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The Relationship Between Serum Endocan Level and Aortic Elastic Properties in Patients With Newly Diagnosed Essential Hypertension

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Abstract

Endothelial dysfunction plays role in the generation of both essential hypertension (EH) and aortic stiffness. We evaluated the relationship between serum endocan level and aortic elastic properties (AEPs) assessed with the aortic strain, aortic distensibility, and aortic stiffness index by echocardiography. Newly diagnosed EH patients (n = 67) and controls (n = 70) were included in the study. The EH group was subdivided into stage 1 and 2 EH groups. A higher endocan level was found in the EH group, compared to the controls (34.2 ± 13.0 vs 24.1 ± 7.3 ng/mL, respectively, $P < .001$). All the AEP parameters were worse in the EH group, compared to the controls. Further, endocan levels correlated with aortic distensibility ($r = -0.305$, $P < .001$) and aortic strain ($r = -0.181$, $P = .038$), but not with aortic stiffness index ($r = 0.162$, $P = .064$) in the whole study population. Aortic elastic properties deteriorate and serum endocan level increases in patients with EH. Moreover, serum endocan level shows a correlation with deteriorated AEPs, and hence may a surrogate marker of escalating aortic stiffness in patients with newly diagnosed EH.

Keywords

serum endocan level, aortic stiffness, essential hypertension

Introduction

Essential hypertension (EH) is a major risk factor for heart failure, stroke, kidney failure, and myocardial infarction.[1,2] While 1.13 billion adults were given the diagnosis of hypertension throughout the world in 2015,[3] its prevalence is rapidly escalating so that the ultimate prevalence is expected to rise up to 1.56 billion adults by 2025.[4]

Endocan is coded by endothelial cell-specific molecule 1 gene and synthesized from endothelial cells as a result of acute or chronic inflammation.[5] Upon secretion, it binds to the lymphocyte function-associated antigen-1 (LFA-1) to exert a negative effect on LFA-1 interaction with endothelial intercellular adhesion molecule-1, thereby hindering leukocyte migration. Endocan also serves as a regulatory molecule of such endothelial and leukocyte cellular activities as adhesion, migration, proliferation, and neovascularization both in health and disease.[6] The expression and secretion of endocan is regulated by a number of cytokines and growth factors, which implicate it in several disease conditions, including diabetes mellitus, hypertension, preeclampsia, and tumorogenesis.[6-9] Therefore, endocan has emerged as surrogate marker of endothelial dysfunction.[10]

As in other arteries, EH also exerts detrimental effects on the aorta mainly through endothelial dysfunction and premature remodeling in the vascular medial layer. Previous studies demonstrated that the aorta becomes stiffer in hypertensive patients compared to healthy participants, and even in nondipper EH patients compared to dipper EH patients.[11] Moreover, other studies suggested a deteriorated cardiovascular performance and increased cardiovascular end points as aortic stiffness increases in patients with hypertension.[12-14]

Although the correlation of aortic stiffness with EH and even the circadian pattern of EH is well recognized, its correlation with serum endocan level in EH patients has yet to be elucidated. In the present study, our primary aim was to assess the relationship between serum endocan levels and the aortic elastic properties (AEPs) in patients with newly diagnosed with EH.

Materials and Methods

Study Population

Our study is single-center, cross-sectional, and prospective in nature. A total of 67 consecutive patients (36 females and 31

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males; mean age: 50.9 ± 9.4 years) admitting to our cardiology outpatient clinic between April 2018 and August 2018 and diagnosed with new EH were included in the study. Moreover, 70 sex-matched normotensive healthy volunteers (35 females and 35 males; mean age: 45.3 ± 11.6 years) were enrolled as the control group. The patients in the EH group had not been on any antihypertensive medication before. All the study participants underwent a thorough physical examination and a detailed inquiry regarding their medical history. Body-mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Among the exclusion criteria were the history of overt diabetes mellitus, severe renal impairment, atherosclerotic cardiovascular disease, endocrine pathology, acute infections or chronic inflammatory diseases, cerebrovascular diseases, history of any anxiety disorder, alcohol or substance addiction, and recent use of vitamin supplementation, anti-inflammatory, or steroid drugs. Informed consent was obtained from each participant. Our study protocol complies with the ethical rules set by the Declaration of Helsinki and the local ethics committee approved our study protocol.

Blood Pressure Measurement and Diagnosis of EH

Office blood pressure (BP) was measured using a mercury sphygmomanometer (Erka Perfect Aneroid, Berlin, Germany) in a quiet environment, with the participant in a sitting position after at least 10 minutes rest. Moreover, 2 more measurements were performed with 5-minute intervals to obtain a total of 3 BP readings. These readings were then averaged to end up with the ultimate BP measurement. All the measurements were performed in the morning between 8 and 10 am. The patients with averaged BP readings $\geq$140/90 mm Hg in the absence of any secondary disease condition likely to induce hypertensive response were diagnosed as EH. Furthermore, the patients in the EH group were subdivided into stage 1 and 2 subgroups, on the basis of their BP readings (systolic BP [SBP] between 140 and 159 mm Hg and diastolic BP [DBP] between 90 and 99 mm Hg for stage 1; SBP between 160 and 179 mm Hg and DBP between 100 and 109 mm Hg for stage 2). Since there were only 6 patients newly diagnosed with stage 3 EH (SBP $\geq$180 mm Hg and DBP between $\geq$110 mm Hg) encountered within the predefined study period, they were not enrolled in the study.

Echocardiography and Assessment of the AEPs (Aortic Stiffness)

All the study participants were subjected to a comprehensive echocardiographic evaluation using a Vivid S5 (GE Vingmed Ultrasound AS, Horten, Norway) by an experienced cardiologist blinded to the study protocol and the participants' clinical data.

The left ventricular dimensions, wall thicknesses, and left atrial diameters were measured in the parasternal long-axis view. Left ventricular ejection fraction (LVEF) was calculated using the modified Simpson's rule. In apical 4 chamber view, early (E) and late (A) diastolic transmitral velocities as well as deceleration time of E velocity were measured with a sample volume located between the tips of the mitral leaflets using pulsed wave Doppler. Moreover, pulse wave tissue Doppler imaging was used with sample volume at the septal and lateral sides of the mitral annulus, thus obtaining respective septal and lateral early (E′) and late (A′) diastolic mitral annular velocities. Then, E/E′ was calculated for each participant. All the conventional echocardiographic examinations were performed according to the standards of the American Society of Echocardiography.[15]

In the parasternal long-axis view, both systolic and diastolic inner diameters of the ascending aorta were measured via M-mode echocardiography 3 cm above the aortic annulus.[16]

The aortic systolic diameter (AoSD) was measured during the maximum anterior motion of the aorta, and the aortic diastolic diameter (AoDD) was measured at the peak of the QRS complex simultaneously.[17]

The echo parameters regarding the AEPs were measured on the basis of 3 consecutively recorded cardiac cycles and 3 measurements were averaged to obtain the ultimate value. The aortic diameter change was calculated by abstracting AoSD from AoDD. The parameters pertaining to the aortic elasticity were calculated by using the formulas as follows: Aortic strain (AS) (%) = (AoSD − AoDD) × 100/AoDD; Aortic stiffness (β) index = ln (SBP/DBP)/(AoS − AoD)/AoD, the ratio of ln (systolic/diastolic pressures) to (relative change in diameter), where "ln" stands for the natural logarithm; and Aortic distensibility (AoD) ($cm^2/dyn/10^3$) = 2 × [100 × (AoSD-AoDD)/AoDD)]/SBP−DBP.[18,19]

Laboratory Analysis

Whole blood was collected after at least 12 hours of hunger through venipuncture into tubes without additives and the serum was separated from the cells by centrifuging at 3000 × *g* for 10 min. The serum was stored at −80°C until assayed. The serum concentration of endocan was measured using a commercially available enzyme-linked immunosorbent assay kit (CUSABIO, Wuhan, People's Republic of China) according to the manufacturer's instructions. Samples were diluted 10-fold into the dilution buffer provided. The detection limit of the assay was 0.039 ng/mL (range: 0.156-10 ng/mL). All samples were assayed in duplicate. The absorbance was measured at 450 nm with a SPECTRO star Nano microplate reader (BMG Labtech, Offenburg, Germany). The data were processed with the MARS software (BMG Labtech) and endocan results were calculated based on the standard curve and multiplied by the sample dilution factor.

Statistical Analysis

The study data was analyzed by using SPSS version 21.0 software for Windows (IBM SPSS Statistics for Windows version 21.0. (IBM Corp, Armonk, New York). The Kolmogorov-Smirnov test was used to assess the normality of the quantitative variables. The qualitative variables, such as smoking or gender, on the other hand, were analyzed using a χ^2 test.

Table 1. Demographic and Echocardiography Characteristics of the Study Groups, Together With a Pair-wise Comparison.[a]

Variables	Controls (n = 70)	Stage 1 EH, Group (n = 35)	Stage 2 EH, Group (n = 32)	*P*
Age (years)	45.3 ± 11.6a	49.5 ± 7.9ab	52.5 ± 10.82b	.005
Gender (Female, %)	35 (50%)	18 (51.4%)	18 (56.3%)	.841
Height (cm)	167.9 ± 9.3	165.7 ± 8.1	168.1 ± 9.5	.453
Weight (kg)	76.2 ± 13.0a	80.8 ± 12.5ab	85.1 ± 14.8b	.007
BMI (kg/m^2)	27.08 ± 4.63a	29.45 ± 4.28b	30.12 ± 4.59b	.003
Smoker (%)	24 (34.3%)	11 (31.4%)	10 (31.3%)	.935
GFR ($mL/min/1.73\text{-}m^2$)	98.2 ± 16.6	91.1 ± 13.8	91.0 ± 13.8	.053
Total cholesterol level (mg/dL)	185.8 ± 38.3	195.7 ± 31.1	197.4 ± 28.8	.264
Triglyceride level (mg/dL)	156.1 ± 118.9	208.7 ± 149.4	178.8 ± 77.4	.161
LDL-C (mg/dL)	106.9 ± 34.1	113.2 ± 31.9	112.4 ± 25.6	.625
HDL-C (mg/dL)	49.0 ± 13.3	44.9 ± 13.9	50.6 ± 17.0	.315
WBC ($\times 10^9/L$)	7.73 ± 1.80	8.60 ± 2.01	8.19 ± 2.04	.096
Hb (g/dL)	14.5 ± 1.8	14.9 ± 1.7	14.4 ± 1.9	.535
Plt ($\times 10^9/L$)	256 ± 62	280 ± 57	266 ± 63	.168
Endocan level (ng/mL)	24.1 ± 7.3a	34.3 ± 13.4b	34.1 ± 12.7b	<.001
LVEDD (mm)	46.11 ± 3.33a	45.62 ± 3.03a	48.09 ± 3.54b	.006
LVESD (mm)	29.48 ± 2.16a	28.85 ± 2.00a	31.12 ± 3.58b	.001
LVEF (%)	63.65 ± 2.84	64.05 ± 2.15	63.43 ± 2.46	.606
AoSD (mm)	32.10 ± 3.69a	32.82 ± 3.76ab	33.96 ± 3.14b	.044
AoDD (mm)	29.14 ± 3.71a	30.45 ± 3.74ab	31.56 ± 3.19b	.006
AoDC (mm)	2.95 ± 0.62a	2.37 ± 0.59b	2.40 ± 0.49b	<.001
IVS (mm)	9.32 ± 0.91a	9.74 ± 1.19ab	10.12 ± 0.97b	.001
PWT (mm)	9.32 ± 0.91a	9.74 ± 1.19ab	10.12 ± 0.97b	.001
LA diameter (mm)	32.71 ± 2.75a	33.71 ± 3.33ab	34.31 ± 2.97b	.031
Transmitral E velocity (cm/s)	80.41 ± 16.87a	68.22 ± 21.55b	69.90 ± 17.43b	.002
Transmitral A velocity (cm/s)	67.00 ± 14.45a	84.54 ± 24.71b	83.87 ± 17.90b	<.001
EDT (ms)	153.62 ± 12.49	158.31 ± 16.69	156.06 ± 19.87	.337
E′ septal (cm/s)	88.67 ± 20.03a	74.88 ± 25.23b	68.34 ± 13.05b	<.001
A′ septal (cm/s)	69.85 ± 21.34a	97.71 ± 21.23b	95.28 ± 19.96b	<.001
E′ lateral (cm/s)	114.38 ± 24.99a	99.05 ± 33.09b	81.62 ± 22.84c	<.001
A′ lateral (cm/s)	86.21 ± 24.69a	106.71 ± 23.10b	101.03 ± 20.28b	<.001
E/E′ septal	0.92 ± 0.17	0.96 ± 0.39	1.04 ± 0.29	.123
E/E′ mean	11.40 ± 2.30a	15.31 ± 2.88b	14.59 ± 3.46b	<.001
Aortic strain (%)	10.30 ± 2.70a	7.65 ± 2.42b	7.67 ± 1.85b	<.001
Aortic stiffness (β) index	1.62 ± 0.46a	2.68 ± 0.19b	2.40 ± 0.67b	<.001
Aortic distensibility ($cm^2/dyn/10^3$)	5.07 ± 1.58a	2.76 ± 0.82b	2.17 ± 0.55c	<.001

[a] There is no statistically significant difference between the pairs marked with the same letter within the same line ($P > .05$).

Abbreviations: A′, late diastolic mitral annular velocity; AoDC, aortic diameter change; AoDD, aortic diastolic diameter; AoSD, aortic systolic diameter; BMI, body-mass index; E′, early diastolic mitral annular velocity; EDT, E-deceleration time; EH, essential hypertension; GFR, glomerular filtration rate; Hb, hemoglobin; HDL-C, high-density lipoprotein cholesterol; IVS, interventricular septum thickness; LA, left atrium; LDL-C, low-density lipoprotein cholesterol; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; PWT, posterior left ventricular wall thickness; WBC, white blood cell count; Plt, platelet count.

Comparison of 2 groups was performed with independent *t* test, while 1-way analysis of variance was utilized in the comparison of >2 groups. Duncan post hoc test was applied so as to classify the groups exhibiting statistical difference. A Pearson correlation analysis was used to assess any possible relationship between serum endocan levels and other parameters. A $P > .05$ was considered significant.

Results

Our study included a total of 137 participants: 70 in the control group and 67 in the EH group. The EH group was further divided into 2 subgroups as stage 1 EH group (35 patients) and stage 2 EH group (32 patients), on the basis of their BP. Comparison of the baseline demographic characteristics of these 3 groups, as well as their pair-wise comparisons, is shown in Tables 1 and 2. As evident in the tables, there was a statistically significant age difference between the groups ($P = .005$). The patients in the stage 2 EH group were slightly older, compared to the stage 1 EH and the control groups. There was no significant gender differentiation between the groups, and gender distribution was homogeneous through the groups. There was no significant difference between the 3 groups with regard to height, smoking habit, glomerular filtration rate, glucose level, white blood cell count, hemoglobin, platelet, and total cholesterol and high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride levels. The participants in the EH group had greater weight and BMI.

Table 2. Demographic and Echocardiography Characteristics of the Essential Hypertension and Control Groups.

Variables	Control Group (n = 70)	Essential Hypertension, Group (n = 67)	*P*
Age (years)	45.3 ± 11.6	50.9 ± 9.5	.002
Gender (Female, %)	35 (50.0)	36 (53.7)	.662
Height (cm)	167.9 ± 9.3	166.8 ± 8.8	.482
Weight (kg)	76.21 ± 13.01	82.89 ± 13.73	.004
BMI (kg/m^2)	27.1 ± 4.6	29.8 ± 4.4	.001
Smoker (%)	24 (34.3)	21 (31.3)	.714
Glucose (mg/dL)	93.9 ± 12.8	97.0 ± 9.9	.130
GFR ($mL/min/1.73\text{-}m^2$)	98.2 ± 16.6	91.1 ± 13.7	.009
Total cholesterol level (mg/dL)	186 ± 38	197 ± 30	.104
Triglyceride level (mg/dL)	156 ± 119	195 ± 121	.094
LDL-C (mg/dL)	107 ± 34	113 ± 29	.334
HDL-C (mg/dL)	49 ± 13	48 ± 16	.596
WBC ($\times 10^9/L$)	7.73 ± 1.80	8.40 ± 2.02	.046
Hb (g/dL)	14.5 ± 1.8	14.7 ± 1.8	.581
Plt ($\times 10^9/L$)	256 ± 62	273 ± 60	.101
Endocan level (ng/mL)	24.1 ± 7.3	34.2 ± 13.0	<.001
LVEDD (mm)	46.11 ± 3.33	46.80 ± 3.48	.237
LVESD (mm)	29.48 ± 2.16	29.94 ± 3.06	.316
LVEF (%)	63.65 ± 2.84	63.76 ± 2.30	.815
AoSD (mm)	32.10 ± 3.69	33.37 ± 3.50	.041
AoDD (mm)	29.14 ± 3.71	30.98 ± 3.50	.003
AoDC (mm)	2.95 ± 0.62	2.38 ± 0.54	<.001
IVS (mm)	9.32 ± 0.91	9.92 ± 1.10	.001
PWT (mm)	9.32 ± 0.91	9.92 ± 1.10	.001
LA diameter (mm)	32.71 ± 2.75	34.00 ± 3.15	.012
Transmitral E velocity (cm/s)	80.41 ± 16.87	69.02 ± 19.56	<.001
Transmitral A velocity (cm/s)	67.00 ± 14.45	84.22 ± 21.57	<.001
EDT (ms)	153.62 ± 12.49	157.23 ± 18.17	.176
E′ septal (cm/s)	88.67 ± 20.03	71.76 ± 20.46	<.001
A′ septal (cm/s)	69.85 ± 21.34	96.55 ± 20.51	<.001
E′ lateral (cm/s)	114.38 ± 24.99	90.73 ± 29.77	<.001
A′ lateral (cm/s)	86.21 ± 24.69	104.00 ± 21.82	<.001
E/E′ septal	0.92 ± 0.17	1.00 ± 0.35	.093
E/E′ mean	11.40 ± 2.30	14.97 ± 3.17	<.001
Aortic strain (%)	10.30 ± 2.70	7.66 ± 2.15	<.001
Aortic stiffness (β) index	1.62 ± 0.46	2.55 ± 1.65	<.001
Aortic distensibility ($cm^2/dyn/10^3$)	5.07 ± 1.58	2.48 ± 0.76	<.001

Abbreviations: A′, late diastolic mitral annular velocity; AoDC, aortic diameter change; AoDD, aortic diastolic diameter; AoSD, aortic systolic diameter; BMI, body-mass index; E′, early diastolic mitral annular velocity; EDT, E-deceleration time; GFR, glomerular filtration rate; Hb, hemoglobin; HDL-C, high density lipoprotein cholesterol; IVS, interventricular septum thickness; LA, left atrium; LDL-C, low density lipoprotein cholesterol; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-systolic diameter; LVEF, left ventricular ejection fraction; PWT, posterior left ventricular wall thickness; WBC, white blood cell count; Plt, platelet count.

Serum endocan level was greater in the EH group compared to the controls (34.2 ± 13.0 vs 24.1 ± 7.3 ng/mL, respectively, $P < .001$); however, a pair-wise comparison of endocan level between the EH subgroups did not yield a significant difference (34.3 ± 13.4 ng/mL for stage 1 EH group and 34.1 ± 12.7 ng/mL for stage 2 EH group, $P > .05$).

Baseline echocardiographic and the aortic stiffness parameters of the 3 groups, together with their pair-wise comparisons, are shown in Tables 1 and 2. There was no significant difference regarding LVEF between the groups. As expected, AoSD and AoDD interventricular septal thickness, posterior wall thickness, and left atrial diameter were greater in the stage 2 EH group, compared to stage 1 EH and control groups. Aortic diameter change was also smaller in the stage 2 hypertension (HT) group. As for the parameters regarding left ventricular diastolic function, transmitral early (E) and late (A) velocities, early diastolic septal mitral annular velocity (E′), and E/E′ ratio were significantly greater in the EH group compared to the controls; however, pair-wise comparisons of these parameters between the EH subgroups did not show any difference. As expected, aortic stiffness (β) index was greater in the EH group compared to the controls. Furthermore, aortic distensibility and aortic strain indices were found to be lower in the EH group compared to the healthy controls. However, a pair-wise comparison of 2 (aortic strain and aortic stiffness [β] index) of these 3 parameters pertaining to aortic stiffness did not yield any significant difference between the stage 1 and 2 EH subgroups, except aortic distensibility which was

Table 3. The Correlation Between Serum Endocan Level and Demographic and Echocardiographic Characteristics Within the Essential Hypertension Group.[a]

Variables	Coefficient of Correlation (r)	P
Aortic strain (%)	0.012	.926
Aortic stiffness (β) index	0.008	.952
Aortic distensibility ($cm^2/dyn/10^3$)	−0.006	.964
Triglyceride level (mg/dL)	0.380[b]	.005
WBC ($\times 10^9$/L)	0.413[b]	.001
Hb (g/dL)	0.372[b]	.002
Plt ($\times 10^9$/L)	0.391[b]	.001

Abbreviations: Hb, hemoglobin; Plt, platelet count; WBC, white blood cell count.
[a]n = 67.
[b]Significant at 1% level.

Table 4. The Correlation Between Serum Endocan Level and Demographic and Echocardiographic Characteristics Within the Whole Study Population.[a]

Variables	Coefficient of Correlation (r)	P
A′ septal (cm/s)	0.215[b]	.013
Aortic strain (%)	−0.181[b]	.038
Aortic stiffness (β) index	0.162	.064
Aortic distensibility ($cm^2/dyn/10^3$)	−0.305[c]	<.001
Triglyceride level (mg/dL)	0.322[c]	.001
WBC ($\times 10^9$/L)	0.391[c]	<.001
Hb (g/dL)	0.186[b]	.036
Plt ($\times 10^9$/L)	0.399[c]	<.001
E/E′ mean	0.250[c]	.004

Abbreviations: A′ septal, late diastolic septal mitral annular velocity; E/E′, the ratio of early diastolic transmitral flow velocity to early diastolic mean mitral annular velocity; Hb, hemoglobin; Plt, platelet count; WBC, white blood cell count.
[a]n = 137.
[b]Significant at 5% level.
[c]Significant at 1% level.

significantly lower in stage 2 EH group compared to stage 1 EH group.

Correlation Analysis

Within the EH group, serum endocan level was found to be positively correlated with the serum triglyceride and hemoglobin levels, and white blood cell and platelet counts ($r = 0.380$, $P = .005$; $r = 0.413$, $P = .001$; $r = 0.372$, $P = .002$; $r = 0.391$, $P = .001$; respectively). On the other hand, there was no significant correlation of serum endocan level either with the 3 aortic stiffness parameters or the other echocardiographic and demographic parameters (Table 3).

Within the whole study population, serum endocan level was found to be positively correlated with septal A′, E/E′, serum triglyceride level, white blood cell, and platelet counts ($r = 0.215$, $P = .013$; $r = 0.250$, $P = .004$; $r = 0.322$, $P = .001$; $r = 0.391$, $P < .001$; respectively). On the other hand, serum endocan level was negatively correlated with the aortic strain ($r = -0.181$, $P = .038$) and aortic distensibility ($r = -0.305$, $P < .001$) indices. However, there was no significant correlation of serum endocan level with aortic stiffness (β) index ($r = 0.162$, $P = .064$), as well as the other echocardiographic and demographic parameters (Table 4).

Discussion

The main findings of our study are that serum endocan levels are raised in EH patients compared to healthy controls and that serum endocan levels show a correlation with aortic stiffness parameters (aortic distensibility and aortic strain, but not aortic stiffness [β] index). It would be rational to extrapolate from our findings that the aorta becomes stiffer as serum endocan levels increase in patients with EH. To our knowledge, this is the first study demonstrating the relationship of serum endocan level with the aortic stiffness parameters in newly diagnosed EH patients compared to healthy individuals.

Previous studies showed a robust relationship between aortic stiffness and EH. Moreover, serum endocan level was reported to escalate in patients with EH compared to healthy individuals.[8,11,20] Musialowska et al[8] showed that in 104 EH patients and 21 healthy volunteers, median serum endocan concentration was significantly greater in the EH group compared to healthy individuals. However, their EH group was composed of the patients with chronic and well-controlled EH, and the patients had already been on a median of 3 antihypertensive medications. The EH group in our study, on the other hand, was composed of patients with newly diagnosed EH. Çimen et al[11] reported an even further increase in serum endocan level in newly diagnosed HT with nondipping circadian pattern compared to those with dipping circadian pattern. As opposed to the findings of the previous studies, serum endocan level in the patients with dipper EH in their study did not show any significant difference compared to healthy controls. In our study, however, the patients with newly diagnosed EH had significantly elevated levels of serum endocan compared to the controls. The reason why serum endocan level in EH group in our study did not differ significantly between stage 1 and 2 EH groups may in part be ascribed to the fact that we had not used 24-hour ambulatory BP monitoring in order to define the stage of HT more accurately and to further document the circadian pattern of HT; we had relied solely on repeated office BP readings. In a similar study to ours,[21] office SBP but not the mean daytime SBP measured by ambulatory monitoring was reported to be an independent predictor of the AEPs assessed by carotid-femoral pulse wave velocity and aortic augmentation index. In contrast to this study, we used 3 echocardiographic parameters (aortic stiffness [β] index, aortic distensibility, and aortic strain) to assess aortic elasticity.

Aortic stiffness shows close association with such a number of conditions as atherosclerosis, acute coronary events, carotid

intima-media thickness, and end-stage renal disease.[12,22-24] These diseases share inflammation and endothelial dysfunction. Further, an association between inflammatory process, endothelial dysfunction, and HT has long been recognized. Accordingly, increased aortic stiffness is likely to be used as surrogate marker of early vascular structural remodeling, vascular inflammation, and subclinical vascular sclerosis in patients with EH.[24,25] In another point of view, increased SBP is quite likely to serve as a crude marker of an increased arterial and aortic stiffening,[26] since exposure to a higher BP can provoke chronic aortic stiffening through escalated arterial wall stress together with the resultant primary structural remodeling in the aortic wall itself and the raised vascular smooth muscle tone.[13,27] Thereby, increased serum endocan level is likely to serve as a marker of a stiffer aorta as well as an increased vascular inflammation. Although aortic distensibility and aortic strain were found to correlate with serum endocan level in favor of increased aortic stiffening, there was no correlation with aortic stiffness (β) index. This situation might have resulted from the relatively small size of our study population and the fact that we did not utilize a 24-hour ambulatory BP monitoring. Accordingly, studies conducted with a larger population are needed.

Our study has limitations. First, our study population was relatively small. Second, we did not use 24-hour ambulatory BP monitoring and relied solely on the repeated office BP readings. Third, we assessed the AEPs by only 3 echo parameters, and did not seek correlation of these parameters with such other AEP indices as carotid-femoral pulse wave velocity and aortic augmentation index. Fourth, we did not differentiate between white coat hypertension and EH; a proportion of high office BP readings may be due to white coat hypertension.

In conclusion, serum endocan levels and aortic stiffness are increased in patients with EH diagnosed by repeated office BP readings. Moreover, serum endocan levels correlate with impaired AEPs, and may turn out to be an early sign of increased aortic stiffness. However, future prospective studies with larger populations are needed to confirm our results.

Author Contributions

M. Ç. substantially contributed to conception and design, or acquisition of data, or analysis and interpretation of data, E. S. and S. S. drafted the article or revised it critically for important intellectual content, C. U. and R. N. critically revised the manuscript, and M. E. gave final approval of the version to be published.

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