



Clinical features of coronary artery ectasia in the elderly

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Abstract

Objective To investigate the incidence, imaging and clinical characteristics in elderly patients with coronary artery ectasia (CAE). **Methods** A retrospective analysis was conducted on patients with CAE who underwent coronary angiography between January 2006 and December 2012. According to age, the enrolled patients were divided into two groups (elderly group, age ≥ 65 years; non-elderly group, age < 65 years). The clinical feature, imaging characteristics and the 5-year survival rate of the two groups were compared. **Results** The prevalence of CAE in elderly patients was 0.33%. Patients in elderly group were found to have significantly higher proportion of female (30.1% vs. 10.1%, $P < 0.001$), three-vessel disease (60.5% vs. 45.2%, $P = 0.003$) and localized ectasia (55.0% vs. 40.2%, $P = 0.003$). In addition, body mass index (20.90 ± 2.71 kg/m² vs. 22.31 ± 2.98 kg/m², $P < 0.001$) and percentage of current smokers (45.0% vs. 64.6%, $P < 0.001$) were significantly lower in elderly group. Cumulative survival curves demonstrated reduced 5-year cumulative survival at the follow-up in the elderly group compared with the non-elderly group (88.0% vs. 96.0%, $P = 0.002$). But the 5-year event free survival rate failed to show a significant difference between the two groups (31.0% vs. 35.0%, $P = 0.311$). **Conclusion** The prevalence of CAE in elderly patients was 0.33%, which was about 1/3 of the entire numbers of CAE patients. There were significant differences between the elderly and the non-elderly patients with CAE in terms of coronary artery disease risk factors and coronary artery ectatic characteristics. CAE might be associated with increased mortality risk in the elderly.

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Keywords: Coronary artery ectasia; Elderly patients; Clinical feature

1 Introduction

Coronary artery ectasia (CAE), which is reported in 0.3%–5.3% of coronary angiograms, has been defined as dilatation of an arterial segment to a diameter at least 1.5 times that of the adjacent normal coronary artery.^[1] There is no consensus about the etiology, prognostic significance and morbidity related to this entity. CAE is associated with increased coronary morbidity such as coronary spasm, dissection and thrombus formation. Previous studies reported that

patients with CAE without significant coronary stenosis may still present with angina pectoris, positive stress tests, or acute coronary syndromes.^[2,3] The optimal treatment has not been really established.

It has been well established that aging affects cardiovascular risk factors, incidence and clinical manifestation of cardiac disease, treatment strategies and prognosis,^[4] and studies on CAE have been performed in various populations.^[1,5,6] However, previous studies have been less focused on the elderly. In the present study, we aimed to describe the clinical feature, angiographic characteristic and long-term outcome of CAE in the elderly.

2 Methods

2.1 Study population

A retrospective analysis was conducted on patients with CAE who underwent coronary angiography at our center between January 2006 and December 2012. The enrolled

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patients were divided into two groups (elderly group, age ≥ 65 years; non-elderly group, age < 65 years). The reasons for catheterization of these patients were history of angina, previous or an acute myocardial infarction, positive treadmill test and/or presence of multiple coronary risk factors. Exclusion criteria were: (1) patients with coronary atherosclerotic disease that was so severe the normal coronary reference diameter could not be determined; (2) patients with ectasia segments appearing within or directly associated with coronary bypass graft; (3) patients with an ectasia segment in an area of previous percutaneous revascularization; (4) patients with CAE directly involving branching of coronary vessels; and (5) patients with valvular, congenital heart disease or cardiomyopathies.

Conventional coronary angiography was performed in all patients after admission. Radial or femoral artery cannulation was used for arterial access site and Judkin's system was applied for cannulation of the left and right coronary arteries. After obtaining images by standard approaches, each angiogram was interpreted by two independent cardiologists. CAE was defined as dilatation of a segment of the coronary artery to a diameter of at least 1.5 times that of normal adjacent segment.^[1] According to the classification system proposed by Markis, *et al.*,^[7] the topographical extent of CAE in the major epicardial coronary arteries was classified as: type I, diffuse ectasia of two or three vessels; type II, diffuse disease in one vessel and localized disease in another vessel; type III, diffuse ectasia in one vessel; and type IV, localized or segmental ectasia. Co-existing obstructive coronary artery disease was defined as stenosis of $\geq 50\%$ of the coronary lumen (Figure 1). CAE without stenosis, namely, isolated CAE was defined as patients who had CAE but no coronary stenosis ($< 50\%$ diameter stenosis of any vessel) (Figure 2). Diabetes mellitus was defined by the documented clinical diagnosis or treatment with oral hypoglycemic agents or insulin. Dyslipidemia was defined by the

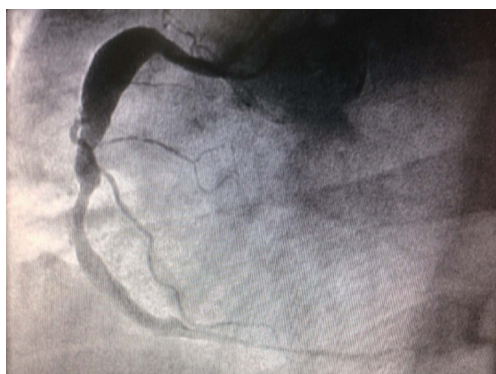


Figure 1. Segmental ectasia in the right coronary artery coexisting stenosis.

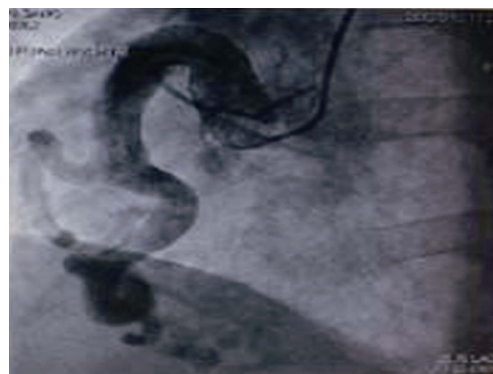


Figure 2. Isolated diffuse ectasia in a right coronary artery.

documentation of the diagnosis, use of lipid-lowering agents, fasting total cholesterol ≥ 6.22 mmol/L or low density lipoprotein cholesterol level ≥ 4.14 mmol/L. Hypertension was defined as blood pressure $\geq 140/90$ mmHg or receiving antihypertensive treatment.

Data were collected from catheterization films and medical records. Follow-up data were obtained by telephone interview and hospital encounters. The patient was considered as an event case if, during the follow-up, there was a death, non-fatal acute myocardial infarction, unstable angina with electrocardiogram (ECG) changes or recurrent chest pain need for hospital admission and for repeat cardiac catheterization or myocardial revascularization. The clinical feature, imaging characteristics and the 5-year survival rate of the two groups were compared.

2.2 Statistical analysis

Data normality was assessed using the Kolmogorov-Smirnov test. Continuous, normally distributed variables are presented as mean \pm SD, non-normally distributed variables are presented as median (interquartile range). Categorical variables are presented as frequencies and/or percentages. We compared means of independent samples using Student's *t* test or non-parametric test, and proportions using the chi-squared test. Cumulative survival rate and event-free survival rate were estimated by the Kaplan-Meier method and compared by the log rank test. $P < 0.05$ was considered significant. Statistical analyses were performed with SPSS for Windows (SPSS, Chicago, IL, USA).

3 Results

3.1 Prevalence of CAE

A total of 80,833 coronary angiograms were performed during the period of the study. Of the total 1029 (1.3%) angiograms showed CAE of both age ≥ 65 years (270, 0.33%) and 18–64 years (759, 0.94%). Among these CAE patients,

525 cases with intact data were divided into the two groups (elderly group, age ≥ 65 years, $n = 129$; non-elderly group, age 18–64 years, $n = 396$).

3.2 Clinical characteristics

Table 1 summarized the cardiovascular risk factors of the study groups. The proportion of female in elderly group was higher than that in non-elderly group (30.1% vs. 10.1%, $P < 0.001$). Patients in elderly group had lower body mass index (BMI) scores (20.90 ± 2.71 kg/m² vs. 22.31 ± 2.98 kg/m², $P < 0.001$) and lower rate of current smokers (45.0% vs. 64.6%, $P < 0.001$), comparing with patients in non-elderly group. However, there was no significant difference in the two groups with regard to history of hypertension, dyslipidemia, diabetes mellitus, family history of coronary heart disease and prior myocardial infarction ($P > 0.05$).

Table 1. Comparison of coronary risk factors between the two groups.

	Elderly ($n = 129$)	Non-elderly ($n = 396$)	<i>P</i>
Age, yrs	71 \pm 4	52 \pm 9	< 0.001
Female	40 (30.1%)	40 (10.1%)	< 0.001
BMI, kg/m ²	20.90 \pm 2.71	22.31 \pm 2.98	< 0.001
Hypertension	91 (70.5%)	265 (66.9%)	0.444
Hyperlipidemia	96 (74.4%)	326 (82.3%)	0.05
Diabetes mellitus	39 (30.2%)	91 (23%)	0.097
Smoking	58 (45%)	256 (64.6%)	< 0.001
FH	20 (15.5%)	69 (17.4%)	0.614
OMI	37 (28.7%)	109 (27.5%)	0.799

Data are presented as mean \pm SD or n (%). BMI: body mass index; FH: family history of coronary artery disease; OMI: old myocardial infarction.

In laboratory findings, compared with non-elderly group, the elderly group showed significantly lower levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltranspeptidase (GGT), uric acid, triglycerides, white blood cell (WBC) count, neutrophil (NEU), lymphocyte (LYM) and neutrophil to lymphocyte ratio (NLR) count but a higher level of high density lipoprotein cholesterol (HDL-C), ($P < 0.05$). There was no significant difference in other laboratory indexes between the two groups ($P > 0.05$). (Table 2)

3.3 Coronary angiographic results

The elderly group had a higher percentage of triple-vessel disease than non-elderly group (60.5% vs. 45.2%, $P = 0.003$). The proportion of Markis' type IV (localized or segmental ectasia) in elderly group was higher than that in

Table 2. Comparison of laboratory indicators between the two groups.

	Elderly ($n = 129$)	Non-elderly ($n = 396$)	<i>P</i>
AST, U/L	19 (16–23)	20 (16.25–26)	0.004
ALT, U/L	18 (14–27)	29 (19–41.75)	< 0.001
ALP, U/L	72.05 \pm 25.49	68.27 \pm 25.62	0.144
GGT, U/L	26 (18–38.5)	33.5 (23–55)	< 0.001
Serum creatinine, μ mol/L	83.44 \pm 21.15	81.65 \pm 20.41	0.391
Uric acid, μ mol/L	324.92 \pm 104.65	350.24 \pm 88.33	0.007
FPG, mmol/L	5.632 \pm 2.083	5.619 \pm 1.796	0.946
Triglycerides, mmol/L	1.55 (1.08–1.97)	1.71 (1.3–2.37)	0.005
Total cholesterol, mmol/L	4.34 \pm 1.07	4.49 \pm 1.28	0.223
HDL-C, mmol/L	1.08 \pm 0.313	0.99 \pm 0.259	0.004
LDL-C, mmol/L	2.53 \pm 0.94	2.68 \pm 1.17	0.172
hs-CRP, mg/L	1.96 (0.99–4.15)	1.96 (1.0–5.24)	0.709
WBC, 10^9 /L	6.796 \pm 1.778	7.632 \pm 2.202	< 0.001
NEU, 10^9 /L	4.351 \pm 1.542	4.954 \pm 1.954	0.001
LYM	1.730 \pm 0.557	1.981 \pm 0.818	0.001
NLR	2.775 \pm 1.398	3.095 \pm 2.291	0.042
LVEF, %	58.43 \pm 9.83	59.76 \pm 9.08	0.158

AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; GGT: gamma glutamyltranspeptidase; FPG: fasting plasma glucose; HDL-C: high density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; hs-CRP: high-sensitive C-reactive protein; WBC: White blood cell; NEU: Neutrophil; LYM: Lymphocyte; NLR: Neutrophil to lymphocyte ratio; LVEF: left ventricular ejection fraction.

non-elderly group (55% vs. 40.2%, $P = 0.003$). There was no significant difference in the two groups with regard to with or without co-existing significant coronary artery disease, involved vessel and other type of Markis' classification ($P > 0.05$), (Table 3).

3.4 Treatment measures

During hospitalization, there was no difference in proportion of medications, percutaneous coronary intervention or coronary artery bypass grafting between the two groups ($P > 0.05$), (Table 4). There was no death during hospital stay in the two groups.

3.5 Cumulative survival rate and event free survival rate

Cumulative survival curves demonstrated reduced 5-year cumulative survival rate in the elderly group compared with the non-elderly group (88.0% vs. 96.0%, $P = 0.002$) (Figure 3). But the 5-year event free survival rate failed to show a

Table 3. Comparison of angiographic characteristics between the two groups.

	Elderly (n = 129)	Non-elderly (n = 396)	P
Isolated CAE	13 (10.1%)	66 (16.7%)	0.069
CAD severity			
50%-70%	12 (9.3%)	16 (4.0%)	0.021
≥ 70%	104 (80.6%)	314 (79.3%)	0.745
One vessel	14 (10.9%)	59 (14.9%)	0.244
Two vessel	24 (18.6%)	92 (23.2)	0.271
Three vessel	78 (60.5%)	179 (45.2%)	0.003
Ectasia artery			
LAD	59 (45.7%)	161 (40.7%)	0.31
LCX	40 (31%)	151 (38.1%)	0.144
RCA	68 (52.7%)	228 (57.6%)	0.333
LM	7 (5.4%)	35 (8.8%)	0.219
Markis' classification			
Type I	18 (14.0%)	72 (18.2%)	0.269
Type II	10 (7.8%)	45 (11.4%)	0.245
Type III	30 (23.3%)	120 (30.3%)	0.124
Type IV	71 (55%)	159 (40.2%)	0.003

Data are presented as n (%). CAE: coronary artery ectasia; CAD: coronary artery disease; LAD: left anterior descending; LCX: left circumflex coronary artery; LM: left main coronary artery; RCA: right coronary artery.

Table 4. Comparison of treatment between the two groups.

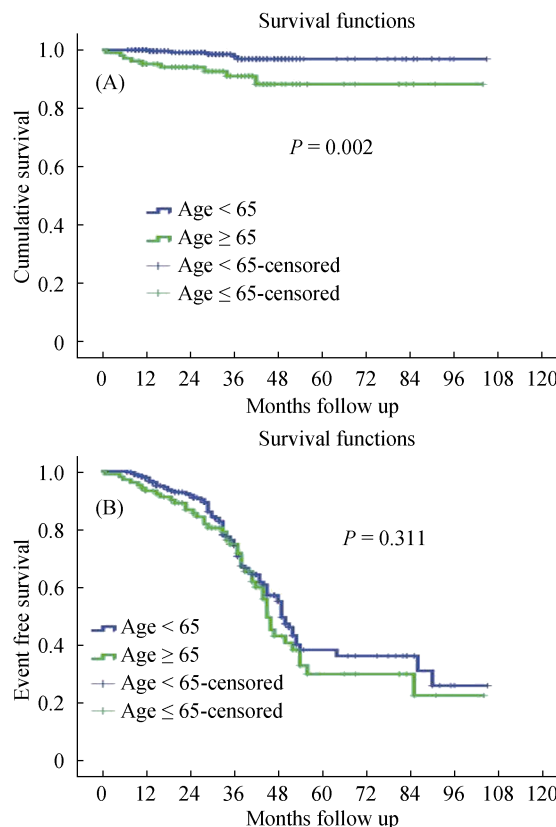
	Elderly (n = 129)	Non-elderly (n = 396)	P
Isolated CAE			
Medical treatment	13 (10.1%)	63 (15.9%)	0.102
PCI	0	0	-
CABG	0	3 (0.75%)	0.320
Mixed CAE			
Medical treatment	51 (39.5%)	120 (30.3%)	0.052
PCI	54 (41.9%)	165 (41.7%)	0.967
CABG	11 (8.5%)	45 (11.4%)	0.365

CABG: coronary artery bypass grafting; CAE: coronary artery ectasia; PCI: percutaneous coronary intervention.

significant difference between the two groups (31.0% vs. 35.0%, $P = 0.311$), (Figure 4).

4 Discussion

The main findings of the present study revealed a prevalence of 0.33% for CAE among the elderly who underwent coronary angiography in a relatively large Chinese cohort. The elderly with CAE presented with more female and localized or segmental ectasia, and with higher percentage of multiple vessel disease compared with the young, but with

**Figure 3. 5-year cumulative survival (A) and free survival (B) curves of elderly group compared with non-elderly group.**

lower BMI scores and less smoking status. Additionally, though the 5-year event free survival rate failed to show a significant difference between the elderly and the younger, but survival curves demonstrated reduced 5-year cumulative survival rate in the elderly CAE patients. It was suggested that CAE may be associated with increased mortality risk in the elderly.

CAE is usually considered a variant of coronary artery atherosclerosis; however, a definite link has not yet been confirmed. Aging represents a major risk factor for coronary artery disease. But the relationship between aging and CAE has not been well-described. Large studies showed that age was inversely associated with incidence of CAE.^[1,8,9] Additionally, the prevalence of CAE in the elderly also differs in some populations. In a Greece study, Giannoglou, *et al.*^[9] found that age constituted a marked negative factor, which was inversely associated with the presence of CAE. However, in their study, this association was only confirmed in men but not in women. In addition, in the early of 1990s, CAE was documented in 10% of Indian patients with ischemic heart disease below 40 years of age, and in 12% of those above 40 years of age though statistical significance was not reached.^[10] Consistent with almost all of literature,

our study showed that CAE was more common in the young, supporting age was inversely associated with the presence of CAE. These data indicated that CAE might not be a simply variant of coronary atherosclerosis.

However, the frequent coexistence of CAE with coronary artery disease and histopathological findings resembling those of atherosclerosis has led to the conception that the underlying mechanism of pathogenesis in the development of CAE may be closely related to that of atherosclerosis.^[11] CAE has a strong male predominance (male: female = 3: 1) which may represent the higher incidence of atherosclerosis in men.^[12] It is well known that women suffer from coronary artery disease five years later than men, which has been inferred by the protective effect of oestrogen. Upon reaching menopause, the incidence of coronary artery disease of women catches up with that of men and more likely to have multiple coronary arterial lesions and more complications.^[13] In accordance with the characteristic of coronary artery disease, our finding showed that the elderly group with CAE was characterized by more female with multiple vessel disease.

Smoking, both active and passive, is an established vascular risk factor. The relationship between tobacco smoking and increased risk of coronary artery disease, cerebrovascular disease, peripheral arterial disease and aortic aneurysm has been well established in numerous longitudinal and cross-sectional epidemiological and basic science studies.^[14] However, whether smoking is an independent risk factor of CAE remains controversial. Swaye, *et al.*^[11] found no clear difference in the incidence of smoking in patients with, and without ectasia. While Pinar, *et al.*^[8] found a different conclusion that smoking was more common in patients with CAE than those with coronary artery disease. In the present study, the percentage of smokers in non-elderly group was significantly higher than those in elderly group (64.6% vs. 45.0%, $P < 0.001$). In parallel with this finding, the incidence of CAE was also significantly higher in non-elderly group (0.94% vs. 0.33%, respectively). It appeared to suggest that smoking may contribute to an increased susceptibility of CAE. One study found that smoking, by interfering with the respiratory tract's ability to defend itself and predisposing to upper and lower respiratory tract infections may accelerate the onset and progression of abdominal aortic aneurysms.^[15] Pathological evidence from abdominal aortic aneurysm showed that CAE are similar in pathogenesis and histology, a thin or absent media of the arterial wall found in patients with abdominal aortic aneurysms.^[16] Smoking, therefore, may play an important role in the initiation and propagation of CAE. But as yet, no evidence has directly confirmed its existence.

The importance of obesity as a risk factor for atherosclerosis has been clearly demonstrated, but the association of the obesity with CAE is currently unknown. Waly, *et al.*^[17] concluded that CAE was not related to any coronary risk factors other than obesity. Çetin, *et al.*^[18] demonstrated that epicardial adipose tissue thickness and BMI were significantly higher in the CAE group compared to the normal coronary artery group. In our findings, the elderly showed lower BMI scores ($20.90 \pm 2.71 \text{ kg/m}^2$ vs. $22.31 \pm 2.98 \text{ kg/m}^2$, $P < 0.001$) and a lower incidence of CAE (0.33% vs. 0.94%) compared to those in the young. These data appeared to indicate that obesity is associated with CAE, but further studies employing more detailed measures are needed. A link between obesity and coronary artery disease development has been repeatedly proposed, possibly in part due to the development of a proinflammatory and prothrombotic state in obese subjects which favors atherosclerosis progression.^[19] CAE is associated with inflammatory response manifested by elevated inflammatory cytokines and C-reactive protein.^[20] Whether the similar physiological mechanisms are expressed in CAE is unknown.

Any of the major epicardial vessels can be affected by CAE. On the basis of their luminal diameter, geometrical shape, vascular wall contains and the dilatation extent, CAE has several classifications.^[21] As for its topographical extent in the major epicardial coronary arteries, Markis, *et al.*^[7] proposed a classification of CAE based on the extent of ectatic involvement. In the decreasing order of severity, diffuse ectasia of two or three vessels was classified as type I, diffuse disease in one vessel and localized disease in another vessel as type II, diffuse ectasia of one vessel only as type III and localized or segmental ectasia as type IV. Williams, *et al.*^[22] regarded that the high incidence of multiple segment involvement suggests that coronary ectasia results from a diffuse abnormality of the vessel wall and in predisposed localized ectasia may follow a stenosis, suggesting poststenotic dilatation. Turhan, *et al.*^[23] detected a statistically significant positive correlation between the total length of ectasia segments and the levels of plasma soluble intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and E-selectin levels. In addition, matrix metalloproteinases-3 levels correlated with diffuse and multi-vessel ectasia.^[24] These data appeared to indicated that a more severe and extensive chronic inflammation in those patients with diffuse ectasia than those with localized or segmental ectasia. In our study, the elderly present with more localized or segmental ectasia (type IV) than the young (55.0% vs. 40.2%, $P = 0.003$) and the markers of inflammation such as WBC, NEU and NLR were found to have significantly

lower levels in the elderly compared to the young ($P < 0.05$). The finding appears to imply that CAE patients may involve different pathogenesis among the elderly and the young or suggest that CAE may have a self-limited characteristic like an autoimmunity disease, which inflammation and immune activation may be more pronounced in young patient but not obvious with aging. CAE consistent with autoimmunity disease such as Kawasaki disease, systemic lupus erythematosus and rheumatic heart disease has been reported.^[25–27] Further investigation should be done in order to better understand this characteristic which would be useful to guide the clinical treatment.

The long-term outcome of CAE is controversial. Some studies regarded that patients with isolated CAE have a good prognosis.^[28] However, in a cohort, the presence of CAE was found to have an independent adverse effect on long-term mortality rate (HR: 1.56, 95%CI: 1.01–2.41) even after controlling for multiple other clinical variables.^[29] In our study, we found there was a lower 5-year cumulative survival rate in the elderly group. Simultaneously, our findings showed that patients in the elderly group were found to have significantly higher proportion of females, three-vessel disease and smokers. CAE whether or not associated with increased mortality risk in the elderly needs to be further studied.

Although it is a relatively large series reported, the research objects were only partially cases with complete data, and this may limit the statistical value of the tests used to detect variables associated with the presence of CAE. In addition, the retrospective design and data from a single center are major limitations of our study.

In conclusion, our findings showed that the prevalence of the CAE in aged 65 years or older who underwent coronary angiography was 0.33%, which was about 1/3 of all CAE patients. There were differences between the elderly and the non-elderly patients with CAE in terms of coronary artery disease risk factors and coronary artery ectatic characteristics. CAE might be associated with increased mortality risk in the elderly.

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