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Prevalence and Angiographic Characteristics of Coronary Artery Ectasia among Patients with Coronary Artery Disease: A Retrospective Analysis between 2014 and 2022

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Coronary artery ectasia (CAE) is defined as segmental dilatation with a diameter of 1.5-fold greater than that of an adjacent normal segment. Whether CAE is a unique clinical finding or results from other clinical entities remains to be determined. The purpose of the study was to investigate the prevalence, and clinical and angiographic characteristics of CAE in patients with coronary artery disease (CAD). Among the 8,845 coronary angiograms reviewed between the years 2014 and 2022, 142 patients had CAE yielding a detection rate of 4.9% among 2,870 CAD angiograms, and 28 patients had isolated CAE showing a detection rate of 0.32% (28/8,845) among total coronary angiography procedures. Overall, the incidence of CAE was 1.92% (170/8,845). The most commonly affected coronary artery by ectasia was the right coronary artery (RCA) (46.28%) among CAE coexisting with CAD cohort. The proportion of obesity, family history of CAD, and the proportion of hyperlipidemia in CAD patients who had ectasia were significantly higher than that in CAD patients who did not have ectasia ($P < 0.05$). In conclusion, CAE is an uncommon finding in coronary angiography, most commonly affecting the RCA. The obesity, family history of CAD, and the coexistence of hyperlipidemia were independent variables associated with CAE in CAD patients.

Keywords: coronary angiography; coronary artery disease; coronary artery ectasia; hyperlipidemia; right coronary artery.
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Introduction

Coronary artery ectasia (CAE) is not uncommonly encountered in patients with or without coronary artery disease (CAD) and commonly defined as the presence of an ectatic segment in one or more coronary arteries with a luminal diameter being at least 50% larger than that of the normal vessel (Kawsara et al. 2018). Localized ectatic segments were characterized by a discrete portion of the artery being affected, while a normal vessel was present adjacent to that segment; diffuse ectatic segments, on the other hand, involved the entire segment without any normal vessel within that specific segment (Li et al. 2017).

Epidemiological evidence has indicated that the diagnosis of CAE before 1,976 mainly depended on postmortem examinations, with a very low detection rate (only 1.2%) (Markis et al. 1976). In many cases, the clinical symptoms even with laboratory tests fail to distinguish CAE from CAD (Eitan and Roguin 2016). With the high selectivity of coronary angiography and improvement in awareness of this disorder, the reported incidence rate of CAE has increased over the years, ranging from 1.4% to 5.3% (Dahhan 2015). The absence of a standardized definition for CAE and the presence of distinct genetic and/or environmental factors may explain these slight differences (Sener 2023). The concurrent presence of CAE and obstructive CAD is common, with approximately 85% of cases showing this coexistence (Eyuboglu and Eyuboglu 2022). Moreover, CAE is frequently observed in patients with sickle cell disease, with an incidence rate of 17.7% reported (Nicholson et al. 2011). Among 40%-70% of patients with CAE, the right coronary artery (RCA) is the most frequently affected vessel, and ectasia involving all three coronary vessels or the left main coronary artery

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(LMCA) is rare (Gahlan et al. 2023). However, for isolated CAE, the prevalence was 1.05%, and the majority of patients had single vessel involvement, with left anterior descending branch being the most common involved vessel (Malviya et al. 2017). CAE is more likely to make individuals predisposing to experience unstable angina, acute myocardial infarction (AMI), heart failure, and even sudden death, owing to vasospasm, slower coronary blood flow, and thrombosis, typically within the dilated segments (Doi et al. 2017; Yao et al. 2018).

Congenital CAE stands at approximately 10%-20% of the cases and is usually associated with cardiac abnormalities, such as bicuspid aortic valve and aortic root dilatation (Mani et al. 2021). The majority of CAE cases are acquired, with atherosclerosis being the most acknowledged cause (Qin et al. 2019; Xi et al. 2023). Other less frequent etiologies refer to inflammatory or connective tissue diseases, such as polyarteritis nodosa, systemic lupus erythematosus, scleroderma, Ehler-Danlos syndrome, collagen vascular disease, Kawasaki disease, and cardiac lymphomas (Aboeata et al. 2012; Brunetti et al. 2014).

The evaluation and characterization of CAE represent a great diagnostic challenge showing clinical and therapeutic implications. Herein, we examine the coronary risk factors and coronary angiographic findings in CAD patients with CAE and to investigate their prevalence, clinical characteristics.

Methods

Patients

In an 8-year period, from the year 2014 to the year 2022, a total of 8,845 consecutive angiographic procedures were performed for typical angina, typical or atypical chest pain suggestive of angina, previous history of myocardial infarction (MI), and/or positive results for exercise test at the Zhoupu Hospital, Shanghai Medical University and Health Science. Out of these, 2,870 angiography reports indicated significant CAD, and 32 angiography reports showed isolated CAE excluding significant CAD, history of myocardial revascularization, or valvular heart disease. The demographic, clinical, angiographic, and follow-up details of included patients were retrospectively reviewed with the approval of the Ethics Committee of the Zhoupu Hospital, Shanghai Medical University and Health Science. The diagnosis of CAD was confirmed by coronary angiography according to the Fourth Universal Definition of Myocardial Infarction (Thygesen et al. 2018). Among the 2,870 coronary angiograms reviewed, there were 144 angiograms reporting CAE. The anatomic distribution and extent of ectasia in the coronary arterial tree were determined. The presence of a discrete localized coronary dilation with a luminal diameter 1.5-2-fold greater than that of an adjacent normal segment was defined as CAE (Devabhaktuni et al. 2016). The inclusion criteria for isolated CAE or CAE coexisting with CAD were: i) an angiographic diagnosis of CAE; ii) complete demographic, clinical and angiographic details; and iii) an age ≥ 18 years. The exclusion criteria for CAE coexisting with CAD were: i) the ectasia developed from or directly related with coronary bypass graft; ii) the ectasia developed after coronary interventions; iii) with a diagnosis of Kawasaki disease; iv) the presence of fistulas or coronary artery anomalies; and v) those with valvular heart disease, infectious endocarditis, cardiomyopathy, congenital heart disease, syphilitic aortitis, rheumatic heart disease, connective tissue disease and ongoing malignant tumors.

Data collection

Patients' age, sex difference, CAD risk factors including smoking history (patient regularly smokes cigarette one or more times per day or has quit smoking during the previous 1 year), body mass index (BMI, BMI ≥ 25 kg/m^2 defined as obese), family history of CAD, comorbid diseases including hyperlipidemia [total cholesterol (TC) ≥ 200 mg/dl, triglyceride (TG) ≥ 150 mg/dl, and high-density lipoprotein cholesterol (HDL-C) ≤ 30 mg/dl], hypertension (systolic blood pressure ≥ 140 and/or diastolic ≥ 90 mmHg and/or on anti-hypertensive treatment), and diabetes, the anatomic distribution and extent of ectasia in the coronary arterial tree were obtained.

Follow-up analysis

Follow-up data of CAE patients included symptoms, such as recurrent chest pain, unstable angina, MI, history of hospitalization, cardiovascular and non-cardiovascular death were retrospectively reviewed.

Statistical analysis

The continuous data were compared by using the t-test and categorical data by using the Fisher's exact test. Odds ratios (ORs) with 95% confidence interval (CI) were calculated by multivariate logistic regression analysis. Data analysis was performed with the aid of SPSS 22 (IBM, Armonk, NY, USA), with the possibility less than 0.05 ($P < 0.05$) used to reflect the presence of significant difference.

Results

The prevalence rate of CAE coexisting with or without CAD

Among the 8,845 coronary angiograms reviewed, 176 patients were reported with CAE including 144 cases of CAE coexisting with CAD and 32 cases of isolated CAE. After final confirmation by the investigator, 142 patients had CAE yielding a detection rate of 4.9% (142/2,870) among CAD angiograms and 28 patients had isolated CAE showing a detection rate of 0.32% (28/8,845) among total coronary angiography procedures (Fig. 1). Overall, the incidence of CAE was 1.92% (170/8,845).

Angiographic characteristics of CAE coexisting with or without CAD

With regard to CAE coexisting with CAD, CAE was presented in 66 cases with angina pectoris, 71 cases with

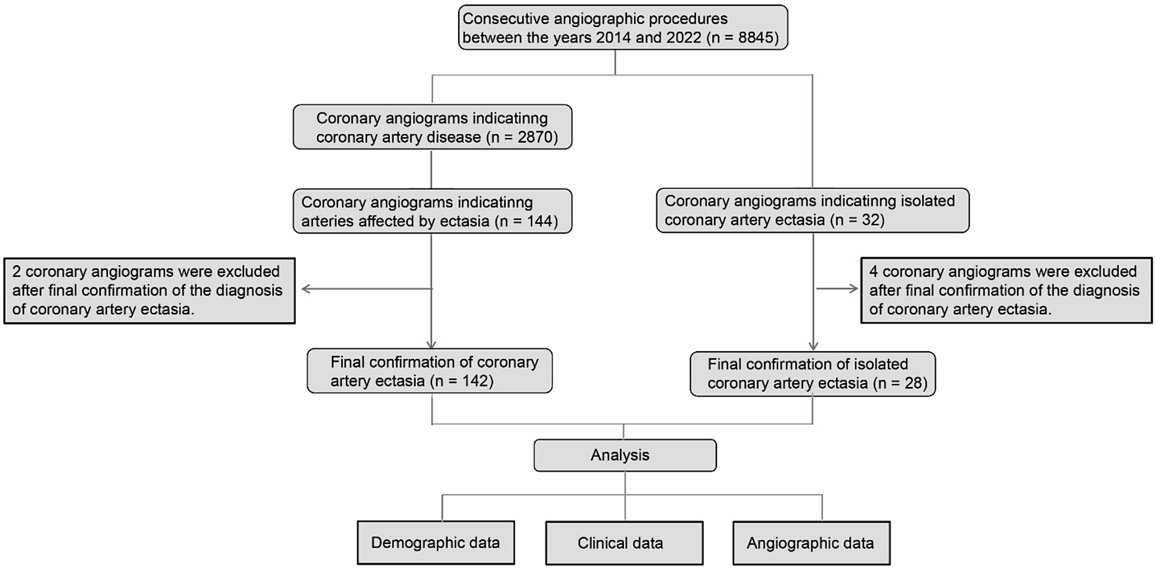

Fig. 1. A flow diagram of coronary angiogram selection.

Table 1. Distribution of coronary artery ectasia (CAE) in different vessels of patients with or without coronary artery disease (CAD).

Affected vessel	CAE with CAD (n = 142)	Isolated CAE (n = 28)
Only RCA	63/142 (44.37%)	5/28 (17.86%)
Only LAD	29/142 (20.42%)	8/28 (28.57%)
Only LCX	29/142 (20.42%)	4/28 (14.29%)
Only LM	0/142	1/28 (3.57%)
Single vessel	121/142 (85.21%)	18/28 (64.29%)
RCA + LAD	7/142 (4.93%)	4/28 (14.29%)
RCA + LCX	5/142 (3.52%)	2/28 (7.14%)
LAD + LCX	4/142 (2.82%)	3/28 (10.71%)
LAD + LM	0/142	1/28 (3.57%)
Double vessels	16/142 (11.27%)	10/28 (35.71%)
Three vessels	5/142 (3.52%)	0/28
Total RCA	87/188 (46.28%)	17/41 (41.46%)
Total LAD	53/188 (28.19%)	13/41 (31.71%)
Total LCX	48/188 (25.53%)	9/41 (21.95%)
Total LM	0/188	2/41 (4.88%)
Localized type	22/142 (15.49%)	5/28 (17.86%)
Diffuse type	120/142 (84.51%)	23/28 (82.14%)

RCA, right coronary artery; LAD, left anterior descending branch; LCX, left circumflex branch; LM, left main coronary artery.

AMI, and 5 cases with old MI. Out of total 188 coronary arteries involved, ectasia was found in 87 RCA (46.28%), 53 left anterior descending branch (LAD) (28.19%), and 48 left circumflex branch (LCX) (25.53%). Ectasia affected single vessel in 121 (85.21%), double vessels in 16 (11.27%), and all the three vessels in only 5 (3.52%). As for isolated CAE, among total 41 coronary arteries involved, ectasia affected 17 LAD (41.46%), 13 RCA (31.71%), 9 LCX (21.95%), 2 LM (4.88%), single vessel in 18 (64.29%), and double vessels in 10 (35.71%). Table 1 presents distribution of CAE in different vessels of 142 CAD patients and 28 isolated CAE. Fig. 2A, B shows volume rendering (VR) and curved planar reformation (CPR) views of RCA and LAD. Fig. 3 shows CAE in different vessels by coronary angiography.

Clinical characteristics of CAE coexisting with or without CAD

Demographic characteristics and CAD risk factors of patients with CAE coexisting with or without CAD are listed in Table 2. The proportion of obesity, family history of CAD, and the proportion of hyperlipidemia in CAD patients who had ectasia were significantly higher than that in CAD patients who did not have ectasia ($P < 0.05$). With regard to age, sex difference, smoking history, the proportions of hypertension and diabetes, and significant stenosis in arteries, no significant difference was noted between CAD patients with CAE and those without ($P > 0.05$). Results showed only age exhibited a significant difference between CAE coexisting with CAD and isolated CAE, with a younger age in CAE coexisting with CAD cohort than isolated CAE cohort ($P < 0.05$). The sex difference, the proportion of obesity, smoking history, family history of CAD, the proportions of hyperlipidemia, hypertension and diabetes showed no significant difference was noted between CAE coexisting with CAD cohort than isolated CAE cohort ($P > 0.05$).

Independent risk factors for CAE in CAD

We included obesity, family history of CAD, and hyperlipidemia into multivariate analysis and then found that the obesity, family history of CAD and the coexistence

Fig. 2. The volume rendering (VR; left) and curved planar reformation (CPR; right) views by computed tomography coronary angiography.
(A) A female patient with coronary artery ectasia (CAE) involved in the right coronary artery (RCA), aged 66 years. (B) A male patient with CAE involved in the left anterior descending branch (LAD), aged 54 years.

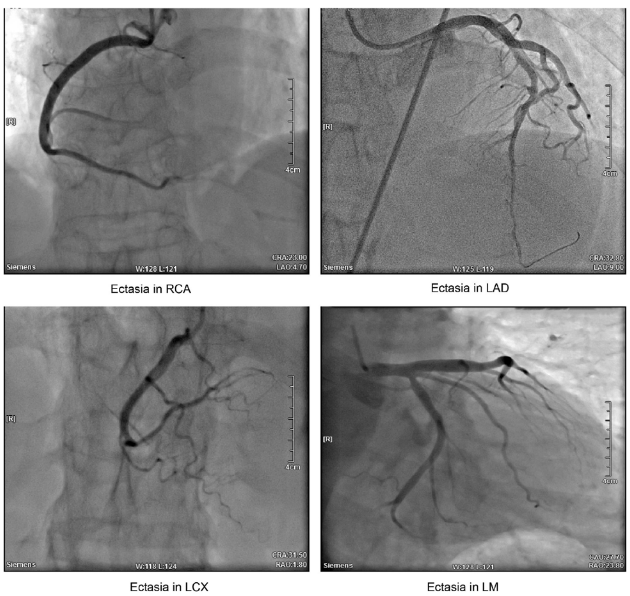

Fig. 3. Representative angiographic images of coronary artery ectasia (CAE) involved in the right coronary artery (RCA), left anterior descending branch (LAD), left circumflex branch (LCX), and left main coronary artery (LM).

of hyperlipidemia were independent variables associated with CAE (Table 3, P < 0.001).

Follow-up analysis for CAE coexisting with CAD

Out of the CAE coexisting with CAD cohort, 129 patients were successfully followed up with a follow-up rate of 90.85% (129/142). The mean follow-up time was 40.64 ± 11.10 months, ranging from 20 to 60 months. During the follow-up period, 97 patients (75.19%) were asymptomatic, 24 patients (18.60%) had recurrent chest pain, 6 patients (4.65%) had unstable angina, and 2 patients (1.55%) had MI. Among the symptomatic patients, 18 (13.95% of 129 patients successfully followed up) had hospital readmission, in which 2 patients were hospitalized twice. None of the patients died due to cardiovascular events during the course of follow-up.

Discussion

CAE is regarded as an uncommonly occurring angiographic finding among CAD patients, and the incidence significantly exhibits regional differences, even in one country. For example, an Indian study reported an incidence rate of 5.45% (270 in 4,950 coronary angiograms) for CAE (Malviya et al. 2017). Another Indian study detected 31 CAE cases out of 2,539 coronary angiograms, with the prevalence of 1.22% (Vasu et al. 2017). However, an incidence rate of 16.02% was also reported for CAE in Indian (Kerr et al. 2016). An Iran study reported an incidence rate of only 1.5% for CAE (Amirzadegan et al. 2014). A Chinese study reported an incidence rate of 9.4% (131 in 1,400 older adults) identified by coronary angiography (Yang et al. 2013). Partially concurring with those reported incidence rates, the incidence rate of CAE was 4.9% among the CAD cohort and 0.32% among total coronary angiography procedures. Overall, the incidence of CAE was 1.92% in our study.

CAE is an uncommon finding in coronary angiography, most commonly affecting the RCA among the 3 epicardial vessels. Willner et al. (2020) analyzed 174 patients with either isolated CAE or CAE coexisting with atherosclerotic heart disease and also found the RCA was the most common artery involved reaching 79%. In addition to the RCA, LAD was the commonly involved artery in the study performed by Amirzadegan et al. (2014) where 93 (61.6%) patients had involvement of the RCA and 92 (60.8%) cases had ectasia in the LAD. Although the rate of involved RCAs was 46.28% in our study, the RCA still ranked the top among 3 epicardial vessels affected by ectasia.

The usual coexistence and similarities in the histological examinations of CAD and CAE supported the notion that ectasia is a variant of atherosclerosis, and the atherosclerotic process play an important role in the pathogenesis of CAE (Yetkin and Waltenberger 2007). Accordingly, several classic CAD risk factors were analyzed in CAE patients. However, there is still a debate on the risk factors for CAE in current studies. In the study of Amirzadegan et al. (2014), CAE patients were older than those with normal coronary arteries, but our data failed to validate significant

Table 2. Demographic characteristics and coronary artery disease (CAD) risk factors of the study groups.

Characteristics	CAE with CAD (n = 142)	CAD (n = 2,728)	Isolated CAE (n = 28)	P_1	P_2
Age (year, mean ± SD)	65.07 ± 4.88	66.00 ± 5.86	58.07 ± 9.44	ns	< 0.0001
Sex [n (%)]				ns	ns
Male	112 (78.87%)	2,103 (74.05%)	20 (71.43%)		
Female	30 (21.13%)	708 (25.95%)	8 (28.57%)		
BMI (kg/m^2)				0.025	ns
≥ 25 (obese)	87 (61.27%)	1,145 (51.32%)	20 (71.43%)		
< 25 (non-obese)	55 (38.73%)	1,583 (48.68%)	8 (28.57%)		
Smoking history				ns	ns
Yes	82 (57.75%)	1,449 (53.12%)	16 (57.14%)		
No	60 (42.25%)	1,279 (46.88%)	12 (42.86%)		
Family history of CAD				< 0.001	ns
Yes	85 (59.86%)	1,227 (44.98%)	13 (46.43%)		
No	57 (40.14%)	1,501 (55.02%)	15 (53.57%)		
Hyperlipidemia				< 0.0001	ns
Presence	90 (63.38%)	1,170 (42.89%)	12 (42.86%)		
Absence	52 (36.62%)	1,558 (57.11%)	16 (57.14%)		
Hypertension				ns	ns
Presence	86 (60.56%)	1,691 (61.99%)	15 (53.57%)		
Absence	56 (39.44%)	1,037 (38.01%)	13 (46.43%)		
Diabetes				ns	ns
Presence	40 (28.17%)	747 (27.38%)	9 (32.14%)		
Absence	102 (71.83%)	1,981 (72.62%)	19 (67.86%)		
No. of stenosed vessels (≥ 50%)				ns	
1	35 (24.65%)	529 (19.39%)			
2	47 (33.10%)	864 (31.67%)			
3	60 (42.25%)	1,335 (48.94%)			

SD, standard deviation; CAE, coronary artery ectasia; BMI, body mass index; ns, not significant.

Table 3. Predictors of coronary artery ectasia (CAE) among coronary artery disease (CAD) patients in multivariate logistic regression analysis.

Variable	OR	95% CI	P value
Obesity (BMI ≥ 25 kg/m^2)	0.456	0.322-0.646	< 0.001
Family history of CAD	0.530	0.375-0.750	< 0.001
Hyperlipidemia	0.437	0.307-0.621	< 0.001

BMI, body mass index; CI, confidence interval; OR, odds ratio.

difference of age between CAE patients and CAD patients without CAE. Morrad et al. (2016) retrospectively analyzed 6,100 consecutive angiography records and found a marked male proportion of 6.9% with regard to female patients (4.5%). In the research by Giannoglou et al. (2006), the male preponderance for CAE was supported with a male-to-female ratio of 2:1. However, no demonstration of male preponderance for CAE was observed between CAE patients and CAD patients without CAE in our study. As similar with our data on BMI analysis, obesity was found in 60% of CAE patients but in 42% of patients without CAE, indicating obesity was associated with the incidence of CAE (Waly et al. 1997). Smoking was a significant predisposing factor for CAE from previous evidence (Gahlan et al. 2023), which was in line with our data that the proportion of current smokers was greater in CAD patients who had ectasia were significantly higher than that in CAD patients who did not have ectasia. Of note, our multivariate analysis found that the family history of CAD and the coexistence of hyperlipidemia were independent variables associated with CAE. In a previous study, although focusing on abdominal aortic aneurysm, family history of atherosclerotic vascular disease contributed to the presence of abdominal aortic aneurysm (Ye et al. 2016). There is a in line research with our study that hyperlipidemia showed a good value for predicting the occurrence of CAE with area under the curve = 0.898 (Qin et al. 2019). The above discussed combined with our data made us believe that the pathogenesis underlying CAE is not simply a variant of coronary atherosclerosis.

Our study has a few limitations. First, retrospective nature of data might cause underestimation of the actual incidence/prevalence of CAE, creating a further need for prospective analysis. Second, the most common affected portion as regards the proximal, mid, and distal portions of the affected arteries as well as the inflammatory activity, such as Adiponectin and hs-CRP, between CAE coexisting with or without CAD cohort should be analyzed in further studies. Third, angiographic characteristics require more data, such as coronary blood flow for each major epicardial coronary artery using the thrombolysis in myocardial infarction (TIMI) frame count which is an angiographic quantification method of contrast opacification in the vessel from proximal to the distal segment.

In conclusion, in this retrospective study of 2,870 consecutive CAD patients undergoing coronary angiography for multiple clinical cardiac indications, 142 (4.9%) angiograms demonstrated definitive CAE. The most common coronary artery affected by ectasia was the RCA. The family history of CAD and the coexistence of hyperlipidemia were independent variables associated with CAE in CAD patients, and clinicians can take into consideration whether lipid-lowering drugs can prevent the incidence of CAE. CAE may lead to hospital readmissions and poor quality of life due to the sustained cardiovascular symptoms, requiring better and more specific considerations. Further perspective studies requiring aggressive risk stratification are needed to thoroughly determine the incidence of CAE among CAD cohort and normal angiographic procedures.

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Conflict of Interest

The authors declare no conflict of interest.

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