The relationship between white coat hypertension and the index of cardiac electrophysiological balance (ICEB)

M Murat Karamanlıoğlu¹, Ekrem Şahan²

¹ Atatürk Chest Disease and Thorax Surgery Training and Research Hospital, Department of Cardiology, Ankara, Turkey
² Ankara Bilkent City Hospital, Department of Cardiology, Ankara, Turkey

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ABSTRACT

Aim: The index of cardiac electrophysiological balance (ICEB) is a new marker that can show the potential for ventricular arrhythmia and indicate the balance between ventricular depolarization and repolarization. A tendency toward ventricular arrhythmia has been shown in non-dipper hypertension and prehypertensive patients in various studies. White coat hypertension (WCH) has been shown to be associated with target organ damage and the actual development of hypertension. In this study, we aimed to evaluate the effect of dipper and non-dipper patterns on the ICEB in patients diagnosed with WCH.

Material and Method: A total of 108 patients were included in this study. Patients were divided into two groups as dipper and non-dipper patterns according to ABPM. QT/QRS (ICEB) and cQT/QRS (ICEBc) were recorded with computerized interpretation of the electrocardiogram.

Results: While electrocardiographic parameters including heart rate, PR interval, QT interval, cQT interval, and ICEB were similar in both groups (p>.05), in the non-dipper group, QRS duration was lower (p=.017) and ICEBc was higher (p=.001).

Conclusion: ICEBc may predict susceptibility to ventricular arrhythmias in WCH patients. Therefore, non-dipper WCH patients with a high ICEBc should be followed for arrhythmia outcomes in addition to hypertensive outcomes.

Keywords: White coat hypertension, non-dipper pattern, the index of cardiac electrophysiological balance, electrocardiography, ventricular arrhythmia, QT interval

INTRODUCTION

White coat hypertension (WCH) is a condition in which home blood pressure (BP) or ambulatory BP measurements (ABPM) are normal, but outpatient measurements are high (1). Although it appears to be a benign condition, it has been shown to be associated with target organ damage and the actual development of hypertension (2,3). Normal blood pressure shows a circadian rhythm. At night, blood pressure decreases by more than 10% compared to the average daytime value; this is called a dipping pattern. A non-dipping pattern is a reduction in blood pressure of less than 10% at night and is associated with increased cardiovascular risk and target organ damage (1,4,5). Supraventricular and ventricular arrhythmias are causes of cardiovascular morbidity and mortality. Predicting these dysrhythmias and initiating early treatment or avoiding the causative conditions can reduce morbidity and mortality. Many studies have shown a predisposition to ventricular arrhythmias in patients with non-dipper hypertension and left ventricular hypertrophy (6–8). A tendency toward ventricular arrhythmia in patients with prehypertensive non-dipping pattern is demonstrated by a fragmented QRS (9). The predictive value of the frontal QRS axis, which demonstrate myocardial repolarization, has been demonstrated in patients with non-dipper hypertension and without left ventricular hypertrophy (10). In the evaluation of arrhythmia, electrocardiographic (ECG) findings such as QT dispersion, QTc, Tp-e (Tp-e=peak-to-end interval of the T wave), Tp-e/QT have been evaluated in many studies (11–14). The index of cardiac electrophysiological balance (ICEB) is the ratio of QT to QRS (QT/QRS), which is a new marker that can show the potential for ventricular arrhythmia and is easily calculated on a surface ECG (15). It has been demonstrated that ICEB can be used in place of cardiac wavelength λ (λ= effective refractory period [ERP] x conduction velocity [CV]), which is measured in an electrophysiology laboratory and can
indicate the balance between ventricular depolarization and repolarization (16). An imbalance may predispose one to Torsades de Pointes (TdP) and other ventricular arrhythmias. In this study, we aimed to evaluate the effect of dipper and non-dipper patterns on ICEB in patients diagnosed with WCH.

MATERIAL AND METHOD

This retrospective study was carried out with the permission of Ankara Keçiören Training and Research Hospital, Non-Invasive Clinical Researches Ethics Committee (Date: 09.11.2021, Decision No: 2012-KAEK-15/2424). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient Selection

In our study, patients with a systolic blood pressure (SBP) of ≥140 mmHg and/or a diastolic blood pressure (DBP) of ≥90 mmHg in a physical examination and who underwent ABPM with suspected WCH (the blood pressure readings in the hospital were higher than they are in other settings, such as the home) were evaluated from May 2020 to July 2021. In accordance with the 2018 European Society of Cardiology (ESC) / European Society of Hypertension (ESH) guidelines (1), 151 patients were diagnosed with WCH. A detailed physical examination was performed on the patients and medical history was taken. Demographic and laboratory data were obtained from the automated hospital system and recorded. Diagnoses of hypertension on ABPM records, diabetes mellitus, chronic kidney disease, coronary artery disease, left ventricular systolic dysfunction (EF<50%) and moderate-severe valve disease in echocardiography, endocrine diseases (hyperthyroidism, anemia), obstructive sleep apnea syndrome, chronic obstructive pulmonary disease, pregnancy, drug use affecting the autonomic nervous system, branch block, atrial fibrillation, and atrioventricular block on an ECG were determined as exclusion criteria. Forty-three patients with one or more of the exclusion criteria were excluded from the study.

ABPM Recordings

Twenty-four-hour ambulatory blood pressure recordings were obtained using the oscillometric system (Altgasse 68 6341 Baar, Switzerland). Daytime recordings were made between 06:00 and 22:00, nighttime recordings were made between 22:00 and 06:00. Blood pressure values were taken every 30 minutes for daytime recordings and were taken every hour at nighttime. Information about sleep duration was obtained from the patients, and no adverse events related to the device were reported during the day or at night. It was required that the false measurement rate be less than 20%. Daytime, nighttime, and 24-hour systolic, diastolic, and mean blood pressures were obtained from ABPM recordings. A 24-hour mean of ≥130/80 mmHg, daytime mean of ≥135/85 mmHg, and nighttime mean of ≥120/70 mmHg were accepted as hypertension, and clinical blood pressure measurements were SBP ≥140 mmHg and/or DBP ≥90 mmHg; those with normal ABPM values were considered WCH (1). A dipper pattern was determined as a ≥10% decrease in mean blood pressure during the nighttime, according to the mean blood pressure value during the daytime, and a ≥10% decrease in mean blood pressure was a non-dipper pattern (1). The patients diagnosed with WCH were divided into two groups, dipper and non-dipper, according to ABPM records.

Electrocardiography and Echocardiography

A 12-lead surface ECG was obtained from all patients, in the supine position, after resting for at least 5 minutes. Heart rate, PR, QRS, QT, and cQT intervals were obtained from computerized interpretation of the electrocardiogram results (Nihon Kohden, Tokyo, Japan). Also, QT/QRs/ICEB and corrected QT (QTc)/QRS (ICEBc) values were calculated from these ECG data for every patient. Transthoracic echocardiography was performed on all patients with GE Healthcare Vivid S60N. Left ventricular diastolic diameter, interventricular septum, and posterior wall measurements were taken on the parasternal long axis just below the mitral valve tips in diastole to calculate the left ventricular mass and index (17). The left ventricular ejection fraction was measured by using the modified Simpson’s method (17). Left ventricular hypertrophy was evaluated according to the LV (left ventricle) mass index. LV mass was calculated with the following formula: $\text{LV mass}=0.8x(1.04x(LVEDD (left ventricle end diastolic diameter)+IVSd (Intraventricular septum distance)+PWd (posterior Wall distance))^3-3xLVEDD3)+0.6$. LV mass index was calculated using the following formula: $\text{LV mass index}=\text{LV mass}/\text{Body surface area (BSA)}$ (17). BSA was calculated with the Mosteller Formula: $\text{BSA}= ((\text{height(cm)}x\text{ weight(kg)})/3600)^{1/2}$. Values >95 g/m² for women and >115 g/m² for men were accepted as left ventricular hypertrophy.

Statistical Analysis

Numerical data were expressed as mean standard deviation, and non-numeric data as a percentage (%). Data were saved in the SPSS version 23.0 statistics program. Continuous variables with normal distribution were compared with the Student t-test. The Pearson method was used in the correlation analysis of the independent variables in each population studied.
RESULTS

The mean age of the entire population in our study was 52.8, and 52% of the dipper group and 50% of the non-dipper group were women. There was no difference between the two groups in terms of body mass index and smoking, respectively (p=0.426, p=0.882). Transthoracic echocardiographic parameters, left ventricular ejection fraction (LVEF), left ventricle end-diastolic diameter (LVEDD), interventricular septum thickness (IVST), and posterior wall thickness (PWT) were examined, and no significant difference was observed in both groups (p>.05). In addition, there was no statistically significant difference between the two groups in terms of left ventricular hypertrophy (p>.05) (Table 1). There was no difference between the two groups in terms of hemoglobin and electrolyte values (p>.05). While for the ABPM records, the 24-h mean SBP was not statistically different between the two groups (p>.05), the 24-h mean DBP was significantly higher in the dipper group (p<.001). Daytime SBP and DBP were significantly higher in the dipper group (p=.024, p<.001), and nighttime SBP was significantly higher in the non-dipper group (p=.002) (Table 2). While electrocardiographic parameters including heart rate, PR interval, QT interval, QTc interval, and ICEB were similar in both groups (p>.05), in the non-dipper group, QRS duration was lower (p=.017) and ICEBc was higher (p<.001) (Table 3).

DISCUSSION

Hypertension is one of the most common diseases in clinical practice (1). Identifying conditions predisposing individuals to hypertension, taking the necessary precautions, and treating them contribute to a reduction of morbidity and mortality (1). In addition, predicting arrhythmias that may be associated with hypertension and taking the necessary precautions may have a positive effect on outcomes in cardiovascular system-related conditions. Although WCH seems to be benign, Mancia et al. (18) showed that hypertension developed in 42.6% of WCH patients in a 10-year follow-up. In another study, it was shown that the development of hypertension was approximately three times more common compared to people with normal blood pressure (19). Not only hypertension, but also WCH has been found to be associated with cardiovascular diseases. Therefore, WCH is a relevant clinical condition. Recent studies have shown that left ventricular hypertrophy and carotid atherosclerosis are more common as target organ damage in patients with WCH than in normotensive patients (20,21). In addition, it has been shown that cardiovascular mortality is higher in patients with WCH than in normotensive or prehypertensive patients (22).

A Non-dipping pattern is a reduction in blood pressure of less than 10% at night compared to the average daytime value and is associated with increased cardiovascular risk and target organ damage (1,4,5). In many studies, it has been shown that the non-dipper
pattern predisposes for VA (ventricular tachycardia and/or ventricular fibrillation) in patients with hypertension (6–14). Therefore, WCH may be a predisposing factor for cardiovascular diseases as well as for arrhythmia. By identifying the WCH population with a predisposition to ventricular arrhythmia, it may be possible to ensure that the agents to be selected as antihypertensives in the future have antiarrhythmic properties or to avoid proarrhythmic agents in different treatment options. LVH has been shown to have a proarrhythmic effect in hypertensive and prehypertensive patients in studies (6–8,10). In our study population, there was no statistically significant difference between the groups in terms of LVH. LVH had no effect on our study population in terms of both ECG findings and arrhythmia. Therefore, the importance of the ICEB value as a proarrhythmic indicator was increased in our study group.

ICEB is a relatively new marker that indicates ventricular arrhythmogenesis and is obtained by dividing QTc/QRS in ECG (15). Lu et al. (16) suggested that a significant increase in ICEB may cause TdP-induced VA, while a decrease may cause non-TdP-induced VA. ICEBc is the QTc/QRS ratio, and in healthy chronic smokers it may predict a tendency toward TdP-induced VA (23). It has also been shown that ICEB can predict cannabinoid-induced VA (24). In our study, ICEB values were higher in the non-dipper group, and ICEBc was found to be significantly higher. The shorter QRS duration on the depolarization side and the longer QTc interval in the direction of repolarization may explain the higher ICEBc values in the non-dipper group. It is known that non-dipper status increases the frequency of left ventricular hypertrophy and causes cardiac conduction problems and autonomic dysfunction and heterogeneity in ventricular repolarization (25,26). Sympathetic activity has been shown to increase in WCH patients compared to normotensive, and, in another study, an increase in sympathetic activity and decrease in vagal activity have been shown to prolong QTc (27,28). In addition, an increase in nocturnal sympathetic activity and a decrease in vagal activity were shown in patients with the non-dipper pattern (29,30). The non-dipper state and increased adrenergic effect may cause deterioration in ventricular homogeneity, and this may be related to the ICEBc results in our study. Ultimately, non-dipper status may lead to increased susceptibility to ventricular arrhythmia in WCH patients.

The main limitations of our study were the small number of patients and its retrospective nature. ABPM could not be used in normotensive patients due to their retrospective nature of the study. Prospective follow-up periods were not performed for the evaluation of arrhythmia in the patients.

CONCLUSION
ICEBc was found to be significantly higher in patients with WCH and non-dipper patterns compared to those with dipper patterns. ICEBc may predict susceptibility to ventricular arrhythmias in WCH patients. Therefore, non-dipper WCH patients with a high ICEBc should be followed for arrhythmia outcomes besides hypertensive outcomes.

ETHICAL DECLARATIONS
Ethics Committee Approval: The study was carried out with the permission of Ankara Keçiören Training and Research Hospital, Non-Invasive Clinical Researches Ethics Committee (Date: 09.11.2021, Decision No: 2012-KAEEK-15/2424).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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