

## PURE CORONARY ARTERY ECTASIA AND MAIN ATHEROSCLEROTIC RISK FACTORS: A STUDY OF IRANIAN POPULATION

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## ЧИСТА ЕКТАЗИЯ НА КОРОНАРНИТЕ АРТЕРИИ И ОСНОВНИ АТЕРОСКЛЕРОТИЧНИ РИСКОВИ ФАКТОРИ: ИЗСЛЕДВАНЕ НА ИРАНСКОТО НАСЕЛЕНИЕ

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### Abstract.

**Introduction:** Coronary artery ectasia (CAE) is an uncommon angiographic finding often associated with atherosclerosis. However, the risk profile of patients with pure CAE (defined as ectasia in the absence of significant obstructive coronary artery disease) remains incompletely understood. This study aimed to evaluate the association between traditional atherosclerotic risk factors and pure CAE in an Iranian population. **Material and methods:** In this retrospective cross-sectional study, 354 patients with pure CAE were identified among 23,000 consecutive coronary angiography reports from two tertiary hospitals (2015–2022). Pure CAE was defined as segmental or diffuse coronary artery dilatation  $\geq 1.5$ -fold the adjacent normal segment in the absence of  $\geq 50\%$  stenosis in any epicardial vessel. Patients with diffuse but non-obstructive atherosclerosis, history of vasculitis, autoimmune disease, congenital syndromes, or incomplete records were excluded. Demographic data and cardiovascular risk factors (hypertension, diabetes, hyperlipidemia, smoking, family history) were collected. Statistical analysis included both univariate comparisons and multivariable logistic regression to identify independent predictors of CAE. **Results:** The mean age was  $57.5 \pm 12.6$  years; 64.1% were male. Hypertension (64.7%) and hyperlipidemia (57.9%) were the most prevalent risk factors. Multivariable regression identified male sex (OR 1.8, 95% CI 1.1–2.9,  $p = 0.01$ ), hypertension (OR 2.1, 95% CI 1.3–3.2,  $p = 0.002$ ), and hyperlipidemia (OR 1.7, 95% CI 1.1–2.5,  $p = 0.01$ ) as independent predictors of CAE. Diabetes mellitus and smoking were not significantly associated. Family history showed borderline significance (OR 1.4,  $p = 0.06$ ). The most common angiographic pattern was three-vessel ectasia (37.9%). **Conclusion:** Pure CAE is more frequent in men and strongly associated with hypertension and hyperlipidemia, supporting a shared risk profile with atherosclerosis. The absence of association with diabetes and smoking suggests a distinct underlying pathophysiology.

### Key words:

coronary artery ectasia, pure CAE, atherosclerosis, risk factors, angiography

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### Резюме.

**Въведение:** Ектазията на коронарните артерии (CAE) е рядко срещано ангиографско нарушение, често свързано с атеросклероза. Въпреки това рисковият профил на пациентите с чиста CAE (определена като ектазия при липса на значителна обструктивна коронарна болест) остава не напълно изяснен. Целта на това проучване е да оцени връзката между традиционните атеросклеротични рискови фактори и чистата CAE при иранската популация. **Материал и методи:** В това ретроспективно кроссекционно проучване бяха идентифицирани 354 пациенти с чиста CAE сред 23 000 последователни доклада за коронарна ангиография от две третични болници (2015-2022 г.). Чистата CAE бе дефинирана като сегментна или дифузна дилатация на коронарната артерия  $\geq 1,5$  пъти по-голяма от съседния нормален сегмент при липса на  $\geq 50\%$  стеноза в някой от епикардиалните съдове. Пациентите с дифузна, но необструктивна атеросклероза, анамнеза за васкулит, автоимунно заболяване, вродени синдроми

или непълни записи бяха изключени от проучването. Бяха събрани демографски данни и данни за сърдечно-съдови рискови фактори (хипертония, диабет, хиперлипидемия, тютюнопушене, фамилна анамнеза). Статистическият анализ включваше както едномерни сравнения, така и многомерна логистична регресия за идентифициране на независими предиктори на САЕ. **Резултати:** Средната възраст на обхванатите в проучването лица беше  $57,5 \pm 12,6$  години; 64,1% бяха мъже. Хипертония (64,7%) и хиперлипидемия (57,9%) бяха най-разпространените рискови фактори. Многовариантната регресия идентифицира мъжкия пол (OR 1,8, 95% CI 1,1–2,9,  $p = 0,01$ ), хипертонията (OR 2,1, 95% CI 1,3–3,2,  $p = 0,002$ ) и хиперлипидемията (OR 1,7, 95% CI 1,1–2,5,  $p = 0,01$ ) като независими предиктори на САЕ. Захарният диабет и тютюнопушенето не показаха статистически значима връзка. Семейната анамнеза показва гранична значимост (OR 1,4,  $p = 0,06$ ). Най-често срещаният ангиографски модел е ектазия на три съда (37,9%). **Заклучение:** Чистата САЕ е по-честа при мъжете и е силно свързана с хипертония и хиперлипидемия, което подкрепя обща рискова характеристика с атеросклерозата. Липсата на връзка с диабета и тютюнопушенето предполага различна основна патофизиология.

**Ключови думи:** ектазия на коронарната артерия, чиста САЕ, атеросклероза, рискови фактори, ангиография

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## INTRODUCTION

Coronary artery ectasia (CAE) is a relatively rare angiographic finding, reported in 1.2–4.9% of patients undergoing coronary angiography worldwide [1]. Pure CAE was defined as segmental or diffuse coronary artery dilatation  $\geq 1.5$ -fold the adjacent normal segment in the absence of  $\geq 50\%$  stenosis in any epicardial vessel [2]. Although CAE is most commonly associated with atherosclerosis, other etiologies such as vasculitis, autoimmune diseases, and congenital syndromes have also been described [3]. From a pathophysiological point of view, CAE is the result of the degradation of the extracellular matrix of the media by matrix metalloproteinase which has been similarly observed in coronary heart disease [1, 2, 4]. More interesting, the clinical manifestations of the two coronary events are comparable as angina and acute coronary syndrome [3, 5]. Therefore, it is now assumed that there must be a significant overlap between the risk factors for coronary artery atherosclerosis and the CAE. Therefore, the present study aimed to investigate the prevalence of traditional atherosclerotic risk factors among patients with pure CAE in an Iranian population and to determine the independent predictors of this condition.

## MATERIAL AND METHODS

This cross-sectional study was approved by the local ethics committee, and written informed consent was obtained. The study was included patients undergoing coronary angiography at two tertiary referral hospitals in Yazd, Iran, between January 2015 and December 2022. Out of 23,000 angiograms, 369 cases of CAE were identified. After applying exclusion criteria, 354 patients with pure CAE were enrolled. Pure CAE was defined as focal or diffuse coronary dilatation  $\geq 1.5$ -fold

compared to an adjacent reference segment in the absence of  $\geq 50\%$  luminal stenosis in any major epicardial vessel [2].

### Exclusion criteria

- Obstructive CAD ( $\geq 50\%$  stenosis);
  - Diffuse atherosclerosis without focal stenosis;
  - Known vasculitis, autoimmune disease, or congenital coronary anomalies;
  - Incomplete demographic or laboratory data.
- A standardized checklist was used to collect data on demographics and cardiovascular risk factors:
- Hypertension: SBP  $\geq 140$  mm Hg or DBP  $\geq 80$  mm Hg, or use of antihypertensive drugs;
  - Diabetes mellitus: Fasting glucose  $\geq 7.0$  mmol/L, use of insulin or oral hypoglycemics;
  - Hyperlipidemia: Total cholesterol  $\geq 4.7$  mmol/L, triglycerides  $\geq 2.3$  mmol/L, or LDL  $\geq 4.1$  mmol/L;
  - Smoking:  $\geq 10$  pack-years;
  - Family history: CAD in male relatives  $< 55$  years or female relatives  $< 65$  years.

Continuous variables were presented as mean  $\pm$  SD and compared using t-test or Mann-Whitney U test as appropriate. Categorical variables were analyzed with chi-square test. Multivariable logistic regression was applied to identify independent associations of risk factors with pure CAE. Results were expressed as odds ratios (OR) with 95% confidence intervals (CI). A p-value  $< 0.05$  was considered significant. Analyses were performed using SPSS v23.

## RESULTS

Of 354 patients with pure CAE, the mean age was  $57.5 \pm 12.6$  years (range 25–89), and 64.1% were male. Hypertension (64.7%) and hyperlipidemia (57.9%) were the most common risk factors, followed by dia-

betes mellitus (30.2%), smoking (45.5%), and positive family history (50.6%). The baseline characteristics are shown in (Table 1). As shown in (Table 2), the pattern of three-vessel involvement with ectasia was significantly higher in the ages ranged 25 to 37 years followed by 64 to 76 years, while other patterns of involvements were seen mostly in the age range of 51 to 63 years indicating an age-dependent difference in the patterns of CAE ( $p = 0.02$ ). Also, multiple vessel ectasia was revealed more in men than in women ( $p = 0.03$ ). Moreover, multiple CAE was significantly higher in hypertensive than in normotensive patients ( $p = 0.004$ ), hyperlipidemic than normal lipid subgroups ( $p = 0.008$ ), and those with family history of CAE ( $p = 0.02$ ). However, we

showed no difference in the pattern of CAE in smoker and non-smoker subgroups ( $p = 0.55$ ). Multivariable regression identified male sex (OR 1.8, 95% CI 1.1–2.9,  $p = 0.01$ ), hypertension (OR 2.1, 95% CI 1.3–3.2,  $p = 0.002$ ), and hyperlipidemia (OR 1.7, 95% CI 1.1–2.5,  $p = 0.01$ ) as independent predictors of CAE. Diabetes mellitus and smoking were not significantly associated. Family history showed borderline significance (OR 1.4,  $p = 0.06$ ). The most common angiographic pattern was three-vessel ectasia (37.9%). The most frequent angiographic pattern was three-vessel ectasia (37.9%), followed by isolated LAD involvement (21.8%). Men and hypertensive patients were more likely to have multivessel ectasia.

**Table 1. Baseline characteristics and cardiovascular profile in study population (n = 354)**

Mean age, year	57.5 ± 12.6	
Male gender, %	227 (64.1)	
History of hypertension, %	229 (64.7)	
History of diabetes mellitus, %	107 (30.2)	
History of hyperlipidemia, %	205 (57.9)	
Family history of coronary disease, %	179 (50.6)	
History of smoking, %	161 (45.5)	
Pattern of coronary artery ectasia	LAD	77 (21.8)
	LCX	25 (7.1)
	RCA	34 (9.6)
	LAD & LCX	36 (10.2)
	LAD & RCA	39 (11.0)
	LCX & RCA	9 (2.5)
	LAD & LCX & RCA	134 (37.9)

## DISCUSSION

In this study of Iranian patients with pure CAE, we found that hypertension, hyperlipidemia, and male sex were independent predictors, whereas diabetes and smoking were not associated. These findings support the hypothesis that CAE shares major risk factors with atherosclerosis but may follow a distinct pathophysiological pathway. CAE, known as aneurysm or ectasia, is a rare condition that is usually seen as an accidental finding in those undergoing angiography, and its prevalence varies from 1.2 to 4.9% [1, 6]. The most common cause is atherosclerosis, followed by Kawasaki disease and congenital aneurysmal diseases [7-9]. Due to the most common cause of this disease, in this study we investigated the role of main risk factors for atherosclerotic diseases in CAE to find prognostic factors and determine their possible association with this disease.

**Table 2. The pattern of coronary CAE according to baseline variables**

Variables		LAD	LCX	RCA	LAD & LCX	LAD & RCA	LCX & RCA	LAD & LCX & RCA
Gender	Male	43 (18.9)	13 (5.7)	25 (11.0)	19 (8.4)	26 (11.5)	6 (2.6)	95 (41.9)
	Female	34 (26.8)	12 (9.4)	9 (7.1)	17 (13.4)	13 (10.2)	3 (2.4)	39 (30.7)
Age (Years)	25 to 37	4 (18.2)	1 (4.5)	0 (0.0)	2 (9.1)	2 (9.1)	0 (0.0)	13 (59.1)
	38 to 50	25 (29.4)	4 (4.7)	9 (10.6)	10 (11.8)	11 (12.9)	0 (0.0)	26 (30.6)
	51 to 63	28 (22.8)	10 (8.1)	14 (11.4)	17 (13.8)	16 (13.0)	4 (3.3)	34 (27.6)
	64 to 76	17 (16.5)	6 (5.8)	9 (8.7)	6 (5.8)	10 (9.7)	3 (2.9)	52 (50.0)
	77 to 89	3 (14.3)	4 (19.0)	2 (9.5)	1 (4.8)	0 (0.0)	2 (9.5)	9 (42.9)
History of hypertension	Positive	42 (18.3)	18 (7.9)	24 (10.5)	21 (9.2)	20 (8.7)	3 (1.3)	101 (44.1)
	Negative	35 (28.0)	7 (5.6)	10 (8.0)	15 (12.0)	19 (15.2)	6 (4.8)	33 (26.4)
History of hyperlipidemia	Positive	37 (18.0)	14 (6.8)	21 (10.2)	17 (8.3)	19 (9.3)	5 (2.4)	92 (44.9)
	Negative	40 (26.8)	11 (7.4)	13 (8.7)	19 (12.8)	20 (13.4)	4 (2.7)	42 (28.2)
History of coronary disease	Positive	32 (17.9)	9 (5.0)	15 (18.4)	16 (8.9)	18 (10.1)	4 (2.2)	85 (47.5)
	Negative	45 (25.7)	16 (9.1)	19 (10.9)	20 (11.4)	21 (12.0)	5 (2.9)	49 (28.0)
History of smoking	Positive	41 (25.5)	11 (6.8)	18 (11.2)	15 (9.3)	19 (11.8)	4 (2.5)	53 (32.9)
	Negative	36 (18.7)	14 (7.3)	16 (8.3)	21 (10.9)	20 (10.4)	5 (2.6)	81 (42.0)

According to the results of our studies, descriptive and demographic findings showed that the mean age of patients was  $57.5 \pm 12.6$  years. It was also shown that the frequency CAE is higher in men than women and the highest frequency of the study population was in the age of 51 to 63 years. Accordingly, in the study of Fariba et al [10] conducted in 2016, 61.3% of patients were male and 38.7% were female, and the average age of patients was 59 years, which was consistent with our study. In a 2011 study by Riffat Sultana et al [11] the mean age was  $52.1 \pm 10.3$  which was closely correlated with our study. Amirzadegan et al. [12] conducted a retrospective cohort study in Iran and showed that patients with CAE are significantly older than patients with normal coronary arteries. Also in the studies of Pinar et al. [7] Qin et al [8], and Swanton et al. [13], the most patients with CAE were men, which was consistent with our study in this regard. In this study, it was shown that most patients (64.7%) with CAE had hypertension and based on our study, there was a significant relationship between hypertension and CAE. Accordingly, in the study of Riffat Sultana et al [11], 55% of patients had high blood pressure and in the study of Fariba et al [10], 57.7% of patients had high blood pressure, which indicates that the majority of patients have high blood pressure. More interestingly, the complexity of CAE was associated with the hypertension, indicating raised blood pressure as the major risk factor for CAE complexity. Regarding the role of diabetes mellitus, in this study, 30.2% of patients were diabetic and 69.8% were non-diabetic, which showed that the prevalence of diabetes in patients with CAE was low. Accordingly, the study by Pinar et al [7] showed that 22.4% of patients had diabetes, which, like our study, indicates a low prevalence of diabetes in this disease. In the study of Riffat et al [11] and Fariba et al [10], the prevalence of diabetes was 22% and 13.4%, respectively. A study by Rashid et al [6] found that diabetes was independently but inversely related to CAE, which is consistent with the results of our study. In this study, 57.9% of the patients had abnormal lipid profiles, which among the patients with concomitant ectasia of LAD & LCX & RCA abnormal lipid profiles was more common. A study by Qin et al [8] showed that high levels of triglyceride and LDL/HDL ratio were identified as risk factors for CAE, which is consistent with the results of our study. In other studies by LAM et al [9] in Singapore 63% of patients with ectasia had abnormal lipid profile and this factor is strongly associated with CAE. In our study, 50.6% of patients with CAE had a positive family history of ischemic heart disease and 49.4% had no family history, which is a significant finding in patients with CAE. A study by Lui et al [14] showed hyperlipidemia and a positive family history as independent variables that were strongly associated with coronary atherosclerosis

but not with CAE. In our study, 45.5% of patients were smokers and 54.5% of patients were non-smokers. In our study, this factor did not show a significant relationship with CAE and the frequency of smokers with ectasia was lower than non-smokers. While in the study of Amirzadegan et al [12] (53.7%) and Pinar et al [7] (56.5%) and Qin et al [8], (56.6%) smoking was also shown as a risk factor for CAE. Fariba et al [10], smoking was a common risk factor for CAE because smoking was considerably prevalent in men than in women. Our study showed that the prominent pattern of coronary involvement was related to simultaneous involvement of three coronary vessels (37.9%), followed by LAD (21.8%) and then LAD & RCA (11%) involvement respectively. In the study by Riffat Sultana et al [11], the left anterior descending artery (LAD) was the most commonly involved vessel (63%) followed by RCA (25%), whereas in the study of George D Giannoglou et al [15], the prevalence of ectasia in the right coronary artery was significantly higher than the LAD and LCX arteries. Therefore, high variability in CAE involvement patterns has been observed in various reports. As the final conclusion, according to our study, the critical role of the main risk factors for coronary artery atherosclerosis, such as raised blood pressure, abnormal lipid profile, positive family history, male gender and old age has been evident in patients with CAE, while the role of diabetes and history of smoking remains already uncertain. Also, the difference in the prevalence of ectasia patterns in single or complex form as well as the type of vessel involved in different communities also needs further pathophysiological studies. But what is clear from our study is the pivotal role of some risk factors for atherosclerosis, including hypertension, hyperlipidemia, and a positive family history in increasing the risk of CAE. Consequently, control of any of these risk factors can be very effective in tracking the occurrence of ectasia and therefore preventing its adverse consequences.

## CONCLUSION

Pure CAE is significantly associated with male gender, hypertension, and hyperlipidemia, but not with diabetes or smoking. These findings suggest that while CAE shares major risk factors with atherosclerosis, its pathophysiology may be partially distinct. Careful risk factor management, especially blood pressure and lipid control, may play a crucial role in preventing complications in these patients.

## LIMITATIONS AND RECOMMENDATIONS

Future prospective studies incorporating multimodality imaging and broader etiologic screening (oth-

er CAE etiologies which were not evaluated in this study) are required to fully elucidate the pathogenesis of pure CAE.

“Compliance with Ethical Standards”

\* Authors have no conflicts of interest.

\* Study protocol was in accordance with the latest Declaration of Helsinki for medical research involving human subjects and was approved by the local ethics committee.

\*This article does not contain any studies with animals performed by any of the authors.

\*Informed consent was obtained from all participants of the study.

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