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Association of dipping pattern of blood pressure and atherosclerotic burden of coronary arteries in hypertensive patients

Aim	The aim of this study was to determine the association between the dipping pattern of BP and coronary artery disease in hypertensive patients.
Material and methods	A total of 356 hypertensive patients were included in the study. The results of ambulatory BP monitoring, echocardiography, and coronary computerised tomographic angiography were evaluated retrospectively. The patients were divided into two groups on the basis of their ambulatory BP monitoring: 1) patients with the dipping pattern of BP; 2) patients with the non-dipping pattern (NDP).
Results	Among the 356 patients, 145 were male (40.7%). The smoking status was higher in patients with NDP (p=0.023). The statin usage in patients with the dipping pattern was higher in patients with NDP (p=0.027). There were no significant differences in the echocardiographic findings. 58.6% of the patients without plaque formation had the dipping pattern of BP (p<0.05), however 84.4% of patients with >50% plaque formation had the NDP of BP (p<0.001).
Conclusion	The NDP of BP might be related to the increased atherosclerotic process in coronary arteries, and patients with NDP might have an increased atherosclerotic burden for coronary arteries when compared with patients with a dipping pattern.

Keywords	Atherosclerosis; coronary artery disease; dipping pattern; hypertension
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Actualization

There is lack of knowledge about the association between the dipping pattern of blood pressure and atherosclerotic process in coronary arteries. This study evaluated the association between pattern of blood pressure and atherosclerotic burden by using coronary computerized tomographic angiography. Non-dipping pattern in blood pressure was found associated with increased atherosclerotic process in coronary arteries. Non-dipping pattern might indicate increased atherosclerotic burden for coronary arteries when compared to the patients with normal dipping pattern.

Introduction

Hypertension is a leading cause of cardiovascular mortality and morbidity. In the current guidelines, hypertension is defined as follows: arterial blood pressure (BP) higher than 140/90 mm Hg; however, there are different cut-off values in certain patient groups, such as patients with diabetes mellitus [1, 2]. BP has a circadian rhythm. In healthy subjects, BP falls by 10% to 20% during the night; this is called the normal dipping pattern. Conversely, if the BP fails to decrease during sleep, this is called the non-dipping pattern (NDP) [3].

Advanced structural vascular disease, i.e., increased vascular resistance and arterial stiffness, as well as increased salt sensitivity and a high-salt diet are the main causes of NDP. NDP is associated with subclinical target organ damage [4, 5]. Guidelines clearly state that nocturnal BP should be carefully controlled in patients with diabetes mellitus. However, this situation is not clear for patients who have other risk factors. Patients with chronic kidney disease

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or obstructive sleep apnoea syndrome (OSAS) also tend to have a non-dipping pattern, and they have an increased risk of cardiovascular morbidity and mortality [6, 7]. Thus, according to current research, the NDP is associated with increased left ventricular hypertrophy and cardiovascular mortality, even in patients who do not have diabetes.

Coronary computed tomographic angiography (CTA) is a new, growing technology that provides clinicians with non-invasively obtained, detailed information about the presence, extension, and composition of obstructive and non-obstructive coronary artery disease (CAD) [8]. CTA is recommended for symptomatic patients, but it has also demonstrated increased coronary atherosclerotic burden in asymptomatic patients with high risk factors, such as diabetes, high serum low-density lipoprotein (LDL) cholesterol, or hypertension [9–11].

In this study, we used CTA to investigate the presence and extent of coronary artery plaque in patients with symptoms associated with ischemic heart disease and with dipping or non-dipping patterns of arterial BP. We also compared these patients in terms of the extent of CAD detected by coronary CTA.

Material and methods

This study was a retrospective, cross-sectional, and single center study. We evaluated the hospital system data of patients with regard to both 24-hr ambulatory BP and coronary CTA. We enrolled 356 patients with similar demographic characteristics who presented with symptoms of ischemic heart disease at our outpatient clinic from January 2017 to September 2021 The demographic and clinical characteristics of the patients were registered and analysed retrospectively. The exclusion criteria were as follows: a previous history of CAD, coronary angiography, myocardial infarction and stroke; signs of heart failure; increased heart rate or absence of sinus rhythm; poor image quality; pregnancy; inability to provide informed consent. The data was statistically analysed as described below. Informed consent was obtained from all patients in accordance with a protocol approved by the local ethics committee (decision number:2021/47).

Demographic data

Height, weight, age and gender data were obtained from the patients' questionnaires. Medical history, current medications, alcohol consumption, and smoking status were registered. Body mass index (BMI) and body surface area (BSA) were calculated. Laboratory records were retrieved from the hospital computer system. When the patients presented with symptoms related to ischemic heart disease, we evaluated the total blood count, creatinine, glucose, hemoglobin A1c, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides and C-reactive protein (CRP) before further evaluations and before non-invasive tests for ischemia.

Echocardiography

Transthoracic echocardiography was performed using an EPIQ 7 ultrasound system (Philips Medical Systems, Andover, MA, USA) for all patient with symptoms of myocardial ischemia. From the echocardiographic data, the left ventricular ejection fraction (EF) was estimated using the biplane Simpson method. Also estimated were the end-diastolic thickness of the interventricular septum (IVS) and of the left ventricular posterior wall (PW) and the end-diastolic antero-posterior diameter of the left atrium (LA).

24-hr ambulatory BP monitoring

As part of the routine evaluation, 24-hr BP monitoring was performed with a Tonoport V Holter system (GE Medical Systems, Milwaukee, WI, USA). BP was measured every 30 min from 7 am to 12 midnight and every 60 min during from 12 midnight to 7 am. A valid record was considered if there were at least 24 valid BP measurements during the day and at least 6 during the night. If the record was invalid, the patients were asked to undergo a repeat Holter monitoring the following day. The dipping pattern was defined as a 10% reduction in the mean of the systolic (SBP) and diastolic BP (DBP) during sleep as compared to the mean of the SBP and DBP during the day. All patients were advised to be asleep by approximately 12 midnight.

Coronary CTA image acquisition

Coronary CTA studies were performed using a 320-row CT scanner (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan) with a gantry rotation time of 350 ms and a minimum temporal resolution of 175 ms. Metoprolol was administered orally (50–100 mg depending on the heart rate) 1 hr before the CT acquisition to patients with a heart rate of >65 beats per minute (bpm), unless contraindicated. The scanning technique was performed according to the patient's heart rate. Prospective gating was 70% – 80% for heart rates ≤65 bpm, 30% – 80% for heart rates 66–70 bpm, 30% – 80% for heart rates of 71–74 bpm. Retrospective gating with the ECG dose modulation technique, i.e., decreasing the tube current during the systolic phase of the R-R interval, was used in patients with a heart rate of >75 bpm.

The tube voltage and tube current depended on the BMI of the patients. The tube voltage was 100 kV (BMI<23 kg/m^2), 120 kV (BMI 23–34 kg/m^2) or 135 kV (BMI>35 kg/m^2), and the tube current was 320–580 mA. A total of 60–80 ml of a non-ionic contrast agent (Iohexol, Omnipaque 350 mgI/mL, GE Healthcare Milwaukee, WI) was injected into the antecubital vein. A triphasic injection

protocol for the contrast agent was used. Firstly, 50–70 ml of the contrast agent was injected at an injection rate of 5–6 ml/s followed by 20 ml of 50% contrast/saline with the same injection rate. Subsequently, 25 ml of a saline chaser was injected at a flow rate of 3 ml/s. The scanning delay was determined using a bolus tracking technique by placing the region of interest (ROI) in the ascending aorta and setting the trigger threshold to 180 Hounsfield units (HU). All images were acquired during an inspiratory breath-hold of approximately 5 s. The raw data set was reconstructed at an R-R interval of 75%, with a slice thickness of 0.5 mm and an interval of 0.25 mm, using an iterative reconstruction algorithm. If multiple phases were acquired, additional reconstructions were explored in the case of motion artefacts to obtain images with the least motion artefacts. For processing and evaluation, the images were transferred to a remote workstation with dedicated CTA analysis software (Version 6.4, Vital Images, Minnetonka, Minn., USA).

CT image analysis

The coronary CTA image analysis was performed by two radiologists in consensus, who were experienced in the assessment of the coronary CTA and blinded to the clinical data of the patients. Coronary anatomy was assessed in a standardised manner by dividing the coronary artery tree into 17 segments according to a modified American Heart Association classification system [12]. Using curved planar reconstructions of all coronary arteries, a coronary CTA image analysis was performed. The data were analysed on a segmental, vessel, and patient basis. Firstly, image quality was evaluated subjectively on a per segment basis by using a four-point grading scale. The image quality was classified as excellent (no artefacts present, optimal depiction of coronary arteries), good (minor artefacts present), moderate (substantial artefacts, but luminal assessment possible) and poor (severe artefacts, luminal assessment impossible). The datasets considered to be of poor image quality were excluded from this study. Secondly, the assessable coronary artery segments were screened for the presence of stenosis. Patients were separated into subgroups: patients with ≤50% stenosis and patients with >50% stenosis. In addition, all patients were analysed in terms of plaque morphology. Coronary plaques were classified as non-calcified, calcified, or mixed according to their structure. The plaques were defined as 1-mm² structures within or adjacent to a vessel lumen that could be clearly distinguished from the lumen and the surrounding pericardial tissue. Plaques with no calcification were defined as non-calcified, plaques with >50% of the plaque area occupied by calcified tissue (density ≥130 HU) were defined as calcified, and plaques with ≤50% calcium were defined as mixed [13]. On a per-patient basis, >50% coronary artery stenosis was diagnosed if one or more >50% stenosis was detected, independent of the segmental location (Figure 1).

Figure 1. Figure shows coronary computed tomographic angiography findings of a 49-year-old male with non-dipping pattern of blood pressure

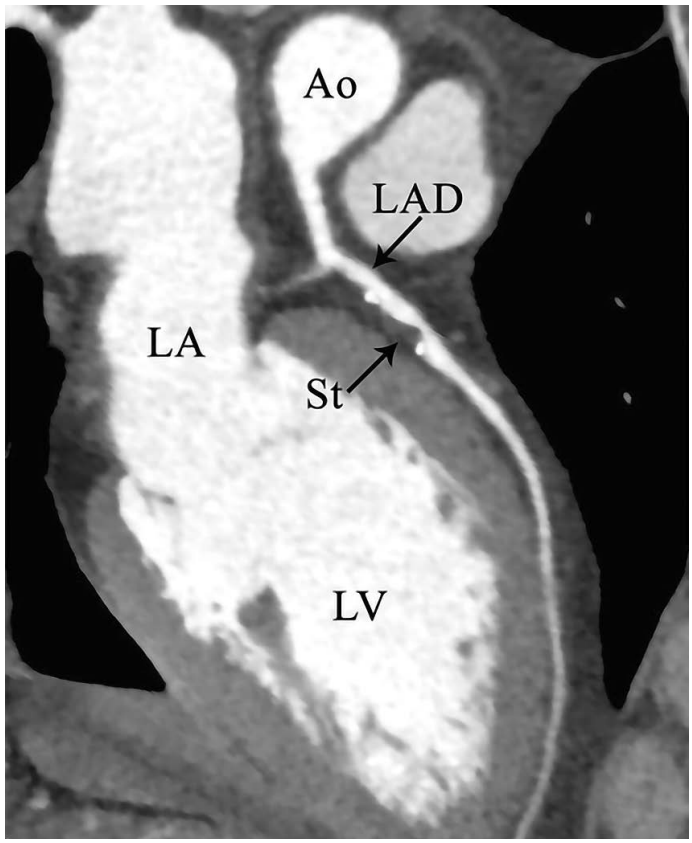

Figure shows a curved planar reconstruction image of the left anterior descending (LAD) artery. The image shows a mixed plaque that causing > 50% stenosis (St) in the proximal LAD. (Ao: aorta, LA: left atrium, LV: left ventricle).

Statistical analysis

Statistical analyses were performed using the SPSS Version 24.0 program (SPSS Inc., Chicago, Illinois, USA). Whether the variables show a normal distribution; evaluated using visual (histograms, probability curves) and analytical methods (Kolmogorov-Smirnov's or Shapiro-Wilk tests), normally distributed numerical variables were expressed as mean +- standard deviation (SD), non-normally distributed numerical variables were expressed as median (interquartile range), and categorical variables were expressed as percentages (%). The statistical analysis of the numerical variables between groups was performed with a Student's t-test or a Mann-Whitney U test, and the categorical variables were analysed using a chi-square or Fisher's exact test. A univariable logistic regression analysis was performed. This was followed by a multivariable logistic regression analysis using the variables found to be significant in the univariable analysis to determine the independent predictors of plaque and lesions <50% or ≥50%. A p value of <0.05 was considered significant.

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Table 1. Demographic and clinical data

Variable	Total (N=356)	Dipper (N=179)	Non-dipper (N=177)	p-value
Age, years	62.9±5.8	62.6±5.0	63.2±6.5	0.371
Gender (male)	145 (40.7%)	71 (39.7%)	74 (41.8%)	0.681
Smoking	88 (24.7%)	35 (19.6%)	53 (29.9%)	0.023
Height, cm	165.9±9.0	165.1±9.2	166.7±8.8	0.101
Weight, kg	83.8±15.4	82.5±15.8	85.1±14.9	0.101
BMI, (kg/m2)	30.4±5.0	30.3±5.3	30.6±4.7	0.482
BMI (kg/m^2) <25 (normal weight) 25-30 (over-weight) >30 (obese)	 56 (15.7%) 116 (32.6%) 184 (51.7%)	 31 (17.3%) 63 (35.2%) 85 (47.5%)	 25 (14.1%) 53 (29.9%) 99 (55.9%)	0.278
BSA, (m^2)	1.92±0.20	1.90±0.20	1.94±0.19	0.059
DM	59 (16.6%)	27 (15.1%)	32 (18.1%)	0.447
Heart rate, beats/min	73.5±12.7	72.0±12.0	75.0±13.3	0.119
LV ejection fraction, %	62.7±3.6	62.9±3.6	62.5±3.7	0.364
IVS thickness, mm	11.4±2.0	11.3±2.0	11.6±2.0	0.280
PW thickness, mm	10.6±1.6	10.5±1.6	10.8±1.7	0.084
ACEi or ARB	279 (78.4%)	139 (77.7%)	140 (79.1%)	0.741
CCB	182 (51.1%)	84 (46.9%)	98 (55.4%)	0.111
Beta Blocker	167 (46.9%)	80 (44.7%)	87 (49.2%)	0.399
Diuretic	229 (64.3%)	115 (64.2%)	114 (64.4%)	0.975
Other antihypertensive medication	47 (13.2%)	18 (10.1%)	29 (16.4%)	0.078
Statin	60 (16.9%)	38 (21.2%)	22 (12.4%)	0.027

Data are number (percentage), mean±standard deviation. BMI, body mass index; BSA, body surface area; DM, diabetes mellitus; IVS, interventricular; septum; PW, posterior wall; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.

Table 2. Laboratory data

Variable	Total (N=356)	Dipper (N=179)	Non-dipper (N=177)	p value
Hemoglobin, g/dl	13.6±1.6	13.8±1.6	13.5±1.7	0.213
Hematocrit, %	41.0±4.6	41.2±4.4	40.8±4.7	0.341
Leukocyte, 10^9/l	7.61±1.94	7.48±1.93	7.74±1.95	0.196
Platelet, 10^9/l	270.5±72.1	268.6±70.8	272.4±73.5	0.614
Neutrophil, mcl	4.50±1.40	4.40±1.40	4.61±1.40	0.152
Lymphocyte, 10^9/l	2.37±0.70	2.36±0.69	2.38±0.70	0.755
Creatinine, mg/dl	0.80±0.22	0.78±0.21	0.81±0.22	0.262
Glucose, mg/dl	100.0 (92.0–116.0)	101.0 (92.5–119.5)	99.5 (92.0–113.5)	0.472
Total Cholesterol, mg/dl	206.0±41.7	203.1±40.0	209.0±43.3	0.184
HDL–C, mg/dl	47.3±12.4	47.1±12.2	47.5±12.6	0.749
LDL–C, mg/dl	128.2±34.0	126.6±32.2	129.8±35.7	0.381
Triglyceride, mg/dl	144 (105–216)	141 (104–203)	146 (107–222)	0.445
HbA1c, %	6.10±1.14	5.98±1.05	6.22±1.22	0.050
CRP, mg/dl	3.3 (1.7–7.2)	2.8 (1.6–5.7)	3.6 (2.0–7.6)	0.022

Data are mean±standard deviation or median (interquartile range). HDL–C, high-density lipoprotein cholesterol; LDC–C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin; CRP, C-reactive protein.

Results

Among the 356 patients presenting with stable angina at our outpatient clinic, 145 were male (40.7%); the mean age was 62.9±5.8 yrs. On the basis of their ambulatory BP, the patients were divided into two groups: patients with a dipping pattern and patients with NDP. In all, 179 of the patients had a dipping pattern, and 177 had NDP. The demographic and clinical characteristics of the study participants are presented in Table 1, and their basal laboratory values are presented in Table 2. Age, gender, diabetes mellitus, BMI, and BSA were not significantly different between the two groups; however, the smoking status was significantly higher in patients with NDP (p=0.023). In terms of medications, no significant differences were observed between the two groups except

Table 3. Ambulatory blood pressure

Variable	Total (N=356)	Dipper (N=179)	Non-dipper (N=177)	p value
Office SBP, mmHg	160.2±30.1	157.1±29.1	163.5±31.0	0.045
Office DBP, mmHg	91.2±11.4	90.3±10.7	92.1±12.1	0.145
24-hr SBP, mmHg	144.6±19.5	141.3±19.0	147.9±19.4	0.001
24-hr DBP, mmHg	88.4±13.3	86.9±13.5	89.9±13.0	0.035
Daytime SBP, mmHg	146.4±19.4	144.8±19.4	148.2±19.3	0.099
Daytime DBP, mmHg	90.7±13.6	90.4±14.1	90.9±13.2	0.705
Nighttime SBP, mmHg	138.4±21.4	129.4±18.3	147.6±20.5	<0.001
Nighttime DBP, mmHg	81.7±13.8	76± 11.6	81.7±13.8	<0.001

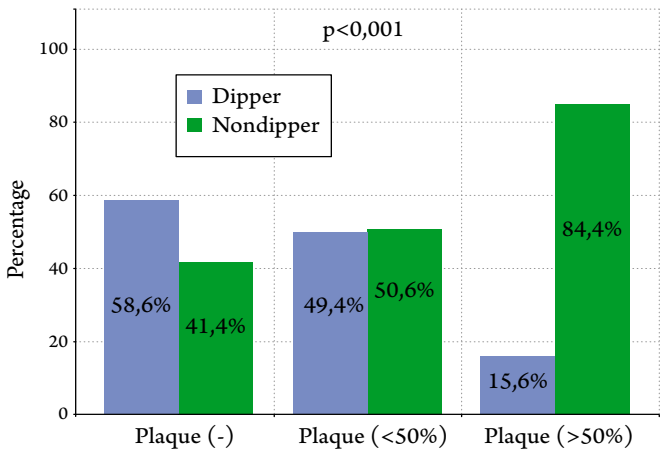
Data are mean±standard deviation. BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 4. Findings from coronary computed tomographic angiography

Variable	Total (N=356)	Dipper (N=179)	Non-dipper (N=177)	p value
Plaque	213 (59.8%)	92 (51.4%)	121 (68.4%)	0.001
Plaque >50%	32 (9.0%)	5 (2.8%)	27 (15.3%)	<0.001
Plaque with mixed morphology	110 (30.9%)	38 (21.2%)	72 (40.7%)	<0.001
Calcific plaque	128 (36.0%)	58 (32.4%)	70 (39.5%)	0.160
Non-calcific plaque	89 (25.0%)	39 (21.8%)	50 (28.2%)	0.159
Number of vessel disease				
0 (no vessel disease)	143 (40.2%)	87 (48.6%)	56 (31.6%)	0.005
1-vessel disease	87 (24.4%)	39 (21.8%)	48 (27.1%)	
2-vessel disease	57 (16.0%)	30 (16.8%)	27 (15.2%)	
3-vessel disease	60 (16.9%)	21 (11.7%)	39 (22.0%)	
4-vessel disease	9 (2.5%)	2 (1.1%)	7 (4.0%)	
Plaque number	1 (0-3)	1 (0-2)	1 (0-3)	0.005

Data are number (percentage) or mean (range).

Figure 2. Figure shows the presence of plaque depending on dipping and non-dipping pattern of blood pressure and the rate of stenosis as over 50% or less than 50% in patients depending on dipping and non-dipping pattern of blood pressure



for statins. More patients with the dipping pattern used statins (p=0.027). The echocardiographic findings are listed in Table 1. No significant differences were observed in the transthoracic echocardiographic findings between the dipping and NDP groups.

With respect to the laboratory values, creatinine, cholesterol, and complete blood count were not significantly different between the two groups. Even though the distribution of diabetes and plasma glucose were similar in the two groups, patients with NDP had higher hemoglobin A1c (p=0.05). In addition, participants with NDP had higher levels of C-reactive protein than those in the dipping pattern group (p=0.022).

The ambulatory BP measurements are summarized in Table 3. Office SBP and DBP, 24-hr SBP and DBP, daytime SBP and DBP, and night-time SBP and DBP values were registered. Patients with NDP had increased office SBP (p=0.045). There were no significant differences in daytime SBP (p=0.099) and DBP (p=0.705). In contrast, patients with NDP had increased night-time SBP and DBP (p<0.001). Moreover, the 24-hr SBP and DBP were higher in the NDP group.

The results of coronary CTA are summarized in Table 4. 58.6% of the patients without plaque formation had a BP dipping pattern, and 41.4% had NDP (p<0.05). Moreover, a majority of the patients with >50% plaque formation (84.4%) had a NDP (p<0.001). However, almost 50% of the patients with ≤50% plaque formation had a dipping pattern (Figure 2).

The univariable and multivariable regression analyses were performed to predict plaque formation cause stenosis

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Table 5. Univariable and multivariable regression analysis: variables that may predict plaque formation cause stenosis less than 50 % in coronary arteries

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, years	1.113 (1.063-1.165)	<0.001	1.114 (1.061-1.171)	<0.001
Gender (male)	1.574 (1.015-2.440)	0.043	1.111 (0.608-2.033)	0.732
Smoking	1.022 (0.625-1.671)	0.930	-	-
Alchol consuming	2.091 (0.743-5.887)	0.163	-	-
BMI, (kg/m^2)	1.088 (1.040-1.139)	<0.001	1.087 (1.034-1.143)	0.001
DM	1.261 (0.706-2.255)	0.433	-	-
Heart rate, beats/min	1.000 (0.977-1.024)	0.996	-	-
LV Ejection fraction, %	0.952 (0.893-1.014)	0.128	-	-
Nighttime SBP, mmHg	1.015 (1.013-1.026)	0.012	0.999 (0.986-1.011)	0.823
Nondiper, n (%)	2.043 (1.327-3.146)	0.001	2.000 (1.174-3.408)	0.011
Hemoglobin, g/dl	1.057 (0.928-1.204)	0.404	-	-
Leukocytes, 10^9 /l	1.082 (0.967-1.210)	0.167	-	-
Platelets, 10^9/l	1.000 (0.997-1.003)	0.858	-	-
Neutrophils, 10^9/l	1.138 (0.973-1.331)	0.105	-	-
Lymphocytes, 10^9/l	1.084 (0.798-1.472)	0.605	-	-
Creatinine, mg/dl	21.945 (6.266-76.861)	<0.001	17.828 (3.747-84.826)	<0.001
Total cholesterol, mg/dl	1.001 (0.996-1.006)	0.634	-	-
HDL-C, mg/dl	0.985 (0.968-1.002)	0.082	0.988 (0.967-1.008)	0.240
LDL-C, mg/dl	1.000 (0.994-1.006)	0.989	-	-
Triglycerides, mg/dl	1.001 (0.999-1.003)	0.225	-	-
HbA1c, %	1.526 (1.199-1.942)	0.001	1.285 (0.985-1.676)	0.065
CRP, mg/dl	1.099 (0.965-1.055)	0.699	-	-

OR, odds ratio; CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; DM, diabetes mellitus;
HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; HbA1c, glycated hemoglobin; CRP: C-reactive protein.

Table 6. Univariable and multivariable regression analysis: Variables predict 50 % or more plaque formation in coronary arteries

Variable	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age, years	1.055 (0.996-1.118)	0.068	1.041 (0.951-1.140)	0.380
Gender (male)	1.512 (0.730-3.130)	0.266	-	-
Smoking	1.958 (0.915-4.188)	0.083	2.132 (0.763-5.955)	0.110
Alchol consuming	1.868 (0.517-6.753)	0.341	-	-
BMI, (kg/m^2)	1.023 (0.953-1.099)	0.528	-	-
DM	2.551 (1.138-5.717)	0.023	-	-
Heart rate, beats/min	1.028 (0.995-1.062)	0.095	1.027 (0.991-1.064)	0.144
LV ejection fraction, %	1.010 (0.909-1.122)	0.855	-	-
Nighttime SBP, mmHg	1.026 (1.009-1.043)	0.002	1.009 (0.986-1.032)	0.466
Nondiper, n (%)	6.264 (2.354-16.672)	<0.001	4.143 (1.237-13.874)	0.012
Hemoglobin, g/dl	0.905 (0.732-1.119)	0.358	-	-
Leukocyte,s 10^9/l	1.153 (0.971-1.370)	0.104	-	-
Platelets, 10^9/l	0.998 (0.982-1.003)	0.414	-	-
Neutrophils, 10^9/l	1.178 (0.928-1.496)	0.177	-	-
Lymphocytes, 10^9/l	1.386 (0.851-2.256)	0.190	-	-
Creatinine, mg/dl	3.203 (0.708-14.491)	0.131	-	-
Total Cholesterol, mg/dl	0.997 (0.988-1.006)	0.519	-	-
HDL-C, mg/dl	0.987 (0.957-1.018)	0.420	-	-
LDL-C, mg/dl	0.997 (0.986-1.008)	0.603	-	-
Triglycerides, mg/dl	1.001 (0.998-1.004)	0.364	-	-
HbA1c, %	1.513 (1.188-1.927)	0.001	1.359 (0.979-1.886)	0.067
CRP, mg/dl	1.004 (0.934-1.079)	0.910	-	-

OR, odds ratio; CI, confidence interval; BMI, body mass index; SBP, systolic blood pressure; DM, diabetes mellitus;
HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; LV, left ventricle;
HbA1c, glycated hemoglobin; CRP: C-reactive protein.

<50% or ≥50% in coronary arteries, and these findings are summarized in Tables 5 and 6. In the univariable and multivariable analyses, respectively, age (p<0.001, p<0.001), serum creatinine (p<0.001, p<0.001), BMI (p<0.001, p<0.001), and NDP (p<0.001, p=0.011) were the variables that predicted plaque formation cause stenosis <50%. NDP was the only variable that predicted stenosis ≥50% in both the univariable (p<0.001) and in the multivariable (p=0.012) regression analysis.

Discussion

This study explored the association between the coronary artery plaque burden detected by CTA and the dipping pattern of BP. We found that the plaque burden was significantly higher in patients with the NDP. Additionally, patients with NDP had significantly higher plaque formation, which caused >50% stenosis in their coronary arteries.

According to Tadic et al. [14], nocturnal hypertension or NDP is associated with subclinical target organ damage, and a reverse dipping pattern, i.e., higher daytime BP than night-time BP, is a predictor of cardiovascular mortality and morbidity. Thus, office BP measurement or even 24-hr Holter monitoring is not always sufficient to detect hypertension. Thus, monitoring of night-time BP has been suggested for more accurate detection and treatment of hypertension and, thus, for preventing cardiovascular mortality and morbidity.

As mentioned above, subclinical target organ damage can occur in patients with NDP. This damage can include increased carotid intima-media thickness, left ventricular hypertrophy, and macro- and microvascular dysfunction, and this damage can occur in different risk groups [15–17]. Erdogan et al. [18] hypothesized that NDP can be a result of decreased dilator response of vascular structures. This clinical situation may lead to a decreased coronary flow reserve. Hence, left ventricle hypertrophy could make a major contribution to microvascular coronary dysfunction in patients with NDP. Hence, no significant difference was observed in the coronary flow reserve between the dipping group and the NDP group, unless the left ventricle was hypertrophied. Our study is unique in that our patient group had similar findings in terms of the interventricular septal thickness, and we focused specifically on the coronary flow and the atherosclerotic burden of the patients with different dipping patterns. Note that, as mentioned above, echocardiographic parameters, and other comorbid diseases might be associated with different dipping patterns in hypertensive patients. Thus, our patient groups were similar when compared with each other in terms of comorbid diseases, echocardiographic findings and body mass index, which might directly determine the association of the outcomes in the CTA and BP pattern differences between the groups.

To evaluate the atherosclerotic burden and the presence of plaque formation, we used coronary CTA. As a result of progress in scanner technology, coronary CTA allows non-invasive visualization of the coronary artery lumen. This has led to improved spatial resolution through thinner slice collimation and to increased temporal resolution through faster gantry rotation. Owing to these developments, coronary CTA has become a robust technology for coronary imaging. A recently published study demonstrated excellent diagnostic accuracy for the evaluation of the obstructive (>50%) CAD when using a 320-row CT scanner [19]. In this study, a negative predictive value of 100% and a diagnostic accuracy of 95% were reported for the detection of >50% stenosis. The authors reported that no patients with significant CAD were missed using the 320-row CTA. Furthermore, the excellent negative predictive value on the segment, vessel and patient basis suggested that coronary CTA might be particularly valuable in the exclusion of significant CAD. Due to these findings and other research data, we used our findings on coronary CTA and evaluated the atherosclerotic burden of every patient.

Some studies have reported the association of the atherosclerotic plaque burden in different groups of hypertensive patients. Costa et al. [20] reported that participants with white coat hypertension had a higher coronary atherosclerotic burden than participants who had normal arterial BP. In another study, Cuspidi et al. [21] evaluated NDP and atherosclerosis, along with evaluating atherosclerosis with carotid atherosclerosis. They concluded that NDP is associated with atherosclerosis, and controlling BP, particularly at night, prevents the progression of vascular damage. They also mentioned that evidence between NDP and CAD is scarce. Meanwhile, Choi et al. [22] showed that NDP is associated with coronary calcification in patients with chronic kidney disease.

The reverse dipping pattern is a specific variant of NDP that shows a higher night-time BP, as compared to daytime values, and it is associated with a higher incidence of CAD. However, the reverse dipping pattern is not associated with increased carotid intima thickness [23]. Aksit et al. showed that patients with NDP tend to have more slow-flow phenomenon than patients with dipper pattern despite having a normal coronary angiogram [24]. These two studies demonstrated that NDP is associated not only with macrovascular changes in coronary arteries, but also with microvascular changes. However, to date there had been no data that directly shows the association between epicardial coronary artery stenosis and NDP. The current study fulfilled this lack of data, and it confirmed that patients having NDP tend to develop coronary artery stenosis as compared to patients with a dipping pattern.

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To the best of our knowledge, this study is the first to compare patients with a dipping pattern and those with NDP in terms of coronary artery stenosis. It also provided detailed information about why such patients should be screened for coronary artery stenosis. In the regression analysis, this study demonstrated that absence or presence of NDP is the only parameter which can predict plaque formations <50% or ≥50%, respectively. This result shows that NDP an important risk factor for CAD. Thus, this study may enlighten clinicians about the importance of NDP assessment. Patients with NDP require strict control of other coronary artery risk factors, such as serum cholesterol levels and smoking status. However, additional information is required about nocturnal BP in certain patient groups, namely those with chronic kidney disease or OSAS.

Conclusion

Our study determined that subclinical damage related to NDP in BP might affect the atherosclerotic process in coronary arteries, and patients with NDP might have higher atherosclerotic burden for coronary arteries as compared to patients with a dipping pattern. Therefore, clinicians should bear in mind that the pattern of BP in hypertensive patients might be a sign of CAD in these patient populations.

Study limitations

This was a single-center, retrospective study, and the number of participants was small. Since it was a retrospective study, and it included a specific subgroup of patients with indications for CTA that suggested CAD, this may have affected the generalizability of the results. Furthermore, coronary CTA has its limitations. Further imaging techniques, such as intravascular ultrasound or optical coherence tomography, may be required to confirm the coronary atherosclerosis burden. Additionally, we do not have long-term follow-up data of the patients, and hence we cannot comment about the endpoints of their CAD.

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