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The Relationship Between Endocan and Serum Inflammatory Markers in Patients with Senile Calcific Aortic Stenosis

ABSTRACT

Background: Endocan is an indicator of many pathologies accompanied by inflammation, endothelial cell activation, and dysfunction. In this study, we examined the relationship between degenerative aortic sclerosis, which progresses in a similar pathophysiologic mechanism as atherosclerosis, and serum inflammatory markers and endocan levels.

Methods: A total of 155 patients without known coronary artery disease, aged between 65 and 80 years, were consecutively included in the prospective cross-sectional study. The study population was analyzed in 4 different groups. The control group consisted of patients with normal aortic valve structure, while patients with aortic stenosis were classified as mild aortic stenosis (2-2.9 m/s), moderate aortic stenosis (3-3.9 m/s), and severe aortic stenosis (≥ 4 m/s) according to their aortic velocity. While there were 39 patients in the control group, there were 58, 24, and 34 patients in the mild, moderate, and severe aortic stenosis groups, respectively.

Results: There was no statistically significant difference between the groups in terms of patient distribution and characteristics. History of dyspnea and angina was correlated with the severity of aortic stenosis ($P < .001$). In this study, no statistically significant correlation was found between serum endocan levels and the severity of aortic stenosis (control group: 17.3 ± 6.3 ng/mL, mild aortic stenosis: 17.6 ± 8.7 ng/mL, moderate aortic stenosis: 16.3 ± 3.8 ng/mL, severe aortic stenosis: 15.2 ± 5.9 ng/mL, $P = .396$). However, it was figured out that there was a positive correlation between endocan levels and hemoglobin (Hg) ($r = 0.308$, $P = .001$), platelet (PLT) ($r = 0.320$, $P < .001$), and albumin (Alb) ($r = 0.206$, $P = .026$).

Conclusion: In this study, no significant correlation was found between serum endocan levels and the severity of aortic stenosis. On the other hand, there was a positive correlation between endocan levels and Hg, PLT, and Alb.

Keywords: Endocan, degenerative aortic stenosis, atherosclerosis, inflammation

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INTRODUCTION

Degenerative aortic stenosis has become more frequent than rheumatic valve disease as a result of prolonged life expectancy and due to more effective treatment of rheumatic valve disease.[1] As a result of the increased mortality and morbidity of degenerative aortic stenosis, studies on aortic stenosis have shifted from rheumatic valve diseases to degenerative aortic stenosis. Aortic stenosis is a slowly progressive disease with a long-term asymptomatic course. On the other hand, when the disease progresses from asymptomatic to symptomatic, it shows a rapid progression.

Although in the past the pathophysiology of degenerative aortic stenosis was defined as chronic shear stress and passive calcium deposition, it is now described as a complex process consisting of mechanical stress, basement membrane damage, chronic lipoprotein deposition, inflammation, osteoblastic transformation, valvular cell apoptosis, and active valve calcification.[1-7] Histologic examination of sclerotic aortic valves has shown that, similar to atherosclerotic plaques, sclerotic areas have high concentrations of oxidative low-density lipoprotein (LDL), small dense LDL, and lipoprotein (a).[8] In addition, tumor necrosis factor alpha,[9]

macrophages,[10] mast cells, CD4 T lymphocytes (CD4 cells), and CD8 T lymphocytes (CD8 cells) have also been shown to be higher in these regions.[11] In support of these studies, an association between inflammatory cell density and aortic stenosis severity, and rate of aortic stenosis progression has been demonstrated.[12] In the advanced stages of degenerative aortic stenosis, mineral deposition, and irregular proliferation of collagen fibers are observed through prostoglandins and leukotyrenes.[13,14] This process is basically similar to the development of atherosclerosis. However, there are some differences between these 2 processes.[4]

There is no effective medical treatment strategy that can slow the progression of aortic stenosis in the early stages of disease. Currently, trans-catheter aortic valve implantation and surgical aortic valve replacement are proven effective methods for the treatment of aortic stenosis.[1,15] Statins, which reduce atherosclerotic plaque burden and induce plaque calcification, have been shown not to be effective in preventing the progression of aortic stenosis.[16-18] Although some recently published studies suggest that proprotein convertase subtilisin/kexin 9[19,20] inhibitors and sodium-glucose-linked transporter 2[21,22] inhibitors may slow the progression of aortic sclerosis, the results are not sufficient to influence clinical practice.

Endocan is a chondroitin sulfate/dermatan sulfate that has an effect on many endothelium-mediated events.[23] The presence of endocan has been demonstrated in many cells where proliferation, inflammation, and neovascularization are active, notably in glandular cells and in the germinal center of lymph nodes. In the cardiovascular system, endocan has been detected in normal cardiomyocytes but not in the endocardium, mesenchymal endothelial cells, stromal fibroblasts, and large vessels.[24]

Endocan affects the balance between inflammatory and vasculoprotective reactions in the direction of inflammatory reactions. It has been stated that endocan can be used as an indicator in many pathologies progressing with endothelial cell activation and dysfunction, especially in atherosclerosis. The effects of endocan on atherosclerosis are mediated by proinflammatory cytokine production, increased microvascular permeability, and regulation of leukocyte migration.[25,26] The relationship between endocan levels and in-hospital mortality, SYNTAX score, and high-sensitivity C-reactive protein levels has been shown in ST elevation myocardial infarction patients.[27] Different studies have shown associations between endocan levels and microvascular angina,[28] coronary slow flow,[29] coronary collateral circulation,[30] coronary ectasia,[31] and cardiac syndrome X.[32,33] It has also been shown that endocan levels are increased in activated endothelial cells and atherosclerotic plaques and are related to neointima formation. Beyond its cardiac effects, endocan, which causes changes in vascular endothelial cells and microvascular bed, has been associated with many diseases, such as diabetes mellitus,[34] chronic renal failure,[35] sepsis,[36] pneumonia,[37] and Behçet's disease.[38] It has also been shown that endocan causes an increase in lymphangiogenesis and tumor vascularity through stimulation of vascular endothelial growth factor (VEGF)-A and VEGF-C in the lymphatic endothelium.[39]

In our study, we examined the relationship between degenerative aortic stenosis, which progresses in a similar pathophysiologic mechanism as atherosclerosis, and serum inflammatory markers and endocan levels.[15]

HIGHLIGHTS

- In the current medical approach, there is a trend toward the use of targeted molecules rather than systemic therapy.
- Endocan affects the balance between inflammatory and vasculoprotective reactions in the direction of inflammatory reactions. It has been stated that endocan can be used as an indicator in many pathologies progressing with endothelial cell activation and dysfunction, especially in atherosclerosis.
- In this study, no statistically significant correlation was found between serum endocan levels and the severity of aortic stenosis.
- Endocan has been significantly correlated with hemoglobin, platelet, and albumin.

METHODS

Patients aged between 65 and 80 years who were admitted to our clinic for outpatient follow-up between June 2018 and October 2021 were enrolled in this prospective cross-sectional study. Patients with known coronary artery disease, bicuspid aortic valve, rheumatic valve disease, congenital heart disease, pulmonary hypertension, reduced ejection fraction (EF) heart failure (HF) (EF ≤ 40%), mildly reduced EF HF (EF 41%-49%), rheumatic diseases, inflammatory or active infectious diseases, history of coronavirus disease 2019, or malignancy were excluded. Patients on dialysis treatment, patients receiving steroid, non-steroidal anti-inflammatory, or anti-inflammatory therapy, and patients with a history of cardiac surgery were also excluded. Finally, 155 patients who met these criteria were enrolled in the study. Patients with stenotic aortic valve structure were classified in 3 separate groups according to the peak velocities of the aortic valve, while the control group was composed of patients with normal aortic valve structure. The peak velocities were grouped as mild (2-2.9 m/s), moderate (3-3.9 m/s), and severe (≥4 m/s).[40] Written informed consent was obtained from the participants included in the study. This study was approved by the Local Ethics Committee (decision number 2018/72, dated April 4, 2018).

The presence of diabetes mellitus (patients on oral antidiabetic therapy or HbA1c ≥ 6.5), hypertension (patients on oral antihypertensive therapy or blood pressure >140/90 mm Hg), cerebrovascular accident, asthma, chronic obstructive pulmonary disease, and peripheral artery disease history were recorded at the admission of the patients. Medications taken by the patients, history of smoking (current or ex-smoker), and regular consumption of alcohol were also recorded. Body mass index (BMI) was calculated as weight (kg)/height $(cm)^2$.

In addition, an electrocardiogram (ECG) was recorded in all patients, and patients with ischemic findings on the ECG and suspected coronary artery disease were excluded from the study.

All patients were echocardiographically evaluated in detail by using Vivid S5 (GE) and Affiniti 50 (Philips) devices. Left ventricular wall thickness and left ventricular cavity diameter were measured at the level of the papillary muscle and chordae junction in the parasternal long axis view. Left ventricular outflow tract (LVOT) diameter was measured 2-3 mm below the aortic annulus in the parasternal long axis view. Ejection fraction was calculated using the modified Simpson's method. Flow velocity in the aortic valve and aortic gradients were evaluated by continuous-wave Doppler in apical 5-chamber view. Left ventricular outflow tract velocity time integral (VTI) was calculated 2-3 mm below the aortic valve by pulsed-wave Doppler. Aortic valve areas were calculated with the continuity equation ($D^2 \times 0.785 \times$ VTI LVOT/VTI aorta). The stroke volume of the patients was determined, and patients with a stroke volume index $\leq$35 mL/m^2 were excluded.

Plasma samples were stored at −80°C. Endocan levels were determined by an experienced biochemist using the enzyme-linked immunosorbent assay (ELISA) method with the Elabscience Human ESM1 (Endothelial Cell Specific Molecule 1) ELISA kit (USA). Calibrators and some samples were studied repeatedly.

Statistical Analysis

Statistical Package for Social Science Statistics software, version 26.0, was used for statistical analysis. A 1-sample Kolmogorov–Smirnov test was used to evaluate the distribution of variables. Mean and SD were defined for normally distributed quantitative data and median and interquartile ranges for non-normally distributed quantitative data. Categorical variables were expressed as percentages and frequencies. A chi-square test was used to evaluate the demographic distribution of the patients. A 1-way analysis of varriance test was used to evaluate laboratory results and endocan levels between groups. In cases of intergroup significance, a Bonferroni post-hoc analysis was performed. Pearson and Spearmen's correlation methods were used to evaluate ratio scale continuous variables and ordinal scale variables, respectively. The results were evaluated using a mean ± 1.96 SD, with a significance level of 0.05.

RESULTS

Baseline Characteristics

A total of 155 patients (90 women and 65 men) were consecutively included in this study. Thirty-nine patients were in the control group, 58 in the mild aortic stenosis group, 24 in the moderate aortic stenosis group, and 34 in the severe aortic stenosis group. Table 1 shows the demographic and clinical characteristics of the patients. There were statistical differences in age (P = .008), mineralocorticoid receptor antagonist (MRA) use (P = .033), and the number of patients with dyspnea (P < .001) and angina complaint (P < .001). The statistical difference in dyspnea and angina is due to the significant difference between the severe aortic stenosis group and the other groups (P < .001). The use of MRA is a statistically significant difference between the control group and all aortic stenosis groups (P = .033). Post-hoc analysis revealed no statistically significant difference between the aortic stenosis groups in terms of age. However, a statistically significant

Table 1. Demographic Characteristics of the Patients

Variables	Control (n = 39)	Mild Aortic Stenosis (n = 58)	Moderate Aortic Stenosis (n = 24)	Severe Aortic Stenosis (n = 34)	*P*
Age (years)	70.6 ± 4.3	74.0 ± 5.9	74.8 ± 5.1	73.1 ± 5.7	.008
Female, n (%)	22 (56.4)	34 (58.6)	17 (70.8)	17 (50.0)	.463
Height (kg)	165 (10)	163 (15)	161.5 (7)	160 (12)	.525
Weight (cm^2)	80 (13)	77.5 (15)	80 (19)	78 (22)	.739
BMI (kg/cm^2)	29.8 ± 4.7	29.5 ± 5.0	30.4 ± 6.8	30.3 ± 6.7	.868
SBP (mm Hg)	128.2 ± 14.3	136.5 ± 17.9	137.3 ± 13.5	128.7 ± 16.3	.420
DBP (mm Hg)	76.1 ± 10.5	79.3 ± 10.5	77.3 ± 8.7	73.1 ± 9.8	.126
HR (/min)	75 (10)	75 (10)	73 (9)	75 (8)	.631
AF, n (%)	3 (7.7)	6 (10.3)	2 (8.3)	4 (11.8)	.935
DM, n (%)	15 (38.5)	21 (36.2)	7 (29.2)	5 (14.7)	.111
HT, n (%)	21 (53.8)	37 (63.8)	17 (70.8)	25 (73.5)	.311
Stroke, n (%)	0 (0)	6 (10.3)	0 (0)	2 (5.9)	.084
Smoking, n (%)	1 (0.7)	8 (5.6)	2 (1.4)	7 (4.9)	.098
Asthma, n (%)	1 (2.6)	6 (10.3)	2 (8.3)	1 (2.9)	.325
COPD, n (%)	1 (2.6)	6 (10.3)	1 (4.2)	3 (8.8)	.456
OAC, n (%)	2 (5.1)	9 (15.8)	4 (16.7)	6 (18.2)	.356
Statins, n (%)	4 (10.3)	8 (13.8)	3 (12.5)	1 (2.9)	.411
ACEİ/ARB, n (%)	11 (28.8)	32 (44.4)	13 (54.2)	16 (48.5)	.056
BB, n (%)	14 (35.9)	14 (24.6)	10 (41.7)	15 (45.5)	.192
MRA, n (%)	0 (0)	2 (3.5)	4 (16.7)	3 (9.1)	.033
CCB, n (%)	8 (20.5)	16 (27.6)	4 (16.7)	7 (21.2)	.686
Nitrates, n (%)	0 (0)	2 (3.5)	1 (4.2)	0 (0)	.429
DU, n (%)	10 (25.6)	19 (33.3)	11 (45.8)	12 (36.4)	.427
OADD, n (%)	12 (30.8)	14 (24.1)	6 (25.0)	3 (9.1)	.149
ASA, n (%)	12 (30.8)	21 (36.8)	5 (20.8)	10 (30.3)	.586
PY12-inh, n (%)	3 (7.7)	3 (5.3)	0 (0)	1 (2.9)	.520
Syncope, n (%)	2 (5.1)	1 (1.7)	1 (4.2)	2 (5.9)	.739
Dyspnea, n (%)	2 (5.1)	9 (15.5)	6 (25.0)	25 (73.5)	<.001
Angina, n (%)	1 (2.6)	3 (5.2)	2 (8.3)	16 (47.1)	<.001
LVEF %	61.9 ± 2.5	61.3 ± 3.2	60.3 ± 5.4	60.5 ± 4.2	.284

ACE/ARB, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker; AF, atrial fibrillation; ASA, acetylsalicylic acid; BB, beta blocker; BMI, body mass index; CCB, calcium channel blockers; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; DM, diabetes mellitus; DU, diuretics; HR, heart rate; HT, hypertension; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonists; OAC, oral anticoagulant drug; OAD, oral antidiabetic drug; SBP, systolic blood pressure.

difference was found between the control group and the mild and moderate aortic stenosis groups in terms of age. In contrast, the rest of the variables, as shown in Table 1, were not significantly different between aortic stenosis groups.

Laboratory Findings

Peripheral blood samples were obtained after 8 hours of fasting, and hemograms and biochemical parameters were evaluated during outpatient clinic visits. Table 2 shows the laboratory and echocardiographic findings. Endocan levels were 17.3 ng/mL ± 6.3 in the control group, 17.6 ng/mL ± 8.7 in the mild aortic stenosis group, 16.3 ng/mL ± 3.8 in the moderate aortic stenosis group, and 15.2 ng/mL ± 5.9 in the severe aortic stenosis group ($P = .396$). There was no statistically significant difference in endocan levels between the groups. However, albumin levels showed a statistically significant difference between the groups ($P = .018$). This difference in albumin levels was due to the difference between the control group and the severe aortic stenosis groups.

Table 3 shows the correlation between endocan levels, inflammatory markers, and aortic stenosis parameters in patients with aortic stenosis. There was a positive correlation between endocan levels and Hg ($r = 0.308$, $P = .001$), PLT ($r = 0.320$, $P < .001$), and Alb ($r = 0.206$, $P = .026$) levels. There was a negative correlation between Hg and aortic gradients [Ao maximum gradient ($r = -240$, $P = .01$), Ao mean gradient ($r = 0.235$, $P = .011$)], while a positive correlation was found for aortic valve area ($r = 0.187$, $P = .044$). Albumin was negatively correlated with Ao maximum velocity ($r = -0.184$, $P = .047$). There was also a negative correlation between neutrophil -to-lymphocyte ratio (NLR) level and albumin ($r = -298$, $P = .001$).

DISCUSSION

Currently, there is no effective medical treatment strategy to prevent the progression of aortic stenosis. In the current medical approach, there is a trend toward the use of targeted molecules rather than systemic therapy. In this study, we investigated the relationship between aortic stenosis and endocan and serum inflammatory markers. There was no correlation between the severity of aortic stenosis and serum endocan levels.

The association between serum endocan levels and coronary artery disease has been demonstrated in many studies in different patient groups.[41] Although aortic stenosis and atherosclerosis seem to be different entities, they share a similar pathophysiologic mechanism with inflammation at its core. However, the fact that a process in which calcification is more prominent than inflammation in the advanced stages of aortic stenosis and inflammation rather than calcification is more prominent in atherosclerotic plaques may explain the results of our study. In support of our findings, in a study in which aortic atheromas and stenotic aortic valves were evaluated by computerized tomography (CT) calcium scoring and positron emission tomography (PET), it was shown that calcium deposition was more intense in stenotic aortic valves, whereas inflammation was more prominent in atherosclerotic plaques.[42] These findings might have been associated with the lack of efficacy of statins in preventing the progression of aortic stenosis.[42] Furthermore, the fact that endocan was not detected in the endocardium, mesenchymal endothelial cells, stromal fibroblasts, and large

Table 2. Laboratory and Echocardiographic Findings of the Patients

Variables	Control (n = 39)	Mild Aortic Stenosis (n = 58)	Moderate Aortic Stenosis (n = 24)	Severe Aortic Stenosis (n = 34)	*P*
Hg (g/dL)	12.95 ± 1.48	13.0 ± 1.65	12.81 ± 1.39	12.17 ± 1.54	.077
WBC (×10³/μL)	7.09 ± 1.94	7.10 ± 2.03	7.70 ± 2.52	7.58 ± 1.84	.468
Neut (×10³/mL)	4.3 ± 1.53	4.54 ± 1.66	4.74 ± 2.20	4.76 ± 1.32	.628
LYMP (×10³/mL)	2.03 ± 0.59	1.96 ± 0.71	1.77 ± 0.67	1.96 ± 0.83	.543
NLR	2 (1.01)	2.48 (1.5)	2.59 (2.08)	2.34 (1.92)	.207
PLT (×10³/mL)	241 (129)	261 (96.3)	255 (106.8)	258 (142.3)	.941
RDW (%)	14.1 (2)	14.2 (1.7)	14.4 (1.5)	14.55 (2.3)	.241
CRP (mg/L)	3.3 (3)	3.27 (2.25)	6.4 (7.75)	3.23 (9.95)	.094
ALB (g/dL)	4.28 ± 0.36	4.14 ± 0.34	4.04 ± 0.40	4.03 ± 0.39	.018
HBA1C (%)	6.1 (1)	6.03 (1.1)	5.9 (1.2)	5.73 (0.8)	.051
ALT (IU/L)	16 (10)	15 (8)	13.5 (6)	12.5 (6)	.073
AST (IU/L)	18 (6)	18 (8)	17 (7)	18.5 (8)	.456
TC (mg/dL)	204.15 ± 47.90	201.93 ± 43.87	206.13 ± 48.32	202.41 ± 44.82	.982
LDL (mg/dL)	125.13 ± 41.118	119.71 ± 35.25	120.51 ± 33.56	123.48 ± 34.20	.893
HDL (mg/dL)	52.90 ± 11.54	54.59 ± 14.65	57.25 ± 13.38	52.30 ± 14.84	.532
TG (mg/dL)	126 (60)	147 (79)	115.5 (127)	132.5 (125)	.880
GFR (mL/min)	67.76 ± 14.14	70.66 ± 14.90	71.29 ± 13.49	65.06 ± 18.07	.296
Endocan ng/mL	17.27 ± 6.31	17.60 ± 8.67	15.25 ± 3.8	15.16 ± 5.85	.396
AA (m/s)	1.39 ± 0.24	2.42 ± 0.27	3.4 ± 0.31	4.51 ± 0.42	<.001
Ao.max.grd (mm Hg)	8.03 ± 2.76	24.03 ± 7.05	46.55 ± 8.6	81.96 ± 15.7	<.001
Ao.mean.grd (mm Hg)	3.92 ± 1.64	12.49 ± 4.27	27.74 ± 7.67	47.55 ± 12.17	<.001
AVA (cm²)	3.31 ± 0.99	2.3 ± 0.6	1.54 ± 0.4	0.95 ± 0.28	<.001

ALB, Albumin; AV, aortic velocity; AVA, aortic valve area; BG, blood glucose; CRP, C-reactive protein; GFR, glomerular filtration rate; HDL, high-density lipoprotein cholesterol; HG, hemoglobin; max grad., aortic valve maximum gradient; mean grad., aortic valve mean gradient; Neut, neutrophil; NLR, neutrophil-to-lymphocyte ratio; LDL, low-density lipoprotein cholesterol; LYMP, lymphocyte; PLT, platelet; RDW, red cell distribution width; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

Table 3. Correlation of Endocan, Inflammatory Markers, and Aortic Stenosis Parameters in Patients with Aortic Stenosis

Variables	Endocan (ng/mL)	AV (m/s)	Ao-max Grd (mm Hg)	Ao-mean Grd (mm Hg)	AVA	WBC (×10³/µL)	HG (g/dL)	PLT (×10³/mL)	NEUT (×10³/mL)	ALB (g/dL)	CRP (mg/L)	NLR	HbA1c (%)
Endocan (ng/mL)	1												
AV (m/s)	−0.140 0.134	1											
Ao-max Grd (mm Hg)	−0.143 0.124	0.988 <0.001	1										
Ao-mean Grd (mm Hg)	−0.133 0.155	0.960 <0.001	0.970 <0.001	1									
AVA (cm²)	0.119 0.204	−0.822 <0.001	−0.793 <0.001	−0.784 <0.001	1								
WBC (×10³/µL)	0.162 0.083	0.099 0.292	0.104 0.267	0.069 0.461	−0.146 0.119	1							
Hg (g/dL)	0.308 0.001	−0.237 0.010	−0.240 0.010	−0.235 0.011	0.187 0.044	0.162 0.083	1						
PLT (×10³/mL)	0.320 <0.001	−0.046 0.624	−0.063 0.502	−0.032 0.731	0.004 0.966	0.278 0.003	−0.081 0.386	1					
NEUT (×10³/mL)	0.173 0.064	0.062 0.506	0.060 0.525	0.044 0.636	−0.105 0.264	0.698 <0.001	−0.043 0.647	0.350 <0.001	1				
Alb (g/dL)	0.206 0.026	−0.184 0.047	−0.178 0.057	−0.182 0.051	0.129 0.169	−0.118 0.209	0.414 <0.001	−0.034 0.716	−0.303 0.001	1			
CRP (mg/L)	0.079 0.401	0.161 0.84	0.162 0.082	0.158 0.090	−0.085 0.363	0.199 0.033	−0.035 0.707	0.168 0.071	0.206 0.026	−0.241 0.009	1		
NLR	−0.035 0.711	0.102 0.274	0.103 0.273	0.099 0.290	−0.079 0.397	0.170 0.069	−0.078 0.405	0.089 0.342	0.594 <0.001	−0.298 0.001	0.214 0.021	1	
HbA1c (%)	0.115 0.219	−0.155 0.097	−0.176 0.059	−0.173 0.063	0.059 0.531	0.091 0.329	−0.013 0.887	0.139 0.138	−0.017 0.852	−0.060 0.520	0.075 0.424	−0.166 0.075	1

ALB, albumin; Ao-max Grd, aortic valve maximum gradient; AV, aortic velocity; AVA, aortic valve area; CRP, C-reactive protein; HG, hemoglobin; Neut, neutrophil; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; WBC, white blood cell.

vessels may have been responsible for the lack of association between endocan and aortic stenosis. However, in this study, a statistically significant correlation was found between endocan levels, which have been proven to be associated with inflammatory conditions, and Hg, PLT, and Alb.[43]

Study Limitations

The relatively limited population is the main limitation of this study. Dobutamine stress echocardiography was not performed during the echocardiographic evaluation. However, this did not affect the results since patients with low-flow aortic stenosis were not included in our study. The fact that the calcium score was not used in the evaluation of aortic stenosis is another limitation of our study. Individuals with known coronary artery disease were not included in our study. Although individuals with known coronary artery disease were not included in our study, no additional evaluation was performed to exclude coronary artery disease during the evaluation of the patients. This was another limitation of our study.

CONCLUSION

In this study, no statistically significant correlation was found between serum endocan level and the severity of aortic stenosis. On the other hand, a statistically significant correlation was found between endocan levels and Hg, Plt, and Alb. This study evaluating a molecule that may play an effective role in the diagnosis and treatment of aortic stenosis is valuable in terms of guiding other researchers.

Ethics Committee Approval: The present study was conducted in accordance with the guidelines proposed in the Declaration of Helsinki and has been approved by the Balıkesir University Faculty of Medicine Ethics Committee (decision number 2018/72, dated April 4, 2018).

Informed Consent: Written informed consent form was obtained from the patients included in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.E.A., E.A., O.A., T.Y.; Design – D.E.A., E.A., T.K., O.S., S.E.Y.; Supervision – D.E.A., E.A., T.K., O.S., A.N., A.Y.; Resources – D.E.A., E.A., O.A., H.K.; Materials – D.E.A., O.S., T.Y., S.E.Y.; Data Collection and/or Processing – D.E.A., E.A., T.K., O.S., A.N., A.Y., H.K., M.G.; Analysis and/or Interpretation – D.E.A., E.A., T.K., T.Y., S.E.Y., A.Y.; Literature Search – D.E.A., O.S., O.A., S.E.Y.; Writing – D.E.A., T.K., O.S., O.A., A.N., A.Y., M.G.; Critical Review – D.E.A., E.A., T.K., T.Y., A.N., H.K., M.G.

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