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# Relationship Between Resting Heart Rate and Carotid Arterial Intima-Media Thickness and Athrosclerotic Plaque in Patients with Essential Hypertension

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## Abstract

**Objective To disscuss the relationship between resting heart rate (RHR) and carotid arterial intima-media thickness (IMT)and athrosclerotic plaque in patients with essential hypertension. Methods To select the patients with essential hypertension from the physical examinationpopulation in The Forth People's Hospital Of Zigong from September, 2015 to August, 2016; and divided into three groups based on RHR, one group: RHR<70 BPM, two group: 70-80 BPM, three group: RHR≥80 BPM. To compare the systolic pressure, diastolic pressure, body mass index (BMI), fasting blood glucose (FPG), total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL), homocysteine (HCY) and carotid arterial intima-media thickness (IMT), athrosclerotic plaque which detected from carotid artery ultrasonography. Results There are 136 patients who had been brought into the study in total,78 patients are male, 58 patients are female, average age is (61.2±10.8)year, one group includes 36 patients (26.5%),two group includes 58 patients(42.6%),three group includes 42 patients(30.9%); age, sex, BMI, diastolic pressure, HCY, FPG, TG, TC, LDL-C, HDL-C in each group has no statistical significance (P>0.05 all); systolic pressure has statistical significance in each group (P<0.001);IMT has statistical significance in each group (P<0.001). RHR is positively associated with IMT in patients with essential hypertension (P<0.01); and RHR is positively associated with systolic pressure, diastolic pressure, BMI (respectively P<0.05, P<0.01, P<0,01). Multivariate logistic regression analysis of athrosclerotic plaque-related factors: increasing RHR can increase the risk of formation of athrosclerotic plaque in patients with essential hypertension (0R=1.162, 95%CI 1.096~1.491); and age, the level of LDL-C also can increase the risk of formation of athrosclerotic plaque(respectively OR=1.051, 95%CI 1.026~1.068; OR=1.368, 95%CI 1.039~1.818).Conclusion There is linear positive correlation between RHR and IMT in patients with essential hypertension, and increased RHR is a risk factor for formation of carotid artery athrosclerotic plaque.**

## Keywords

**Hypertension; heart rate; carotid arterial intima-midia; athrosclerotic plaque.**

## 1. INTRODUCTION

Hypertension is a common chronic disease as well as a progressive disease, which can lead to damage to the heart, brain, kidney and other important organs. Regardless of acute coronary heart disease events, acute ischemic events or hemorrhagic stroke events, hypertension is the first risk factor [1]. 70% of stroke is related to hypertension, and common carotid artery IMT has a better predictive value for stroke [2]. Increased heart rate is a reliable indicator of

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sympathetic overactivation [3]. Previous studies have shown that heart rate is an independent risk factor for carotid atherosclerosis in patients with essential hypertension [4], and carotid intima media thickness (IMT) is the most commonly used indicator to evaluate carotid atherosclerosis. In this study, the relationship between RHR and IMT in patients with essential hypertension, as well as the risk factors for the occurrence of carotid atherosclerosis plaque, was investigated by measuring RHR and carotid ultrasound examination in patients with essential hypertension, so as to provide certain clinical evidence for the comprehensive and effective management of hypertension patients.

## 2. OBJECTS AND METHODS

### 2.1. Objects

A total of 136 patients with essential hypertension were randomly selected from the physical Examination center of The Fourth People's Hospital of Zigong city from September 2015 to August 2016. There were 78 males and 58 females, aged 40-75 years. Inclusion criteria :(1) meet the diagnostic criteria of hypertension in the Chinese guideline for hypertension prevention and treatment 2010[5]; (2) Complete basic data; (3) Agree to participate in this study and sign the informed consent. Exclusion criteria :(1) clear the history of secondary hypertension; (2) Severe hepatic and renal insufficiency, severe valvular heart disease, heart failure, severe hyperlipidemia, and tumor; (3) Diseases affecting heart rate, such as hyperthyroidism and severe anemia; (4) Patients who are taking drugs that affect their heart rate, such as beta-blockers.

### 2.2. Methods

(1) In this cross-sectional study, general information of patients, including gender and age, was obtained through the physical examination information management system, height and weight were measured using standard methods, and body mass index (BMI) was calculated according to BMI= weight (kg)/height (m2). The blood pressure values were obtained by using the corrected omron arm electronic sphygmomanometer. Before measurement, the blood pressure of the brachial artery in the right upper arm was measured for 3 times and the mean value was obtained. The values of fasting blood glucose (FPG), blood lipid and homocysteine were determined by Olympus AU automatic biochemical analyzer in the morning.

(2) RHR measurement: All patients were in a quiet environment. Standard 12-lead electrocardiogram was recorded by a three-channel electrocardiogram machine, and the RHR was calculated using the mean R-R interval. According to the RHR value, the patients were divided into three groups: group 1: RHR<70 BPM, group 2:70-80 BPM, and group 3: RHR≥80 BPM.

(3) Measurement of carotid intima thickness (IMT) : By special survey work in the ultrasonic 5 years full-time physicians determination, philips A50 ultrasound diagnostic instrument, frequency of the probe is 5-12 MHZ, the object of study in recumbent head thrown back, head to check for side, fully exposed to the neck, the probe from the inside along the common carotid artery to bottom-up, longitudinal and transverse scan for common carotid artery, bifurcate department and the internal carotid artery segments and in the end of the bilateral common carotid artery 1-2 cm range, measure the actual IMT, avoid take back wall plaque longitudinal section of this study is to take the larger value of bilateral common carotid artery IMT cadres were analyzed. The criteria of carotid atherosclerotic plaque were local eminence and thickening, protruding into the lumen, and thickness ≥1.2mm.

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### 2.3. Statistical Methods

SPSS13.0 statistical software was used for processing. The measurement data of normal distribution were expressed as mean ± standard deviation (x±s), and the count data were expressed as an example (%). The comparison of the rates was performed by chi-square test. Single-factor analysis of variance was used for the comparison between groups, and linear correlation analysis was used for the correlation between two factors. Correlation between carotid atherosclerotic plaque formation and risk factors was analyzed by multivariate logistic regression, and the difference was statistically significant with P<0.05 (bilateral test).

## 3. RESULTS

1. Basic information: age, sex, BMI, diastolic blood pressure, HCY, FPG, TG, TC, LDLl-c and HDL-c in each RHR group of patients with essential hypertension were not statistically significant (all P>0.05). The difference in systolic blood pressure between the three groups was statistically significant (P<0.001) (Table 1).

2. Comparison of measurement parameters of carotid artery IMT: IMT of 0.76±0.12 (mm) in the first group, 0.88±0.18 (mm) in the second group, and 1.10±0.32 (mm) in the third group were statistically significant (P<0.001) (Table 2).

3. RHR linear correlation analysis: IN patients with essential hypertension, RHR was positively correlated with IMT (r =0.238, P<0.01); RHR was positively correlated with systolic blood pressure (r=0.229, P<0.05), diastolic blood pressure (r=0.323, P<0.01), and BMI (r =0.278, P<0.01) (Table 3).

4. Multivariate logistic regression analysis of influencing factors for carotid plaque formation: with the presence or absence of carotid plaque as the dependent variable, increased RHR in patients with essential hypertension would increase the risk of carotid plaque formation (0R=1.162,95%CI 1.096-1.491); In addition, age also increased the risk of carotid atherosclerosis plaque formation (OR=1.051,95%CI 1.026 ~ 1.068). Increased LDL-C level also increased the risk of carotid atherosclerotic plaque formation (OR=1.368,95%CI 1.039-1.818) (Table 4).

**Table 1.** General conditions of the research objects

| parameter | Different heart rate groups | | | | |
|---|---|---|---|---|---|
| | <70BPM | 70-80BPM | ≥80BPM | F/χ2 | P |
| case | 36 | 58 | 42 | | |
| Age(x±s) | 62.1±11.2 | 60.7±10.1 | 62.6±11.3 | 0.42 | 0.658 |
| Male(%) | 21(58.3) | 38(65.5) | 30(71.4) | 1.470 | 0.479 |
| BMI(kg/m$^2$,x±s) | 24.7±3.3 | 24.6±3.9 | 24.8±3.5 | 0.0373 | 0.963 |
| SBP(mmHg,x±s) | 129.5±9.8 | 136.3±15.2 | 142.2±16.1 | 7.656 | <0.001 |
| DBP(mmHg,x±s) | 88.2±9.6 | 90.3±11.7 | 89.4±10.8 | 0.413 | 0.662 |
| HCY(umol/L,x±s) | 8.59±4.23 | 9.27±4.16 | 10.42±4.58 | 1.829 | 0.165 |
| FPG(mmol/L,x±s) | 5.2±1.6 | 5.4±1.8 | 5.6±2.2 | 0.437 | 0.647 |
| TG(mmol/L,x±s) | 1.28±0.19 | 1.31±0.15 | 1.30±0.20 | 0.319 | 0.728 |
| TC(mmol/L,x±s) | 4.53±0.16 | 4.55±0.18 | 4.60±0.21 | 1.540 | 0.218 |
| LDL-C(mmol/L,x±s) | 3.08±0.15 | 3.06±0.13 | 3.05±0.17 | 0.406 | 0.667 |
| HDL-C(mmol/L,x±s) | 1.01±0.17 | 0.98±0.14 | 1.02±0.15 | 0.95 | 0.389 |

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**Table 2.** Comparison of measurement parameters of carotid artery IMT in 3 groups

| group | case | IMT(mm,x±s) |
|---|---|---|
| <70BPM | 36 | 0.76±0.12 |
| 70-80BPM | 58 | 0.88±0.18 |
| ≥80BPM | 42 | 1.10±0.32 |
| F/χ2 | | 24.097 |
| P | | <0.001 |

**Table 3.** Linear correlation analysis of resting heart rate

| virable | RHR | |
|---|---|---|
| | r | P |
| SBP | 0.229 | <0.05 |
| DBP | 0.323 | <0.01 |
| BMI | 0.278 | <0.01 |
| IMT | 0.238 | <0.01 |

**Table 4.** Results of multivariate logistic regression analysis of influencing factors for carotid atherosclerotic plaque formation

| virable | β | SE | χ2 | P | OR(95%CI) |
|---|---|---|---|---|---|
| age | 0.048 | 0.012 | 16.862 | 0.000 | 1.051 (1.026-1.068) |
| RHR | 0.241 | 0.101 | 4.412 | 0.039 | 1.162 (1.096-1.491) |
| LDL-C | 0.315 | 0.147 | 4.852 | 0.031 | 1.368 (1.039-1.818) |

## 4. DISCUSS

Hypertension is the most common cardiovascular disease, according to the fourth national nutrition and health survey in 2002, our country adult hypertension prevalence rate of 18.8% above the age of 18, with 60 years of age or older prevalence rate is as high as 49.1%, according to calculations, hypertension is now more than 200 million people in China [6], and high blood pressure is the most important risk factor for stroke, so also is the high incidence of stroke in China region, stroke has become the leading cause of death in China [7]. Carotid atherosclerosis is a high risk factor for stroke in hypertensive patients, and heart rate is an independent risk factor for carotid atherosclerosis in patients with essential hypertension. Studies have shown that stroke risk is reduced by about 40% for every 10mmHg reduction in systolic blood pressure or 5mmHg reduction in diastolic blood pressure [8]. Therefore, it is necessary for us to comprehensively manage and control the heart rate and blood pressure of hypertensive patients, so as to make them reach the standard comprehensively, improve the prognosis of hypertensive patients and improve their quality of life.

Carotid artery IMT has been used as a good substitute for the observation and evaluation of atherosclerosis, and has become a "window" reflecting systemic atherosclerosis, because its measurement method is simple, non-invasive and reproducible. This group of data showed that with the increase of RHR in patients with essential hypertension, the carotid artery IMT was also thickened, and the difference between the groups was statistically significant. Correlation analysis showed that RHR was positively correlated with IMT in hypertensive patients ($r=0.238$, $P<0.01$). The reasons for IMT thickening caused by RHR acceleration may be related to the following factors :(1) increased heart rate can enhance the pulsation of arterial blood flow, resulting in shock along the direction of shear stress, which in the long run can damage the vascular endothelium, promote platelet and lipid deposition, and produce atherosclous plaque; (2) Patients with high RHR have strong sympathetic nerve activity, and sympathetic activation can increase the concentration of plasma norepinephrine and other neuroendocrine factors

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through neuroendocrine effect, while excessive concentration of some neuroendocrine factors may have toxic effect on vascular endothelium [9]. (3) The high frequency shear force generated by the high speed blood flow can activate superoxidase and inflammatory factors, etc., thus producing the relevant oxidative stress response and affecting the gene expression of vascular endothelial cells [10]. This research shows that other RHR faster, systolic pressure, diastolic blood pressure and BMI also increases accordingly, now consider associated with an increased sympathetic nervous activity, studies have shown that the sympathetic nerve excitement can lead to heart rate increase fast, vasoconstriction, blood pressure, obesity and metabolic abnormalities, such as sugar, sympathetic activation and heart rate increase fast, metabolic disorders, etc have certain correlation [11]. There are limitations in this study. Although resting heart rate is found to be associated with carotid artery intima thickening and atherosclerotic plaque formation, the causal relationship between the two is not clear. There are still confounding factors that have not been corrected.

To sum up, the rate of RHR in patients with essential hypertension is related to the incidence of atherosclerosis. However, the occurrence of atherosclerosis is not solely caused by the rapid RHR, but is the result of the combined effect of multiple factors. But RHR is an easy and accurate measurement and obtain parameters, monitoring RHR the occurrence of atherosclerosis in patients with primary hypertension is of certain guiding role, for RHR increase quickly to control the heart rate in the treatment of hypertension patients can improve the process of atherosclerosis, in patients with primary hypertension management should strive to make their blood pressure, heart rate, etc, to avoid the occurrence of atherosclerosis and stroke.

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