RESEARCH LETTER

Coronary artery ectasia carries a worse prognosis: a long-term follow-up study

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Introduction Coronary artery ectasia (CAE) is defined as coronary dilation that exceeds the diameter of the normal adjacent segments or the diameter of the largest coronary artery by 1.5-fold.[1] The prevalence of CAE varies between 1.5% and 5%, and could be as low as 0.4% in nonatherosclerotic CAE.[2] Early reports of CAE supported the aggressive nature of the disease, with frequent presentation of major adverse cardiac events (MACEs)[3] that was attributed to disturbed inflammatory response, leading to the damage of the coronary artery intima.[4] Furthermore, the pro-inflammatory response seen in the abnormal cytokine response may influence disease severity and prognosis.[5]

This study investigated the long-term clinical outcome of patients with CAE from Northern Europe. To the best of our knowledge, this is the first study to provide such long-term follow-up data on this population.

Patients and methods **Patient selection** We reviewed 16 464 angiograms performed between 2003 and 2011 at the Umeå Heart Centre of Umeå University Hospital, Sweden, and Letterkenny University Hospital, Ireland, in patients with clear evidence of CAE. The following inclusion criteria were used: coronary artery diameter exceeding the original caliber of the artery or the diameter of the adjacent artery by more than 1.5-fold, the ectatic segment not localized in the artery (ie, >20 mm long and/or includes more than one-third of the artery length).[2] Criteria for the selection of patients with CAE were described before[5]; based on that, we selected only individuals with minimal atherosclerosis (≤20% luminal stenosis) and CAE. Medical therapy was optimized according to the clinical need and using national and European guidelines, regardless of the presence of CAE.

Follow-up data collection A total of 66 patients fulfilled the predefined inclusion criteria. Complete follow-up data with information on MACEs (ie, acute coronary syndrome, acute myocardial infarction [MI], and death from cardiac events) were collected. Data were obtained from hospitals or health center registries, clinical notes, or by a telephone interview conducted by a research nurse.

Follow-up data on CAE were compared with those from a control group of 41 consecutive patients with minimal coronary artery disease (CAD defined as ≤20% luminal stenosis on conventional coronary angiography). Data on follow-up periods were collected for patients with CAE and controls who underwent coronary angiography between January 2008 and December 2011 (Supplementary material, *Figure S1*). The follow-up period was similar in both groups.

We excluded patients or controls who had prior coronary intervention, more than mild valve disease, or congenital heart disease at the time of the diagnostic coronary angiogram.

The study was approved by the Regional Ethics Committee of Umeå (Sweden) and Letterkenny University Hospital (North West Health Service Executive, Ireland).

Cardiovascular risk factors Data on cardiovascular (CV) risk factors for CAD, MACEs, and CV mortality were obtained from patients' medical records at the time of presentation, including hypertension, diabetes mellitus, current or former smoking, family history of CAD, and dyslipidemia. We used standard definitions for risk factors according to conventional guidelines.[6,7] None of the patients with CAE or controls had documented inflammatory disorder or advanced kidney disease at the time of the study.

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TABLE 1 Demographic and cardiovascular data in patients with coronary artery ectasia and controls

Parameter		Controls (n = 41)	CAE (n = 41)	*P* value
Age, y, median (IQR)		61 (56–68)	68 (60–74)	0.003
Female sex, n (%)		12 (29.3)	11 (26.8)	0.81
Risk factors, n (%)	Hypertension	24 (58.5)	22 (53.7)	0.82
	Diabetes	8 (19.5)	7 (17.1)	0.78
	Smoking	15 (36.6)	30 (73.2)	0.001
	Dyslipidemia	22 (53.7)	27 (65.6)	0.26
	Family history of CAD	12 (29.3)	22 (53.7)	0.02
Overall mortality, n (%)		0	9 (22)	0.001
Cardiovascular mortality, n (%)		0	5 (12.2)	0.03
MACEs, n (%)		13 (31.7)	18 (43.9)	0.26
Follow-up, y, median (IQR)		10.0 (9.7–10.3)	11.4 (10.1–12.2)	0.001

A *P* value of less than 0.05 was considered significant.

Abbreviations: CAD, coronary artery disease; CAE, coronary artery ectasia; IQR, interquartile range; MACE, major adverse cardiac event

Statistical analysis Statistical analysis was performed using the IBM SPSS Statistics program for Macintosh, version 24.0 (IBM Corp., Armonk, New York, United States). The data were reported as median (interquartile range) or as number and percentage of patients. Differences between patients and controls were assessed using the Mann–Whitney test. Proportions were analyzed by the χ^2 or Fisher exact test, as appropriate. Since our hypothesis was that the CV mortality rate and number of MACEs were higher in the CAE group, the 1-sided Fisher exact test was used. However, 2-sided tests were applied to compare the prevalence of risk factors in different groups, since we expected that the prevalence could be both higher and lower in the group with the highest risk of cardiac events. Statistical significance was defined as a *P* value of less than 0.05.

Results

Demographic data and cardiovascular risk factors The baseline demographic data, CV risk factors, MACEs, and CV mortality during the follow-up were assessed in the CAE and control groups (TABLE 1). Controls were slightly younger and had a shorter follow-up period than patients with CAE, but there were no differences between groups with respect to sex, hypertension, hypercholesterolemia, and diabetes mellitus. However, the prevalence of smoking and family history of CAD was significantly higher in patients with CAE than in controls ($P = 0.001$ and $P = 0.02$, respectively). On the other hand, the CAE group had higher CV mortality ($P = 0.03$) but the same rate of readmission with MACEs ($P = 0.26$) (TABLE 1).

Follow-up Follow-up data on MACEs and mortality were retrospectively collected for patients with CAE and controls (median duration, 10 years and 11.4 years, respectively; $P = 0.001$). The data were complete in 41 patients with CAE (62.1%; median age, 61 years; 12 women) (Supplementary material, *Figure S1*). Medical therapy was standardized according to the clinical indications regardless of the presence of CAE.

Cardiovascular mortality in patients with coronary artery ectasia Cardiovascular mortality was documented in 5 of the 41 patients (12%). There were no differences in demographic characteristics or CV risk factors between survivors and nonsurvivors ($P > 0.05$). Mortality in the CAE group was related to ventricular arrhythmia in 2 patients, atrial fibrillation complicated by stroke in 1 patient, as well as dilated cardiomyopathy and heart failure in 2 patients (the same 2 patients were also known to have increased alcohol intake). Data are presented in Supplementary material, *Figure S2A*. Finally, all nonsurvivors were smokers and had dyslipidemia, with a noticeable but nonsignificant difference between subgroups (Supplementary material, *Table S1*).

Cardiovascular profile of patients with major adverse cardiac events During the follow-up, 18 patients with CAE (44%) developed MACEs, including 14 survivors (34%). Most events were related to the development of atrial fibrillation (4 patients), acute coronary syndrome or acute MI (3 patients), urgent coronary artery bypass surgery (2 patients), dilated cardiomyopathy leading to heart failure (2 patients), and cardiac arrest (2 patients who primarily presented with ventricular arrhythmias) (Supplementary material, *Figure S2B*). The patients with CAE who developed MACEs, as compared with those without MACEs, were relatively older ($P = 0.09$), mostly female (8 patients, $P = 0.03$), and had less relevant family history of CAD ($P = 0.03$). The other CV risk factors did not differ between groups (Supplementary material, *Table S2*).

Discussion

This study presented data from a relatively long-term follow-up of patients with CAE

(11.4 years; interquartile range, 10.1–12.2 years). Overall and CV-related mortality rates were significantly higher in CAE patients compared with controls. In comparison with controls, patients with CAE were slightly older, were more often smokers, and more often had a family history of CAD. Apart from smoking, the remaining conventional CV risk factors did not differ between the CAE group and controls. Overall, a subanalysis revealed that the CV risk profile failed to predict MACEs or mortality among patients with CAE, probably because of the small sample size.

Coronary artery ectasia with major adverse cardiac events Adverse cardiac events are well-established consequences of CAE.[8] A 3-year follow-up study showed similar clinical outcomes in patients with CAE and those with high burden of CAD.[9] On the other hand, another study reported a nonbenign course of CAE as a result of dilated lumens with disrupted flow, a substrate for potential thrombus formation.[10] In our study, patients with CAE had no significant coronary stenosis as a sign of severe atherosclerosis but demonstrated higher long-term mortality, with higher rates of CV mortality or hospital admissions due to chest pain, acute coronary syndrome, and arrhythmia. The previously suggested coronary slow flow phenomenon could explain the poorer clinical outcome, as well as the development of dilated cardiomyopathy with heart failure in 2 patients, as documented before.[11] Perhaps the long-term outcome shown in our patients provides stronger evidence for a worse clinical outcome in CAE compared with controls.

Cardiovascular risk profile and major adverse cardiac events in coronary artery ectasia Although conventional CV risk factors were not found to affect the development of MACEs in CAE,[2] another study showed that smoking was independently associated with CAE-related MACEs, particularly MI.[10] Our study may support this finding, as it showed that smoking and dyslipidemia were associated with a higher risk of mortality in CAE. However, most CV risk factors (except the family history of CAD and female sex) were similar among CAE patients with and without MACEs, thus refuting the potential impact of these factors on MACEs in patients with CAE. Similarly, the CV risk factors did not affect CV mortality in the same group of patients. This finding supports our previous suggestion that CAE (particularly nonatherosclerotic) is quite different from conventional atherosclerosis, as suggested also by other studies,[5,12] as well as showed significantly higher CV mortality and trends towards higher morbidity and occurrence of MACEs in the long-term follow-up.[10,11]

Study limitations Despite the long-term follow-up of our study and the use of strict criteria for the diagnosis of CAE, the cohort was rather small, especially the number of patients with complete follow-up data. This limits the relevance of statistical findings and adjustments for confounding factors. Another limitation is the fact that controls were relatively younger, but this was due to the specific criteria for inclusion of patients with minimal disease rather than those with a significant atherosclerotic burden. Finally, there may be some differences between patients and controls in terms of individual habits and exercise training.

Conclusion Patients with CAE have a worse prognosis, with higher CV mortality than individuals with minor CAD. Among patients with CAE, older women were shown to have higher mortality. Smoking and dyslipidemia seem to have an important prognostic role in CAE.

SUPPLEMENTARY MATERIAL

Supplementary material is available with the article at www.mp.pl/paim.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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