Heart rate turbulence in masked hypertension and white-coat hypertension

C.-L. SONG¹, X. ZHANG², Y.-K. LIU³, W.-W. YUE², H. WU²

1Shandong Provincial Hospital Affiliated to Shandong University, Ji’nan, China
2The Fourth People’s Hospital of Ji’nan, Ji’nan, China
3Laiwu Health School, Laiwu, China

Abstract. – OBJECTIVE: To observe the heart rate turbulence (HRT) in patients with masked hypertension (MH), and white-coat hypertension (WCH).

PATIENTS AND METHODS: Patients were classified on the basis of clinic and 24 h ambulatory blood-pressure monitoring: essential hypertension (H, n = 32), masked hypertension (MH, n=26), white-coat hypertension (WCH, n = 29) and normotension (NT, n = 30). For each subject, we recorded 24 hours holter monitoring electrocardiogram, calculated the turbulence onset (TO) and turbulence slope (TS) and compared the differences.

RESULTS: Compared with NT controls, the differences of TO and TS in the patients with EH, MH and WCH were statistically significant (p < 0.01). No significant differences were found between the EH, MH and WCH groups.

CONCLUSIONS: The HRT in EH, MH and WCH patients is significantly lower, when their autonomic nerve function is damaged.

Key Words: Masked hypertension, White-coat hypertension, Essential hypertension, Heart rate turbulence.

Introduction

Essential hypertension (EH) is a common ailment in cardiovascular medicine. Cardiovascular changes and autonomic neuropathy are common complications of EH. However, clinicians don’t fully understand masked hypertension (MH) and white-coat hypertension (WCH). Heart rate turbulence (HRT) is a new electrocardiology index of forecasting a malignant cardiovascular event. Heart rate turbulence is an index that is sensitive and specific, and is used to forecast the fatality rate of organic cardiopathy, myocardial infarction, chronic heart failure, and myocardiosis.¹² Heart rate turbulence is considered to be an indicator that could reflect the regulating function of the cardiac autonomic nerve¹ and is an important factor to predict the risk of sudden death. For this study, the relationship between HRT and ambulatory blood-pressure was observed in order to investigate the cardiac autonomic nervous function in MH and WCH patients.

Patients and Methods

Patients
According to the The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7)², patients with essential hypertension (EH, n = 32) were observed and considered as grade 1 or 2 hypertensive, based on clinic and 24h ambulatory blood-pressure monitoring (140 ≤ systolic pressure < 180 mmHg and/or 90 ≤ diastolic pressure < 110 mmHg). Masked hypertensive patients (n = 26) were observed according to the diagnostic criteria of MH, and classified on the basis of clinic blood-pressure of less than 140/90 mmHg and 24h ambulatory blood-pressure over 135/85 mmHg. White-coat hypertensive patients (n = 29) were observed according to the diagnostic criteria of WCH, classified on the basis of clinic blood-pressure over 140/90 mmHg and 24 h ambulatory blood-pressure over 135/85 mmHg. White-coat hypertensive patients (n = 29) were observed according to the diagnostic criteria of WCH, classified on the basis of clinic blood-pressure over 140/90 mmHg and 24 h ambulatory blood-pressure over 135/85 mmHg. White-coat hypertensive patients (n = 29) were observed according to the diagnostic criteria of WCH, classified on the basis of clinic blood-pressure over 140/90 mmHg and 24 h ambulatory blood-pressure over 135/85 mmHg. White-coat hypertensive patients (n = 29) were observed according to the diagnostic criteria of WCH, classified on the basis of clinic blood-pressure over 140/90 mmHg and 24 h ambulatory blood-pressure over 135/85 mmHg.
antihypertensives or other medication that could affect the autonomic nervous system or heart rate during the two months of the study. There were no significant differences in gender, age, and body mass index amongst the groups.

Methods

Blood-Pressure Measurement in Clinic

Blood-pressure was measured by platform mercury sphygmomanometer. Patients had to rest for five minutes before measuring their blood-pressure. The blood-pressure of right brachial artery was measured in sitting stance for three times, and the final result was taken.

Ambulatory Blood-Pressure Monitoring

Ambulatory blood-pressure monitoring was recorded by a CB-2302-A12 leading 24h ambulatory electrocardio and blood pressure two-in-one monitor (Biox Instruments Co., Ltd, Wuxi, China). Blood pressure was measured once each 30 mins during the day (from 6 am to 10 pm), and once each hour during the night (from 10 pm to 6 am). Valid data had to be more than 85% or be retested. The data of 24h systolic blood pressure (24hSBP) and 24h diastolic blood pressure (24hDBP), day and night systolic blood pressure (dSBP, nSBP), day and night diastolic blood pressure (dDBP, nDBP) were analyzed.

Heart Rate Turbulence Monitoring

Twenty-four hour holter monitoring electrocardiogram was recorded by 24h ambulatory electrocardiogram and blood pressure two-in-one monitor. Atrial fibrillation, artifacts and interference were automatically excluded by man-machine interaction software. The qualification for calculating heart rate turbulence was set before testing. The selected conditions of the qualified ventricular premature beat (n > 5) were the following: (1) It should be a normal sinus tachycardia before ventricular premature beat. (2) The minimum advance rate of the ventricular premature beat is 20%. The compensatory pause after ventricular premature beat should exceed the normal R-R interval by 20%. Heart rate turbulence monitoring was calculated and taken by the average. The formula used is as follows:

\[ \text{TO} = \frac{(\text{RR}_1+\text{RR}_2) - (\text{RR}_1+\text{RR}_2)}{(\text{RR}_1+\text{RR}_2)} \times 100\% \]

The TO means the acceleration of initial sinus rhythm after ventricular premature beat. TO > 0 indicates normal. TO < 0 indicates abnormal that means initial sinus rhythm decelerates after ventricular premature beat. RR1 and RR2 mean the average of RR interval between initial two sinus rhythms which follow the ventricular premature beat. RR-1 and RR-2 means the average of RR interval between two sinus rhythms which are after ventricular premature beat.

The TS is an indicator for quantitative analyzing should there be any deceleration of sinus rhythm after ventricular premature beat. Firstly, measure the RR interval of the initial twenty sinus rhythms after ventricular premature beat and draw the distributing graph of RR interval according to RR interval as a vertical ordinate, and the serial number of the RR interval as the horizontal ordinate. Secondly, by taking linear regression treatment by RR, stair step plots of any five consecutive sinus rhythms. The result of TS is the maximum of a positive slope. The TS was indicated by ms change of each RR interval. TS > 2.5 ms/RR indicates normal, which means sinus rhythm decelerates after ventricular premature beat. TS ≤ 2.5 ms/RR indicates abnormality, which means that the sinus rhythm does not decelerate after a ventricular premature beat.

Statistical Analysis

The statistical analysis was taken using SPSS 12.0 statistical software. The result was indicated by average ± standard deviation (\( \overline{x} \pm s \)). Measurable data was tested by \( t \) and count data was tested by \( \chi^2 \). It was statistically significant, when the difference was \( p < 0.05 \).

Results

Comparison of General Date of Each Group

The groups in observation were the EH group (n = 32), MH group (n = 26), WCH group (n = 29) and NT group (n = 30). There was no statistically significant difference (\( p > 0.05 \)) of gender, age, body mass index (BMI), blood glucose and blood-lipid among the groups (Table I).

Comparison of TO and TS Among Groups (\( \overline{x} \pm s \))

There was a statistically significant difference (\( p < 0.05 \)) in the HRT indicators testing results between the EH group, MH group, WCH group and NT group. There was no statistically significant difference (\( p > 0.05 \)) amongst the three hypertensive groups (Table II).
Heart rate turbulence in masked hypertension and white-coat hypertension

Dysfunction is low, so that the value of HRT diminishes or disappears. There is an internal relationship between the autonomic nervous system and sudden cardiac death. Furthermore, ventricular premature beat will cause arrhythmia and predict an increase risk in sudden death. These will be the pathophysiologic basis of organic heart disease forecasted by heart rate turbulence.

Previous studies have shown that changes of heart autonomic nervous activity have an important role in the occurrence and maintenance of hypertension. An increase in sympathetic nerve activity, and a rise and drop in vagus nerve activity will be considered the main occurrence mechanism of primary hypertension. Primary hypertension can cause cardiac muscular reconstruction, myocardial receptors deformation, and lower sensitivity in the sympathetic and vagus nerve. Furthermore, heart rate turbulence will diminish or disappear after the ventricular premature beat of patient.

In this study, we compared groups EH, MH, WCH with NT, and found that the TO increases, TS decreases, and the abnormal occurrence of TO and TS is significantly higher. There is no statistical significance between group EH, MH and WCH. It also indicates that patients with WCH, MH or primary hypertension, have autonomic nervous system dysfunction. Conversely,

### Table I. Comparison of baseline date of each group (x ± s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases (male/female)</th>
<th>Age</th>
<th>BMI (kg/m²)</th>
<th>Fasting blood glucose (mmol/L)</th>
<th>Triacylglycerol (mmol/L)</th>
<th>Total cholesterol (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td>30 (19/11)</td>
<td>62.12 ± 8.71</td>
<td>22.52 ± 4.33</td>
<td>4.90 ± 0.43</td>
<td>1.28 ± 0.65</td>
<td>4.44 ± 0.85</td>
</tr>
<tr>
<td>EH</td>
<td>32 (20/12)</td>
<td>63.40 ± 9.23</td>
<td>23.72 ± 3.91</td>
<td>4.81 ± 0.54</td>
<td>1.34 ± 0.59</td>
<td>4.65 ± 0.72</td>
</tr>
<tr>
<td>MH</td>
<td>26 (16/10)</td>
<td>62.24 ± 10.65</td>
<td>22.84 ± 3.15</td>
<td>5.01 ± 0.65</td>
<td>1.48 ± 0.40</td>
<td>4.78 ± 0.47</td>
</tr>
<tr>
<td>WCH</td>
<td>29 (18/11)</td>
<td>61.14 ± 10.12</td>
<td>23.43 ± 2.92</td>
<td>5.10 ± 0.17</td>
<td>1.56 ± 0.33</td>
<td>4.51 ± 0.56</td>
</tr>
</tbody>
</table>

### Discussion

Investigators found that, after adjusting age, gender or other cardiovascular risk factors, patients with WCH, MH or hypertension will be more at risk of having continuous hypertension compared to normotensive patients. Furthermore, the cardiovascular and all-cause mortality risk will increase definitely.

In HRT, the heart-rate has a characteristic bipolar type fluctuation after a single ventricular premature beat. It accelerates and decelerates after a ventricular premature beat. This can be found in normal or low risk patients with organic heart disease. In patients with a high risk of sudden cardiac death, the heart-rate appears diminished or non existent.

The exact mechanism of HRT is not clear. But the sinus nod and aortic arch depressor reflex activation are considered to be the main reason of the transient changes in heart rate after a ventricular premature beat. Heart-rate turbulence is mainly dependant on the vagus nerve. Heart-rate turbulence is marked that the autonomic nervous system and antiarrhythmic protective mechanisms of vagus nerve are complete. When there is organic heart disease, for example, myocardial infarction, cardiomyopathy, heart failure etc, the heart reconstructs and the heart geometry changes. The autonomic nervous reflex dysfunction is low, so that the value of HRT diminishes or disappears. There is an internal relationship between the autonomic nervous tension and sudden cardiac death.

Furthermore, ventricular premature beat will cause arrhythmia and predict an increase risk in sudden death. These will be the pathophysiologic basis of organic heart disease forecasted by heart rate turbulence.

Previous studies have shown that changes of heart autonomic nervous activity have an important role in the occurrence and maintenance of hypertension. An increase in sympathetic nerve activity, and a rise and drop in vagus nerve activity will be considered the main occurrence mechanism of primary hypertension. Primary hypertension can cause cardiac muscular reconstruction, myocardial receptors deformation, and lower sensitivity in the sympathetic and vagus nerve. Furthermore, heart rate turbulence will diminish or disappear after the ventricular premature beat of patient.

In this study, we compared groups EH, MH, WCH with NT, and found that the TO increases, TS decreases, and the abnormal occurrence of TO and TS is significantly higher. There is no statistical significance between group EH, MH and WCH. It also indicates that patients with WCH, MH or primary hypertension, have autonomic nervous system dysfunction. Conversely,

### Table II. Comparison of TO and TS among groups (x ± s).

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>TO (%)</th>
<th>TS (ms/RR)</th>
<th>Abnormal TO (%)</th>
<th>Abnormal TS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension</td>
<td>30</td>
<td>-4.97 ± 0.37</td>
<td>8.37 ± 4.11</td>
<td>4 (13)</td>
<td>5 (16)</td>
</tr>
<tr>
<td>EH</td>
<td>32</td>
<td>-1.95 ± 0.37*</td>
<td>5.86 ± 3.78*</td>
<td>8 (25)*</td>
<td>8 (25)*</td>
</tr>
<tr>
<td>MH</td>
<td>26</td>
<td>-1.86 ± 0.16*</td>
<td>3.51 ± 3.68*</td>
<td>6 (26)*</td>
<td>7 (27)*</td>
</tr>
<tr>
<td>WCH</td>
<td>29</td>
<td>-2.03 ± 0.22*</td>
<td>4.63 ± 3.34*</td>
<td>7 (24)*</td>
<td>8 (28)*</td>
</tr>
</tbody>
</table>

Note: Comparing with normotensive group, *p < 0.05; Comparison of MH group, WCH group and EH group, p > 0.05.
the change in cardiac autonomic nervous activity plays an important role in the appearance and development of hypertension and has an important influence on the prognosis.

Conclusions

The presence of MH and WCH significantly weakens the HRT and can predict cardiovascular disease. Monitoring MH and WCH patients by paying attention to their dynamic and controlling blood pressure, and preventing the development of atherosclerosis, plays an important role in reducing target organ damage and cardiovascular disease. Through early detection of HRT, left ventricular hypertrophy can be reversed and the autonomic nerve can be improved by early treatment intervention.

---

Conflict of Interest
The Authors declare that there are no conflicts of interest.

References


