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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Comparison of neutrophil to lymphocyte ratio in patients with coronary artery ectasia versus patients with obstructive coronary artery disease

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Abstract

Background: Previous studies have demonstrated that inflammation, neurohormonal process and cardiovascular risk factors are associated with the development of coronary artery ectasia (CAE). However, the underlying mechanisms responsible for ectasia formation are not fully understood. The neutrophil to lymphocyte (N/L) ratio has recently emerged as a new inflammation marker for cardiovascular disease.

Aim: In this study, we hypothesised that CAE could be associated with more severe inflammation compared to obstructive coronary artery disease (O-CAD) with regard to N/L ratio values.

Methods: A total of 405 patients with isolated CAE, O-CAD and insignificant CAD (controls) were enrolled. Severity of isolated CAE was determined according to the Markis classification. N/L ratio values were compared between the three groups.

Results: We determined that the patients with isolated CAE had significantly elevated N/L ratio values compared to O-CAD and control groups (2.5 vs. 1.9, $p < 0.001$ and vs. 1.6, $p < 0.001$, respectively). In multivariate analysis adjusted for age, sex, diabetes meliteis (DM) and hypertension, N/L ratio was independently associated with the presence (N/L ratio, OR = 2.48, 95% CI 2.03–3.02, $p < 0.001$) and severity (DM, OR = 2.90, 95% CI 1.02–8.18, $p = 0.044$, N/L ratio, OR = 1.88, 95% CI 1.47–2.41, $p = 0.004$) of isolated CAE. ROC curve analysis revealed that a N/L ratio value of > 2.06 identified the patients with isolated CAE.

Conclusions: We showed that patients with isolated CAE had a significantly higher N/L ratio than patients with O-CAD and control groups. This finding suggests that a more severe inflammatory process could be involved in the development of CAE.

Key words: coronary artery ectasia, neutrophil to lymphocyte ratio, coronary artery disease

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INTRODUCTION

Coronary artery ectasia (CAE) has been defined as localised or diffuse non-obstructive lesions of the epicardial coronary arteries, with a luminal dilation ≥ 1.5 times normal of the adjacent segments or vessel diameter. Isolated CAE has been defined as CAE without significant coronary artery stenosis [1]. This abnormal dilatation of coronary arteries can cause angina pectoris and even myocardial infarction due to vasospasm, dissection or thrombus in patients without coronary artery disease (CAD) [2]. Therefore, determination of the factors associated with the presence and severity of CAE may have a salutary influence on the management of these patients. Previous studies have demonstrated that inflammation, neurohormonal process and cardiovascular risk factors are associated with the development of CAE. However, the underlying mechanisms responsible for ectasia formation are still not fully understood [3].

Inflammation plays a major role in atherosclerosis and all stages of CAD [4]. As CAE is associated with inflammation

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and frequently accompanies CAD, it has been suggested that CAE may be a variant of CAD [5]. However, it is unclear why similar risk factors lead to dilatation in the arterial lumen in some patients, but to obstruction in others [6]. Postmortem histopathologic studies showed that extensive vascular inflammatory infiltration involving all layers of the vascular wall in the coronary circulation was usually observed in patients with CAE [1]. Based on the findings obtained from previous studies, it has been suggested that a more severe inflammation could be involved in the pathogenesis of CAE [5].

The circulating white blood cell count (WBC) and its subtypes have been studied as potential predictors of cardiovascular outcomes [7]. The neutrophil to lymphocyte (N/L) ratio has emerged as a new inflammation marker. Recent literature has shown that N/L ratio elevation has been also associated with the presence and severity of CAD [8], poor prognosis in acute coronary syndromes (ACSs) and stable coronary heart diseases (CHD) [9, 10]. These clinical studies have also shown a possible relationship between N/L ratio and systemic inflammation [11].

Although preliminary data has shown that N/L ratio is a predictor of long-term cardiovascular risk, its role and importance in the presence and severity of isolated CAE have not been adequately evaluated. Our study was performed on the hypothesis that a more severe inflammation might be involved in the development of isolated CAE compared to obstructive CAD (O-CAD); and patients who had angiographically insignificant CAD.

METHODS

In this study, 418 patients who underwent coronary angiography (CAG) in our hospital between February 2011 and May 2012 were retrospectively evaluated. Of these, 151 patients with isolated CAE constituted the first group. During this period, initial 128 consecutive patients who had O-CAD without CAE comprised the second group, and 139 consecutive patients with insignificant CAD comprised the last group (controls). Indication for CAG was either the presence of typical angina or positive or equivocal results of non-invasive screening tests for myocardial ischaemia in the patient groups.

Patients with ACS, previous myocardial infarction, left ventricular systolic dysfunction (left ventricular ejection fraction [LVEF] < 40%), severe valvular heart disease, coronary artery by-pass grafting, immunologic or inflammatory disease, haematological disease, sepsis, active local or systemic infections, chronic renal disease (creatinine > 1.6 mg/dL), a history of recent infection (< 3 months before the study) or a history of malignancy were excluded. A total of 405 patients were finally enrolled (Fig. 1).

Selective CAG was performed by Judkin's technique in multiple projections without the use of nitroglycerin. CAGs were analysed by two experienced angiographers who were blinded to clinical status and N/L ratio values of the patients. Right anterior oblique and left anterior oblique views were used for the evaluation of ectasia of the left and right coronary system, respectively. The vessel diameter was calculated quantitatively in case of conflicts about CAE. The CAEs were defined based on the criteria used in the Coronary Artery Surgery Study. According to the angiographic definition used in that study, a vessel was considered to be ectasic when its diameter was ≥ 1.5 times that of the adjacent normal segment in segmental ectasia. When there was no identifiable adjacent normal segment, the mean diameter of the corresponding coronary segment in the control group served as the normal value [12]. Isolated CAE was defined as CAE without significant coronary artery stenosis. The severity of isolated CAE was determined according to the Markis classification [1]. In decreasing order of severity, diffuse ectasia of two or three vessels was classified as type 1, diffuse disease in one vessel and localised disease in another vessel as type 2, diffuse ectasia of only one vessel as type 3 and localised segmental ectasia as type 4. Types 1 and 2 which indicate severe ectasic involvement according to Markis classification constituted group 1, while types 3 and 4, indicating milder ectasic involvement, constituted group 2. Significant CAD was defined as stenosis of more than 50% of the diameter at one or more major epicardial artery.

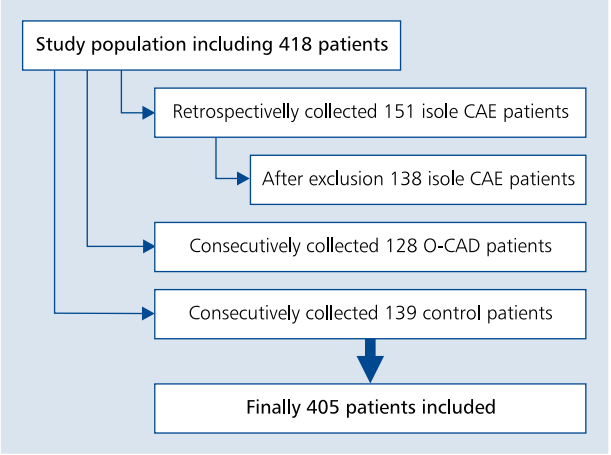

Figure 1. Flow-chart of the study population; CAE — coronary artery ectasia; O-CAD — obstructive coronary artery disease

Laboratory and clinical characteristics of the patients, such as age, sex, diabetes mellitus (DM), hypertension (HT), hypercholesterolaemia, smoking, family history of cardiovascular disease, medical history, weight and height were recorded. HT was defined as previous use of antihypertensive medications, systolic pressure > 140 mm Hg or diastolic pressure > 90 mm Hg in at least two separate measurements. Diagnosis of DM was based on previous history of diabetes with or without drug therapies or fasting blood glucose ≥ 126 mg/dL. Hyperlipidaemia was defined as total cholesterol of ≥ 200 mg/dL or current statin therapy. Body mass index (BMI) was calculated

as weight [kg]/height [m^2]. A BMI of ≥ 30 kg/m^2 was defined as obese. Current smokers were defined as those who had smoked for some period during the past year. Estimated glomerular filtration rate was calculated by the Modification of Diet in Renal Disease (MDRD) Study equation [13].

Peripheral venous blood samples were drawn after overnight fasting. Total and differential leukocyte counts were measured using an automated haematology analyser Advia 2120 (Siemens). Absolute cell counts were used in this analysis. Total and high-density lipoprotein cholesterol, triglycerides and fasting glucose were also measured. Concentrations of low-density lipoprotein were calculated using the Friedewald equation.

Echocardiography (VIVID S-5 General Electric Medical System 3.6 MHz) was performed according to the American Society of Echocardiography guidelines, and LVEF was evaluated using the biplane Simpson method [14]. Informed consent was obtained from all patients and the local ethics committee approved this study.

Statistical analysis

SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA) and the MedCalc software program, release 12.3.0.0 (MedCalc Software, Belgium) were used for statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range, as appropriate. Categorical variables were expressed as percentages. Group means for continuous variables were compared with the Student's t-test, the Mann-Whitney U or Bonferroni-corrected Mann-Whitney U test, ANOVA or the Kruskal-Wallis test, as appropriate. Categorical variables were compared with the χ^2 test. Tukey's honestly significant difference test was used for *post hoc* analysis. Variables with a $p \leq 0.05$ criterion were selected for logistic regression analysis. Logistic regression analysis was performed in order to find independent predictors of presence and severity of isolated CAE. Receiver-operating characteristic (ROC) curve analysis was performed to detect the cut-off value of the N/L ratio in predicting CAE. A p value of ≤ 0.05 was considered statistically significant.

RESULTS

The study population consisted of 405 patients. The mean age of the patients was 61.4 ± 11.8 years and male gender constituted 55.3% of the patients ($p < 0.001$). General characteristics of the patients, as well as distribution and the severity of isolated CAE, are presented in Table 1. The patients with isolated CAE and O-CAD were relatively older and had higher prevelance of male gender and history of DM and HT. The patients with isolated CAE had significantly elevated N/L ratio values compared to the others. Significant differences were observed in N/L ratio values between the CAE vs. O-CAD, CAE vs. control and O-CAD vs. control groups ($p < 0.001$, $p < 0.001$, $p = 0.001$, respectively). Significant differences were also identified in terms of neutrophil values between the CAE vs. O-CAD, CAE vs. control and O-CAD vs. control groups ($p < 0.001$, $p < 0.001$, $p < 0.001$, respectively). Moreover, we found that isolated CAE were most likely to occur in right coronary arteries (81.9%) and mostly involved two vessels (42%). According to the Markis classification, type 4 (32.6%) and type 2 (31.9%) were the most common types of isolated CAE (Table 1). N/L ratio values according to the groups are shown in Figure 2.

A multivariate logistic regression model was built to find the independent associates of the presence of isolated CAE. Age [years], male sex, DM, HT and N/L ratio were entered into the model as independent variables. N/L ratio was found to be independently associated with the presence of isolated CAE (OR = 2.48, 95% CI 2.03–3.02, $p < 0.001$) (Table 2).

The patients with severe ectasia (group 1, types 1 and 2) and milder ectasia (group 2, types 3 and 4) are compared in Table 3. The patients in group 1 had higher rates of DM and HT, as well as significantly elevated N/L ratio values. At multivariate logistic regression analysis, DM and N/L ratio were identified as independent predictors of the severity of isolated CAE (OR = 2.9, 95% CI 1.02–8.18, $p = 0.044$; OR = 1.88, 95% CI 1.47–2.41, $p = 0.004$, respectively) (Table 4).

ROC curve analysis was performed in isolated CAE and control groups to detect the cut-off value of N/L ratio in predicting patients with isolated CAE. The analysis showed that N/L ratio values of > 2.06 identified the patients with isolated CAE with a specificity of 74.1% (95% CI 66–81.2%) and a sensitivity of 69.6% (95% CI 61.2–77.1%) (AUC 0.752, 95% CI 0.697–0.802, $p < 0.001$). Likelihood ratio (LR) (+) and (–) were 2.7 (95% CI 2.0–3.6) and 0.4 (95% CI 0.3–0.5), respectively (Fig. 3A).

Furthermore, ROC curve analysis was performed in isolated CAE and O-CAD groups to detect the cut-off value of N/L ratio in predicting patients with isolated CAE. The analysis showed that N/L ratio values of > 2.07 identified the patients with isolated CAE with a specificity of 60.9% (95% CI 51.9–69.4%) and a sensitivity of 68.8% (95% CI 60.4–76.4%) (AUC 0.657, 95% CI 0.597–0.714, $p < 0.001$). LR (+) and (–) were 1.8 (95% CI 1.4–2.2) and 0.5 (95% CI 0.4–0.7), respectively (Fig. 3B).

DISCUSSION

This study showed that N/L ratio was independently associated with the presence and the severity of isolated CAE. So, isolated CAE may be related to more severe inflammation when compared to O-CAD and control groups. A cut-off value > 2.06 was able to identify the patients with isolated CAE.

Several studies have shown that patients with CAE have an increased risk of mortality, equivalent to that of patients with O-CAD [2]. Although it has been suggested that CAE is commonly a variant of O-CAD, a definitive link between atherosclerosis and ectasia has not been confirmed [15].

Table 1. Baseline characteristics of the study population

Variables	CAE (n = 138)	O-CAD (n = 128)	Control (n = 139)	P
Age [years]	63.5 ± 11.1	64.7 ± 10.9	56.3 ± 11.8	< 0.001
Male sex	82 (59.4%)	91 (71.1%)	52 (37.4%)	< 0.001
Diabetes mellitus	24 (17.4%)	43 (33.6%)	21 (15.1%)	< 0.001
Hypertension	86 (62.3%)	99 (77.3%)	70 (50.4%)	< 0.001
Hyperlipidaemia	86 (62.3%)	89 (69.5%)	83 (59.7%)	0.229
Current smoker	13 (9.4%)	11 (8.6%)	7 (5%)	0.347
Family history	14 (10.1%)	16 (12.5%)	21 (15.1%)	0.460
Body mass index ≥ 30 kg/m^2	60 (43.5%)	60 (46.9%)	63 (45.3%)	0.856
MDRD eGFR < 60 mL/min/1.73 m^2	19 (13.8%)	19 (14.8%)	15 (10.8%)	0.592
Use of β-blocker	43 (31.2%)	40 (31.3%)	31 (22.3%)	0.167
Use of ACE inhibitor	34 (24.6%)	38 (29.7%)	23 (16.5%)	0.085
Use of angiotensin receptor blocker	32 (23.2%)	17 (13.3%)	22 (15.8%)	0.037
Use of statin	39 (28.3%)	37 (28.9%)	29 (20.9%)	0.242
Left ventricular ejection fraction [%]	59 (52–65)	60 (54.2–65)	59 (52–65)	0.636
Total cholesterol [mg/dL]	200.4 ± 40.6	198.3 ± 52.5	198.1 ± 43.7	0.886
LDL [mg/dL]	131.2 ± 33.7	132.6 ± 40.4	132.3 ± 32.3	0.946
HDL [mg/dL]	40 (35–46)	42 (36.2–48.7)	43 (35–52)	0.240
Triglyceride [mg/dL]	145.5 (99–183.7)	150 (103.5–204.5)	140 (99–212)	0.662
Glucose [mg/dL]	100 (92.7–109)	105 (95–141)	95 (88–103)	< 0.001
Haemoglobin [g/dL]	14.2 ± 1.2	13.9 ± 1.4	13.6 ± 1.2	0.002
Platelet count [× 10^9/L]	233.7 ± 62.4	232.5 ± 58.3	247.2 ± 47.3	0.057
White blood cell count [× 10^9/L]	7.7 ± 1.8	7.6 ± 1.6	6.8 ± 1.7	< 0.001
Neutrophil count [× 10^9/L]	5.3 (3.9–7.2)	4.2 (3.6–5.2)	3.6 (3–4.6)	< 0.001
Lymphocyte count [× 10^9/L]	2.0 (1.6–2.5)	2.2 (1.7–2.6)	2.1 (1.8–2.6)	0.139
Neutrophil/lymphocyte ratio	2.5 (1.8–3.6)	1.9 (1.4–2.7)	1.6 (1.3–2.2)	< 0.001
Distribution of ectasia:				
Left anterior descending artery	86 (62.3%)			
Left circumflex artery	69 (50%)			
Right coronary artery	113 (81.9%)			
Number of ectasic vessels:				
1 vessels	44 (31.9%)			
2 vessels	58 (42%)			
3 vessels	36 (26.1%)			
Markis classification:				
Type 1	32 (23.2%)			
Type 2	44 (31.9%)			
Type 3	17 (12.3%)			
Type 4	45 (32.6%)			

Data are expressed in numbers (percentages), mean ± one standard deviation, or median and (interquartile range). Percentages are rounded; CAE — coronary artery ectasia; O-CAD — obstructive coronary artery disease; MDRD — Modification of Diet in Renal Disease; eGFR — estimated glomerular filtration rate; ACE — angiotensin converting enzyme; LDL — low-density lipoprotein; HDL — high-density lipoprotein

The smooth muscle-containing medial layer of the vascular wall also includes extracellular matrix proteins, elastin and collagen, which are arranged in layers with smooth muscle cells to form a structure that can withstand the stresses on the vascular wall and maintain vascular wall integrity [16]. Postmortem histopathologic examination of the ectasic segment has demonstrated extensive destruction of the media of the vessel wall. Markis et al. [1] proposed the destruction

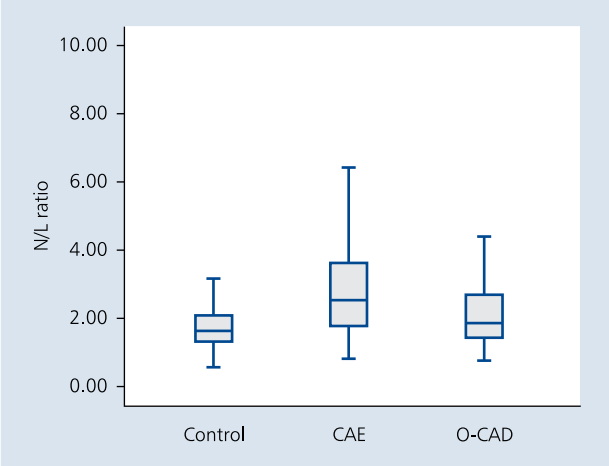

Figure 2. Box-plot graph showing neutrophil to lymphocyte (N/L) ratio values of the groups; CAE — coronary artery ectasia; O-CAD — obstructive coronary artery disease

Table 2. Independent predictors of angiographic ectasia in multivariate logistic regression analysis

Variables	Multivariate: OR (95% CI)	P
Age [years]*	11.91 (11.68–12.15)	0.191
Male sex	1.10 (0.70–1.74)	0.681
Diabetes mellitus	1.42 (0.80–2.51)	0.227
Hypertension	1.28 (0.78–2.09)	0.323
N/L ratio*	2.48 (2.03–3.02)	< 0.001

*OR expressed as per standard deviation; OR — odds ratio, CI — confidence interval; N/L — neutrophil/lymphocyte

of the vascular media as the cause of ectasia. Infiltration of the media layer by inflammatory cells is another finding that can be seen in ectasic segments [15].

The relation between inflammation and CAE was evaluated based on the findings of postmortem studies. Higher levels of high sensitive C-reactive protein (hs-CRP) [5], adhesion molecules (ICAM-I, VCAM-I, E-selectine) [17], interleukin-6 (IL-6) [18] and matrix metalloproteinase-3 (MMP-3) [19] have been reported in patients with isolated CAE, compared to patients with O-CAD. Additionally, Kocaman et al. [20] reported that patients with isolated CAE had significantly higher leukocyte, monocyte and neutrophil levels than patients with non-obstructive CAD and normal coronary arteries (NCAs).

However, several previous studies had conflicting results. Although a few studies reported increased levels of CRP in CAE, most did not find any siginificant difference [21]. Dogan et al. [22] evaluated IL-6, hs-CRP, MMP-3 and MMP-9 in patients with isolated CAE, O-CAD and NCAs and reported that only MMP-9 was significantly elevated in the isolated CAE group, compared to the other two groups. In addition, the majority of these studies did not evaluate the association between severity of CAE and inflammation markers (apart from ICAM-I, VCAM-I, MMP-3), in contrast to our study. However, previous studies showed that besides the presence of CAE, the extent of CAE was also associated with cardiovascular mortality [23]. In our study, we demonstrated that N/L ratio was correlated with both presence and severity of isolated CAE.

Clinical outcomes support the hypothesis that an inflammation marker, in addition to being a predictor of CAD, could also have a prognostic value to be used in clinical practice. Although epidemiological studies have shown that these inflammation markers (IL-6, ICAM-I, VCAM-I, E-selectine, etc.) are associated with a rise in vascular risk, CRP has been regarded as the most promising prognostic prediction marker in clinical use because it is easily available, has a long life-time, and affords stability of levels with no observable circadian variation [24]. So, CRP has been the most extensively studied and clinically applied cardiovascular risk prediction marker to date. But, compared to major established risk factors, CRP concentration was a relatively moderate predictor of CHD risk. So, researchers have suggested that recent recommendations regarding the use of measurements of CRP in the prediction of CHD may need to be reviewed [25].

Recently, N/L ratio has emerged as a potential new biomarker for cardiovascular events (CVEs) and prognosis [9]. Leukocytes and especially neutrophils play a central role in atherogenesis and atherothrombosis. Low lymphocyte counts have been shown in ACS patients. Increased number of neutrophils and decreased lymphocytes are risk indicators for future CVEs. Therefore, an elevated N/L ratio integrates the predictive risk of these two leukocyte subtypes into a single risk factor [8]. The WBC and its subtypes are classic markers of inflammation in CAD. But recently it has been suggested that the N/L ratio is a better predictor of CVEs compared to WBC or neutrophil count. So N/L ratio may appear additive to conventional risk factors and commonly used biomarkers [26]. In addition, interestingly, the N/L ratio has remained as a predictor of all-cause mortality in patients with normal WBC counts [27].

Previous studies have stated that neutrophil elastase (NE), a serine proteinase, may play a role in the pathogenesis of CAE [15]. NE is predominantly present in neutrophils and can digest elastin, collagen and proteoglycans. It also swings the proteolytic balance in favour of matrix breakdown by MMP-1, MMP-3 and MMP-9. In addition, it regulates the activity of cytokines (IL-8, TNF-α, etc.) [28]. Akyel et al. [21] determined that higher neutrophil gelatinase-associated protein (NGAL) levels were detected in patients with CAE compared to those with NCAs. NGAL is a protein that is secreted from activated neutrophils, and it prevents degradation of MMP-9 which has a crucial role in the degradation of collagen [21]. Therefore, we consider that these factors, NE or NGAL, may explain the relationship between N/L ratio and CAE.

Balta et al. [11] recently investigated the relationship between the N/L ratio and isolated CAE. Although they found

Table 3. Baseline characteristics with and without severe CAE

Variables	Group 1 (n = 76)	Group 2 (n = 62)	P
Age [years]	63.8 ± 11.3	63.1 ± 10.8	0.701
Male sex	50 (65.8%)	32 (51.6%)	0.092
Diabetes mellitus	18 (23.7%)	6 (9.7%)	0.031
Hypertension	55 (72.4%)	31 (50%)	0.007
Hyperlipidaemia	50 (65.8%)	36 (58.1%)	0.352
Current smoker	7 (9.2%)	6 (9.7%)	0.926
Family history	7 (9.2%)	7 (11.3%)	0.687
Body mass index ≥ 30 kg/m^2	34 (44.7%)	26 (41.9%)	0.741
MDRD eGFR < 60 mL/min/1.73 m^2	13 (17.1%)	6 (9.7%)	0.208
Use of β-blocker	26 (34.2%)	17 (27.4%)	0.392
Use of ACE inhibitor	17 (22.4%)	17 (27.4%)	0.493
Use of angiotensin receptor blocker	18 (23.7%)	14 (22.6%)	0.879
Use of statin	23 (30.3%)	16 (25.8%)	0.563
Left ventricular ejection fraction [%]	59.5 (51–64.3)	59 (53.8–65)	0.667
Total cholesterol [mg/dL]	198.1 ± 41.2	203.3 ± 40	0.462
LDL [mg/dL]	128.3 ± 32.4	134.9 ± 35.1	0.257
HDL [mg/dL]	40.5 (35–46)	40 (35–46)	0.591
Triglyceride [mg/dL]	148 (101–203.8)	142 (94–171)	0.175
Glucose [mg/dL]	101 (95–113)	98 (90–107.3)	0.019
Haemoglobin [g/dL]	14.4±1.3	14.1 ± 1.2	0.168
Platelet count [× 10^9/L]	230.3 ± 61.9	237.9 ± 63.2	0.475
White blood cell count [× 10^9/L]	7.7 ± 1.8	7.6 ± 1.8	0.808
Neutrophil count [× 10^9/L]	5.8 (4.2–7.2)	5.0 (3.7–7.2)	0.226
Lymphocyte count [× 10^9/L]	1.9 (1.4–2.5)	2.2 (1.8–2.8)	0.011
Neutrophil/lymphocyte ratio	2.8 (2.1–4.8)	2.3 (1.6–3.3)	0.008

Data are expressed in numbers (percentages), mean ± one standard deviation, or median and (interquartile range). Percentages are rounded; CAE — coronary artery ectasia; MDRD — Modification of Diet in Renal Disease; eGFR — estimated glomerular filtration rate; ACE — angiotensin converting enzyme; LDL — low-density lipoprotein; HDL — high-density lipoprotein

Table 4. Independent predictors severity of ectasia in multivariate logistic regression analysis

Variables	Univariate: OR (95% CI)	P	Multivariate: OR (95% CI)	P
Diabetes mellitus	2.89 (1.07–7.81)	0.031	2.90 (1.02–8.18)	0.044
Hypertension	2.61 (1.29–5.31)	0.007	2.06 (0.98–4.35)	0.057
N/L ratio*	1.88 (1.49–2.40)	0.008	1.88 (1.47–2.41)	0.004

*OR expressed as per standard deviation; OR — odds ratio, CI — confidence interval; N/L — neutrophil/lymphocyte

a higher N/L ratio in the CAE and O-CAD groups compared to the NCA group, they reported no difference between CAE and O-CAD groups and no correlation between the severity of CAE and N/L ratio, in contrast to our findings. However, this study included fewer patients than our study population, and especially the number of patients with severe isolated CAE was much lower compared to those with milder isolated CAE. The difference between the scale of these two studies may lead to this discrepancy. Additionally, the fact that the four subgroups established by Balta et al. [11] on the basis of severity of CAE included few patients for significant comparison may also have led to our findings being incompatible with theirs.

CAE, which may lead to ischaemic symptoms and findings, could be identified by more sensitive and specific cardiovascular imaging modalities. However, these tools are expensive and time consuming, with potential unwanted effects such as exposure to radiation. Therefore, N/L ratio, which is cheap and easily obtained, could be used as an initial filter criterion, especially in small centres, to determine the need for further imaging modalities in the assessment of CEA.

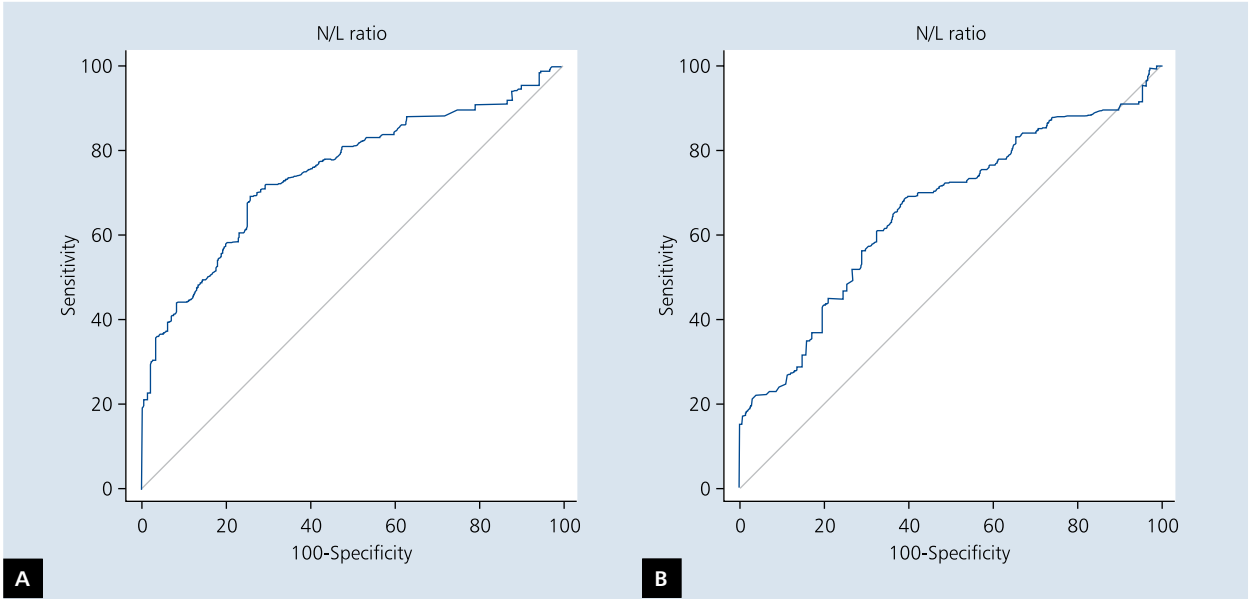

Figure 3. **A**. Receiver-operating characteristic (ROC) curve analysis of neutrophil to lymphocyte (N/L) ratio for predicting coronary artery ectasia (CAE) in CAE and control groups; **B**. ROC curve analysis of N/L ratio for predicting CAE in CAE and obstructive coronary artery disease groups

Limitations of the study

Some limitations should be considered for this study. Inflammatory markers such as CRP, IL-6, TNF-α and MMP were not analysed and not compared to the N/L ratio. However, such inflammatory biomarkers are expensive and are not immediately available in everyday practice. In contrast, calculation of the N/L ratio is inexpensive and routinely performed on admission. It therefore imposes no additional cost. Another limitation of our study is that the evaluation of CAG was performed on visual assessment and the vessel diameter was calculated quantitatively by QCA (quantitative coronary angiography) in case of conflicts about CAE. However, the angiograms, as in previous studies, were evaluated by two experienced cardiologists. Another limitation is that our AUC values for ROC curve analysis were relatively small according to the traditional academic point system. Morever, the fact that the study group did not include subjects with CAE and concurrent O-CAD is also a limitation. This should be addressed in future studies. In addition, the relatively small sample size of the study population may limit the generalisability of our findings. Hence, large scale further studies are needed to support our findings.

CONCLUSIONS

This study shows that a more severe inflammatory process may be involved in the development of CAE.

Conflict of interest: *none declared*

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W dniu 26 marca 2014 roku nominację profesorską
z rąk Prezydenta RP Bronisława Komorowskiego otrzymali

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Panom Profesorom
serdeczne gratulacje i okolicznościowe życzenia składają:
Redaktor Naczelny oraz Rada Redakcyjna i Naukowa „Kardiologii Polskiej"

Porównanie stosunku liczby neutrofilów do limfocytów u pacjentów z tętniakiem tętnicy wieńcowej i chorych z istotnym zwężeniem tętnicy wieńcowej

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Streszczenie

Wstęp: Wcześniejsze badania wykazały, że zapalenie, proces neurohormonalny i czynniki ryzyka sercowo-naczyniowego wiążą się z rozwojem tętniaka tętnicy wieńcowej (CAE). Jednak mechanizmy prowadzące do powstania tętniaka nie zostały w pełni poznane. Ostatnio uznano stosunek liczby neutrofili do limfocytów (N/L) za nowy wskaźnik zapalenia w chorobach układu sercowo-naczyniowego.

Cel: W niniejszym badaniu autorzy postawili hipotezę, że CAE może się wiązać z bardziej nasilonym procesem zapalnym niż istotne zwężenie tętnicy wieńcowej (O-CAD), czego miarą są wartości współczynnika N/L.

Metody: Do badania włączono 405 osób z izolowanym CAE, O-CAD i nieistotną klinicznie CAD (grupa kontrolna). Ciężkość izolowanego CAE określono na podstawie klasyfikacji Markisa. Wartości współczynnika N/L porównano między grupami.

Wyniki: Autorzy ustalili, że u chorych z CAE wartości współczynnika N/L były istotnie podwyższone w porównaniu z pacjentami z O-CAD i osobami z grupy kontrolnej (odpowiednio 2,5 *vs*. 1,9; $p < 0,001$ i 1,6; $p < 0,001$). W analizie wieloczynnikowej skorygowanej względem wieku, płci, cukrzycy i nadciśnienia tętniczego współczynnik N/L był niezależnie związany z obecnością (współczynnik N/L, OR = 2,48; 95% CI 2,03–3,02; $p < 0,001$) i ciężkością (cukrzyca, OR = 2,90; 95% CI 1,02–8,18; $p = 0,044$; współczynnik N/L, OR = 1,88; 95% CI 1,47–2,41; $p = 0,004$) izolowanego CAE. Analiza krzywych ROC wykazała, że wartość współczynnika N/L wynosząca ponad 2,06 pozwala zidentyfikować pacjentów z izolowanym CAE.

Wnioski: Autorzy wykazali, że u chorych z izolowanym CAE współczynnik N/L jest istotnie wyższy niż u pacjentów z O-CAD i u osób z grupy kontrolnej. Te obserwacje sugerują, że bardziej nasilony proces zapalny może wpływać na rozwój CAE.

Słowa kluczowe: tętniak tętnicy wieńcowej, stosunek liczby neutrofilów do leukocytów, choroba wieńcowa

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