The Association between Obesity, Blood Pressure Variability, and Right Ventricular Function and Mechanics in Hypertensive Patients

Marijana Tadic, MD, PhD, Cesare Cuspidi, MD, Vladan Vukomanovic, MD, Vesna Kocijancic, RN, Vera Celic, MD, PhD, and Dejana Stanisavljevic, MD, *Belgrade, Serbia; and Meda, Italy*

Background: The purpose of this investigation was to evaluate the association between blood pressure (BP) variability and right ventricular (RV) mechanical function in normal-weight, overweight, and obese untreated patients with hypertension.

Methods: This retrospective cross-sectional study included 127 untreated subjects with hypertension who underwent 24-hour ambulatory BP monitoring and complete two-dimensional and three-dimensional echocardiographic examination. All participants were divided into three groups according to body mass index (BMI): normal-weight patients (BMI < 25 kg/m^2), overweight patients (25 ≤ BMI < 30 kg/m^2), and obese patients (BMI ≥ 30 kg/m^2).

Results: Daytime, nighttime, and 24-hour BP variability parameters were higher in overweight and obese subjects with hypertension than in lean subjects. Two-dimensional RV longitudinal strain and systolic strain rate were significantly lower in obese patients with hypertension than in normal-weight patients (−24.1 ± 3% vs −23.3 ± 3.2% vs −21.7 ± 3.3%, P = .004). Three-dimensional echocardiographic RV volumes indexed to body surface area were lower in lean and overweight subjects than in obese participants with hypertension (mean RV end-diastolic volume index, 65 ± 6 vs 67 ± 7 vs 71 ± 8 mL/m^2, P = .001), while three-dimensional RV ejection fraction decreased in the same direction (60 ± 4% vs 58 ± 3% vs 57 ± 3%, P < .001). Nighttime BP variability indices, more than daytime BP variability parameters, correlated with two-dimensional RV global longitudinal strain and three-dimensional echocardiographic RV volumes.

Conclusions: BP variability and RV structure, function, and mechanics are significantly affected by obesity in patients with untreated hypertension. BP variability is significantly associated with RV remodeling in patients with hypertension. (J Am Soc Echocardiogr 2016;■:■-■.)

Keywords: Hypertension, Right ventricle, Obesity, Overweight, Two-dimensional strain, Three-dimensional echocardiography

Blood pressure (BP) variability has appeared as a complex phenomenon that includes both short-term and long-term BP changes. A recently published large study that included 25,814 patients from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial showed that higher visit-to-visit BP variability of systolic BP was associated with increased risk for cardiovascular morbidity (nonfatal cardiac infarction, heart failure, stroke) and all-cause mortality.[1] The Pressioni Arteriose Monitorate e Loro Associazioni study demonstrated that short-time BP variability (over 24 hours) could predict mortality in general population.[2] Investigations of BP variability in overweight and obese subjects with or without arterial hypertension are scarce. A recent large study demonstrated that high nocturnal BP variability greatly increased the risk for mortality related to obesity.[3]

The Multi-Ethnic Study of Atherosclerosis included 4,127 participants and revealed that overweight and obesity were independently associated with right ventricular (RV) remodeling even after adjustment for the respective left ventricular (LV) measures.[4] However, to our knowledge no study has investigated the mutual relationship among BP variability, RV remodeling, and overweight or obesity in patients with arterial hypertension.

Considering that BP variability, RV remodeling, and obesity are related to worse cardiovascular outcomes, we aimed to investigate the relationship between BP variability and RV function and mechanics in normal-weight, overweight, and obese patients with hypertension because this association could partially explain unfavorable outcomes in obese patients with hypertension. We hypothesized that BP variability indices are related with parameters of RV function and deformation in patients with hypertension with different body sizes, from normal weight to obese.

From the University Clinical Hospital Center “Dr. Dragisa Misovic – Dedinje,” Cardiology Department, Belgrade, Serbia (M.T., V.V., V.K., V.C.); the Faculty of Medicine, Belgrade, Serbia (M.T., V.C., D.S.); the University of Milan-Bicocca and Istituto Auxologico Italiano, Clinical Research Unit, Meda, Italy (C.C.); and the Institute for Medical Statistics and Informatics, Belgrade, Serbia (D.S.).

Reprint requests: Marijana Tadic, MD, PhD, University Clinical Hospital Center “Dr. Dragisa Misovic – Dedinje”, Heroja Milana Tepica 1, 11000 Belgrade, Serbia (E-mail: *marijana_tadic@hotmail.com*).

0894-7317/$36.00

http://dx.doi.org/10.1016/j.echo.2016.04.001

Abbreviations
BMI = Body mass index
BP = Blood pressure
CV = Coefficient of variation
LV = Left ventricular
PASP = Right ventricular systolic blood pressure
RA = Right atrial
RV = Right ventricular
3D = Three-dimensional
2D = Two-dimensional

METHODS

The present retrospective cross-sectional study included 127 recently diagnosed subjects with untreated hypertension referred to the outpatient clinic of University Hospital "Dr. Dragisa Misovic – Dedinje" (Belgrade, Serbia) for echocardiographic examination or ambulatory BP monitoring. Patients with heart failure ($n = 7$), sleep apnea syndrome ($n = 3$), coronary artery disease ($n = 2$), previous cerebrovascular insult ($n = 4$), atrial fibrillation ($n = 7$), congenital heart disease ($n = 1$), valve heart disease ($n = 8$), neoplastic disease ($n = 4$), cirrhosis of the liver ($n = 2$), kidney failure ($n = 7$), or endocrine diseases including type 2 diabetes mellitus ($n = 11$) were also excluded from the study. Stress testing was performed in 14 patients because of suspected coronary artery disease; the results of two tests were positive for decreased coronary reserve, and these patients were excluded from further study. Polysomnography was performed in eight patients (two overweight and six obese) because they reported symptoms that could be related to obstructive sleep apnea syndrome, and in three patients obstructive sleep apnea was confirmed (one overweight and two obese). Subjects with poor quality three-dimensional (3D) acquisition ($n = 6$) or poor two-dimensional (2D) RV visualization ($n = 4$) were also excluded from any further analyses. Dropout of one segment during RV strain analysis was detected in 12 subjects. Patients in whom two or more segments dropped out were excluded from the study ($n = 14$); three patients were excluded from the normal-weight group, five patients from the overweight group, and six patients from the obese group. Ultimately, 127 patients with hypertension were analyzed in our study.

Anthropometric measures (height and weight) and laboratory analyses (fasting glucose, total cholesterol, triglycerides, and serum creatinine) were performed in all subjects included in the study. Body mass index (BMI) was calculated for each patient. Patients were divided into three groups according the definition of the World Health Organization using BMI[5]: normal-weight patients (BMI < 25 kg/m^2), overweight patients ($25 \leq$ BMI < 30 kg/m^2), and obese patients (BMI ≥ 30 kg/m^2).

The study was approved by the ethics committee of the University Clinic "Dr. Dragisa Misovic – Dedinje," and informed consent was obtained from all participants.

Clinic BP Measurement and 24-Hour Ambulatory BP Monitoring

All participants underwent 24-hour BP monitoring. Clinic arterial BP values were obtained by aneroid manometer in the morning hours by measuring the average value of three consecutive measurements in the sitting position, taken within an interval of 5 to 10 min, after the subject had rested for ≥5 min in that position.

Noninvasive 24-hour ambulatory BP monitoring was performed on the nondominant arm, using the Schiller BR-102 plus system (Schiller AG, Baar, Switzerland). The device was programmed to obtain BP readings at 20-min intervals during the day (7 AM to 11 PM) and at 30-min intervals during the night (11 PM to 7 AM). Patients were asked to attend to their usual daily activities but to keep still at times of measurement and to keep a diary of daily activities, including the times of awakening and going to bed. Nighttime BP was defined as the average of BPs from the time when patients went to bed until the time they got out of the bed and daytime BP as the average of BPs recorded during the rest of the day. The recording was then analyzed to obtain 24-hour daytime and nighttime average systolic BP, diastolic BP, mean arterial pressure, and heart rate. When the readings exceeded ≥70% of the total readings programmed for the testing period, the recording was considered valid and satisfactory. Arterial hypertension was defined according to current guidelines.[6]

BP variability was evaluated using two different groups of indices: (1) the SD of average daytime, nighttime, and 24-hour BPs and (2) the coefficient of variation (CV) of daytime, nighttime, and 24-hour BPs, which represents the average SD of BP divided by the corresponding mean BP and multiplied by 100 (CV = [SD/BP average values] × 100).

Echocardiography

Echocardiographic examination was performed using a 2.5-MHz transducer with harmonic capability and real-time 3D data set acquisition of the left ventricle obtained using a 3D volumetric transducer and a Vivid 7 ultrasound machine (GE Vingmed Ultrasound AS, Horten, Norway).

Conventional Echocardiographic Examination

The values of all 2D parameters were obtained as the average value of three consecutive cardiac cycles. LV end-systolic and end-diastolic diameters and interventricular septal thickness were determined by using 2D-guided linear measurements.[7] Relative wall thickness was calculated as (2 × posterior wall thickness)/LV end-diastolic diameter. LV ejection fraction was assessed using the biplane method. Two-dimensional echocardigoraphic LV mass was calculated by using the formula of the American Society of Echocardiography[7] for indexing by body surface area, and Penn's formula was used for indexing by height.[8]

Left atrial volume was measured just before mitral valve opening, according to the biplane method in four- and two-chamber views, and all values were indexed to body surface area.

Transmitral Doppler inflow and tissue pulsed Doppler velocities were obtained in the apical four-chamber view. Pulsed Doppler measurements included the ratio between transmitral early and late diastolic peak flow velocity (E/A).[9] The spectral tissue Doppler method was used to obtain LV myocardial velocities in the apical four-chamber view, with a sample volume placed just above the septal and lateral segment of the mitral annulus during early diastole (e′). The average of the peak early diastolic velocity (e′) of the septal and lateral mitral annulus obtained by the tissue Doppler was calculated, and the E/e′ ratio was computed.

Right Ventricle and Right Atrium

RV internal diameter was measured in the parasternal long-axis view.[10] RV thickness was measured in the subcostal view. Right atrial (RA) maximal volume was obtained in the four-chamber view during ventricular end-systole and indexed to body surface area.

Tricuspid flow velocities were assessed using pulsed-wave Doppler in the apical four-chamber view at end-expiration during quiet breathing to determine early diastolic peak flow velocity (E_t). Doppler tissue imaging was used to obtain RV myocardial velocities in the apical four-chamber view, with a sample volume placed just above the