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Research Article

Increased morning blood pressure surge and coronary microvascular dysfunction in patient with early stage hypertension

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Abstract

Morning blood pressure surge (MBPS) is defined as an excessive increase in blood pressure (BP) in the morning from the lowest systolic BP during sleep, and it has been reported as a risk factor for cardiovascular events in current clinical studies. In this study, we evaluated the association between the rate of BP variation derived from ambulatory BP monitoring data analysis and coronary microvascular function in patients with early stage hypertension. One hundred seventy patients with prehypertension and Stage 1 hypertension who fulfilled the inclusion and exclusion criteria were included in the study. We divided our study population into two subgroups according to the median value of coronary flow reserve (CFR). Patients with CFR values <2.5 were defined as the impaired CFR group, and patients with CFR values ≥ 2.5 were defined as the preserved CFR group, and we compared the MBPS measurements of these two subgroups. CFR was measured using transthoracic Doppler echocardiography (TTDE). Ambulatory 24-hour systolic and diastolic BP, uric acid, systolic MBPS amplitude, diastolic MBPS amplitude, high-sensitivity C-reactive protein, and mitral flow E/A ratio were statistically significant. These predictors were included in age- and gender-adjusted multivariate analysis; ambulatory 24-hour systolic BP (ß = 0.077, $P < .001$; odds ratio [OR] = 1.080; 95% confidence interval [CI] [1.037–1.124]) and systolic MBPS amplitude (ß = 0.043, $P = .022$; OR = 1.044; 95% CI [1.006–1.084]) were determined to be independent predictors of impaired CFR (Hosmer–Lemeshow test, $P = .165$, Nagelkerke's $R^2 = 0.320$). We found that increased changes in MBPS values in patients with prehypertension and Stage 1 hypertension seemed to cause microvascular dysfunction in the absence of obstructive coronary artery disease. J Am Soc Hypertens 2014;8(9):652–659.

Keywords: Coronary flow reserve; morning blood pressure surge; prehypertension.

Introduction

The incidence of cardiovascular events such as myocardial infarction, sudden death, and stroke reaches the highest point in the early hours after waking up in the morning.[1–5] Morning is associated with various hormonal and physiological alterations, such as activation of the sympathetic nervous system, elevation of blood pressure (BP), and increased heart rate.[6,7] A significant rise in BP upon awakening is called morning BP surge (MBPS), and it may indicate a normal physiological BP response to the change in physical activity, which is part of the normal circadian BP rhythm. MBPS has a threshold, and values above the threshold have been shown to be associated with target organ damage such as left ventricular hypertrophy and increased carotid intima media thickness.[8]

In the absence of epicardial coronary stenosis, decreased coronary flow reserve (CFR) is considered to be a marker of coronary microvascular dysfunction. Hypertensive patients have decreased CFR, even if they have normal epicardial coronary arteries.[9] Hypertension impairs CFR during the early stages of hypertension, even before the development

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of left ventricular hypertrophy.[9] Impaired CFR is a sensitive indicator of hypertensive vascular damage and signifies increased risk of cardiovascular morbidity and mortality. Therefore, there might be an association between MBPS values (also defined as changes in morning systolic BP [SBP]) and CFR in patients with early stages of hypertension. The possible association between elevated MBPS values and CFR has not been examined in asymptomatic patients with early stage hypertension until now. In this cross-sectional study, we searched for an association between MBPS and CFR in patients with early stage hypertension.

Materials and Methods

Study Population

In this cross-sectional study, we enrolled 195 consecutive patients from a cardiology outpatient clinic who underwent 24-hour ambulatory blood pressure monitoring (ABPM) between January 2007 and December 2013. Each patient was advised to continue their usual daily activities during ABPM recording; to avoid unusual physical exercise or behavioral changes; and to log their main activities, including the times of meals, bed rest, and sleep and awakening times, in a diary. Each patient was questioned regarding major cardiovascular risk factors, including diabetes mellitus, family history of coronary artery disease, current smoking status, and alcohol consumption. None of the patients had any symptoms of hypertension or coronary artery disease. The exclusion criteria were presence of secondary hypertension etiologies; obstructive sleep apnea; stroke and/or transient ischemic attack; congestive heart failure; and the presence of any systemic disease, such as hemolytic, hepatic, or renal diseases, diabetes mellitus, impaired glucose tolerance, and familial dyslipidemia. The exclusion criteria included excessive alcohol consumption (>120 g/d), morbid obesity (body mass index >35 kg/m^2), cigarette smoking, and use of any vasoactive drug. Subjects with ST segment or T wave changes specific for myocardial ischemia and Q wave and left bundle branch block on electrocardiogram (ECG) were also excluded. After taking into account the inclusion and exclusion criteria, 170 patients with prehypertension and Stage 1 hypertension were included in the study.

Office BP Measurements

BP was measured three times with the patient in a sitting position after 20 minutes of rest, using an appropriately sized arm cuff and a mercury sphygmomanometer, by skilled staff in the office. The first and fifth phases of Korotkoff sounds were used for SBP and diastolic BP (DBP) values, respectively. The average of the BP measurements was documented, and office BP was calculated by averaging nine measurements acquired during three separate episodes over a 3-week period. Height (cm), weight (kg), and a resting 12-lead ECG were also recorded.

ABPM

All of the patients underwent 24-hour ABPM on a typical working day. BP and heart rate were recorded every 15 minutes during the day (between 07:00 and 23:00) and every 30 minutes at night (between 23:00 and 07:00) by the oscillometric method with an automatic monitoring device (Model 92,512; Spacelabs Medical Inc., Redmond, VA), and analyzed using the software (Model 90,207; Spacelabs Medical Inc.). More than 80% of successful readings were required to consider a test adequate for subsequent analysis. The mean values of daytime, nighttime, and 24-hour SBPs and DBPs were calculated for each patient on the basis of hourly averages of ABPM recordings. MBPS was calculated by subtracting the mean SBP value of the hour when the lowest SBP was measured during sleep from the SBP of the second hour after awakening. Participants showing a nocturnal fall of ≥10% in SBP were considered dippers. Likewise, patients whose nocturnal SBP fell by <10% or even rose were considered ''nondippers.'' Shift workers and patients who did not rest or sleep at night were not included in the study. The accuracy of the ABPM devices was checked monthly by obtaining 10 automatic BP measurements via a Y-tube. In all instances, the value did not differ by more than 5 mm Hg for each reading.

Biochemical Assessment

The patients' blood tests and clinical data collection were conducted on the day of ABPM. All blood samples were taken after overnight fasting and a 24-hour period of abstinence from alcohol and vigorous physical exercise. Total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglyceride levels were calculated using enzymatic methods. Insulin resistance was measured using the homeostasis model assessment insulin resistance index.[10] the homeostasis model assessment insulin resistance index was calculated with the following formula: fasting serum insulin (micro-units per milliliter) × fasting plasma glucose (micromoles per liter/22.5, which has been found to correlate with glucose clamp measurement in non-diabetic, diabetic, and hypertensive populations).[11] Diabetes mellitus was defined as having a fasting glucose level >126 mg/dL, a random non-fasting glucose level >200 mg/dL, or use of an oral hypoglycemic agent or insulin. Plasma levels of high sensitivity C-reactive protein (hs-CRP) were measured with a highly sensitive sandwich enzyme-linked immunosorbent assay technique.

Echocardiographic Examination

Echocardiographic examinations were performed with an Acuson Sequoia C256 Echocardiography System equipped