ORIGINAL ARTICLE

Impaired oscillometric arterial stiffness parameters in patients with coronary artery ectasia

Koroner arter ektazisi olan hastalarda bozulmuş osilometrik arteriyel sertlik parametreleri

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ABSTRACT

Objective: The aim of this study was to investigate the oscillometric measurements of the elastic properties of the aorta in patients with isolated coronary artery ectasia (CAE).

Methods: This study included 137 patients (92 men and 45 women; mean age: 60.8±11.7 years) who underwent coronary angiography to investigate ischemic heart disease. The patients were divided into 3 groups; the first group consisted of 51 patients with CAE, the second group comprised 36 patients with coronary artery disease (CAD), and the third group was made up of 50 patients with normal coronary arteries. Aortic stiffness (AS) measurements, including pulse wave velocity (PWV) and augmentation index (AIx), were measured using the oscillometric method.

Results: The mean PWV was significantly higher in the CAE group compared with the CAD and control groups (9.1±2.3 *vs.* 8.2±1.3 and 8.0±1.6; p=0.008), whereas the median AIx was significantly lower in the CAE group compared with the CAD and control groups (10.0% [-3.0–63.0] *vs.* 15.5% [-2.0–57.0] and 21.5% [-1.0–45.0]; p=0.010). Multinomial logistic regression analysis demonstrated that gender, hypertension, high-density lipoprotein cholesterol level, PWV, and AIx were independently associated with CAE.

Conclusion: The oscillometric elastic properties of the aorta, including PWV and AIx, are impaired in patients with CAE.

ÖZET

Amaç: Bu çalışmada, izole koroner arter ektazisi (KAE) olan hastalarda aortanın elastik özelliklerinin osilometrik ölçümlerini araştırmayı amaçladık.

Yöntemler: Bu çalışmaya, iskemik kalp hastalığı araştırılma endikasyonu bulunan ve koroner anjiyografi yapılan toplam 137 (92 erkek, 45 kadın; ortalama yaş: 60.8±11.7 yıl) hasta dahil edildi. Hastalar üç gruba ayrıldı; birinci grup KAE'si olan 51 hasta, ikinci grup koroner arter hastalığı (KAH) olan 36 hasta ve üçüncü grup normal koroner arterli 50 hastadan oluşmaktaydı. Nabız dalga hızı (NDH) ve augmentasyon indeksi (Aİx) dahil aort sertliğinin (AS) ölçütleri, osilometrik yöntemle araştırıldı.

Bulgular: Ortalama NDH, KAE grubunda KAH ve kontrol gruplarına göre daha yüksek iken (9.1±2.3'e karşılık 8.2±1.3 ve 8.0±1.6, p=0.008) medyan Aİx, KAE grubunda KAH ve kontrol gruplarına göre daha düşüktü (10.0 [-3.0–63.0]'e karşılık 15.5 [-2.0–57.0] ve 21.5 [-1.0–45.0], p=0.010). Çoklu terimli (multinomial) lojistik regresyon analizinde cinsiyet, hipertansiyon, yüksek yoğunluklu lipoprotein kolesterol seviyesi, NDH ve Aİx'in, KAE ile bağımsız olarak ilişkili olduğu saptandı.

Sonuç: Nabız dalga hızı ve Aİx dahil olmak üzere aortun osilometrik elastik özellikleri KAE'li hastalarda bozulmuştur.

Coronary artery ectasia (CAE) is defined as coronary artery dilatation to a diameter at least 1.5 times that of the adjacent normal coronary artery.[1] It is considered isolated unless accompanied by other cardiac disorders, such as coronary or valvular heart disease. The incidence of CAE in patients undergoing coronary angiography has been reported as 1.2% to 4.9%.[2] However, isolated CAE comprises a small portion of total CAE cases, with an incidence of 0.1% to 0.79%.[3] CAE can be either localized or

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diffuse when affecting the entire coronary artery. This entity is associated with atherosclerosis in 50% of the patients. However, 10% to 20% of CAE cases have been demonstrated to be associated with inflammatory and/or connective tissue diseases, including scleroderma, Ehlers-Danlos syndrome, anti-neutrophil cytoplasmic antibody-associated vasculitis, syphilitic aortitis, and Kawasaki disease. In addition, several studies have demonstrated a relationship between CAE and non-coronary aneurysms, including aortic, popliteal, and pulmonary aneurysms.[4,5] It is noteworthy that 20% to 30% of CAE cases are congenital.[6]

Abbreviations:

ACE	*Angiotensin-converting enzyme*
AIx	*Augmentation index*
AP	*Augmentation pressure*
ARB	*Angiotensin receptor blocker*
AS	*Aortic stiffness*
BMI	*Body mass index*
BP	*Blood pressure*
CAD	*Coronary artery disease*
CAE	*Coronary artery ectasia*
CI	*Confidence interval*
DM	*Diabetes mellitus*
HDL	*High-density lipoprotein*
HT	*Hypertension*
HPL	*Hyperlipidemia*
LAD	*Left anterior descending*
LV	*Left ventricle*
NLR	*Neutrophil-to-lymphocyte ratio*
OR	*Odds ratio*
PWV	*Pulse wave velocity*
RCA	*Right coronary artery*
WBC	*White blood cell*

Arterial stiffness (AS), defined as arterial rigidity caused by a loss of elastic tissue of the arterial wall, is associated with a decrease in arterial widening capacity. It has been established that as the stiffness of large arteries, including the aorta, increases, cardiovascular morbidity and mortality increase.[7] Evaluation of AS, which is associated with cardiovascular risk factors[8] and atherosclerotic coronary artery disease (CAD),[9] is a simple method to identify the degree of rigidity. The association between AS parameters, including pulse wave velocity (PWV) and augmentation index (Ax), and CAE has not yet been investigated.

The aim of this study was to evaluate oscillometric AS parameters in patients with isolated CAE.

METHODS

Study design and population

This study included a total of 137 patients (92 male; mean age: 60.8±11.7 years) who underwent coronary angiography indicated for the investigation of ischemic heart disease based on clinical conditions, including typical angina and/or positive or equivocal results of non-invasive myocardial ischemia screening tests. The patients were divided into 3 groups: (1) The CAE group consisted of 51 patients with isolated and localized CAE who had ectatic coronary segments without any stenotic lesion observed on coronary angiography, (2) the CAD group consisted of 36 patients with obstructive coronary artery lesions, and (3) the control group consisted of 50 patients with normal coronary arteries. Data concerning cardiovascular risk factors, including age, gender, hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HPL), smoking status, and family history, as well as biochemical measurements and AS parameters were noted. Body mass index (BMI) measurements were calculated based on the following formula: BMI=weight (kg)/height^2 (m^2).

Patients with acute/chronic infective and/or inflammatory disease; severe congestive heart failure (left ventricular [LV] ejection fraction <40%); moderate to severe valvular heart disease; history of coronary artery bypass grafting; cardiac arrhythmia including, atrial fibrillation, bradycardia, and tachycardia; malignancy; chronic kidney disease (glomerular filtration rate <90 mL/minute/1.73 m^2); or a history of anti-inflammatory agent and/or antibiotic use were excluded. The institutional ethics committee approved the study protocol and each participant provided written informed consent.

Blood samples and laboratory analysis

Venous blood samples were obtained from all of the patients on admission. Complete blood counts were measured using a Sysmex K-1000 auto-analyzer (Sysmex Corp., Kobe, Japan). Routine blood chemistry and lipid panels were measured using a standard auto-analyzer. The neutrophil-to-lymphocyte ratio (NLR) was calculated as the ratio of the neutrophil count to the lymphocyte count.

Coronary angiography and assessment of coronary arteries

Coronary angiography procedures were performed using commercially available Siemens (Axiom Sensis XP; Erlangen, Germany) and Toshiba (Infinix CSI; Tokyo, Japan) devices by an experienced interventional cardiologist in the cardiac catheterization laboratory. All patients underwent an elective procedure following the appropriate patient preparation. The coronary arteries were evaluated regarding appearance, luminal wall irregularities, and epicardial local or diffuse caliber reduction and stenosis by at

least 2 experienced, blinded interventional cardiologists. Isolated CAE was defined as a localized luminal dilatation of any epicardial coronary artery segment exceeding 1.5-fold diameter of the normal adjacent coronary segment without stenotic lesion. CAD was defined as >50% stenosis in the left main coronary artery and/or >70% stenosis in any other coronary artery.

Measurement of arterial stiffness

The ARC Solver Method

The ARC Solver method, which is commercially available in the oscillometric Mobil-O-Graph NG 24-hour PWA monitor (IEM GmbH, Stolberg, Germany), is considered a novel method for assessing aortic systolic blood pressure (BP), aortic BP curves, and AIx based on oscillometric BP measurements. Measurement of AS using this method has been previously reported in several studies.[10,11] It utilizes pulse waves obtained from the brachial artery. After the conventional oscillometric BP assessment, peripheral pressure waves are recorded, using an appropriate brachial cuff and a high-fidelity pressure sensor (MPX5050; Freescale Semiconductor Inc., Tempe, AZ, USA), at diastolic BP level for 10 seconds. The sensor is connected to a 12-bit A/D converter by means of an active analogue band bass filter (0.425 Hz). Following digitalization, signal processing is performed using a 3-step algorithm. In the first step, single pressure waves are verified for their plausibility by testing the position of the minima and the corresponding wavelengths. The minima are detected using an iterative procedure evaluating higher order time derivations of the pressure signal. The second stage involves a comparison of all single pressure waves to recognize artifacts. Then, aortic pulse waves are generated via a general transfer function. Finally, the coherence of the measured parameters is verified and displayed within the Mobil-O-Graph software package.

Measurement of the aortic pulse wave velocity and augmentation index

Measurements of AS parameters were performed in accordance with international recommendations.[12] A blinded observer performed all of the measurements. The patients were asked to fast for 12 hours and discontinue the use of vasoactive medications, alcohol, and caffeine 24 hours prior to measurement. At least 2 consecutive measurements were performed. If the second measurement varied significantly from the first, a third measurement was performed. The measurements were performed after resting for at least 15 minutes to minimize "noise" due to incomplete basal resting condition, in the supine position, in a quiet, temperature-controlled room, using the Mobil-O-Graph ARC Solver algorithm with an appropriate BP cuff attached to the patient's right arm. With the cuff inflated at the diastolic BP level, a 10-second pulsed wave analysis record was obtained, followed by the aortic BP curve, aortic systolic BP, and aortic pulse pressure (aortic systolic BP-aortic diastolic BP) using the same device. A characteristic point of the aortic BP curve, called the inflection point, indicates the arrival of the reflected wave in the ascending aorta. BP at this point is called inflection pressure. The difference between aortic systolic BP and inflection pressure is called augmentation pressure (AP). Then, AIx is calculated as AP/aPPx100. The Mobil-O-Graph software package allowed us to calculate aortic PWV and AIx automatically.

Statistical analysis

Data analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Analysis of normality was performed using the Kolmogorov-Smirnov test. Analysis of homogeneity of variances across samples was performed using Levene's test. Continuous variables were expressed as mean±SD and median (minimum-maximum). Categorical variables were expressed as a number (percentage). Comparison of continu¬ous variables between groups was performed using one-way analysis of variance with the Tukey post hoc test or the Kruskal-Wallis test with Dunn's post hoc test, depending on the fulfillment of each test's assumptions. Comparison of categorical variables between groups was performed using a chi-square test. All possible factors ($p<0.1$) in the univariate analysis (gender, HT, HPL, smoking status, white blood cell [WBC] count, high-density lipoprotein [HDL] cholesterol, LV ejection fraction, PWV, and AIx) were selected for the multivariate model and a multinomial logistic regression analysis was used to determine the independent predictors of CAE and CAD. The odds ratio (OR) and 95% confidence interval (CI) of each variable were calculated. A 2-tailed p-value of less than 0.05 was considered significant.

RESULTS

There was no significant difference between groups with regard to the clinical and demographic characteristics of the patients, except in terms of gender, prevalence of HT, prevalence of HPL, smoking status, HDL cholesterol level, LV ejection fraction, PWV, and AIx (Table 1). Male gender was significantly dominant in the CAE group compared with the CAD and control groups (86.3% *vs*. 66.7% and 48.0%; p<0.001). Hypertension, HPL, and smoking rates were higher in the CAE group compared with the CAD and control groups (84.3% *vs*. 44.4% and 48.0%, p<0.001 for HT; 72.5% *vs*. 41.7% and 34.0%, p<0.001 for HPL; 49.0%

Table 1. Clinical and demographic characteristics of the patients

Variable	CAE group (n=51)	CAD group (n=36)	Control group (n=50)	*p*[a]
Age (years)	61.9±14.6	60.7±8.4	59.8±10.5	0.670
Gender, (male) n (%)	44 (86.3)[b]	24 (66.7)	24 (48.0)	<0.001
Body mass index (kg/m^2)	29.4±5.3	29.6±5.6	29.0±4.9	0.849
Systolic blood pressure (mm Hg)	129±17.0	130±17.2	128±16.9	0.724
Diastolic blood pressure (mm Hg)	77±13.0	79±10.0	79±12.0	0.117
Hypertension, n (%)	43 (84.3)[c]	16 (44.4)	24 (48.0)	<0.001
Diabetes mellitus, n (%)	13 (25.5)	14 (38.9)	13 (26.0)	0.329
Hyperlipidemia, n (%)	37 (72.5)[d]	15 (41.7)	17 (34.0)	<0.001
Smoking, n (%)	25 (49.0)[e]	13 (36.1)	10 (20.0)	0.008
Family history, n (%)	26 (51.0)	15 (41.7)	19 (38.0)	0.413
Hemoglobin (g/dL)	13.5±1.8	13.6±1.6	13.5±1.3	0.968
White blood cell, x10^3/uL	8.4 (5.2–18.3)	8.1 (5.9–16.5)	8.0 (4.7–10.0)	0.073
Neutrophil (x10^3/uL)	5.2±1.5	5.2±1.7	4.8±1.3	0.290
Lymphocyte (x10^3/uL)	2.1 (1.1–4.3)	2.3 (1.5–3.7)	2.1 (1.1–4.3)	0.220
Neutrophil-to-lymphocyte ratio	2.4 (1.1–6.2)	2.2 (1.3–3.8)	2.3 (1.1–5.0)	0.748
Platelet count (x10^3/uL)	215 (156–373)	236 (161–366)	246 (171–389)	0.171
Creatinine (mg/dL)	0.85 (0.50–1.20)	0.90 (0.50–1.20)	0.80 (0.50–1.20)	0.121
Triglyceride (mg/dL)	164 (64–646)	174 (81–514)	161 (65–329)	0.356
Total cholesterol (mg/dL)	160 (103–299)	184 (64–320)	185 (129–285)	0.234
High-density lipoprotein cholesterol (mg/dL)	32 (18–49)[f]	34 (20–73)	42 (23–68)	<0.001
Low-density lipoprotein cholesterol (mg/dL)	129.0±44.3	114.6±40.5	115.3±26.6	0.123
Left ventricle ejection fraction (%)	58 (44-66)[g]	60 (47-68)	61 (50-69)	0.002
Pulse wave velocity (m/s)	9.1±2.3 h	8.2±1.3	8.0±1.6	0.008
Augmentation index (%)	10.0 (-3.0–63.0)[i]	15.5 (-2.0–57.0)	21.5 (-1.0–45.0)	0.010
ACEI or ARB use, n (%)	40 (78.4)	27 (75.0)	42 (84.0)	0.575
Beta-blocker use, n (%)	38 (74.5)	26 (72.2)	35 (70.0)	0.880
Calcium channel blocker use, n (%)	7 (13.7)	1 (2.8)	7 (14.0)	0.188
Statin use, n (%)	40 (78.4)	29 (80.6)	38 (76.0)	0.878

Data are presented as number (percentage), mean value±SD or median (minimum-maximum).

[a]P value was calculated using one-way analysis of variance (ANOVA) or the Kruskal–Wallis test for continuous variables and a chi-square test for categorical variables. The ANOVA test was performed for age, BMI, SBP, DBP, hemoglobin, neutrophil count, LDL cholesterol and PWV.

[b]p=0.037 vs. CAD group; p<0.001 vs. Control group. [c]p<0.001 vs. CAD group; p<0.001 vs. Control group. [d]p=0.007 vs. CAD group; p<0.001 vs. Control group. [e]p=0.276 vs. CAD group; p=0.003 vs. Control group. [f]p=0.038 vs. CAD group; p<0.001 vs. Control group. [g]p=0.020 vs. CAD group; p=0.001 vs. Control group. [h]p=0.043 vs. CAD group; p=0.006 vs. Control group. [i]p=0.027 vs. CAD group; p=0.003 vs. Control group.

CAE: Coronary artery ectasia; CAD: Coronary artery disease; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker.

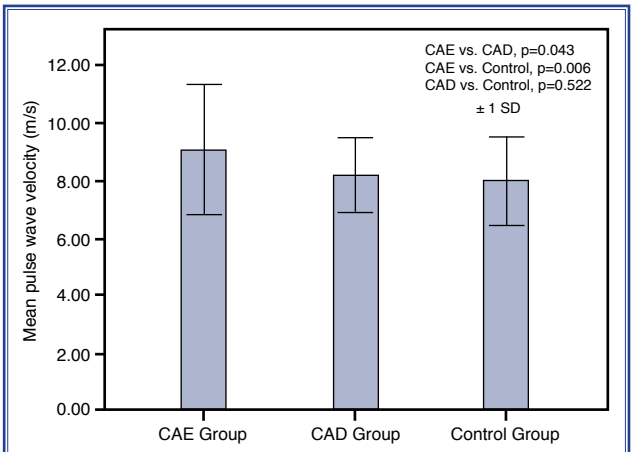

Figure 1. Comparison of pulse wave velocity levels of the patients. Mean pulse wave velocity was significantly higher in the coronary artery ectasia (CAE) group compared with the coronary artery disease (CAD) and control groups.

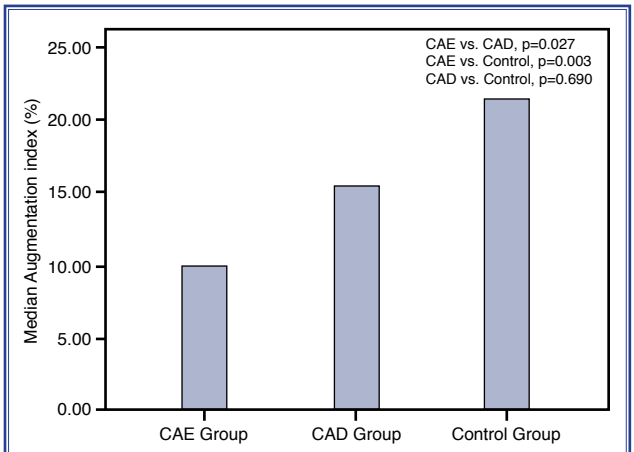

Figure 2. Comparison of augmentation index levels of the patients. Median augmentation index was significantly lower in the coronary artery ectasia (CAE) group than in the coronary artery disease (CAD) and control groups.

vs. 36.1% and 20.0%, p=0.008 for smoking). The median HDL cholesterol level was significantly lower in the CAE group compared with CAD and control groups (32 mg/dL [18–49] *vs*. 34 mg/dL [20–73] and 42 mg/dL [23–68]; p<0.001). The median LV ejection fraction was significantly lower in the CAE group compared with the CAD and control groups (58% [44–66] *vs*. 60% [47–68] and 61% [50–59]; p=0.002).

The mean PWV was significantly higher in the CAE group compared with the CAD and control groups (9.1±2.3 *vs*. 8.2±1.3 m/s and 8.0±1.6 m/s; p=0.008) (Fig. 1). However, the median AIx was significantly lower in the CAE group compared with the CAD and control groups (10.0% [-3.0–63.0] *vs*. 15.5% [-2.0–57.0] and 21.5% [-1.0–45.0]; p=0.010) (Fig. 2).

A multinomial logistic regression analysis of all of the significant parameters (p<0.1) in the univariate analysis, including gender, HT, HPL, smoking status, WBC count, HDL cholesterol, LV ejection

Table 2. Results of multinomial logistic regression analysis

Predictor variable	Coronary artery ectasia (n=51)		Coronary artery disease (n=36)	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Gender				
Male vs female	5.966 (1.131–31.471)	0.035	1.971 (0.516–7.533)	0.321
Hypertension				
HT (+) vs HT (-)	7.917 (1.561–40.144)	0.012	1.335 (0.347–5.139)	0.675
Hyperlipidemia				
HPL (+) vs HPL (-)	2.320 (0.518–10.395)	0.271	2.082 (0.562–7.711)	0.272
Smoking status				
Smoker vs. non-smoker	4.341 (0.996–18.926)	0.051	3.828 (1.012–14.477)	0.048
White blood cell	0.996 (0.652–1.519)	0.984	1.423 (0.992–2.040)	0.055
High-density lipoprotein cholesterol	0.867 (0.785–0.957)	0.005	0.976 (0.920–1.034)	0.408
Left ventricle ejection fraction	0.883 (0.756–1.032)	0.118	0.941 (0.810–1.094)	0.428
Pulse wave velocity	2.058 (1.260–3.362)	0.004	1.305 (0.866–1.968)	0.204
Augmentation index	0.940 (0.884–0.998)	0.044	1.018 (0.972–1.066)	0.444

Reference category: normal coronary arteries. OR: Odds ratio; CI: Confidence interval; HT: Hypertension; HPL: Hyperlipidemia.

Table 3. Distribution of ectatic vessels in coronary artery ectasia patients

Retained coronary vessel (s)	n[a]	%
Left main coronary artery	1	2.0
LAD	12	23.5
Left circumflex artery	10	19.6
RCA	15	29.4
LAD + left circumflex artery	3	5.9
LAD + RCA	5	9.8
Left circumflex artery + RCA	4	7.8
LAD + left circumflex artery + RCA	1	2.0

[a]Total number of patients with coronary artery ectasia is 51.
LAD: Left anterior descending artery; RCA: Right coronary artery.

fraction, PWV, and AIx, was used to determine the independent predictors of CAE and CAD (Table 2). When compared with female gender, male gender was significantly associated with an OR greater than 1 in patients with CAE versus normal coronary arteries (OR:5.966; p=0.035). In addition, compared with non-hypertensive patients, CAE patients with HT were significantly associated with an OR greater than 1 versus those with normal coronary arteries (OR:7.917; p=0.012). HDL cholesterol level was also significantly associated with an OR less than 1 in patients with CAE versus those with normal coronary arteries (OR:0.867; p=0.005). Although PWV was significantly associated with an OR greater than 1 in patients with CAE compared with those with normal coronary arteries (OR:2.058; p=0.004), AIx was significantly associated with an OR less than 1 in the same population (OR:0.940; p=0.044).

Regarding the distribution of ectatic vessels in patients with CAE, the right coronary artery (RCA) was the most frequently affected coronary artery, followed by the left anterior descending (LAD) artery (Table 3).

DISCUSSION

The major results of our study include the finding that oscillometric AS parameters, including PWV and AIx, are impaired in patients with CAE. To the best of our knowledge, this is the first report demonstrating an association between oscillometric AS parameters, including PWV and AIx, and CAE.

Evaluation of AS, which is a measure of distensibility representing elasticity of the aorta, is a simple method to assess arterial elasticity. Impaired AS, defined as deteriorated arterial rigidity caused by a loss of the elastic tissue of the arterial wall, is associated with cardiovascular risk factors, including HT, DM, and smoking,[13–16] and consequently contributes to cardiovascular morbidity and mortality.[7] The deterioration in aortic elasticity properties plays a role in the development of atherosclerosis.[17] A stiff aorta increases the LV load and myocardial oxygen demand and results in deleterious effects on LV function, coronary perfusion, and arterial wall integrity. As yet, the pathophysiology of CAE has not been clearly identified, although multiple factors, including inflammation, endothelial dysfunction, vasculitis, and atherothrombosis have been involved. CAE is associated with connective tissue disorders, including scleroderma, Ehlers-Danlos syndrome, syphilitic aortitis and Kawasaki disease. Previous studies have demonstrated that histopathological findings of ectatic lesions are similar to those of atherosclerotic lesions, and that ectatic segments are associated with extensive atherosclerotic changes, as well as thinning of the vascular media.[18,19] In our study, an increased AS in patients with CAE was demonstrated. This finding indicates that CAE is a focal coronary manifestation of a generalized vascular disorder. Although the underlying mechanisms of aortic elasticity impairment in patients with CAE have not been definitively clarified, atherosclerosis, which involves endothelial dysfunction and inflammation, may play a key role in the pathophysiology of this disease. Decreased nitric oxide production due to inflammation negatively affects AS. Thus, endothelial dysfunction may affect functions of the vessel wall, leading to increased AS. Moreover, vasa vasorum originating in the epicardial arteries, which supplies the ascending aorta and contributes to the remodeling process, involving blood flow, wall stretch, and shear stress, as well as cytokines, vasoactive substances,[20–22] and various matrix-metalloproteinases,[23] which arrange the structure of the extracellular matrix, may play a crucial role in this entity. In this study, unlike previous studies in which transthoracic echocardiography was used to determine the distensibility of large arteries by measuring aortic systolic and diastolic diameters,[24,25] we utilized the Mobil-O-Graph arteriography system for the oscillometric measurements of AS.

Earlier studies regarding gender difference in CAE have reported contradictory results.[26–28] Hartnell et

al.[26] found that there was a significant gender difference among patients with CAE and reported that 0.5% of female and 2.2% of male patients with CAD had concomitant CAE. Morrad et al.[27] analyzed 6100 angiograms and found that among patients with ectasia, 6.9% were men and 4.5% were women. Similarly, Malviya et al.[28] recently reported a greater incidence of CAE in men than in women. Pinar et al.[29] demonstrated that CAE was associated with cardiovascular risk factors, with the exception of DM. Swaye et al.[30] reported a greater prevalence of HT in CAE patients and Sudhir et al.[31] found that there was an increased prevalence of ectasia in familial hypercholesterolemia, although ectasia was not related to age, HT, smoking, or ethnicity. On the other hand, Demopoulos et al.[32] found no specific predisposing factors. In the present study, we also found that male gender was significantly dominant in patients with CAE. In addition, HT, HPL, and smoking rates were significantly higher in CAE patients.

HDL cholesterol counteracts macrophage migration during inflammation.[33] Murphy et al.[34] demonstrated that HDL cholesterol and its protein apolipoprotein A-1 exhibited anti-inflammatory effects on human monocytes by inhibiting activation of CD11b. Moreover, HDL cholesterol has been shown to defend endothelial cells against the unfavorable effects of low-density lipoprotein cholesterol and to prohibit oxidation of these molecules.[35] Therefore, monocytes exert a pro-inflammatory effect, but HDL cholesterol functions as a reversal factor during this process. An association between the monocyte to HDL cholesterol ratio and CAE has been reported recently.[36] In the present study, HDL cholesterol levels were significantly lower in patients with CAE. However, the role of HDL cholesterol in the pathogenesis of CAE is still not well known.

Recent data suggest that CAE is associated with LV systolic and diastolic dysfunctions. Amirzadegan et al.[37] demonstrated that the LV ejection fraction was significantly lower in patients with CAE than in patients with CAD and normal coronary arteries. Similar findings were observed in our study.

Various methods have been employed to assess AS. PWV and AIx have been used as reliable indicators of AS.[38] Aortic PWV is useful to predict future CAD or stroke.[39] In the Framingham heart study, subjects with a higher aortic PWV had a 48% increase in the risk of cardiovascular disease, including myocardial infarction, unstable angina, heart failure, and stroke.[40] In addition to PWV, AIx is another useful marker for increased AS. The AIx was greater in patients with CAD. However, AIx was not a predictor of future cardiovascular events in the Framingham heart study.[40] Recent studies[41,42] have demonstrated that AS parameters measured by echocardiography, including systolic and diastolic aortic diameter, strain, beta index, distensibility, and end-systolic wall stress, were impaired in patients with CAE and that the impairment in the CAE group was more severe than that observed in a CAD group. In our study, oscillometric AS parameters were impaired in patients with CAE and those with CAD. The impairment in the CAE group was more severe than that observed in the CAD group. This may indicate that destruction of the arterial media layer is greater in the setting of CAE. These findings reveal the fact that CAE is a focal coronary manifestation of a generalized vascular disorder and that impairment of these parameters may play an essential role in the pathophysiology of CAE. However, more data regarding this issue are needed. Interestingly, there was no significant difference between the CAD and control groups regarding AS parameters, including PWV and AIx. We suppose that this finding is related to antihypertensive agents and their effects on AS. In our study, beta-blocker and angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) use was significantly different between the CAD and control groups. These antihypertensive agents have been well studied regarding their effect on peripheral and central arterial BP. Recent data suggest that some beta-blockers,[43,44] ACE inhibitors,[45,46] and ARBs[47] affect AS by altering pulse wave reflection and increasing AIx.

Several studies have demonstrated that the RCA was the most commonly involved vessel in the setting of CAE,[48–50] whereas others have reported that the LAD artery was the vessel most often affected.[27,28] In our study, the RCA was the most commonly involved vessel, and 2-vessel involvement of the RCA and LAD artery and/or left circumflex artery was common in patients with isolated CAE.

Our study has limitations that warrant consideration. First, it was a single-center study and a limited number of patients were included. A study involving more patients could have more significant results and

data. Second, we did not analyze the echocardiographic features of AS, which have traditionally been used in previous studies. Third, anatomical imaging modalities, including intravascular ultrasound or optical coherence tomography to assess the ectatic vessels were not used.

Conclusion

Oscillometric elastic properties of the aorta, including PWV and AIx, are impaired in patients with CAE.

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