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Association of indexed aortic dimensions with the presence and extent of coronary artery ectasia in patients with acute coronary syndrome

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ABSTRACT

Background: Conflicting findings have been reported on the potential association between CAE and aortic dilatation. This study aimed to investigate the relationship between CAE extent and aortic dimensions in patients with acute coronary syndrome (ACS).

Methods: This retrospective cohort study included 448 adult patients who underwent coronary angiography for ACS between 2004 and 2015. The cohort was divided into 224 patients with CAE and 224 control patients without CAE, matched for age, sex, and hypertension. Aortic dimensions at the annulus, sinus of Valsalva (SOV), sinotubular junction (STJ), and ascending aorta were measured using transthoracic echocardiography and indexed to body surface area (BSA). The extent of CAE was classified using the Markis and Markis-Harirkrishnan systems. Statistical analysis included ANOVA to assess differences in aortic dimensions and their correlation with CAE extent.

Results: Patients with CAE had significantly larger non-indexed aortic dimensions compared to those without CAE (e.g., ascending aorta diameter: 35.2 ± 4.0 mm vs. 33.6 ± 3.7 mm, $p < 0.0001$). However, when indexed to BSA, these differences were not significant. No significant correlation was found between CAE extent and aortic dimensions (e.g., indexed ascending aorta: $F = 1.161$, $p = 0.325$). The incidence of bicuspid aortic valve was similar between both groups (0.9 % vs. 0.4 %, $p = 0.554$).

Conclusion: In patients with ACS, there were no significant differences in indexed aortic diameters in those with and without CAE. Additionally, no correlation was found between CAE extent and aortic dimensions and the incidence of bicuspid aortic valve was comparable in both groups.

1. Introduction

Coronary artery ectasia (CAE) is commonly defined as a coronary segment with a diameter 1.5 times the sizes of an adjacent healthy segment. Unlike coronary aneurysms, which are saccular or fusiform, CAE is characterized by a diffuse dilation of the coronary arteries [1]. The incidence of CAE ranges from 0.3 % to 5.3 % in the general population [2], with a higher prevalence observed in males and patients with diastolic hypertension [3–4]. In patients with atherosclerotic obstructive coronary artery disease, 85 % of CAE are pre- or post-stenotic [5]. However, CAE is often detected in the absence of atherosclerotic coronary artery disease [6].

CAE has been independently associated with an increased rate of major adverse cardiovascular events and a higher thrombus burden in patients presenting with acute myocardial infarction (MI) [7]. There have been suggestions of an association between the presence and extent of CAE and an enlargement of the aortic root and ascending aorta, although the findings in this regard are contradictory [8–11]. As ascending aortic dilatations pose a risk of dissection or rupture, determining the presence or absence of a correlation with CAE could provide

Abbreviations: ACS, acute coronary syndrome; BMI, body mass index; BSA, Body surface area; CAE, Coronary artery ectasia; LV, left ventricle; MI, Myocardial infarction; SOV, Sinus of Valsalva; STJ, Sinotubular junction; TIMI, Thrombolysis in Myocardial Infarction; TTE, transthoracic echocardiogram.

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prognostic value [12]. Additionally, a correlation between the presence of CAE and aortic valve anomalies such as a bicuspid aortic valve has been shown, with or without ascending aortic dilatation present [13]. These associations underline the importance of understanding the broader cardiovascular implications of CAE beyond the coronary arteries.

The aim of this study is to investigate whether the dimensions of the ascending aorta, both in raw measurements and adjusted for body surface area, are larger in patients with acute coronary syndrome (ACS) who exhibit CAE on coronary angiography compared to those without CAE. Furthermore, this study seeks to determine whether there is a correlation between the extent of CAE and aortic dimensions. The analysis will adjust for potential confounding factors, including age, sex, and hypertension

2. Methods

2.1. Study population

In the present retrospective analysis, consecutive adult patients (>18 years) who underwent emergent coronary angiography because of ACS between 2004 and 2015 in a tertiary academic center were considered for inclusion. The procedure was performed following standard protocols and culprit vessel revascularization was performed following contemporary guidelines. Patients were treated according to the institutional care-track protocol for MI [14–15], and remained hospitalized under ECG monitorization for at least 48 h. A two-dimensional transthoracic echocardiography (TTE) was performed prior to discharge. Patients with previous history of coronary artery bypass grafting and unavailable of coronary angiograms or TTE images were excluded from the analysis. Baseline clinical and demographic characteristics were collected from the departmental information system (EPD vision, Leiden, The Netherlands).

The study population consisted of patients with ACS and CAE on index coronary angiography and a control group comprised by patients with ACS without CAE, adjusted to age, gender and presence of hypertension. This retrospective study of clinically acquired data was approved by the Institutional Review Board and the need for patient written informed consent was waived.

2.2. Angiographic and procedural analysis

All coronary angiograms obtained during the index procedure were retrospectively evaluated by two experienced interventional cardiologist. CAE was defined as a coronary segment with a diameter 1.5 times larger than the diameter of an adjacent healthy segment [16]. The angiographic anatomical distribution of CAE was defined according to both Markis and the Markis-Harikrishnan classifications. The Markis classification [1] categorizes CAE in 4 different subgroups: type I, defined as the presence of diffuse CAE in 2 or 3 coronary vessels; type II, defined as diffuse CAE in one coronary vessel and localized CAE in another vessel; type III, defined as diffuse CAE in only one coronary vessel and type IV, defined as localized or segmental CAE. The Markis-Harikrishnan classification [17–18] builds upon the foundational Markis classification by introducing additional subcategories, allowing a more precise differentiation between focal and diffuse ectasia. Hence, type I is defined as the presence of diffuse CAE in 2 or 3 vessels, and is further subdivided in type IA (diffuse CAE in 3 vessels), type IB (diffuse CAE in 2 vessels and focal in 1 vessel) and type IC (diffuse CAE in 2 vessels). Type 2 is defined as diffuse CAE in one vessel and is subdivided in IIA (diffuse CAE in 1 vessel and focal in 1 vessel) and IIB (diffuse CAE in 1 vessel and focal in 2 vessels). Type III is defined as diffuse CAE in only 1 vessel. Type IV is characterized by the presence of focal CAE, and is subdivided in type IVA (1 vessel involved), type IVB (2 vessels involved) and type IVC (3 vessels involved). Both classifications, along with angiographic examples, are depicted in Fig. 1. Multivessel disease was defined by the presence of a stenosis > 50 % in at least to two coronary arteries. Coronary flow was measured using the Thrombolysis in Myocardial Infarction (TIMI) frame count method [19]. Thrombus burden was rated from 0 to 5 on the TIMI-thrombus scale, with a high burden defined as a score of 4 or higher [20]. Angiographic success was defined as TIMI 3 distal flow with less than 20 % residual stenosis and no immediate mechanical issues at the end of the procedure. No-reflow phenomenon was defined as final TIMI flow of ≤ 2 in the absence of mechanical obstruction [21].

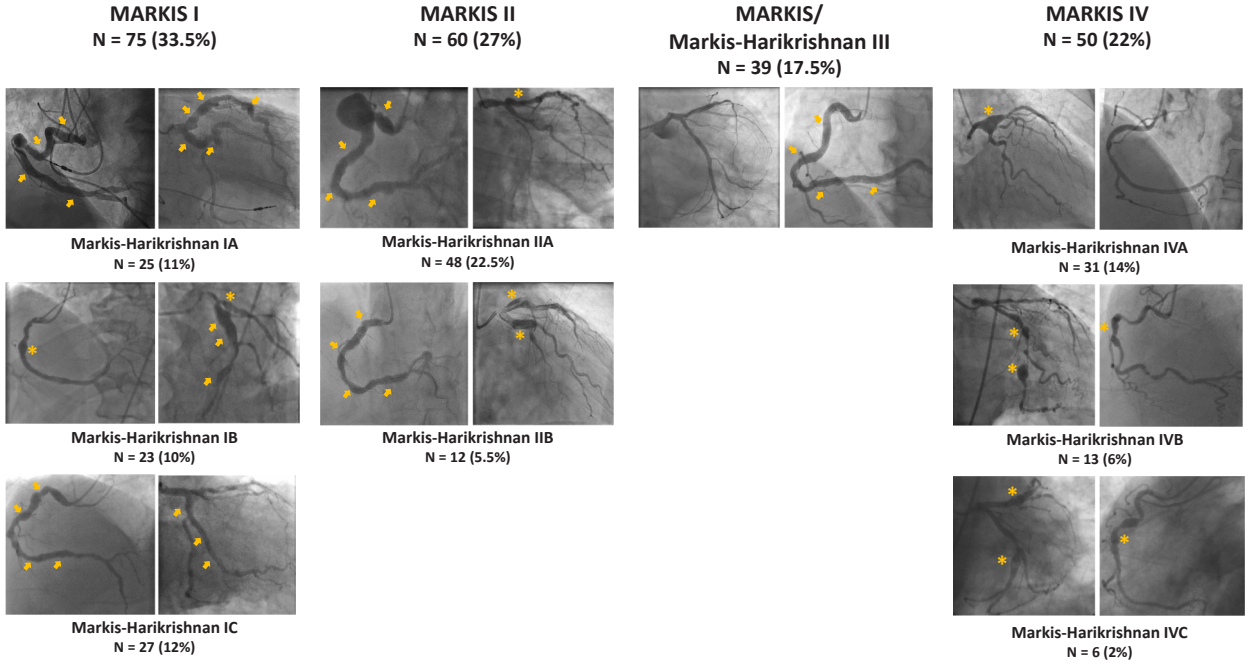

Fig. 1. Distribution of the CAE phenotypes based on the Markis and Markis-Harikrishnan classification of CAE. Diffuse CAE is indicated with arrows. Areas or focal CAE are marked with asterisks.

2.3. Echocardiographic characteristics

Transthoracic echocardiography was performed with the patients at rest, lying in the left lateral decubitus position, using commercially available ultrasound systems (GE Vingmed Ultrasound, General Electric, Milwaukee, Wisconsin) equipped with 3.5 MHz or M5S transducers. The echocardiographic data were digitally stored in cine-loop format, and data were retrospectively analyzed using commercially available software (EchoPAC version 203; GE Vingmed Ultrasound AS). Two-dimensional and Doppler data were acquired from parasternal, apical, and subcostal views. Left ventricular (LV) end-diastolic diameter was measured on the parasternal long-axis view [22]. The apical 2- and 4-chamber views were used to measure the LV end-diastolic and end-systolic volumes, and LVEF was calculated according to Simpson's biplane method. Aortic regurgitation grade was assessed using a multiparametric approach including the measurement of the jet width relative to the left ventricular outflow tract width and the vena contracta in the parasternal and apical views. Aortic regurgitation was graded as grade 2 (mild to moderate; jet width/ left ventricular outflow tract width ratio of 0.25–0.45 and/or vena contracta of 3.0–4.5 mm), grade 3 (moderate to severe; jet width/left ventricular outflow tract width ratio of 0.46–0.64 and/or vena contracta of 4.6–5.9 mm), or grade 4 (severe; jet width/ left ventricular outflow tract width ratio $\geq$ 0.65 and/or vena contracta $\geq$ 6.0 mm).

Measurement of aortic dimensions was performed at the levels of the aortic annulus, sinus of Valsalva (SOV), sinotubular junction (STJ) and ascending aorta using the parasternal long axis view. To measure the STJ, SOV and ascending aorta the leading edge to leading edge method was used during end-diastole. Measurements of the annulus were performed with the inner edge to inner edge method in mid-systole as per the current recommendations [22]. Body surface area (BSA) was calculated according to the Dubois and Dubois formula as follows, BSA = = 0.007184 x (Height(m)$^{0.725}$) x (Weight(kg)0.425. [23] Indexed values were obtained by dividing the mentioned measurements (mm) by BSA (m^2).

2.4. Study endpoints

The primary endpoint of this study is to investigate whether the dimensions of the aortic root and ascending aorta, both in raw measurements and adjusted for body surface area (BSA), are larger in patients with ACS who present with CAE on coronary angiography compared to those without CAE.

Secondary endpoints include:

1. The relationship between aortic root and ascending aorta dimensions and the extent of CAE, as classified by the Markis and Markis-Harirkrishnan systems.
2. The correlation between the presence of CAE and the incidence of bicuspid aortic valve.

2.5. Statistical analysis

Continuous variables are presented as either the mean ± standard deviation or median with interquartile range (25th-75th percentile), as appropriate. Differences between unpaired continuous variables were assessed with the unpaired *t*-test if normally distributed, and with the Mann-Whitney *U* test if not normally distributed. Categorical variables were reported as frequencies and percentages and were analyzed using the $\chi 2$ or Fischer exact test. One way ANOVA analysis was performed to determine whether CAE extent classified using both the Markis and Markis-Harikrishnan classifications could predict a significantly larger aortic diameter at the levels of the annulus, SOV, STJ and ascending aorta with and without adjusting for BSA. Results of the ANOVA test are reported as an F-value to represent variance between groups and the corresponding P-value. Associations between clinical variables and CAE were assessed using univariable and multivariable binary logistic regression. The multivariable model accounted for potential confounding factors to identify variables independently associated with CAE. Results are reported as odds ratios (OR) with 95 % confidence intervals (CI) and P-values. Statistical analysis was performed with SPSS for Windows version 25.0 (IBM, Armonk, New York). All tests were two-sided, and a $P < 0.05$ was considered statistically significant.

3. Results

A total of 448 patients were included in the analysis, with 224 patients exhibiting CAE and 224 control patients without CAE adjusted to age, sex and presence of hypertension. The baseline characteristics of the study population are presented in Table 1. Notably, patients with CAE had a higher BSA compared to those without CAE (2.03 ± 0.2 m^2 vs. 1.98 ± 0.2 m^2, p = 0.010). Other baseline characteristics such as body mass index, diabetes prevalence, smoking history, cholesterol levels, hypertension, and hemoglobin levels showed no significant differences between the groups. Low-density lipoprotein levels were significantly lower in the CAE group (3.3 ± 1.1 mmol/L vs. 3.5 ± 1.0 mmol/L, p = 0.014), and C-reactive protein levels were higher in the CAE group (3.0 (3.0–6.4) mg/L vs. 3.0 (3.0–5.0) mg/L, p < 0.0001). Prior MI was more common in the CAE group (12.5 % vs. 4.5 %, p = 0.002). Estimated glomerular filtration rate was significantly lower in the CAE group (72.7 ± 17.9 mL/min/1.73 m^2 vs. 79.0 ± 20.8 mL/min/1.73 m^2, p = 0.024).

Angiographic characteristics are detailed in Table 2. Multivessel disease was present in 51.9 % of the overall cohort, with no significant difference between the CAE and non-CAE groups (p = 0.143). The distribution of the culprit vessel did not vary significantly between groups, with the left anterior descending artery being the most common culprit vessel in both groups.

Final TIMI flow grade < 3 was more frequent in the CAE group (14.5 % vs. 6.6 %, p = 0.009). Creatinine kinase levels were significantly lower in the CAE group (1016 (377–2029) U/L vs. 1399 (688–3290) U/

Table 1
Baseline patient characteristics.

	Overall (N = 448)	CAE (N = 224)	No CAE (N = 224)	P-Value
Age, years	62.2 ± 11.7	62.1 ± 11.6	62.3 ± 11.7	0.894
Females, n(%)	74(16.5)	37(16.5)	37(16.5)	1.000
BSA, m^2	2.01 ± 0.2	2.03 ± 0.2	1.98 ± 0.2	**0.010**
BMI, kg/m^2	27.1 ± 4.3	27.4 ± 4.4	26.9 ± 4.2	0.272
Diabetes, n(%)	49(10.9)	25(11.2)	24(10.7)	1.000
Hypertension, n(%)	199(44.4)	100(44.6)	99(44.2)	0.924
Family history premature CAD, n(%)	154(34.4)	71(31.7)	83(37.1)	0.139
Smoking history, n(%)	236(52.7)	117(52.2)	119(53.1)	0.702
Cholesterol, mmol/L	5.2 ± 1.1	5.2 ± 1.2	5.4 ± 1.1	0.170
LDL, mmol/L	3.4 ± 1.1	3.3 ± 1.1	3.5 ± 1.0	**0.014**
eGFR, mL/min/1,73 m2	76.8 ± 20	72.7 ± 17.9	79.0 ± 20.8	**0.024**
Creatinine, umol/L	80.6 ± 18.6	82.4 ± 20.8	78.8 ± 15.9	0.054
CRP, mg/L	3.0 (3.0–5.6)	3.0 (3.0–6.4)	3.0 (3.0–5.0)	**<0.0001**
Hemoglobin, mmol/L	9.2 ± 6.3	9.7 ± 9.2	8.9 ± 1.1	0.215
Prior TIA/stroke, n(%)	20(4.5)	14(6.3)	6(2.7)	0.067
Prior PCI, n(%)	26(5.8)	18(8.1)	8(3.6)	**0.043**
Prior MI, n(%)	38(8.5)	28(12.5)	10(4.5)	**0.002**
ACS type, n(%)				**<0.0001**
STEMI	404(90.2)	183(81.7)	221(98.7)	
NSTEMI	44(9.8)	41(18.3)	3(1.3)	

ACS = acute coronary syndrome; BMI = body mass index; BSA = body surface area; CAE = coronary artery ectasia; CRP = C-reactive protein; eGFR = estimated glomerular filtration rate; LDL = low density lipoprotein; MI = myocardial infarction; NSTEMI = non ST-elevated myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST-elevated myocardial infarction; TIA = transient ischemic attack.

Table 2
Angiographic characteristics.

	All (N = 448)	CAE (N = 224)	No CAE (N = 224)	P-Value
Multivessel disease, n (%)	232 (51.9)	108(48.4)	124(55.4)	0.143
Culprit vessel				
LM, n(%)	5(1.1)	3(1.3)	2(0.9)	0.653
LAD, n(%)	183(41.0)	85(38.1)	98(43.9)	0.211
LCx, n(%)	83(18.6)	35(15.7)	48(21.5)	0.114
RCA, n(%)	157(35.2)	82(36.8)	75(33.6)	0.488
Final TIMI flow				
0, n(%)	8(1.9)	6(3)	2(0.9)	0.131
1, n(%)	5(1.2)	4(2)	1(0.5)	0.157
2, n(%)	30(7.3)	19(9.5)	11(5.2)	0.092
3, n(%)	369(89.6)	171(85.5)	198(93.4)	**0.009**
Final TIMI flow < 3, n (%)	43(10.4)	29(14.5)	14(6.6)	**0.009**
Creatinine Kinase, U/L	1200 (494–2530)	1016 (377–2029)	1399 (688–3290)	**<0.0001**
Balloon predilatation, n(%)	360(81.6)	170(78)	190(85)	0.050
Balloon postdilatation, n (%)	138(31.4)	65(30)	73(32.7)	0.530
Stenting, n(%)	383 (85.9)	170(76.2)	213(95.5)	**<0.0001**
Stent type DES, n(%)	267(70)	104(61)	163(76)	**<0.0001**
CAE in infarct related area	–	172(80.4 %)	–	–
Thrombus load*				
0	55(12.8)	18(8.0)	37(18.0)	**0.002**
1	23(8.5)	19(8.5)	4(1.9)	**0.003**
2	24(4.7)	13(5.8)	7(3.4)	0.237
3	63(14.7)	33(14.7)	30(14.6)	0.961
4	99(23.0)	39(17.4)	60(29.1)	**0.004**
5	170(39.5)	102(45.5)	68(33)	**0.008**
Thrombectomy, n(%)	62(13.8)	36(16.1)	26(11.6)	0.171
Anti-GPI periprocedural, n (%)	353(81.5)	164(73.5)	189(90)	**<0.0001**
Dual antiplatelet therapy at discharge, n(%)	439(98.2)	216(96.4)	223(100)	**0.004**
Anticoagulant therapy at discharge, n(%)	45(10.1)	28(12.5)	17(7)	0.087

*0 = no angiographic evidence of thrombus; 1 = possible thrombus (reduced contrast density, haziness, irregular lesion contour, smooth convex meniscus); 2 = definite thrombus with largest dimension measuring ≤ ½ the vessel diameter; 3 = definite thrombus with largest dimension measuring > ½ but ≤ 2 vessel diameters; 4 = definite thrombus with the largest dimension measuring > 2 vessel diameters; 5 = total occlusion.
CAE = coronary artery ectasia; GP = glycoprotein; LAD = Left anterior descending coronary artery; LCx = left circumflex artery; LM = left main; RCA = right coronary artery; TIMI = thrombolysis in myocardial infarction; DES = drug eluting stent.

Table 3
Echocardiographic findings.

	All (N = 448)	CAE (N = 224)	No CAE (N = 224)	P-Value
LVEDd, mm	48.7 ± 6.6	48.7 ± 6.3	48.6 ± 6.9	0.884
LVESd, mm	34 ± 7.7	35.9 ± 8.1	32.3 ± 7.0	**<0.0001**
IVST, mm	10.9 ± 2.0	10.8 ± 2.0	11.0 ± 1.9	0.246
PWT, mm	10.2 ± 1.9	10.5 ± 2.2	10.1 ± 1.7	**0.027**
LVEDV, ml	128 ± 42.7	123.8 ± 4.6	131.7 ± 43.4	0.061
LVESV, ml	67.5 ± 27.2	67.2 ± 27.4	67.7 ± 27.1	0.833
LVEF (%)	48.0 ± 9.0	47.1 ± 9.9	48.9 ± 8.1	**0.037**
Aortic anulus maximum diameter, mm	21.1 ± 2.1	21.3 ± 1.9	20.9 ± 2.2	**0.029**
Indexed aortic annulus maximum diameter, cm/m^2	10.6 ± 1.1	10.5 ± 1.1	10.6 ± 1.2	0.684
SOV diameter, mm	35.7 ± 3.9	36.4 ± 3.8	35.1 ± 3.9	**<0.0001**
Indexed SOV diameter, cm/m^2	17.9 ± 2.1	18 ± 2.1	17.8 ± 2.1	0.435
STJ diameter, mm	31.2 ± 3.7	31.8 ± 3.6	30.7 ± 3.7	**0.002**
Indexed STJ diameter, cm/m^2	15.7 ± 1.9	15.7 ± 1.8	15.6 ± 1.9	0.373
Ascending aortic diameter, mm	34.4 ± 4	35.2 ± 4.0	33.6 ± 3.7	**<0.0001**
Indexed ascending aortic diameter cm/m^2	1.7 ± 0.23	1.7 ± 0.2	1.7 ± 0.2	0.111
Ascending aortic dilatation (>40 mm), n(%)	33(7.6)	20(9.2)	13(5.9)	0.200
Indexed ascending aortic dilatation (>2,1cm/m^2), n(%)	24(5.8)	14(6.6)	10(4.9)	0.457
Aortic valve regurgitation grade > 2, n(%)	11(2.5)	6(2.7)	5(2.2)	0.749
Bicuspid aortic valve, n(%)	3(0.7)	2(0.9)	1(0.4)	0.554

AR = aortic regurgitation; IVST = interventricular septum thickness; LVEF = left ventricular ejection fraction; LVEDd = left ventricular end diastolic diameter; LVEDV = left ventricular end diastolic volume; LVESd = Left ventricular end systolic diameter; LVESV = left ventricular end systolic volume; PWT = posterior wall thickness; SOV = sinus of Valsalva; STJ = Sinotubular junction;

L, $p < 0.0001$). The rate of stenting was lower in the CAE group (76.2 % vs. 95.5 %, $p < 0.0001$). The thrombus load was significantly higher in the CAE group (p-values ranging from 0.002 to 0.008 across different grades).

Echocardiographic findings are summarized in Table 3. There were no significant differences in LV end-diastolic diameter between the CAE and non-CAE groups (48.7 ± 6.3 mm vs. 48.6 ± 6.9 mm, $p = 0.884$). However, the LV end-systolic diameter was significantly larger in the CAE group (35.9 ± 8.1 mm vs. 32.3 ± 7.0 mm, $p < 0.0001$). Posterior wall thickness was also greater in the CAE group (10.5 ± 2.2 mm vs. 10.1 ± 1.7 mm, $p = 0.027$). LV ejection fraction was slightly lower in the CAE group (47.1 ± 9.9 % vs. 48.9 ± 8.1 %, $p = 0.037$).

The aortic annulus maximum diameter was significantly larger in the CAE group (21.3 ± 1.9 mm vs. 20.9 ± 2.2 mm, $p = 0.029$). Similarly, the SOV diameter (36.4 ± 3.8 mm vs. 35.1 ± 3.9 mm, $p < 0.0001$), the STJ diameter (31.8 ± 3.6 mm vs. 30.7 ± 3.7 mm, $p = 0.002$), and the ascending aorta diameter (35.2 ± 4.0 mm vs. 33.6 ± 3.7 mm, $p < 0.0001$) were also larger in the CAE group. When the aortic diameters were indexed to BSA, the differences between the CAE and non-CAE groups were not significant. Specifically, the indexed aortic annulus maximum diameter (10.5 ± 1.1 cm/m^2 vs. 10.6 ± 1.2 cm/m^2, $p = 0.684$), indexed SOV diameter (18 ± 2.1 cm/m^2 vs. 17.8 ± 2.1 cm/m^2, $p = 0.435$), indexed STJ diameter (15.7 ± 1.8 cm/m^2 vs. 15.6 ± 1.9 cm/m^2, $p = 0.373$), and indexed ascending aortic diameter (1.7 ± 0.2 cm/m^2 in both groups, $p = 0.111$) did not show significant differences. Furthermore, there was no significant difference in the prevalence of ascending aortic dilatation (defined as diameter > 40 mm) or indexed ascending aortic dilatation (defined as > 2.1 cm/m^2) between the groups ($p = 0.200$ and $p = 0.457$, respectively), and the incidence of bicuspid aortic valves, did not differ significantly between the CAE and non-CAE groups (0.9 % vs. 0.4 %, $p = 0.554$).

An analysis of variance (ANOVA) was conducted to evaluate the relationship between both indexed and non-indexed aortic diameters with the classifications of CAE extent according to Markis and Markis-Harirkrishnan. For the indexed diameters, the results showed no statistically significant differences among the levels of the Markis-Harirkrishnan classification (aortic annulus $F = 2.544$, $p = 0.057$; SOV $F = 0.640$, $p = 0.590$; STJ $F = 0.810$, $p = 0.490$; ascending aorta $F = 1.161$, $p = 0.325$; indexed diameters > 2.1 cm/m^2 $F = 0.800$, $p = 0.603$). The eta-squared values ranged from 0.029 to 0.060, suggesting small

effect sizes.

Similarly, for the Markis classification, the ANOVA results indicated no statistically significant differences for the aortic annulus ($F = 1.929$, $p = 0.126$), SOV ($F = 2.624$, $p = 0.051$), STJ ($F = 3.484$, $p = 0.017$), ascending aorta ($F = 2.324$, $p = 0.076$), and indexed diameters > 2.1 cm/m^2 ($F = 1.655$, $p = 0.178$). Eta-squared values ranged from 0.023 to 0.046, indicating small to moderate effect sizes.

For the non-indexed diameters, there were no significant differences among the levels of the Markis-Harirkrishnan classification (aortic annulus $F = 0.931$, $p = 0.492$; SOV $F = 1.222$, $p = 0.287$; STJ $F = 1.595$, $p = 0.128$; ascending aorta $F = 1.470$, $p = 0.170$; diameters > 40 mm $F = 1.143$, $p = 0.336$). Eta-squared values ranged from 0.034 to 0.057, suggesting small to moderate effect sizes. Similarly, for the Markis classification, there were no significant differences (aortic annulus $F = 0.931$, $p = 0.492$; SOV $F = 1.222$, $p = 0.287$; STJ $F = 1.595$, $p = 0.128$; ascending aorta $F = 1.470$, $p = 0.170$; diameters > 40 mm $F = 1.143$, $p = 0.336$), with eta-squared values ranging from 0.034 to 0.057.

Overall, the results indicate no significant relationships between aortic diameters at various anatomical levels and the extent of coronary artery ectasia as classified by Markis and Markis-Harirkrishnan, with effect sizes suggesting limited practical significance.

On multivariate analysis (Table 4), dyslipidemia ($p = 0.037$) and previous MI ($p = 0.020$) were independently associated with CAE.

4. Discussion

The main findings of the present study indicate that there are no statistically significant differences in indexed aortic diameters at various anatomical levels (aortic annulus, SOV, STJ and ascending aorta) between ACS patients exhibiting CAE and those without CAE. Additionally, the study found no significant correlation between the extent of CAE, classified by the Markis and Markis-Harirkrishnan systems, and aortic dimensions. These results suggest that aortic dimensions, whether raw or adjusted for BSA, do not have a strong association with the extent of CAE. Importantly, this study utilized a control group adjusted for age, sex, and the presence of hypertension to minimize confounding effects.

In contrast to previous literature, we found no association between aortic diameters and the presence of CAE. Previous studies [9–10] suggested a relationship between CAE and ascending aorta aneurysm. The discrepancy of results could be explained by several reasons. Firstly, these studies evaluated the presence of CAE on coronary angiography in patients with aneurysms who were candidates for surgery. This approach is markedly different from our study, which evaluated aortic dimensions in patients with CAE. The presence of an aortic aneurysm with indication for surgery may have predispose patients to a higher detection of CAE, resulting from the potential interaction of several pathophysiological mechanisms [24]. Secondly, our cohort was conform exclusively by patients with ACS, a population excluded from previous studies. Thirdly, our study differentiates itself by adjusting aortic measurements to BSA, which may explain the lack of association. After this adjustment, no significant differences were found, raising the question of whether previous findings might have been confounded by differences in body size rather than a true pathophysiological link. While structural factors like aortic dimensions may not correlate with CAE, multivariate analysis identified dyslipidemia and previous MI as independent predictors of CAE. The findings reinforce the role of metabolic factors in CAE pathophysiology and suggest a potential link between prior ischemic events and CAE.

Interestingly, we found that patients with CAE had a significantly higher BSA compared to those without CAE (2.03 ± 0.2 m^2 vs. 1.98 ± 0.2 m^2, $p = 0.010$). This difference in BSA could influence the raw measurements of aortic diameters, potentially confounding the relationship between aortic dimensions and CAE. By indexing aortic diameters to BSA, we aimed to control for this confounding factor. Qin et al. [4], conducted a study in which 100 patients with CAE were compared to a control group of 100 patients with atherosclerosis without CAE. Among other variables including sex, diastolic blood pressure, D-dimer, triglyceride, and LDL/HDL ratio, BMI was found an independent predictor of CAE. It should be pointed out that, while BMI is useful for general assessments, BSA is often preferred for indexing echocardiographic measures because it provides a more precise estimation of body size. Moreover, it has been demonstrated that indexing measures of cardiac and aortic size by BSA improves prognostic performance regardless of BMI, showing better clinical prognostic performance that any other analyzed body size metric (lean body mass, height, and/or weight raised to different powers) [25]. Therefore, the lack of adjustment for BSA may significantly impair the interpretation of previous studies analyzing the relationship between CAE and aortic dimensions.

The study found no significant correlation between the extent of CAE, classified by the Markis and Markis-Harirkrishnan systems, and aortic dimensions as previously suggested. Ghetti et al. [11] retrospectively analyzed 135 patients with CAE on coronary angiography, and classified them in four categories based on their ascending aorta diameters. The authors found a linear correlation between CAE extension (defined as total estimated ectatic area) and an enlarged aorta. Again, lack of indexation of the aortic diameters, may have influenced the results of this study. Additionally, the method used to define the extent of CAE is not based on the globally accepted classifications of CAE [1,17].

In the procedural aspect, our study noted that the thrombus burden was significantly higher in the CAE group. This finding is consistent with previous reports showing a greater thrombus burden in patients with CAE, which can lead to complications such as the no-reflow phenomenon and higher rates of adverse events [7]. The management of thrombus burden is crucial in CAE patients undergoing percutaneous coronary intervention, and our results underscore the need for tailored therapeutic strategies to address this issue effectively. Specifically, the CAE group showed higher final TIMI flow < 3 (14.5 % vs. 6.6 %, $p = 0.009$) and lower stenting rates (76.2 % vs. 95.5 %, $p < 0.0001$), highlighting procedural challenges.

The incidence of bicuspid aortic valve, which has been associated with aortic dilatation, did not differ significantly between the CAE and non-CAE groups (Table 3). Meindl et al. [13] found and increased prevalence of CAE (detected by invasive coronary angiography) in patients with bicuspid aortic valves ($n = 94$) compared with those with tricuspid aortic valves ($n = 83$) (17 % vs. 44 %, $P < 0.0001$) angiography analysis, respectively of the presence of aortic dilatation. The authors found as well a similar incidence of CAE in a large bicuspid aortic valve

Table 4
Univariate and multivariate binary logistic regression analysis of variables associated with CAE.

Variable	Univariable analysis			Multivariable analysis		
	Odds ratio (OR)	95 % confidence interval	P-value	Odds ratio (OR)	95 % confidence interval	P-value
BMI	1.025	0.981–1.072	0.273	1.020	0.974–1.069	0.401
Diabetes	1.047	0.578–1.895	0.880	0.919	0.480–1.758	0.798
Dyslipidemia	1.948	1.271–2.984	**0.002**	1.621	1.030–2.552	**0.037**
Smoking history	0.937	0.646–1.360	0.733	0.968	0.653–1.435	0.872
Prior MI	3.057	1.448–6.456	**0.003**	2.486	1.157–5.343	**0.020**
Prior TIA/stroke	2.422	0.914–6.421	0.075	2.723	0.948–7.819	0.063

BMI = body mass index; MI = myocardial infarction; TIA = transient ischemic attack.

registry comprising 600 patients. The different methodology of our study and the infrequent and anecdotal occurrence of BAV in our sample limits our ability to draw definitive conclusions or establish connections between our findings and those of previous studies.

Several limitations should be acknowledged. The single-center, retrospective design may introduce selection bias, and the sample size, while adequate for detecting moderate to large effects, may not be sufficient to identify smaller effect sizes. Moreover, only ACS patients where included. Future research should aim to include larger, more diverse populations and utilize longitudinal designs to track changes in aortic dimensions and their potential impact on CAE over time.

5. Conclusions

In this cohort study of patients with ACS, comparing those with CAE to a control group without CAE adjusted for age, sex, and hypertension, non-indexed aortic dimensions were found to be larger in patients with CAE. However, when adjusted for BSA, there was no significant difference between the groups. Additionally, there was no significant correlation between the extent of CAE and aortic dimensions, and the incidence of bicuspid aortic valve was similar in both groups.

CRediT authorship contribution statement

Martijn J.H. van Oort: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Federico Oliveri:** Writing – review & editing, Writing – original draft, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **Florens W.J. de Lange:** Writing – original draft, Investigation, Formal analysis, Data curation. **Madelien V. Regeer:** Writing – review & editing, Validation, Supervision. **B.O. Bingen:** Writing – review & editing, Validation, Supervision, Conceptualization. **J.Wouter Jukema:** Writing – review & editing, Resources, Project administration, Funding acquisition. **Frank van der Kley:** Writing – review & editing. **Ibtihal Al Amri:** Writing – review & editing, Validation, Supervision, Project administration, Formal analysis, Conceptualization. **Jose M. Montero-Cabezas:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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