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High prevalence of coronary artery events and non-coronary events in patients with coronary artery aneurysm in the observational group

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ABSTRACT

Background: Coronary artery aneurysm (CAA) is occasionally detected on a small percentage of coronary angiography or multi-detector computed tomography (MDCT). CAA itself is considered benign entity despite the potential risks of rupture, thromboembolism, and compression of surrounding structures. However, the optimal management including other vascular comorbidity has yet to be fully clarified.
Objective: The aim of this study was to evaluate cardiovascular events in the patients with CAA in the observational group.
Methods: Between January 2010 and August 2015, 48 CAAs were identified in 37 patients out of consecutive 10,010 patients (0.37%) by MDCT. Twenty-eight patients treated conservatively were included in this study. Their major adverse cardiovascular events (MACE) were evaluated retrospectively: death, non-fatal myocardial infarction (MI), revascularizations; coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI), and other vascular events.
Results: The average age was 62.0 ± 15.5 year sold, and median follow-up period was 49.6 months (IQR 23.6 to 78.1). Mean CAA diameter was 7.5 ± 2.8 mm. Twenty-two MACE occurred in 15 patients (53.6%): 1 sudden death, 4 MI, 1 CABG for CAA, 3 PCI for CAA, 7 PCI for non-CAA lesions, and 6 other vascular treatments for aorta and cerebral and peripheral artery. Follow-up MDCT was performed for 22 CAAs in 16 patients. In 9 CAAs of them, the maximal diameter increased significantly (Δ diameter: 1.5 ± 1.1 mm).
Conclusions: Presence of CAA may be associated with adverse vascular events including non-coronary diseases. This study could suggest the management for CAA should include the evaluation of not only CAA itself but also other vascular diseases.

1. Introduction

Coronary artery aneurysm (CAA) is occasionally detected on a small percentage of coronary angiography (CAG) or multi-detector computed tomography (MDCT). The prevalence of CAA is reported as 0.3–5.3% in CAG and MDCT [1–4], and as 1.4% in autopsy [5]. The majority of patients have CAA that is due to atherosclerosis [1,4,6], and the prognosis of CAA is considered directly related to the severity of the concomitant obstructive coronary artery disease [3,7,8]. So, CAA itself is considered as benign entity despite the potential risks of rupture, thromboembolism, and compression of surrounding structures. However, CAA is sometimes associated with other vascular diseases, such as cerebrovascular disease, macro-vascular disease like abdominal aortic aneurysm (AAA), and peripheral artery disease [1,5,8]. Otherwise, only a few reports mention the risk of these comorbidities [9–11]. So, the optimal management for CAA including other vascular comorbidity has yet to be fully clarified. The purpose of this study was to evaluate cardiovascular events in the patients with CAA, not only about coronary artery but also other vascular diseases.

2. Method

2.1. Patients

Between January 2010 and August 2015, 48 CAAs were identified in 37 patients out of consecutive 10,010 patients by MDCT (0.37%). All of MDCT was performed aimed to close investigation for ischemic heart disease and rule out of coronary artery disease before non-cardiovascular surgical operation. CAA is defined as localized coronary artery dilatation 1.5 times the diameter of the adjacent coronary artery segment [1]. The term "localized" means involving less than 50% of the total length of the vessel. By this definition, the term "ectasia", defined

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as diffuse coronary artery dilatation 1.5 times the diameter of the adjacent coronary artery segment that involves 50% or more of the length of the artery [12], was not included in this study. The patients were retraced when their CAAs were first detected (the data was defined as "onset") and their long-term major adverse cardiovascular events (MACE) were evaluated retrospectively. MACE was defined as death, non-fatal myocardial infarction (MI), revascularizations; coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI), and intervention for other vascular events, such as cerebrovascular disease, macro-vascular disease like AAA, and peripheral artery disease. Because 9 patients (11 CAAs) immediately treated with invasive therapy after first detection of CAAs were excluded, 28 patients (37 CAAs) treated conservatively at first were included in this study as an observational group. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and all patients gave written informed consent approved Research Ethics Committee in our institution. The study flow was shown in Fig. 1.

2.2. Statistical Analysis

Continuous variables were expressed as mean and (±) standard deviation (SD) or as median accompanied by interquartile range (IQR), as appropriate. All the statistical analysis was performed using SPSS 20.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Patient and aneurysm characteristics

The average age at onset was 62.0 ± 15.5 year-old, and median follow-up period was 49.6 months (IQR 23.6 to 78.1). Men were observed in 64.3%. Diabetes mellitus and chronic kidney disease were less observed than other coronary risk factors. Other patient characteristics ware shown in Table 1. Mean CAA diameter at onset was 7.5 ± 2.8 mm. About the distribution of CAA, the right coronary artery was most frequently involved (48.6%), followed by the left descending coronary artery (40.5%). Three-vessel involvement was not observed. On the basis of morphologic appearance, saccular aneurysm, defined as the transverse diameter is greater than the longitudinal measurement of the aneurysm [12], was observed in 24.3%. Fusiform aneurysm, defined as the longitudinal diameter is greater than the transverse measurement of the aneurysm [12], was more frequently seen (75.7%). Almost 60% of CAA occurred as a consequence of atherosclerosis, followed by Kawasaki disease (14.3%). Iatrogenic CAA as a consequence of complication of PCI and Bentall operation was observed in one and one each. Other aneurysm characteristics were shown in Table 2. Aspirin was most frequently administered to these patients (71.4%), followed by clopidogrel (42.9%). Anticoagulant agent was less administered (14.3%) than antiplatelet agent, and novel oral anticoagulant (NOAC) was not administered at all (Table 3).

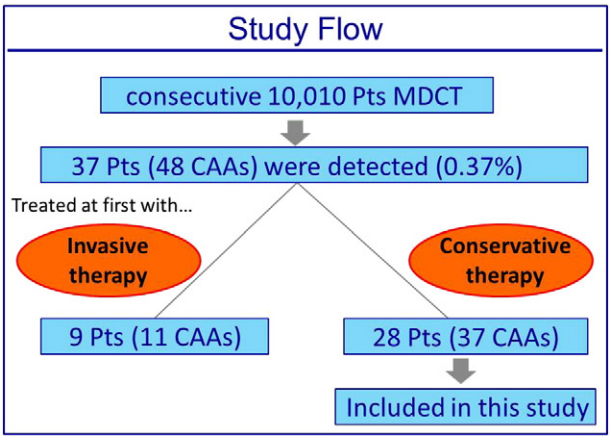

Fig. 1. Study flow. Between January 2010 and August 2015, 48 CAAs were identified in 37 patients out of consecutive 10,010 patients (0.37%) by MDCT. Twenty-eight patients treated conservatively at first were included in this study. Pts = patients, MDCT = multi-detector computed tomography, CAA = coronary artery aneurysm.

Table 1
Patient characteristics.

Patient characteristics	28 patients
Age, y	62.0 ± 15.5
Men, n (%)	18 (64.3)
Median f/u period, m	49.6 (IQR 23.6 to 78.1)
Coronary Risk Factors	
HT, n (%)	18 (64.3)
DL, n (%)	16 (57.1)
DM, n (%)	4 (14.1)
CKD, n (%)	4 (14.1)
Smoke, n (%)	16 (57.1)
Family History of CAD, n (%)	4 (14.1)
systolic BP, mmHg	130.0 ± 15.1
diastolic BP, mmHg	74.5 ± 9.5

HT = hypertension, DL = dyslipidemia, DM = diabetes mellitus, CKD = chronic kidney, disease, CAD = coronary artery disease, BP = blood pressure.

3.2. Outcome

Clinical outcome was shown in Table 4. MACE occurred in 15 patients out of 28 patients (53.6%), and total 22 adverse events were counted. One sudden death (3.6%), 4 MI (14.3%), including 3 CAA related MI, 1 CABG for CAA with stenosis (3.6%), 3 PCI for CAA with stenosis (10.7%), 7 PCI for non-CAA lesions (25.0%), 2 coil embolization for cerebral artery aneurysm (7.1%), 2 surgical operation for AAA (7.1%), 1 surgical operation for annuloaortic ectasia (3.6%), and 1 percutaneous transluminal angioplasty for arteriosclerosis obliterans (3.6%). At each physician's discretion, follow-up MDCT was performed for 22 CAAs in 16 patients. In 9 CAAs of them, the maximal diameter increased significantly: Δ diameter 1.5 ± 1.1 mm in the median follow-up period of 66.5 months (IQR 61.3–77.2).

4. Discussion

According to this study, presence of CAA seemed highly associated with major adverse cardiovascular events. In general, the prognosis of

Table 2
Aneurysm characteristics.

Aneurysm characteristics		28 Pts, 37 CAAs
Size at onset, mm		7.5 ± 2.8
Distribution, n (%)	LMT	3 (8.1)
	LAD	15 (40.5)
	LCx	1 (2.7)
	RCA	18 (48.6)
Form, n (%)	Saccular	9 (24.3)
	Fusiform	28 (75.7)
Etiology, n (%)	atherosclerosis	16 (57.1)
	Kawasaki disease	4 (14.3)
	polycystic kidney disease	1 (3.6)
	fistula	2 (7.1)
	Marfan syndrome	1 (4.5)
	post-Bentall operation	1 (4.5)
	post-stent	1 (4.5)
	unknown	2 (7.1)

Pts = patients, CAA = coronary artery aneurysm, LMT = left main trunk, LAD = left anterior descending artery, LCx = left circumflex, RCA = right coronary artery,

Table 3
Medication.

Medication, n (%)		28 patients
Antiplatelet	Aspirin	20 (71.4)
	Clopidogrel	12 (42.9)
	Cilostazol	1 (3.6)
Anticoagulant	Warfarin	4 (14.3)
	NOAC	0 (0.0)

NOAC = novel oral anticoagulant.

CAA is considered directly related to the severity of the concomitant obstructive coronary artery disease [3,7,8]. However, almost one third of MACE in this study was concerning non-coronary vascular disease. Indeed, several literatures describe that CAA is sometimes associated with other vascular diseases, particularly aortic and iliofemoral aneurysms [1,5,8,13,14]. Otherwise, only a few reports mention the risk of these comorbidities [9–11]. That may due to insufficient estimation of other vascular diseases and asymptomatic entities of aortic, carotid and cerebral artery diseases. To the best of our knowledge, this study put first clearly emphasis on the risk of multi-vascular diseases of the patients with CAA, except for case report [15].

This study included various type of CAA. However, etiology, distribution, morphologic appearance and patient characteristics such as high prevalence of hypertension and dyslipidemia, and low prevalence of diabetes mellitus in this study were very similar to those described in former studies [1,3,4,6,12,14,16]. So, the population in this study could represent overview image of CAA in the real world.

MACE seemed more frequently in CAA due to atherosclerosis, 16 events in 16 patients, compared to 6 events in 12 non-atherosclerotic patients, although lacking statistical power. Saccular aneurysm is considered more prone to thrombosis and rapture [17]. It is also considered aneurysm size is not associated with mortality [18] and rapture of aneurysm is rare and unpredictable [3,19]. We found 9 saccular aneurysms and 9 enlarging aneurysms. But we could not find out whether these features contained the risk of MACE or not because of insufficient statistical power. Further studies including multicenter registries are needed in order to clarify what type of CAA has more risk of multi-vascular diseases.

5. Study Limitations

This study had several limitations, such as single center, small size, and retrospective study. Original selection bias as many of patients who underwent MDCT were suspected coronary artery disease was inevitable. Follow-up period was not uneven for each patient in this study design. There was excluded population, such as moderate and severe chronic kidney disease and contra-indication of MDCT. The late stent malposition and aneurysmal formation is often seen in drug-eluting stent era [20–21]. However, there was only one post-stent aneurysm observed despite a study in high volume PCI center. It was mainly because these CAAs were usually closely followed with intravascular ultrasound imaging or optical coherence tomography in our institution.

Table 4
Clinical outcome.

MACE, n (%)	15/28 patients (53.6)
Sudden death	1 (3.6)
non-fatal MI	4 (14.3)
CABG for CAA	1 (3.6)
PCI for CAA	3 (10.7)
PCI for non-CAA lesions	7 (25.0)
Coil embolization for cerebral aneurysm	2 (7.1)
Surgical operation for AAA	2 (7.1)
Surgical operation for AAE	1 (3.6)
PTA for ASO	1 (3.6)

MACE was defined as death, non-fatal myocardial infarction, revascularization, and other vascular events. MACE occurred in 15 patients out of 28 patients (53.6%), and total 22 adverse events were counted.
MI = myocardial infarction, CABG = coronary artery bypass grafting, CAA = coronary artery aneurysm, PCI = percutaneous coronary intervention, AAA = abdominal aortic aneurysm, AAE = annuloaortic ectasia, PTA percutaneous transluminal angioplasty, ASO = arteriosclerosis obliterans.

6. Conclusions

Cardiovascular events in the patients with CAA in the observational group cannot be ignored. This study suggested the management of these patients should include not only evaluation of CAA itself but also other vascular diseases.

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Conflict of interest statement

None.

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