Underlying factors relating to acute myocardial infarction for coronary artery ectasia patients

Qianqian Sheng, MD, Huiqiang Zhao, MD, PhD, Shanshan Wu, PhD, Ruifeng Liu, MD, PhD[*] ⓘ

Abstract

Coronary artery ectasia (CAE) patients were more prone to present with acute myocardial infarction (AMI), this case-control research aimed to explore the underlying factors relating AMI for them.

This study investigated a serial of 119 patients who underwent coronary angiography and were diagnosed as CAE between the years 2016 and 2017 at the Beijing Friendship Hospital; 32 of the patients developed AMI and 87 did not develop AMI. The possible factors relating to AMI, including disease history, cardiovascular risk factors, thrombotic condition, inflammation status, and coronary imaging characteristics, were comprehensively compared between CAE patients with and without AMI.

CAE patients with AMI had a lower antiplatelet rate, a higher blood low-density lipoprotein cholesterol level, increased neutrophil to lymphocyte (NL) ratio, higher Gensini score, and larger proportions of Markis type II. Logistic regression analysis also indicated that AMI history, lower antiplatelet rate, higher NL ratio, higher low-density lipoprotein cholesterol level and Gensini score, as well as Markis type II were associated with AMI in CAE patients.

AMI history, lower antiplatelet treatment rates, poor blood lipid control and higher coronary stenosis extent, higher inflammatory response, and Markis type II were closely related to the incidence of AMI in CAE patients.

Abbreviations: AMI = acute myocardial infarction, CAE = coronary artery ectasia, CAG = coronary angiography, CHD = coronary heart disease, hs-CRP = high sensitivity C-reactive protein, LDL-c = low-density lipoprotein cholesterol, LVEF = left ventricular ejection fraction.

Keywords: acute myocardial infarction, coronary artery ectasia, Markis classification

1. Introduction

Coronary artery ectasia (CAE) is defined as dilatation of the coronary arteries to a diameter of more than 1.5 times its normal adjacent segment.[1] Epidemiology data showed the incidence of CAE is about 1.4% to 12% in autopsies and during coronary angiography (CAG) or multidetector computed tomography angiography (MD-CTA),[2–4] and more than 80% of CAE patients also had atherosclerotic stenosis. CAE can be divided into four types by the Markis classification method according ectasia extent.[3] The main clinical manifestations were angina, acute myocardial infarction (AMI), arrhythmia, and sudden

death, while some patients had no obvious symptoms.[2] CAE was more likely a thrombotic disease, as Swaye PS reported that AMI prevalence in CAE populations was 52.9%, which was higher than in patients with coronary heart disease (CHD) and in other non-CAE patients.[5] According to our limited clinical practices, a portion of but not all CAE patients were more prone to present with AMI[6] and even recurring AMI. The exact underlying mechanisms as to why some patients with CAE tended to develop AMI remain unclear. Thus, it was necessary to distinguish CAE patients with high AMI risk in the early screening stage in order to prevent AMI events from interfering with the controllable factors. This study aimed to explore the underlying factors relating to AMI in CAE patients by systematically evaluating the disease histories, cardiovascular risk factors, thrombotic systems, inflammation conditions, and coronary imaging characteristics in CAE populations. These results would be useful for clinical practice and future research in this field.

2. Patients and method

2.1. Patient population

This research was a case-control study. A total of 5012 subjects who underwent CAG at the cardiac catheterization center of Beijing Friendship Hospital between January 2016 and December 2017 were screened for participation in the study; among them, 119 (2.37%) were eligible according to inclusion and exclusion criteria as following and identified as having CAE. These 119 patients were then divided into 2 groups: 1 group of 32 CAE patients with AMI (CAE+AMI group) and another group of 87 patients without AMI (CAE group).

The baseline data, key laboratory tests, and imaging character were compared and analyzed comprehensively between the above 2 groups. Then the effect of ectasia extent on AMI prevalence was investigated by comparing the different Markis types. Furthermore, logistic analysis was applied by setting AMI as the dependent factor and other items as independent parameters.

This study was approved by the ethics committee of Beijing Friendship Hospital Affiliated to Capital Medical University and was in accord with the Declaration of Helsinki. Informed consent was obtained from all study participants.

2.2. Inclusion criteria

A diameter of the ectatic segment that was 1.5 times greater than that of the adjacent normal segment was defined as CAE.[4] According to current consensus,[7] AMI was defined by an elevated cardiac biomarker and at least 1 of the following:

(1) symptoms relating to ischemia,
(2) changes on an electrocardiogram, such as ST segment changes, new left bundle branch block, or Q waves,
(3) changes in the motion of the heart wall on imaging, and/or
(4) discovery of a thrombus on angiogram or at autopsy.

2.3. Exclusion criteria

Exclusion criteria were cardiomyopathy, myocarditis, valvular heart disease, chronic heart failure, aneurysm in other vessels, collagen tissue diseases, vasculitis, syphilis, explicit diagnosis of pulmonary embolism and aortic dissection, severe liver and kidney dysfunction, hemagglutination disorders, pregnancy, active bleeding, malignant neoplasm, infectious diseases, previous history of infection (<3 months), other inflammatory diseases, and poor compliance.

2.4. Basic clinical characteristics

The medical records and angiography databases were intact and detailed. Most of the data were obtained from the medical record system and the radiography database, including demographics (such as age and sex), history of past diseases (such as hypertension, diabetes, coronary heart disease, etc), family history, personal history (such as smoking and drinking), and history of past drug use. Body mass index was calculated by dividing weight in kilograms by height in meters squared (kg/m^2). The left ventricular ejection fraction (LVEF) and the peak flow rate ratio (E/A) in early and late diastolic phase were evaluated by transthoracic echocardiography (Philips EPIQ 7C with a S5-1 probe). The LVEF for all subjects was first measured by M-mode ultrasound method. Then if the patient was with enlarged heart, or segmental abnormal wall motion, or ventricular aneurysms, the biplane Simpson method would be applied to introduce a new LVEF value as the final measurement.

2.5. Biochemical indicators

For all subjects, blood samples were analyzed by the Clinical Laboratory of Beijing Friendship Hospital. For most laboratory measurements, the vein blood sample was extracted in the morning after the patient was admitted to the hospital. The main items included were total cholesterol; triglycerides; high density lipoprotein cholesterol; low density lipoprotein cholesterol (LDL-c); leukocyte count; neutrophils; lymphocytes; monocytes; neutrophil to lymphocyte (NL) ratio; total bilirubin and direct bilirubin, which functioned as anti-oxidant factors to some degree;[8] high sensitivity C-reactive protein (hs-CRP); and erythrocyte sedimentation rate. The thrombelastography was analyzed after the patient was admitted to the hospital to ensure systematic evaluation of the thrombotic condition.

2.6. Coronary artery imaging features

Coronary angiograms were performed via a radical artery or femoral artery approach, without the use of adenosine or calcium channel blockers. According to the Markis classification method, the CAE could be classified into 4 groups based on the extent of coronary involvement: type I, diffuse ectasia of 2 or 3 vessels; type II, diffuse disease in 1 vessel and localized disease in another vessel; type III, diffuse ectasia of 1 vessel only; and type IV, localized or segmental ectasia.[3] The thrombolysis in myocardial infarction (TIMI) frame count (TFC)[9] of left anterior descending coronary artery, left circumflex coronary artery, and right coronary artery were intuitively determined by 2 experienced cardiac interventionist experts according to strict anatomical signs and imaging characteristics. The Gensini scores[10] were calculated to evaluate the coronary stenosis extent at the same time.

2.7. Statistical analysis

The Statistical Package for Social Sciences software (SPSS 25.0, IBM SPSS Statistics, Armonk, New York) was used for the analyses. All data were initially analyzed using the Kolmogorov-Smirnov test to assess for normality. Continuous data are presented as mean ± SD when normally distributed and median with interquartile range (IQR) when non-Gaussian in distribution. Unpaired t-tests and Mann-Whitney-U rank sum tests were used for bivariate analyses of normally and non-normally distributed continuous data, respectively. Then, the logistic analysis was applied by setting with forward method and threshold of 0.05; P value <.05 was considered significant.

3. Results

3.1. Baseline characteristics for enrolled subjects

According the medical database from January 2016 to December 2017 in our hospital, CAE prevalence was 2.37% (119/5012) in the subjects who underwent CAG evaluation. There were 105 CAE patients with CHD (105/119 = 88.24%) and 29 CAE + AMI patients with CHD (29/32 = 90.63%), while the CHD prevalence was 92.03% (4503/4893) in non-CAE patients. The AMI prevalence rate in CAE patients was 26.89% (32/119), which was higher than in non-CAE population who underwent coronary angiograms 19.15% (937/4893).

The baseline characteristics of the 2 groups are shown in Table 1. The 2 groups were balanced with regard to age, sex, CHD history, hypertension, blood pressure, diabetes, smoking, alcohol, and body mass index. CAE + AMI patients had higher AMI history rates (28.13% versus 8.05%, P = .012). The LVEF were 61.61% ± 6.45% for CAE + AMI patients and 66.07% ± 6.98% for CAE group (P = .003).

There was no significant difference between the CAE + AMI group and CAE group regarding total cholesterol and triglycer-

Table 1

Baseline characteristics for enrolled subjects.

	CAE + AMI (n = 32)	CAE (n = 87)	P value
Age, yr	65.56 ± 14.39	64.77 ± 9.58	.774
Sex, male (%)	25 (78.13%)	59 (67.82%)	.365
CHD history, n (%)	9 (28.13%)	39 (44.83%)	.140
AMI history, n (%)	9 (28.13%)	7 (8.05%)	.012
Hypertension, n (%)	18 (56.25%)	59 (67.82%)	.054
SBP, mm Hg	126.61 ± 20.59	124.92 ± 14.55	.675
DBP, mm Hg	74.94 ± 10.05	74.84 ± 9.87	.963
Diabetes, n (%)	9 (28.13%)	37 (42.53%)	.206
Smoking, n (%)	17 (53.13%)	46 (52.87%)	1.000
Alcohol, n (%)	9 (28.13%)	21 (24.14%)	.642
BMI, kg/m^2	26.14 ± 4.02	26.71 ± 3.93	.505
TC, mmol/L	4.41 ± 1.18	4.15 ± 1.1	.284
TG, mmol/L	1.46 ± 0.59	1.65 ± 1.03	.338
HDL-c, mmol/L	0.95 ± 0.17	1.06 ± 0.31	.019
LDL-c, mmol/L	2.65 ± 0.88	2.27 ± 0.71	.020
LVEF, %	61.61 ± 6.45	66.07 ± 6.98	.003
E/A ratio	1.19 (0.79–1.85)	0.77 (0.72–0.92)	.108
Antiplatelet, n (%)	7 (21.88%)	39 (44.83%)	.033
Antianginal n (%)	3 (9.38%)	18 (20.69%)	.184
Statin, n (%)	9 (28.12%)	44 (50.57%)	.038
β-blocker, n (%)	7 (21.88%)	34 (39.08%)	.087
CCB, n (%)	15 (46.87%)	39 (44.83%)	1.000
ACEI/ARB, n (%)	14 (43.75%)	31 (35.63%)	.274
Diuretic, n (%)	3 (9.37%)	3 (3.45%)	.341

P values for comparisons between the 2 groups. Significance level was .05. CAE = coronary artery ectasia, CHD = coronary heart disease, AMI = acute myocardial infarction, SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = body mass index, TC = total cholesterol, TG = triglyceride, HDL-c = high-density lipoprotein cholesterol, LDL-c = low-density lipoprotein cholesterol, LVEF = left ventricular ejection fraction. CCB = calcium-channel blockers, ACEI = Angiotensin-Converting Enzyme Inhibitors, ARB = angiotensin receptor blocker.

ide. High-density lipoprotein cholesterol was lower and LDL-c was higher, with significant statistical differences (0.95 ± 0.17 vs 1.06 ± 0.31, *P* = .019, 2.65 ± 0.88 vs 2.27 ± 0.71, *P* = .020) in CAE + AMI group compared to the CAE group (Table 1).

At the same time, the antiplatelet treatment rate, and the statin treatment rate before admission was lower in CAE + AMI group (21.88% vs. 44.83%, *P* = .033; 28.12% vs 50.57%, *P* = .038) while most of medications before admission were balanced between the 2 groups (Table 1).

3.2. Thrombotic system evaluation and inflammation indicators

The thrombotic system, including platelet functions, coagulation system, and fibrinolytic system could be evaluated by thrombelastogram in Table 2. There was no significant difference in thrombelastogram between the 2 groups (*P* > .05).

The white blood cell count (7.64 ± 2.54 vs 6.14 ± 1.42, *P* = .003), neutrophil count (5.43 ± 2.25 vs 4.01 ± 1.41, *P* = .002), NL ratio (2.89 [2.39–4.39] vs 2.47 [1.81–3.02], *P* = .009) and hs-CRP (5.58 [1.81–12.24 vs. 1.13 [0.54–2.45], *P* = .000) in the CAE + AMI group were significantly higher than those in the CAE group (Table 2).

3.3. Coronary imaging characteristics

This study showed in Table 3 that in general Markis type III was the most common type in CAE patients. Markis type II was higher with AMI (34.38% vs 14.94%, *P* = .037) in the CAE + AMI group than

Table 2

The thrombelastogram analysis and inflammation indicators.

Item	CAE + AMI (n = 32)	CAE (n = 87)	P value
R (min)	7.00 (5.98–8.45)	6.8 (5.80–7.70)	.351
K (min)	1.70 (1.35–2.30)	1.70 (1.40–2.00)	.552
Angle (deg)	64.89 ± 8.04	66.23 ± 7.50	.445
MA (mm)	64.38 ± 7.21	63.78 ± 5.61	.663
EPL (%)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	.280
LY30 (%)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	.302
G (kd/sc)	9.45 (6.65–11.55)	8.50 (7.50–10.07)	.535
A	64.87 ± 7.14	63.46 ± 6.62	.363
A30	63.96 ± 7.17	63.18 ± 6.51	.610
CLT	5.95 (4.65–7.95)	5.40 (4.00–6.50)	.131
TPL	52.70 (37.10–72.20)	55.85 (36.88–92.63)	.686
TMA	27.30 (23.05–28.58)	26.80 (22.90–28.60)	.646
SP	6.40 (4.68–7.50)	5.80 (5.20–6.80)	.420
WBC, 10^9/L	7.64 ± 2.54	6.14 ± 1.42	.003
NEUT, 10^9/L	5.43 ± 2.25	4.01 ± 1.41	.002
MONO, 10^9/L	0.39 ± 0.19	0.32 ± 0.19	.054
LY, 10^9/L	1.66 ± 0.73	1.68 ± 0.53	.884
NL ratio	2.89 (2.39–4.39)	2.47 (1.81–3.02)	.009
hs-CRP, mg/L	5.58 (1.81–12.24)	1.13 (0.54–2.45)	.000
ESR, mm/h	11.50 (6.25–29.50)	8.00 (5.75–14.5)	.214
Tbil, μmol/L	12.51 (9.23–15.97)	11.51 (9.65–14.96)	.771
Dbil, μmol/L	2.32 (1.52–3.35)	2.46 (1.87–2.91)	.988

P values for comparisons between the 2 groups. Significance level was .05. CAE = coronary artery ectasia, AMI = acute myocardial infarction, R = reaction time, K = kinetics, Angle = slope of line between R and K, MA = maximum amplitude, A30 or LY30 = amplitude at 30 minutes, CLT = clot lysis time (s), TMA = time to maximum amplitude(s), WBC = white blood cells, NEUT = neutrophils, MONO = monocytes, LY = lymphocytes, NL ratio = neutrophil lymphocyte ratio, hs-CRP = high sensitivity C-reactive protein, ESR = Erythrocyte sedimentation rate, Tbil = total bilirubin, Dbil = direct bilirubin.

in the CAE group, while Markis type IV was lower with AMI (9.38% vs 31.03%, *P* = .017). The ectasia sites were more common in right coronary artery with an incidence of 66.39% (79/119). The incidence of infarction within ectasia part was 59.38%.

Table 3

Coronary imaging characteristics for enrolled subjects.

	CAE + AMI (n = 32)	CAE (n = 87)	P value
LAD TFC	41.67 ± 11.93	40.41 ± 11.25	.606
LCX TFC	37.06 ± 9.90	38.09 ± 12.24	.670
RCA TFC	29.13 ± 10.15	31.05 ± 10.98	.406
LM ectasia, n (%)	1 (3.13%)	10 (11.49%)	.287
LAD ectasia, n (%)	10 (31.25%)	32 (36.78%)	1.000
LCX ectasia, n (%)	10 (31.25%)	34 (39.08%)	.824
RCA ectasia, n (%)	20 (62.5%)	59 (67.82%)	1.000
Markis I, n (%)	5 (15.63%)	14 (16.09%)	1.000
Markis II, n (%)	11 (34.38%)	13 (14.94%)	.037
Markis III, n (%)	13 (40.63%)	33 (37.93%)	.834
Markis IV, n (%)	3 (9.38%)	27 (31.03%)	.017
Infarction within ectasia part, n (%)	19 (59.38%)	-	-
LM stenosis, n (%)	4 (12.50%)	5 (5.75%)	.224
LAD stenosis, n (%)	29 (90.63%)	72 (82.76%)	.021
LCX stenosis, n (%)	27 (84.38%)	60 (68.97%)	.012
RCA stenosis, n (%)	28 (87.50%)	71 (81.61%)	.067
1 vessel stenosis, n (%)	0 (0.00%)	6 (6.90%)	.334
2 vessels stenosis, n (%)	3 (9.38%)	13 (14.94%)	.758
3 vessels stenosis, n (%)	26 (81.25%)	57 (65.52%)	.016
Gensini score	58.00 (32.00–86.00)	26.00 (8.00–57.00)	.000

P values for comparisons between the 2 groups. Significance level was .05. CAE, coronary artery ectasia; AMI = acute myocardial infarction; LM = left main coronary artery; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; TFC = thrombolysis in myocardial infarction (TIMI) frame count.

Table 4

The comparisons among CAE subgroups classified by Markis method.

	Markis I (n=19)	Markis II (n=24)	Markis III (n=46)	Markis IV (n=30)	P
Age, yr	64.05±9.20	64.63±14.74	64.91±10.79	65.97±9.27	.942
Sex, male (%)	13 (68.42%)	19 (79.17%)	30 (65.22%)	22 (73.33%)	.650
CHD history, n (%)	6 (31.58%)	11 (45.83%)	16 (34.78%)	15 (50.00%)	.447
AMI history, n (%)	0 (0.00%)[a]	5 (20.83%)	5 (10.87%)	6 (20.00%)	.142
Anti-platelet, n (%)	4 (21.05%)	8 (33.33%)	18 (39.13%)	16 (53.33%)	.139
AMI, n (%)	5 (26.32%)[a]	11 (45.83%)	13 (28.26%)[b]	3 (10.00%)[c]	.032
Hypertension, n (%)	16 (84.21%)	15 (62.50%)	28 (62.50%)	15 (60.87%)	.119
Diabetes, n (%)	10 (52.63%)	9 (37.50%)	19 (41.30%)	8 (41.30%)	.305
Smoking, n (%)	11 (57.89%)	16 (66.67%)	19 (41.30%)	17 (41.30%)	.198
Alcohol, n (%)	4 (21.05%)	10 (41.67%)	9 (19.57%)	7 (23.33%)	.216
LVEF, %	66.13±4.06	62.52±5.91	66.41±7.48	63.61±8.23	.115
LAD TFC	46.11±13.82	40.91±11.82	38.96±10.84	39.93±9.61	.138
LCX TFC	47.32±16.49	37.71±9.32	36.22±10.47	34.21±7.96	.001
RCA CTFC	35.83±14.06	32.18±9.35	30.42±10.67	25.85±7.52	.017
Gensini score	39.00 (7.00–76.00)	46.50 (21.00–63.50)	28.50 (11.75–53.25)	38.50 (8.00–70.25)	.432

P values for comparisons among the four groups. Significance level was .05. CHD = Coronary heart disease; AMI = acute myocardial infarction; LVEF = left ventricular ejection fraction; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery; CTFC = corrected thrombolysis in myocardial infarction (TIMI) frame count; Subgroup analysis for AMI prevalence: Markis II vs Markis I [a]$P<.05$; Markis II vs Markis III [b]$P<.05$; Markis II vs Markis IV [c]$P<.05$.

The Gensini score was significantly higher in patients with AMI compared to patients without AMI (58.00 [32.00–86.00] vs 26.00 [8.00–57.00], $P=.000$). The CAE + AMI group had higher rates of left anterior descending coronary artery stenosis and left circumflex coronary artery stenosis (90.63% vs 82.76%, $P=.021$; 84.38% vs 68.97%, $P=.012$) and 3-vessels stenosis (81.25% vs 65.52%, $P=.016$) than the CAE group (Table 3).

3.4. Subgroup analysis for CAE patients

According to the Markis classification method,[3] the 119 patients were divided into four groups. The results showed the AMI prevalence for Markis II CAE patients was 45.83%, which was higher than that of the other 3 groups. And another result is the corrected thrombolysis in myocardial infarction (TIMI) frame count of Markis I patients was higher than other 3 groups. (Table 4).

3.5. Logistic regression analysis for AMI in CAE patients

Logistic regression analysis was applied in Table 5 to explore the factors relating to AMI for CAE patients. In this setting, AMI was the dependent variable, and other factors that may relate to AMI were arranged as independent variables. This study used the forward method and set the corresponding p value at less than

0.05. The logistic regression analysis revealed that AMI history, lower antiplatelet rate before admission, higher NL ratio, higher blood LDL-c level (means poor lipid control), Gensini score (higher Gensini score means more extent in stenosis), as well as Markis type II were associated with AMI in CAE patients.

4. Discussion

As known more than 80% of CAE were combined with CHD stenosis,[2–4] and in CAE patients including those with CHD and without CHD, AMI and sudden death rate were higher than that of pure CHD patients,[10–13] thromboembolism might be the main reason.[14,15] The expansion site was often the site of thrombus formation (culprit vessels).[12,16] If CAE patients have coronary artery thrombotic events, the reperfusion treatment success rate is lower than in non-CAE patients, the large thrombus also increased the no reflow phenomenon and distal embolization and other incidence of adverse events during percutaneous coronary intervention,[2,14] and after percutaneous coronary intervention it was also prone to have stent thrombosis.[17] Thus CAE is a kind of thrombotic disease in some degree and it is necessary to find out the underlying reasons especially the controllable factors relating to AMI in CAE patients. In this research, by comparisons between the AMI + CAE group and CAE group, by comparison among the 4 Markis subgroups, and

Table 5

Logistic regression for possible items relating to AMI for CAE patients.

	Beta	Standard error	Wald	P value	Exp(B)	95.0% CI for Exp(B)	
AMI history	2.770	0.913	9.215	.002	15.965	2.669	95.503
Antiplatelet	−1.725	0.708	5.937	.015	0.178	0.044	0.714
NL ratio	0.364	0.156	5.450	.020	1.439	1.060	1.952
LDL-c	1.095	0.389	7.933	.005	2.989	1.395	6.405
Markis II*	1.156	0.623	3.446	.063	3.177	0.938	10.762
Log(Gensini)†	1.433	0.596	5.784	.016	4.190	1.304	13.469
constant	−7.156	1.656	18.675	.000	0.001		

Significance level was 0.05. AMI = acute myocardial infarction, NL ratio = neutrophil lymphocyte ratio, LDL-c = low-density lipoprotein cholesterol.

* the CAE patients here were grouped into Marks type II and non-Markis type II subgroups, CI = confidence interval, Exp(B) = exponentiation of the B coefficient.

† The Gensini score was replaced with Log (Gensini score) in logistic regression part.

by logistic regression analysis in which AMI was dependent variable, it was founded possible factors relating to AMI in CAE patients were:

(1) AMI history, lower antiplatelet rate,
(2) higher NL ratio and other inflammation indicators,
(3) higher Gensini score, and higher LDL-c level,
(4) as well as Markis type II CAE. Those risk factors relating to AMI for CAE founded in this research were very similar to those for CHD.

In fact, most of CAE patients did have obvious atherosclerosis manifestations in coronary and other vessels: the coronary calcification score,[18,19] the carotid artery intima-media thickness[20–23] and pulse wave velocity[24] were all significantly increased in CAE patients. As to pathological characteristics in coronary:

(1) there was significant atherosclerotic change in intimal and media of coronary artery;
(2) inflammatory cells (neutrophils, lymphocytes, plasma cells, eosinophils and mononuclear cell) were infiltrated in the vessel wall.[3,25]

The pathological features of CAE in general were similar to CHD except the damage of smooth muscle and elastic fiber layer on the middle coronary wall which might be due to proteolysis.[25–27] And also similar to CHD, CAE patients were in a systemic inflammatory state with higher level of hsCRP and NL ratio.[28–31] It was suggested CAE and CHD might have a common pathological process with a viewpoint that CAE was a variation from CHD.[32] Theoretically some novel candidate indicators for atherosclerosis, inflammation and prognosis in CHD and AMI patients such as pentraxin 3[33] and osteoprotegerin[34] might be also important for CAE patients. Those AMI relating factors for CAE patients founded in this study might have important clinical significance.

First, CAE patients with high AMI risk could be distinguished if they presented with 1 or more following characters: AMI history, lower antiplatelet treatment rates, poor blood lipid control and higher coronary stenosis extent, higher inflammatory response, and Markis type II. There might be unknown intrinsic factors relating to thrombotic event for CAE patients, thus the patients with AMI history and lower rate of antiplatelet were more likely to undertake AMI, a special CAE case in our hospital had experienced AMI four times within 1 year with dual antiplatelet treatment. The severer inflammation status and atherosclerosis changes in coronary artery might contribute to this kind of higher AMI risk in some degree. The inflammation status and poorer-controlled blood lipid were promotive factors for atherosclerotic plaques formation indicated by higher Gensini scores. As to why Markis type II patients was with highest AMI prevalence, TA Zografos also observed AMI was more frequent in patients with diffuse ectasia,[35] but the relationship between AMI risk and Markis type had not been clearly addressed until present.

Secondly, this research indicated the possible solutions for preventing AMI in CAE patients might include antiplatelet treatment, anti-atherosclerosis treatment including lipid-lowering treatment, and so on. Correspondingly in practices, most proposals for CAE were based the treatment of CHD currently, and anti-thrombotic agent and statin were the main treatments. For antiplatelet treatment, there is no consensus whether to select a single antiplatelet agent, dual antiplatelet therapy or the combination of antiplatelet agent and anticoagulant therapy. Some research notes the larger coronary aneurysms require aggressive treatment through a combination of antiplatelet and anticoagulant therapy.[36] For the anti-atherosclerosis treatment, in theory the application of statin was essential for CAE patients not only by lipid-lowering effect but also by anti-inflammation as for CHD patients, but the lipid-lowering goal, the anti-thrombosis effect of statin were unknown as so far. More clinical trails were needed to evaluate the efficacy of anti-thrombotic agent and statin for CAE patients and to observe the long-term prognosis.

5. Conclusion

The possible factors relating to AMI for CAE patients were higher AMI history, lower antiplatelet treatment rate, poor blood lipid control and higher coronary stenosis extent, higher inflammatory status, and Markis type II. More attention should be paid to these factors in order to decrease the AMI rate for CAE patients.

5.1. Limitations

This research has some deficiencies and limitations that need to be further improved:

(1) it was a small sample size and single centre study because it was not easy to enroll enough subjects due to the low prevalence of CAE and it was usually diagnosed by special methods such as CAG and coronary MD-CTA but not by other easier and more popularized methods;
(2) this study did not conduct a follow-up observation, and the short and long-term effects of those underlying factors especially the treatments of anti-platelet agent and statin needed to be further evaluated.
(3) It was a clinical research by analysis of the data from routine medical practices, other molecules and biological mechanisms which might be also related with AMI for CAE patients were not considered and evaluated by this research.

Author contributions

Conceptualization: Qianqian Sheng and Ruifeng Liu
Formal analysis: Qianqian Sheng and Ruifeng Liu
Investigation: all of authors
Methodology: Shanshan Wu
Project administration: Qianqian Sheng and Ruifeng Liu
   Qianqian Sheng and Ruifeng Liu conceived the study and its design;
Resources: Qianqian Sheng and Ruifeng Liu
Software: Qianqian Sheng and Ruifeng Liu
Validation: all of authors
Writing – original draft: Qianqian Sheng
Writing – review & editing: Ruifeng Liu and Qianqian Sheng

References

[1] Hartnell GG, Parnell BM, Pridie RB. Coronary artery ectasia. Its prevalence and clinical significance in 4993 patients. Br Heart J 1985;54:392–5.

[2] Eitan A, Roguin A. Coronary artery ectasia: new insights into pathophysiology, diagnosis, and treatment. Coron Artery Dis 2016;27:420–8.

[3] Markis JE, Joffe CD, Cohn PF, et al. Clinical significance of coronary arterial ectasia. Am J Cardiol 1976;37:217–22.

[4] Devabhaktuni S, Mercedes A, Diep J, et al. Coronary artery ectasia-a review of current literature. Curr Cardiol Rev 2016;12:318–23.

[5] Swaye P, Fisher L, Litwin P, et al. Aneurysmal coronary artery disease. Circulation 1983;67:134–8.

[6] Liang S, Zhang Y, Gao X, et al. Is Coronary artery ectasia a thrombotic disease? Angiology 2019;70:62–8.

[7] Barrabes J. Comments on the 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent st-segment elevation. Rev Esp Cardiol (Engl Ed) 2015;68:1061–7.

[8] Demir M, Demir C, Keceoglu S. The relationship between serum bilirubin concentration and coronary artery ectasia. Postepy Kardiol Interwencyjnej 2015;11:202–5.

[9] Tony H, Meng K, Wu B, et al. Among ectasia patients with coexisting coronary artery disease, TIMI frame count correlates with ectasia size and markis type IV Is the commonest. Cardiol Res Pract 2015; 2015:282170.

[10] Shakerian F, Sanati H, Kiani R, et al. Comparison of outcomes of diseased coronary arteries ectasia, stenosis and combined. Res Cardiovasc Med 2015;4:e25206.

[11] Antonopoulos AS, Siasos G, Oikonomou E, et al. Characterization of vascular phenotype in patients with coronary artery ectasia: the role of endothelial dysfunction. Int J Cardiol 2016;215:138–9.

[12] Ozturk C, Balta S, Demir M, et al. The relation between coronary artery ectasia and psychological-environmental factors. J Saudi Heart Assoc 2016;28:127–8.

[13] Amirzadegan AR, Davoodi G, Soleimani A, et al. Association between traditional risk factors and coronary artery ectasia: a study on 10057 angiographic procedures among iranian population. J Tehran Heart Cent 2014;9:27–32.

[14] Erden I, Erden EC, Ozhan H, et al. Outcome of primary percutaneous intervention in patients with infarct-related coronary artery ectasia. Angiology 2010;61:574–9.

[15] Swanton RH, Thomas ML, Coltart DJ, et al. Coronary artery ectasia–a variant of occlusive coronary arteriosclerosis. Br Heart J 1978;40:393–400.

[16] Pasha AK, Jokerst CE, Janardhanan R. Myocardial infarction related to a coronary artery aneurysm. Am J Med 2015;128:e5–6.

[17] Feng T, Yundai C, Hongbin L, et al. Evaluation neointimal coverage in patients with coronary artery aneurysm formation after drug-eluting stent implantation by optical coherence tomography. Int J Cardiovasc Imaging 2013;29:1677–83.

[18] Erkan H, Agac MT, Akyol S, et al. Coronary artery calcification score is increased in patients with isolated coronary artery ectasia. Clin Invest Med 2013;36:E191–6.

[19] Farrag A, Faramawy AE, Salem MA, et al. Coronary artery ectasia diagnosed using multidetector computed tomography: morphology and relation to coronary artery calcification. Int J Cardiovasc Imaging 2013;29:427–33.

[20] Demirkol S, Balta S, Celik T, et al. Carotid intima media thickness and its association with total bilirubin levels in patients with coronary artery ectasia. Angiology 2020;71:425–30.

[21] Kosar F, Sincer I, Aksoy Y, et al. Increased aortic stiffness in patients with coronary artery ectasia. Coron Artery Dis 2005;16:499–504.

[22] Celik S, Erdogan T, Kasap H, et al. Carotid intima-media thickness in patients with isolated coronary artery ectasia. Atherosclerosis 2007; 190:385–7.

[23] Yetkin E, Acikgoz N, Aksoy Y, et al. Decreased carotid intima-media thickness in patients with coronary artery ectasia compared with patients with coronary artery disease. Coron Artery Dis 2005;16:495–8.

[24] Kiris A, Bostan M, Korkmaz L, et al. Carotid-femoral pulse wave velocity in patients with isolated coronary artery ectasia: an observational study. Anadolu Kardiyol Derg 2012;12:313–9.

[25] Lee N, Park H, Park C, et al. Analysis of systemic endothelin-1, matrix metalloproteinase-9, macrophage chemoattractant protein-1, and high-sensitivity C-reactive protein in normal-tension glaucoma. Curr Eye Res 2012;37:1121–6.

[26] Sarli B, Baktir A, Saglam H, et al. Neutrophil-to-lymphocyte ratio is associated with severity of coronary artery ectasia. Angiology 2014; 65:147–51.

[27] Li J, Nie S, Qian X, et al. Chronic inflammatory status in patients with coronary artery ectasia. Cytokine 2009;46:61–4.

[28] Dogdu O, Koc F, Kalay N, et al. Assessment of red cell distribution width (RDW) in patients with coronary artery ectasia. Clin Appl Thromb Hemost 2012;18:211–4.

[29] Virmani R, Robinowitz M, Atkinson JB, et al. Acquired coronary arterial aneurysms: an autopsy study of 52 patients. Hum Pathol 1986;17: 575–83.

[30] Lamblin N, Bauters C, Hermant X, et al. Polymorphisms in the promoter regions of MMP-2, MMP-3, MMP-9 and MMP-12 genes as determinants of aneurysmal coronary artery disease. J Am Coll Cardiol 2002;40:43–8.

[31] Finkelstein A, Michowitz Y, Abashidze A, et al. Temporal association between circulating proteolytic, inflammatory and neurohormonal markers in patients with coronary ectasia. Atherosclerosis 2005; 179:353–9.

[32] Yetkin E, Waltenberger J. Novel insights into an old controversy: is coronary artery ectasia a variant of coronary atherosclerosis? Clin Res Cardiol 2007;96:331–9.

[33] Altay S, Cakmak HA, Kemaloglu Oz T, et al. Long-term prognostic significance of pentraxin-3 in patients with acute myocardial infarction: 5-year prospective cohort study. Anatol J Cardiol 2017;17:202–9.

[34] Flora Özkalaycı, Öykü Gülmez, Betül Uğur-Altun, et al. The role of osteoprotegerin as a cardioprotective versus reactive inflammatory marker: the chicken or the egg paradox. Balkan Med J 2018;35:225–32.

[35] Zografos T, Korovesis S, Giazitzoglou E, et al. Clinical and angiographic characteristics of patients with coronary artery ectasia. Int J Cardiol 2013;167:1536–41.

[36] Baman TS, Cole JH, Devireddy CM, et al. Risk factors and outcomes in patients with coronary artery aneurysms. Am J Cardiol 2004;93: 1549–51.