Journal of the American Society of Hypertension 8(10) (2014) 699–708

Research Article

The association between heart rate variability and biatrial phasic function in arterial hypertension

Marijana Tadic, MD, PhD[a,*], Cesare Cuspidi, MD[b], Biljana Pencic, MD[a], Tamara Marjanovic, RN[a], and Vera Celic, MD, PhD[a,c]

[a]*University Clinical Hospital Center ''Dr. Dragisa Misovic – Dedinje'', Department of Cardiology, Heroja Milana Tepica 1, Belgrade 11000, Serbia;*

[b]*University of Milan-Bicocca and Istituto Auxologico Italiano, Clinical Research Unit, Viale della Resistenza 23, Meda 20036, Italy; and*

[c]*Faculty of Medicine, Doktora Subotica 6, Belgrade 11000, Serbia*

Manuscript received June 2, 2014 and accepted July 25, 2014

Abstract

We sought to investigate (1) left atrial (LA) and right atrial (RA) phasic function and mechanics; (2) heart rate variability (HRV); and (3) their relationship in untreated hypertensive patients. This cross-sectional study involved 73 untreated hypertensive patients and 51 subjects without cardiovascular risk factors with similar gender and age. All the subjects underwent a 24-hour Holter monitoring and comprehensive two- and three-dimensional echocardiography examination. LA and RA reservoir and conduit function, estimated by total and passive atrial emptying fractions and systolic and early diastolic strain rates, were reduced in the hypertensive patients. On the other hand, LA and RA booster function, assessed by active atrial emptying fraction and late diastolic strain rate, was increased in this group. All time and frequency domain heart-rate variability parameters were reduced in the hypertensive subjects. In the whole study population, parameters of cardiac sympathovagal balance (standard deviation of all normal RR intervals, root mean square of the difference between the coupling intervals of adjacent R-R intervals, 24-hour low-frequency domain [0.04–0.15 Hz], 24-hour high-frequency domain [0.15–0.40 Hz], and 24-hour total power [0.01–0.40 Hz]) correlated with LA and RA volume indexes, biatrial booster function assessed by active emptying fraction, biatrial longitudinal function evaluated by longitudinal strain; and biatrial expansion index. LA and RA phasic function and mechanics are significantly impaired in the untreated hypertensive patients. Heart-rate variability parameters are also deteriorated in the hypertensive population. Biatrial function and mechanics correlated with cardiac autonomic nervous system indexes in the whole study population. J Am Soc Hypertens 2014;8(10):699–708.

Keywords: Arterial hypertension; heart rate variability; left atrium; mechanics; phasic function; right atrium.

Introduction

The left atrial (LA) volume, at the same time, reflects the diastolic filling of the left ventricle (LV), represents a sensitive marker of LV diastolic dysfunction,[1] and is a valuable indicator of cardiovascular morbidity and mortality.[2] LA mechanics has been proved as an important independent predictor of the outcome in patients with atrial fibrillation, heart failure, myocardial infarction, or valve heart disease.[3]

Similarly to the LA, the right atrium (RA) mirrors the diastolic filling pressure of the right ventricle (RV). The RA has long been considered unimportant for overall cardiac function. However, recent investigations have demonstrated that RA volume and/or function are important predictors of morbidity and mortality in patients with heart failure, coronary artery disease, pulmonary embolism, or Eisenmenger syndrome.[4–7] LA phasic function and mechanics have been investigated in arterial hypertension previously,[8–10] whereas the data about RA functional remodeling are scarce and mostly provided by our study group.[11,12]

Sympathovagal disbalance in systemic hypertension evaluated by heart rate variability (HRV) parameters has been revealed earlier.[13–15] The investigators also demonstrated the relationship between HRV and cardiovascular

*Corresponding author: Marijana Tadic, MD, PhD, University Clinical Hospital Center "Dr. Dragisa Misovic – Dedinje", Cardiology Department, Heroja Milana Tepica 1, Belgrade 11000, Serbia. Tel: +381658107085; Fax: +381112411464.

E-mail: marijana_tadic@hotmail.com

1933-1711/$ - see front matter
http://dx.doi.org/10.1016/j.jash.2014.07.032

events.[16] Nevertheless, to our knowledge, there is no study that investigated the relationship between biatrial phasic function and HRV in arterial hypertension.

We aimed at evaluating LA and RA phasic function using (1) traditional methods—atrial volumes and emptying fractions; and (2) sophisticated echocardiographic tool—two-dimensional echocardiography examination (2DE) speckle tracking, in a population consisting of untreated hypertensive subjects and normotensive controls. Furthermore, our objective was to examine the difference in HRV parameters between two observed groups, and to define the relation between atrial mechanics and HRV in the whole study population.

Methods

In the present study, we enrolled 73 untreated, recently diagnosed, hypertensive patients and 51 normotensive subjects without cardiovascular risk factors. Exclusion criteria were age >60 years, antihypertensive treatment, heart failure, coronary artery disease, previous cerebrovascular events, atrial fibrillation, pace-maker, congenital heart disease, valve heart disease, obesity (body mass index [BMI] $\geq$30 kg/m^2), neoplastic disease, cirrhosis of the liver, kidney failure, or endocrine diseases including type 2 diabetes mellitus.

Clinic blood pressure (BP) values were obtained in two separate visits 3 weeks apart. BP was measured by conventional sphygmomanometer in the morning hours by taking the average value of three consecutive measurements in the sitting position 10 minutes apart. BP was calculated as average values between all the measurements. Arterial hypertension was diagnosed according to the current guidelines.[17]

Anthropometric measures (height, weight) and laboratory analyses (level of fasting glucose, blood creatinine and urea, total cholesterol, and triglycerides) were obtained from all the subjects included in the study. BMI and body surface area (BSA) were calculated for each patient. The metabolic syndrome was defined by the presence of three or more criteria of the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (AHA-NHLB) definition [18]: high blood pressure ($\geq$130/85 mm Hg), abdominal obesity (waist circumference $\geq$102 cm in men and $\geq$88 cm in women), increased fasting triglycerides ($\geq$1.7 mmol/L), decreased high-density lipoprotein (HDL) cholesterol (<1.0 mmol/L in men and <1.3 mmol/L in women), and increased level of fasting glucose ($\geq$5.6 mmol/L). The study was approved by the local Ethics Committee, and informed consent was obtained from all the participants.

24-hour Holter Monitoring

24-hour Holter monitoring was performed with a three-channel digital Schiller Microvit MT-101 system (Schiller AG, Baar, Switzerland) and analyzed by Schiller software (Schiller AG, Baar, Switzerland). The minimum duration of recording was 18 hours (after exclusion of non-sinusal cardiac cycles). Time-domain HRV parameters were calculated on 24-hour, daytime, and nighttime recordings after excluding non-sinusal cardiac cycles, according to the guidelines.[18] SDNN was defined as the standard deviation of all normal RR intervals. SDANN, which reflects long-term HRV and therefore mainly sympathetic activity or sympathovagal balance, was defined as the standard deviation of the averaged normal RR intervals for all 5-minute segments. rMSSD was calculated as the root mean square of the difference between the coupling intervals of adjacent RR intervals. pNN50, which reflects short-term beat-to-beat HRV and consequently primarily vagal activity, was calculated as the proportion of adjacent RR intervals that varied by more than 50 ms. After power spectral density estimation, four standard frequency-domain HRV measures were calculated for 24-hour, daytime, and nighttime recordings.[19] Low-frequency domain (LF) was defined between 0.04 and 0.15 Hz; high-frequency domain (HF) was defined between 0.15 and 0.4 Hz; total spectral power (TP) for all the intervals up to 0.4 Hz; and ratio of low to high frequency power (LF/HF).

Echocardiography

Echocardiographic examinations were performed by using Vivid 7 (GE Vingmed, Horten, Norway) ultrasound machine equipped with both a 2.5 MHz transducer and a 3V matrix probe for three-dimensional echocardiography examination (3DE) data set acquisitions.

Reported values of all 2DE parameters were obtained as the average value of three consecutive cardiac cycles. LV diameters and septum thickness were measured according to the current recommendations.[20] Relative wall thickness was calculated according to the formula. LV ejection fraction (EF) was calculated by using the biplane method. LV mass was calculated by using the Devereux formula,[21] and indexed for the height powered to 2.7.

Pulsed-wave Doppler assessment of transmitral LV was obtained in the apical four-chamber view according to the guidelines.[22] Tissue Doppler imaging was used to obtain LV myocardial velocities in the apical four-chamber view, with a sample volume placed at the septal and lateral segments of the mitral annulus. The average of the peak early diastolic relaxation velocity (é) of the septal and lateral mitral annulus was calculated, and the E/é ratio was computed.

Assessment of LA Volume and Function

LA volumes were measured in three different sequences of the cardiac cycle: maximal LA volume was measured just before the mitral valve opening, pre-A LA volume was determined at the onset of atrial systole (peak of P wave in electrocardiogram [ECG]), whereas minimal LA volume was measured at the mitral valve closure. All the