

Cardiovascular Topics

A new inflammatory marker: elevated eosinophil-to-lymphocyte ratio associated with presence and severity of isolated coronary artery ectasia

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Abstract

Objectives: The pathophysiology of isolated coronary artery ectasia (CAE) involves atherosclerosis and inflammation. Eosinophils and lymphocytes have been found to play a significant role in inflammation, atherosclerosis and endothelial dysfunction. Many studies have explored the relationship between isolated CAE and systemic inflammation. However, there are no data regarding the relationship between eosinophil-to-lymphocyte ratio (ELR) and isolated CAE. Therefore, this study analysed the relationship between ELR and isolated CAE.

Methods: All patients who underwent coronary angiography between January 2009 and June 2018 were investigated retrospectively. Of 16 240 patients, 232 patients with isolated CAE (141 males) and 247 age- and gender-matched control subjects (130 males) with normal coronary angiography (NCA) were enrolled in this study. Baseline demographic and laboratory data were obtained from the hospital database. The severity of isolated CAE was determined according to the Markis classification, vessel count and diffuseness of ectasia.

Results: Patients with angiographic isolated CAE had significantly elevated white blood cell (WBC) and eosinophil counts and ELR values compared to patients with NCA [8.11 ± 1.75 vs $7.49 \pm 1.80 \times 10^9$ cells/l, $p < 0.0001$; 0.22 (0.13 – 0.32) vs 0.19 (0.12 – 0.28) $\times 10^9$ cells/l, $p = 0.02$; 0.11 (0.06 – 0.17) vs 0.08 (0.05 – 0.12), $p < 0.0001$. The ELR value for Markis I was significantly higher than for Markis IV ($p = 0.04$), and three-vessel isolated CAE was significantly higher than one-vessel isolated CAE ($p = 0.04$). Additionally, the ELR value for diffuse ectasia (Markis class I, II and III) was significantly higher compared to focal (Markis class IV) ectasia ($p = 0.02$). In receiver operating characteristics (ROC) analyses, it was determined that an ELR value > 0.099 , measured in isolated CAE patients at application, had a predictive specificity of 60.3% and a sensitivity of 56.5% (area under the curve: 0.604, 95% confidence interval: 0.553–0.655, $p < 0.0001$).

Conclusion: Patients with isolated CAE had higher blood eosinophil counts and ELR. Furthermore, the ELR was significantly correlated with severity of isolated CAE. These findings demonstrate that ELR may have a significant role in the aetiopathogenesis of isolated CAE.

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Coronary artery ectasia (CAE) is a congenital or acquired coronary anomaly. CAE is described as the local or wide extension of a partial or entire epicardial coronary artery that is 1.5 times larger than the diameter of the adjacent normal coronary artery.¹⁻⁵ CAE aetiology has been attributed to atherosclerosis (50% of cases), congenital malformations

(20–30% of cases) and inflammatory or connective tissue disease (10–20% of cases).⁶ CAE is considered a unique form of atherosclerotic cardiovascular disease. Various studies have indicated that CAE is characterised by a denser vascular inflammation than occlusive coronary artery disease.^{7,8}

Some publications have reported that CAE causes coronary slow flow in the coronary arteries, resulting in thrombosis. CAE has also been suggested to cause clinical symptoms of ischaemic heart disease and myocardial infarction without occlusive coronary artery disease.⁹ The ischaemic mechanism in patients with CAE has not been fully clarified, as the basic cause of ischaemia and angina is considered to be microvascular perfusion impairment. The slow or turbulent flow during vasodilation is believed to cause thrombosis in the ectatic segment or embolus formation in the distal coronary artery, resulting in ischaemia.³ Güleç *et al.* indicated that epicardial and microvascular perfusion is destroyed in ectasia patients. The same study noted that the thrombolysis in myocardial infarction score could be used to predict microvascular perfusion impairment when ectatic and non-ectatic arteries were compared.¹⁰

Eosinophil and lymphocyte cells are associated with an immune response and inflammation. A low number of lymphocyte cells is considered one of the main reasons for progression of cardiovascular disease.^{11,12} Eosinophil elevation and low lymphocyte levels reflect systemic inflammation and physiological stress.^{13–15} Therefore the eosinophil-to-lymphocyte ratio (ELR) is an indicator of systemic inflammation.^{16,17}

Eosinophils have a significant status in endothelial dysfunction, inflammation, vasoconstriction and thrombosis.^{18,19} Eosinophils stimulate platelet activation and aggregation and contribute to thrombus formation by inhibiting thrombomodulin.²⁰ Some publications have revealed that vascular anomalies, such as aneurysms, may be associated with hypereosinophilic syndrome.^{21,22}

Can eosinophils (with their strong vasoactive and procoagulant effects) and the ELR (which is a good indicator of systemic inflammation) be associated with isolated CAE and its microvascular perfusion impairment? Although there is a small study examining the relationship between blood eosinophil concentration and CAE, no large studies that could indicate a correlation between blood eosinophil level and ELR, and CAE severity were found in the literature.¹³ This study aimed to determine whether there was an association between plasma eosinophil level, ELR and the existence and severity of CAE.

Methods

Angiographic records of 16 240 Turkish patients who had coronary angiography between January 2009 and June 2018 in the Elazığ Education and Research Hospital were retrospectively investigated for the presence of isolated CAE. The study included 232 subjects with isolated CAE and 247 age- and gender-matched subjects who had normal coronary anatomy (NCA). The routine clinical and laboratory tests (complete blood count, total biochemistry values and demographic data) of the subjects were obtained from their files (Fig. 1).

The study was conducted according to the Helsinki principles, and ethical approval was obtained from the TC Firat University ethics committee. The ethics committee did not require informed written consent forms as the data are anonymous.

Coronary angiographies were performed with Siemens Axiom Artis FC diagnostic equipment using the Judkins technique (Siemens Healthcare GmbH, Forchheim, Germany).²³ Nitroglycerin was not used during the coronary angiographies.

Coronary angiography records were gained from the left and right anterior oblique cranial, anterior–posterior (AP) cranial, right anterior oblique, caudal and horizontal positions. Isohexol 350 mg/ml (Amersham Health Co, Cork, Ireland) was used for opacity when performing the coronary angiogram; 6 ml was administered into the coronary arteries at each position. The angiography was recorded digitally with a frame rate of 25 frames/ms. The coronary artery diameters were determined by computerised quantitative angiography. These evaluations were gained by analysing the digital inputs obtained from the coronary angiographies.

Scientific quantification coronary analysis software (Siemens Healthcare GmbH, Forchheim, Germany) was used for these procedures. The computations were obtained at the proximal, mid and distal segments of the coronary arteries to define the artery segment as ectatic. The largest diameter of the segments was taken into account.

CAE was defined as 1.5 times or more enlargement of the coronary artery compared to the adjacent coronary artery. Isolated CAE was defined as regional or widespread expansion without significant coronary artery stenosis. Angiographic stenosis of more than 50% of the coronary artery was considered as significant occlusion. Patients without significant coronary artery stenosis who had ectatic segments were included in the isolated CAE group. The characteristics of CAE were categorised as diffuse or discrete ectasia to classify the severity of CAE. Fusiform dilatations of the coronary arteries were defined as diffuse ectasia, and localised/focal vesicular or spheroidal dilatation of the coronary arteries was defined as discrete ectasia⁶ (Figs 2–5).

Classification by Markis *et al.* was used to determine the distribution of CAE. This classification depends on the diffuseness of ectasia. Accordingly, patients who have isolated CAE were classified into four groups. Diffuse ectasia in two or three vessels was defined as type I, diffuse ectasia in one vessel and focal ectasia in another vessel was defined as type II, diffuse ectasia in only one vessel was defined as type III and focal ectasia was defined as type IV.⁴

The coronary angiographies were evaluated by two angiography experts who specialise in coronary angiography and had no knowledge about the history of the patients.

Study exclusion criteria: subjects with acute coronary syndrome at study entrance, significant coronary artery stenosis (angiographic stenosis > 50%) or isolated coronary slow flow, anaemia (Htc < 30%), cardiac failure, thyroid dysfunction, malignancy, chronic renal deficiency [glomerular filtration rate (GFR) < 60 ml/min/1.73 m²], chronic liver failure, chronic obstructive pulmonary disease and/or bronchial asthma, or were found to have used immunosuppressive therapy or steroids, or subjects who had a body mass index of > 30 kg/m² were excluded. Subjects who had a recent past of an acute infection and/or high body temperature > 37.2°C or an inflammatory or allergic disease were also excluded from the analysis.

Subjects who had taken antihypertensive medication and had systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg were defined as hypertensive. Diabetes



Fig. 1. Flow-chart diagram of subject inclusion.

mellitus was defined as having a fasting blood glucose level > 126 mg/dl (6.99 mmol/l) or current use of a diet or drug to lower blood glucose level. Hyperlipidaemia was defined as having

total serum cholesterol > 200 mg/dl (5.18 mmol/l), low-density lipoprotein cholesterol > 130 mg/dl (3.37 mmol/l), triglycerides > 150 mg/dl (1.69 mmol/l) or the use of a lipid-lowering drug.

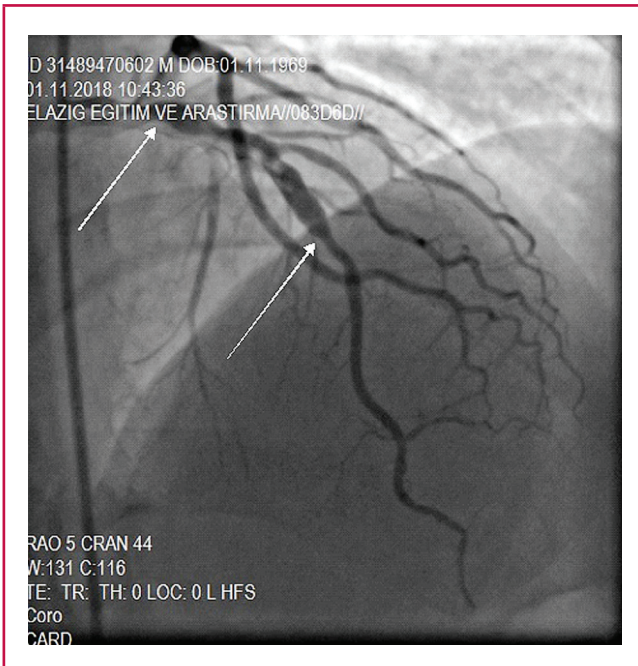


Fig. 2. Demonstration of a fusiform ectasia in the left anterior descending artery in the region between the white arrows.

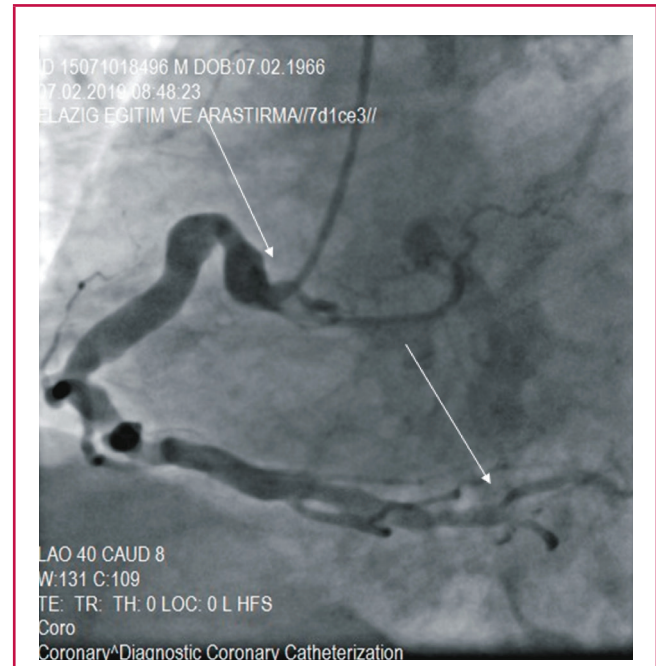


Fig. 4. Demonstration of a fusiform ectasia in the right coronary artery in the region between the white arrows.

Statistical analysis

The results were statistically evaluated with SPSS 16.0 (SPSS Inc, Chicago, IL, USA) analysis program for Windows. The distribution of the results was determined with the Kolmogorov–Smirnov test. Continuous variables are shown as means with standard deviations or medians in the 25th–75th percentiles. Categorical variables are represented as numbers with

percentages. Continuous data were analysed with the Student's *t*-test for normally distributed variables and the Mann–Whitney *U*-test was used for non-normally distributed variables. Aside from white blood cells (WBC) and calcium, all continuous variables were not distributed normally, and the Mann–Whitney *U*-test was used to compare these variables. Categorical data were analysed using the chi-squared test. The Bonferroni test was used to validate one-way ANOVA analysis for comparison

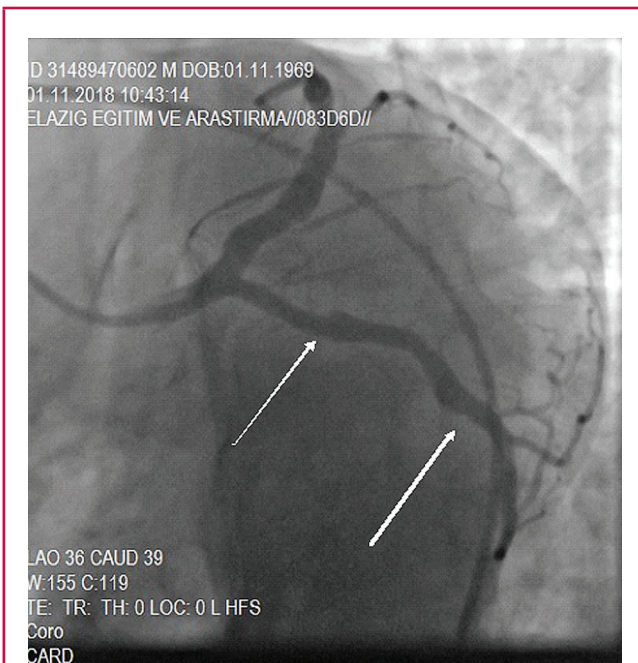


Fig. 3. Demonstration of a fusiform ectasia in the circumflex artery in the region between the white arrows.



Fig. 5. Demonstration of a saccular ectasia in the left anterior descending artery, shown with a white arrow.

Table 1. Inter-group comparison of demographic and laboratory data

Parameters	Isolated CAE (232)	NCA (247)	p-value
Gender, n (male/ female)	141/91	130/117	0.07
Hypertension, n (%)	72/232 (31.0)	64/247 (25.9)	0.21
Hyperlipidaemia, n (%)	82/232 (35.3)	71/247 (28.7)	0.12
Diabetes mellitus, n (%)	50/232 (21.6)	49/247 (19.8)	0.64
Smoking, n (%)	79/232 (34.1)	76/247 (30.8)	0.44
Age (year)	56.0 (53.0–60.0)	55.0 (52.0–59.0)	0.15
Platelets ($\times 10^9$ cells/l)	257.0 (223.0–296.75)	250.0 (209.0–292.0)	0.10
Glucose (mg/dl)	100.0 (89.25–110.30)	99.0 (90.0–109.0)	0.25
(mmol/l)	5.55 (4.95–6.12)	5.49 (5.0–6.05)	
Triglycerides (mg/dl)	133.5 (100.25–190.25)	131.7 (95.0–152.0)	0.09
(mmol/l)	1.51 (1.13–2.15)	1.49 (1.07–1.72)	
LDL-C (mg/dl)	115.0 (92.0–134.25)	112.0 (88.0–125.0)	0.06
(mmol/l)	2.98 (2.38–3.48)	2.90 (2.28–3.24)	
Total cholesterol (mg/dl)	186.0 (160.0–213.5)	185.2 (161.0–203.0)	0.65
(mmol/l)	4.82 (4.14–5.53)	4.80 (4.17–5.26)	
HDL-C (mg/dl)	42.0 (36.0–49.0)	47.0 (40.9–55.2)	< 0.0001
(mmol/l)	1.09 (0.93–1.27)	1.22 (1.06–1.43)	
Eosinophils ($\times 10^9$ cells/l)	0.22 (0.13–0.32)	0.19 (0.12–0.28)	0.02
Lymphocytes ($\times 10^9$ cells/l)	2.05 (1.62–2.54)	2.18 (1.80–2.90)	0.002
ELR	0.11 (0.06–0.17)	0.08 (0.05–0.12)	< 0.0001
Haemoglobin (g/dl)	14.4 (13.6–15.1)	14.1 (13.5–15.0)	0.09
Haematocrit (%)	43.1 (41.0–45.5)	42.0 (41.0–45.0)	0.07
White blood cells ($\times 10^9$ cells/l)	8.11 \pm 1.75	7.49 \pm 1.80	< 0.0001*
Urea (mg/dl)	30.0 (25.0–36.0)	29.2 (23.7–35.0)	0.10
Creatinine (mg/dl)	0.67 (0.54–0.78)	0.66 (0.55–0.77)	0.50
Sodium (mmol/l)	140.0 (138.0–142.0)	140.0 (138.0–142.0)	0.36
Potassium (meq/l)	4.3 (4.0–4.6)	4.3 (4.1–4.6)	0.40
Calcium (mg/dl)	9.21 \pm 0.49	9.27 \pm 0.47	0.23*

CAE: coronary artery ectasia; NCA: normal coronary arteries; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; ELR: eosinophil-to-lymphocyte ratio.
 *Normality of the distribution was evaluated by the Kolmogorov–Smirnov test, and the Mann–Whitney U-test was applied to compare for continuous variables except for white blood cells and calcium.

between groups (among Markis I, II, III and IV and among one-, two- and three-vessel disease). The receiver operating characteristics (ROC) test was used to estimate the sensitivity and specificity of ELR and its optimal cut-off value. Correlation analyses were fulfilled using Spearman’s correlation test; $p < 0.05$ was considered to indicate statistical significance.

Results

The records of 16 240 patients who underwent coronary angiography were retrospectively screened, of whom 232 patients with isolated CAE (141 males) and 247 age- and gender-matched subjects with NCA (130 males) were detected. It was observed that WBC and eosinophil counts and ELR for the isolated CAE group were significantly higher than in the NCA group 8.11 ± 1.75 vs $7.49 \pm 1.80 \times 10^9$ cells/l, $p < 0.0001$; $0.22 (0.13–0.32)$ vs $0.19 (0.12–0.28) \times 10^9$ cells/l, $p = 0.02$; $0.11 (0.06–0.17)$ vs $0.08 (0.05–0.12)$ $p < 0.0001$, respectively (Table 1, Fig. 6). However, high-density lipoprotein cholesterol (HDL-C) level and lymphocyte count for the NCA group were significantly higher than in the isolated CAE group $[47.0 (40.9–55.2)$ vs $42.0 (36.0–49.0)$ mg/dl = $1.22 (1.06–1.43)$ vs $1.09 (0.93–1.27)$ mmol/l, $p < 0.0001$; $2.18 (1.80–2.90)$ vs $2.05 (1.62–2.54) \times 10^9$ cells/l, $p = 0.002$, respectively) (Table 1).

Eosinophil and lymphocyte counts were not significantly

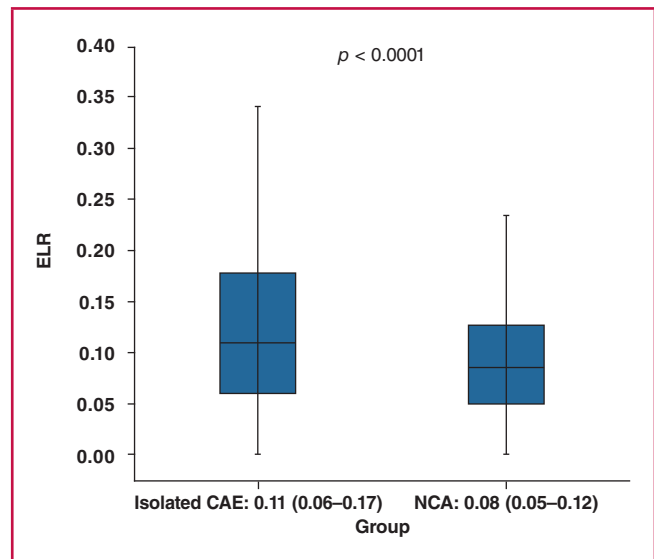


Fig. 6. Comparison of ELR between isolated CAE and NCA.

different among patients with one-, two- and three-vessel isolated CAE (Table 2). Likewise, the eosinophil and lymphocyte counts were not significantly different among Markis types I, II, III and IV (Table 3). However, the ELR for three-vessel isolated CAE was significantly higher than for one-vessel isolated CAE ($p = 0.04$) (Table 2). Furthermore, the ELR for Markis I was significantly higher than for Markis IV ($p = 0.04$) (Table 3, Fig. 7). There were no statistically significant differences between focal (Markis type IV) and diffuse ectasia (Markis type I, II and III) in terms of eosinophil count ($p = 0.54$) (Table 4). In contrast, the ELR for diffuse ectasia (Markis type I, II and III) was significantly higher compared to focal (Markis type IV) ectasia, and the lymphocyte count for diffuse ectasia (Markis types I, II and III) was significantly lower than for focal (Markis type IV) ectasia ($p = 0.02$; $p = 0.001$, respectively) (Table 4).

No significant correlations were observed between eosinophil count and any Markis classification ($p = 0.314$, $r = -0.066$) or between eosinophil count and diffuse ectasia ($p = 0.544$, $r = 0.040$) (Table 5). Likewise, there was no correlation between

Table 2. Eosinophil and lymphocyte counts and ELR values according to vessel count

Vessels	Noun	Eosinophil count ($\times 10^9$ cells/l)	Lymphocyte count ($\times 10^9$ cells/l)	ELR value
One vessel	135	0.22 \pm 0.12	2.23 \pm 0.81	0.11 \pm 0.07
Two vessels	42	0.26 \pm 0.14	2.05 \pm 0.59	0.14 \pm 0.10
Three vessels	55	0.24 \pm 0.12	1.96 \pm 0.79	0.14 \pm 0.09

All p-values for eosinophil and lymphocyte counts > 0.5.
 p-value for ELR (between one and three vessels): 0.04.

Table 3. Eosinophil and lymphocyte counts and ELR values according to the Markis classification

Markis classification	Noun (%)	Eosinophil count ($\times 10^9$ cells/l)	Lymphocyte count ($\times 10^9$ cells/l)	ELR value
Type I	51 (21.98)	0.25 \pm 0.12	1.93 \pm 0.79	0.15 \pm 0.10
Type II	38 (16.38)	0.24 \pm 0.12	1.98 \pm 0.60	0.14 \pm 0.09
Type III	41 (17.67)	0.21 \pm 0.13	2.15 \pm 0.94	0.11 \pm 0.07
Type IV	102 (43.96)	0.23 \pm 0.13	2.29 \pm 0.73	0.11 \pm 0.08

All p-values for eosinophil and lymphocyte counts > 0.5.
 p-value for ELR (between Markis type I and IV): 0.04.

Table 4. Comparison of ELR values, and eosinophil and lymphocyte counts between focal (Markis type IV) and diffuse ectasia (Markis type I, II, III)

Counts	Focal ectasia (n = 102)	Diffuse ectasia (n = 130)	p-value
Eosinophil count ($\times 10^9$ cells/l)	0.20 (0.12–0.32)	0.22 (0.14–0.33)	0.54
Lymphocyte count ($\times 10^9$ cells/l)	2.21 (1.81–2.67)	1.93 (1.55–2.36)	0.001
ELR	0.10 (0.05–0.15)	0.12 (0.06–0.18)	0.02

eosinophil count and vessel count ($p = 0.103$, $r = 0.107$) (Table 5). However, the ELR significantly correlated with the Markis classification and diffuse ectasia and vessel count ($p = 0.005$, $r = -0.182$; $p = 0.027$, $r = 0.145$; $p = 0.005$, $r = 0.185$, respectively), and the lymphocyte count significantly correlated with the Markis classification and diffuse ectasia ($p = 0.001$, $r = 0.211$; $p = 0.001$, $r = -0.211$, respectively) (Table 5).

ROC curve analysis revealed that the specificity of an ELR > 0.099 (measured before coronary angiography) in predicting isolated CAE was 60.3%, and the sensitivity was 56.5% [area under the curve (AUC): 0.604, 95% CI: 0.553, 0.655; $p < 0.0001$] (Fig. 8). No differences were observed between the two groups with regard to other analysed laboratory data (Table 1).

Discussion

The analysis revealed that ELR, and eosinophil and WBC counts were significantly higher in the isolated CAE group compared to the NCA group. However, HDL-C levels and lymphocyte counts were significantly lower for the isolated CAE group than for the NCA group (Table 1). In addition, the study revealed no relationship between eosinophil count and number of ectatic vessels, the diffuseness of the ectatic segment and Markis classification. However, it was found that ELR values were significantly related to the stated classifications.

Coronary artery ectasia may be acquired or congenital.^{24–28} The associated diseases reported in its aetiology are 50% atherosclerosis, 20–30% congenital diseases and 10–20%

Table 5. Spearman's correlation analysis between vessel count, extension of isolated CAE and Markis classification, and eosinophil and lymphocyte counts and ELR value.

	Eosinophil count		Lymphocyte count		ELR value	
	r	p	r	p	r	p
Vessel count	0.107	0.103	-0.127	0.052	0.185	0.005
Extension of isolated CAE (as diffuse)	0.040	0.544	-0.211	0.001	0.145	0.027
Markis classification	-0.066	0.314	0.211	0.001	-0.182	0.005

inflammatory or connective tissue diseases.⁶ The association between inflammation and CAE has been revealed using well-recognised inflammatory markers such as WBC, neutrophil and monocyte counts, and interleukin-6, matrix metalloproteinase, tumour necrosis factor- α and C-reactive protein (CRP) levels.^{29,30}

The ischaemic mechanism in patients with CAE has not been fully understood. However, it is accepted that the leading cause of ischaemia and angina is impaired microvascular perfusion. Slow or turbulent flow in dilated vessels has been reported to cause ischaemia by causing thrombosis in the ectatic segment and embolism in the distal coronary artery.³ Eosinophils are loaded with many granule-associated molecules that cause vascular thrombosis and endothelial damage. Major basic protein and eosinophil peroxidase, as the most well-known of these granules, are also platelet agonists and play an important role in thrombus formation.²⁰ Eosinophils may additionally cause thrombosis by secreting tissue factor and stimulating platelets and leukocytes, in addition to secreting major basic protein and eosinophil peroxidase.^{20,31}

These three proteins (tissue factor, basic protein and eosinophil peroxidase) contribute considerably to thrombus formation by stimulating thrombocytes and inhibiting thrombomodulin. It has been reported that eosinophils and their granule-associated molecules have been isolated from necrotic and thrombotic lesions, and these structures were extracted from small arterial walls, especially after acute ischaemic damage to

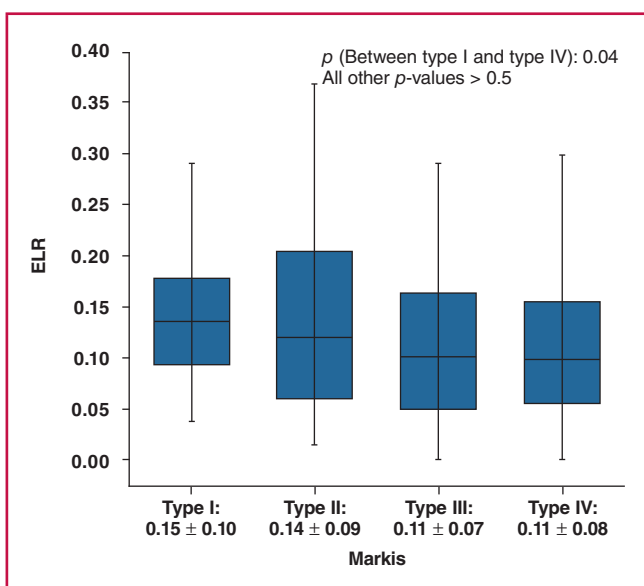


Fig. 7. Comparison of ELR among Markis type I, II, III and IV.

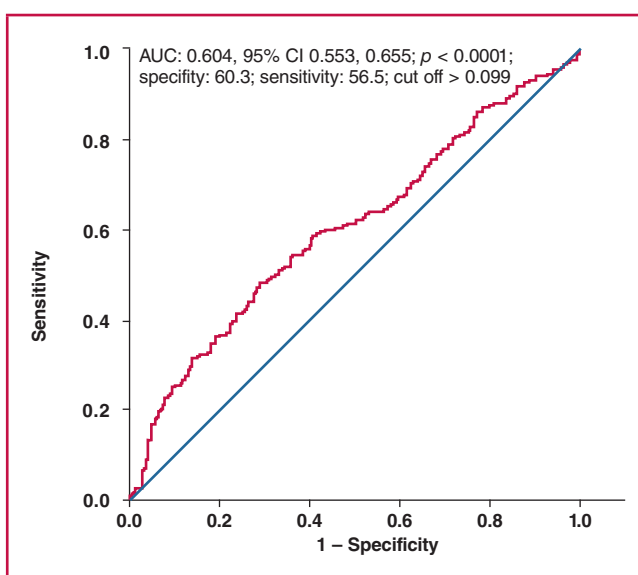


Fig. 8. ELR ROC analysis between isolated CAE and NCA. AUC: area under the curve; CI: confidence interval; ELR: eosinophil-to-lymphocyte ratio; ROC: receiver operating characteristics.

the endocardium. These findings suggest that eosinophils may cause inflammation, thrombosis and embolus-induced vascular damage.³²⁻³⁴

It has been reported that eosinophils are related to arterial tortuosity, thrombosis, cardiac syndrome X, dilatation and aneurysm in patients with hypereosinophilic syndromes.^{35,36} Cytotoxic secretions secreted from eosinophils have been suggested to cause direct medial destruction leading to aneurysmal formation or spontaneous intimal dissection and sudden cardiac death.³⁷ This suggests that eosinophil secretion may be one of the causes of vascular injury, therefore eosinophils may affect the cardiovascular system via an inflammatory mechanism.

Lymphocytes are related to the immune response and systemic inflammation. Stress-induced low lymphocyte levels (lymphopaenia) have been found to be associated with inflammatory conditions and adverse cardiovascular events.^{11,12} Low lymphocyte counts might result from increased cortisol levels that induce apoptosis specifically in lymphocytes but also increase the total WBC count.³⁸ Eosinophil elevation and low lymphocyte levels reflect systemic inflammation and physiological stress and contribute to the development of cardiovascular disease.^{13-15,20}

A strong correlation was found between CAE and low HDL-C levels, and this study suggests that low HDL-C levels could lead to isolated CAE.³⁹ Several studies have previously reported that HDL-C levels decrease in the presence of systemic inflammation, and systemic and vascular inflammation impair the structure of HDL-C and disrupt its function, reducing its protective effect on the vascular endothelium.⁴⁰⁻⁴³

In this study, we observed that HDL-C levels were lower in the isolated CAE group than in the NCA group (Table 1). This finding may be reflective of the systemic and vascular inflammation consistent with previous studies. Moreover, the low HDL-C levels observed in the isolated CAE group may be considered one of the mechanisms responsible for endothelial dysfunction and vascular destruction. Nevertheless, larger studies that focus only on this issue are necessary to draw more concrete conclusions.

Increased WBC count, WBC sub-type and sub-type ratios have been accepted as important inflammatory markers in forecasting cardiovascular outcomes.^{11,44} Elevated eosinophil count and ELR values and decreased lymphocyte levels are associated with systemic inflammation and atherosclerosis.^{13,16,17,45,46} In some studies, the relationship between some haematological parameters actively functioning in inflammation, such as neutrophils, lymphocytes, monocytes and eosinophils, and parameters such as the monocyte-to-HDL-C ratio (MHR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) and their relationship with coronary artery ectasia has been revealed.^{13,14,47-49} However, as far as we know, the relationship between CAE and ELR has not previously been studied.

Based on the role of inflammation in the aetiopathogenesis of isolated CAE and in light of the study results, we hypothesised that ELR may be associated with isolated CAE. The present study revealed an increased eosinophil count and a decreased lymphocyte count in isolated CAE patients compared to subjects with NCA (Table 1). However, we did not observe a significant association between eosinophil count and Markis classification, diffuse ectasia or vessel count (Tables 2–5). Likewise, we did

not observe a significant difference between lymphocyte count and Markis classification or vessel count (Tables 2–5). However, the study showed that ELR was significantly associated with these parameters (Tables 2-5). In addition, correlation analyses revealed a significant association between lymphocyte count and Markis classification, diffuse ectasia and vessel count (Table 5).

This indicates that the eosinophil count was higher in isolated CAE compared to NCA but was not correlated with the severity of CAE. However, lymphocyte count and ELR value not only increased in isolated CAE patients but also were significantly correlated with the severity of isolated CAE. The data obtained in this study suggest that an analysis of only lymphocyte and eosinophil levels may not provide reliable results, whereas the use of ELR as a systemic inflammatory marker may be more reliable. Although the sensitivity and specificity of ELR for predicting isolated CAE were low in the ROC analysis, all correlation analyses in other areas found that ELR indicated the presence and severity of isolated CAE.

Since the study was designed retrospectively, data on acute or chronic diseases that may affect ELR were obtained in accordance with patient statements. Some patients may not have been aware of inflammatory diseases such as allergic rhinitis, conjunctivitis or atopic dermatitis, or they may not have declared these diseases. Because advanced equipment such as intravascular ultrasound could not be used in this study, the coronary arteries of the subjects examined could not be confirmed to be completely normal. These factors may explain the results of the ROC analysis.

Limitations

Although there may be an atherosclerotic plaque over large segments, the related vessel can be observed as normal angiographically.^{50,51} In this study, it was not possible to confirm that the coronary arteries were completely normal because a device such as intravascular ultrasound could not be used. Second, as the study was retrospective, inflammatory markers such as CRP could not be investigated or compared to ELR.

Conclusions

The results of this study may contribute to the aetiopathogenesis of isolated CAE. As a new, simple, effortless and cost-effective inflammatory marker, ELR may be able to forecast isolated CAE in daily clinical practice. Increased ELR may explain the vascular destruction, endothelial dysfunction, thrombosis and distal microvascular embolisation seen in isolated CAE patients.

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