstable angina	15	12.2
Stable angina	14	11.5
NSTEMI	25	20.6
Anterior wall STEMI	33	27
Inferior wall STEMI	35	28.7

Table no. 5: Distribution of isolated coronary ectasia, coronary ectasia with obstructive coronary artery disease, obstructive coronary artery disease alone and normal coronary arteries in the study population

Parameter	**N**	**Percentage (%)**
Coronary ectasia with obstructive coronary artery disease	100	27.3
Isolated coronary ectasia	22	6%
Obstructive coronary artery disease without ectasia	122	33.3
Normal coronary arteries	122	33.3

Table 6: Distribution of ectatic coronary arteries as per Markis classification in study population

Markis classification	**N**	**Percentage (%)**
1	15	12.3
2	33	27
3	15	12.3
4	59	48.4

DISCUSSION

The study investigated the distribution of age and gender, comorbidities and the prevalence of ischemic heart disease in patients with coronary ectasia. Out of the 122 patients diagnosed with coronary ectasia, 22 had solitary coronary ectasia, while the remaining 100 showed both coronary ectasia and coronary artery disease. These individuals were then paired with two separate groups: 122 patients with a normal coronary angiogram, and those with coronary artery disease but without ectasia. The study found that males were the majority in the study population, with an average age of 56.62 years. These results were consistent with findings from other studies, and coronary ectasia was more common in males. Additionally, coronary artery disease was a significant

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www.jchr.org
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factor associated with coronary ectasia, and it was more prevalent in males compared to females.

In terms of comorbidities and risk factors, 38.5% of patients with coronary ectasia had diabetes mellitus, which was higher than reported in other studies. Smoking was observed as a risk factor in 24% of the patients, leading to oxidative stress and inflammation that could promote coronary ectasia.

Regarding the presentation of ischemic heart disease in the study population, ST-segment elevation myocardial infarction was the most common, accounting for 56.7% of cases. This could be attributed to disturbances in coronary flow and endothelial stress, which led to a prothrombotic state and compromised myocardial blood supply. The coexistence of coronary ectasia and atherosclerotic coronary artery disease was frequently observed, consistent with previous studies.

In summary, the study found a male predominance in the population with coronary ectasia, highlighted the association between diabetes, smoking, and the condition, and emphasized the frequent occurrence of ST-segment elevation myocardial infarction in these patients due to coronary flow disturbances. This information aligns with previous research in the field.

The study examined the distribution of coronary ectasia in the study population based on the Markis classification. The most common type observed was Markis type 4, which is characterized by localized and segmental ectasia. This finding was consistent with a study by Tony et al. The reported findings indicated that the prognostic implications of coronary ectasia were influenced by the distribution and scope of the condition. Specifically, individuals with widespread ectasia faced an elevated risk of experiencing significant adverse cardiovascular events. In terms of frequency, the right coronary artery (RCA) was the most commonly impacted, followed by the left anterior descending (LAD) and left circumflex (LCX) arteries, with the left main coronary artery (LMCA) showing the least occurrence. The reasons behind this topographical preference remain unexplained. Additionally, the RCA had longer ectatic segments with larger diameters, leading to larger ectatic areas. This observation was in line with studies by Wu et al and Tony et al. [9] [10]

The study also explored the relationship between diabetes mellitus and coronary ectasia. It found that diabetic patients with coronary ectasia had ectatic segments with smaller diameters, shorter lengths, and smaller ectatic areas. The estimated ectatic ratio was significantly lower in diabetic patients compared to non-diabetic patients. Diabetes mellitus negatively affected arterial remodeling during the atherosclerotic process, possibly due to the downregulation of matrix metalloproteinases (MMP) in smooth muscle cells and monocytes.

Inflammation was recognized as a significant contributor to the onset of coronary ectasia.. Neutrophils were found to infiltrate the tunica media of ectatic coronary arteries, secreting proteolytic enzymes and oxygen free radicals. Neutrophil : lymphocyte ratio and C-reactive protein were associated with the severity of inflammation and coronary ectasia. Elevated C-reactive protein levels were also linked to vulnerable plaques.

Dyslipidemia, particularly elevated LDL-C levels, was associated with coronary ectasia. Oxidation of LDL-C promoted the binding of LDL-C to components of the extracellular matrix, leading to the secretion of metalloproteases and proteolysis of the extracellular matrix.

Elevated serum homocysteine levels were observed in patients with coronary ectasia and atherosclerotic disease. Serum homocysteine is known to induce endothelial dysfunction and promote atherogenesis, correlating positively with the incidence of coronary ectasia. Vitamin D deficiency was positively correlated with coronary ectasia, possibly due to its role in controlling renin-angiotensin-aldosterone system activity, inflammation, and atherogenesis.The long-term outcomes of coronary ectasia remain underexplored, with some studies suggesting increased rates of angina and ischemia in these patients. Nonetheless, the mortality rates among individuals with coronary ectasia mirrored those observed in patients with coronary artery disease who did not have ectasia. The study also examined blood flow in coronary ectasia using TIMI frame counts and found a positive correlation between the magnitude of ectasia and TIMI frame count. Slow blood flow and alterations in blood flow patterns were observed in patients with ectatic coronary arteries. The management varied and was largely case-based, depending on factors such as clinical presentation, operator experience, and coronary anatomy. Medical care was prevalent among individuals with solitary coronary ectasia and non-blocking coronary artery disease.

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JCHR (2023) 13(4), 2111-2117 | ISSN:2251-6727

CONCLUSION

Coronary ectasia is a relatively uncommon finding in coronary angiography. In our present study, we sought to investigate the prevalence of coronary ectasia among patients undergoing angiography and its associations with risk factors, coronary blood flow, and biochemical factors. Our findings revealed that the Markis type 4 subtype of coronary artery ectasia (CAE) was the most frequently encountered. A robust link was observed between the Markis classification and the extent of ectasia, with the right coronary artery (RCA) being the most frequently affected and displaying more severe cases of coronary ectasia. Additionally, we noted a negative correlation between the occurrence of diabetes mellitus, HbA1c levels, and the presence of coronary ectasia. The presence of elevated inflammatory markers in patients with ectasia supported the hypothesis that inflammation may contribute to the development of this condition. Although we did not identify any significant major adverse cardiovascular events in the group of individuals with ectasia in our study, it underscores the imperative need for standardized treatment guidelines for coronary artery ectasia.

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