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Analysis of risk factors of cardiac metabolic abnormality in patients with hypertension.

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Abstract

Objective: This study was designed to investigate the potential risk factors of cardiac metabolic abnormality in hypertension patients during the early stage.
Methods: In total, 1649 participants were enrolled in this clinical trial. Baseline data of all participants were collected and analysed. In the advanced-stage hypertension group, 530 patients diagnosed with hypertension were assigned, 562 patients with early-stage hypertension in the early-stage hypertension group and 557 with normal blood pressure in the control group. The potential risk factors of cardiac metabolic abnormality were statistically analysed in this case-control study.
Results: In the early-stage hypertension group, the blood pressure, age, Body Mass Index (BMI), waistline, serum levels of uric acid and hypersensitivity C-reactive protein were significantly higher, whereas the high-density lipoprotein cholesterol level was significantly lower compared with those in the control group (all P<0.05). Logistic regression analysis revealed that age and BMI were risk factors of the incidence of early-stage hypertension. In the advanced-stage hypertension group, 68.9% of patients were complicated with at least one metabolic disorder, and 52.0% in the early-stage hypertension group.
Conclusion: Age and BMI were risk factors of the incidence of early-stage hypertension. For early-stage hypertension patients, active measures should be implemented to prevent and treat the potential risk of cardiovascular metabolic disorders.

Keywords: Early-stage hypertension, Hypertension, Cardiac metabolic abnormality, Risk factor.

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Introduction

Hypertension is defined as having a blood pressure higher than 140 over 90 mmHg, with a consensus across medical guidelines [1-3]. Long-term high blood pressure is a major risk factor for coronary artery diseases, stroke, heart failure, peripheral vascular disease, vision loss and chronic kidney disease, etc. [4,5]. Lifestyle changes and medications can lower blood pressure and decrease the risk of health complications. Lifestyle changes include weight loss, decreased salt intake, physical exercise, and a healthy diet. If lifestyle changes are not sufficient then blood pressure medications are used. Up to three medications can control blood pressure in 90% of people. The treatment of moderately high arterial blood pressure (defined as >160/100 mmHg) with medications is associated with an improved life expectancy. The effect of treatment of blood pressure between 140/90 mmHg and 160/100 mmHg is less clear, with some reviews finding benefit and others finding a lack of evidence for benefit. High blood pressure affects between 16 and 37% of the population globally. In 2010, hypertension was believed to have been a factor in 18% (9.4 million) deaths [6]. Effective lifestyle modification may lower blood pressure as much as an individual antihypertensive drug. Combinations of two or more lifestyle modifications can achieve even better results. There is considerable evidence that reducing dietary salt intake lowers blood pressure, but whether this translates into a reduction in mortality and cardiovascular disease remains uncertain. Estimated sodium intake ≥ 6 g/day and <3 g/day are both associated with high risk of death and/or major cardiovascular disease, but the association between high sodium intake and adverse outcomes is only observed in people with hypertension [7-9]. In this case-control study, healthy controls, early-stage hypertension and hypertension patients were recruited to investigate the potential risk factors of cardiac metabolic abnormality and analyse the association between the incidence of cardiac metabolic abnormality and hypertension, aiming to provide more evidence for clinical prevention and treatment of hypertension complicated with cardiac metabolic disorder.

Materials and Methods

Study subjects

In this case-control study, 557 healthy controls with normal blood pressure during physical examination in Jiangxia Street

Health Service Center, Haishu District, Ningbo were enrolled. Moreover, clinical data of 530 advanced-stage hypertension (both abnormal IGT and OGTT) patients and 562 patients diagnosed with early-stage hypertension (OGTT range: 7.8-11.0 mmol/L, and abnormal IGT) [2-4] admitted to Department of Cardiovascular Medicine, Ningbo First Hospital were retrospectively analysed. Among all participants, 986 subjects were male and 663 female, aged ranging from 35.0 to 85.0 y with a mean age of 52.0 y. All enrolled subjects have signed the written informed consents. All study procedures were approved by the ethics committee of Ningbo First Hospital.

Diagnostic criteria

A subject was considered hypertensive if he or she had a mean systolic blood pressure of ≥ 140 mmHg, a mean diastolic blood pressure of ≥ 90 mmHg and/or was already taking anti-hypertensive medication. A systolic blood pressure of ≥ 160 mmHg or a diastolic blood pressure of ≥ 100 mmHg was considered indicative of stage II hypertension, while corresponding values of ≥ 180 and ≥ 110 mmHg were considered indicative of stage III. Hypertensive persons who had previously received a doctor's diagnosis of hypertension or simply claimed to be hypertensive were considered to be aware of their hypertension. Hypertensive persons who claimed to be receiving any form of anti-hypertensive medication were considered to have treated hypertension. Hypertensive persons whose systolic blood pressure was<140 mmHg or whose diastolic blood pressure was<90 mmHg or both were considered to be controlling their hypertension well.

Overweight and obese criteria

BMI>25.0 kg/m^2; hyperglycemia: fasting plasma glucose (FPG) ≥ 6.1 mol/L (110 mg/dL) and/or diagnosed with diabetes mellitus; fasting triacylglycerol level ≥ 1.7 mmol/L (150 mg/dL); fasting High-Density Lipoprotein Cholesterol (HDL-C)<0.9 mmol/L (35 mg/dL) for male individuals or <1.0 mmoL/L (39 mg/dL) for female counterparts.

Exclusion criteria

Those diagnosed with or having a medical history of coronary heart diseases, stroke, alternative cardiovascular diseases, malignant tumor, type II diabetes mellitus, dyslipidemia or those receiving medication therapy were excluded from subsequent analysis.

Baseline data measurement

Body height, body weight, BMI, hip circumference, waist circumference, blood pressure and heart rate were quantitatively measured and calculated. The blood pressure was measured triple times when the patients were in sitting position. Prior to the measurement, the patients were prohibited from smoking, drinking caffeine beverage or doing intensive physical activity. The mean value was calculated from three times measurement.

Laboratory examination

Intravenous blood samples were collected in the early morning under fasting status. Then, the obtained samples were sent to the laboratory for parameter examination including routine blood test, detection of triacylglycerol, total cholesterol, HDL-C, LDL-C, FPG, uric acid, mean platelet volume, hypersensitive C-Reactive Protein (hs-CRP).

Statistical analysis

SPSS 20.0 statistical software was utilized for data analysis (SPSS Inc., Chicago, USA). All continuous variables were subject to test of normality. The mean values among different groups were statistically compared by using analysis of variance. Measurement data were analysed using t-test. Enumeration data were studied by χ^2 test. The risk factors of cardiac metabolic abnormality in hypertension were analysed using Logistic regression analysis. A value of P<0.05 was considered as statistical significance.

Results

Baseline data

Among three groups, gender, smoking habit, drinking alcohol and physical activity did not significantly differ (all P>0.05). In the early-stage and advanced-stage hypertension groups, age, blood pressure, BMI, WC, uA, TG and hs-CRP levels were significantly higher, whereas the HDL-C level was significantly lower compared with those in the control group with statistical significance (all P<0.05). In the advanced-stage hypertension group, the proportion of patients with a family history of hypertension was the highest among all three groups with statistical significance (all P<0.01). In addition, the TC, FPG and WBC in the advanced-stage hypertension group were significantly higher than those in the control group (all P<0.05), as illustrated in Table 1.

Risk factors of cardiac metabolic abnormality in patients with hypertension

Age, BMI, WC, TC, HDL-C, LDL-C, TG, uA, FPG, WBC, hs-CRP and MPV were classified into three categories and subject to multivariate logistic regression analysis. The results demonstrated that age, BMI, FPG and uA were the risk factors of the incidence of hypertension. Meantime, age and BMI served as the risk factors of the occurrence of early-stage hypertension, as illustrated in Table 2.

Cardiac metabolic abnormality

In the advanced-stage hypertension group, approximately 68.9% of hypertension patients were complicated with at least one metabolic disorder. In the early-stage hypertension group, 52.0% of these patients were complicated with ≥ 1 metabolic disorder. The proportion of patients complicated with metabolic disorders in two groups was significantly higher compared with that in the control group (both P<0.01), as illustrated in Table 3.

Table 1. *Comparison of baseline data among three groups.*

Parameter	Hypertension group (n=530)	Early-stage hypertension group (n=562)	Control group (n=557)
Male	312	336	338
Female	218	226	219
Age (y)	62.9 ± 10.3*	56.3 ± 11.1*	52.5 ± 10.1
Family history of hypertension (n)	160**	109	125
DBP (mmHg)	82.2 ± 9.6*	77.4 ± 5.9*	68.8 ± 5.5
SBP (mmHg)	133.9 ± 16.3*	123.1 ± 6.9*	106.7 ± 7.6
BMI (kg/m^2)	23.9 ± 3.5*	23.0 ± 3.3*	21.8 ± 2.7
WC (cm)	83.7 ± 9.7*	80.4 ± 8.7*	77.4 ± 8.1
TC (mmol/L)	5.8 ± 1.4*	5.7 ± 1.3	5.6 ± 1.2
HDL-C (mmol/L)	1.3 ± 0.3*	1.3 ± 2.3*	1.4 ± 0.3
LDL-C (mmol/L)	3.7 ± 1.3	3.6 ± 1.1	3.6 ± 0.8
TG (mmol/L)	1.9 ± 1.2*	1.8 ± 1.3*	1.5 ± 0.8
uA (μmol/L)	379.1 ± 91.1*	344.6 ± 88.1*	331.1 ± 82.1
FPG (mmol/L)	5.5 ± 1.7*	5.0 ± 1.5	4.9 ± 1.4
WBC (× 10^9/L)	7.4 ± 4.6	6.8 ± 4.3	6.8 ± 4.8
MPV (fL)	10.1 ± 0.8	10.0 ± 0.5	10.1 ± 0.6
hs-CRP (mg/L)	3.3 ± 6.6**	2.8 ± 0.8*	1.8 ± 0.3
Note: *represents statistical significance compared with the control group.			

Table 2. *Logistic regression analysis of multiple parameters among three groups.*

Parameter	Regression coefficient	P value	OR value	95% CI
Hypertension group*				
Age	0.085	0	1.088	1.022-1.105
WC	0.021	0.049	1.024	1.001-1.058
BMI	0.141	0	1.154	1.088-1.201
TC	-0.022	0.881	0.971	0.665-1.431
FPG	0.092	0.032	1.902	1.002-1.191
HDL-C	-0.365	0.221	0.685	0.371-1.253
LDL-C	-0.008	0.925	0.99	0.766-1.251
TG	0.132	0.102	1.145	0.965-1.321
uA	0.002	0.004	1.001	1.001-1.006
MPV	-0.047	0.587	0.952	0.801-1.123
WBC	0.025	0.045	1.021	1.000-1.054
hs-CRP	-0.003	0.854	0.995	0.971-1.022
Early-stage hypertension group*				

Age	0.031	0.001	1.033	1.021-1.048
WC	0.014	0.235	1.011	0.991-1.036
BMI	0.085	0.004	1.088	1.024-1.158
TC	0.154	0.195	1.166	0.921-1.477
FPG	0.011	0.817	1.012	0.921-1.100
HDL-C	-0.381	0.152	0.685	0.401-1.168
LDL-C	-0.185	0.105	0.826	0.652-1.045
TG	0.033	0.758	1.022	0.875-1.211
uA	0.001	0.699	1.002	0.995-1.021
MPV	-0.031	0.711	0.985	0.822-1.120
WBC	0.004	0.656	1.002	0.958-1.036
hs-CRP	0.005	0.485	1.005	0.985-1.035
*represents statistical significance compared with the control group				

Table 3. *Comparison of the prevalence of metabolic abnormality among three groups.*

Parameter	**Hypertension group (n=530)**	**Early-stage hypertension group (n=562)**	**Control group (n=557)**
Complicated with one metabolic abnormality			
Lipid metabolic disorder	121 (22.8%)	136 (24.2%)	112 (20.1%)
High glucose level	31 (5.9%)	15 (2.7%)	13 (2.3%)
Overweight and obesity	69 (13.1%)	53 (9.4%)	47 (8.4%)
Complicated with two metabolic abnormalities			
Lipid metabolic disorder and high glucose level	31 (5.8%)	15 (2.7%)	11 (1.9%)
High glucose level and obesity	18 (3.2%)	3 (0.5%)	5 (0.9%)
Lipid metabolic disorder and obesity	69 (13.1%)	63 (11.2%)	27 (4.9%)
Complicated with three metabolic abnormalities			
Lipid metabolic disorder, high glucose level and obesity	30 (5.7%)	9 (1.6%)	3 (0.5%)
Total	368 (69.4%)*	294 (52.1%)*	218 (37.6%)
*represents statistical significance compared with the control group			

Discussion

Hypertension is classified as either primary high blood pressure or secondary high blood pressure. Approximately 90 to 95% of cases are primary, defined as high blood pressure due to nonspecific lifestyle and genetic factors [10]. Lifestyle factors that increase the risk include excess salt, excess body weight, smoking, and alcohol. The remaining 5-10% of hypertensive cases is categorized as secondary high blood pressure, defined as high blood pressure due to an identifiable cause, such as chronic kidney disease, narrowing of the kidney arteries, an endocrine disorder, or the use of birth control pills, etc.

In this case-control study, 1649 healthy controls, early-stage and advanced-stage hypertension patients were recruited to investigate the potential risk factors of cardiac metabolic abnormality and analyse the association between the incidence of cardiac metabolic abnormality and hypertension, aiming to provide more evidence for clinical prevention and treatment of hypertension complicated with cardiac metabolic abnormality.

Blood pressure rises with aging and the risk of becoming hypertensive in later life is considerable [11]. Several environmental factors influence blood pressure. High salt intake raises the blood pressure in salt sensitive individuals; lack of exercise, obesity, and depression can play a role in individual cases. The possible role of other factors such as caffeine consumption, and vitamin D deficiency are less clear [12,13]. In this investigation, both BMI and WC in the early-stage hypertension and hypertension groups were significantly higher compared with those in the control group, suggesting that active measures and interventions should be implemented to counteract BMI and WC for patients with early-stage hypertension. Logistic regression analysis demonstrated that a more significant association was observed between blood pressure and BMI compared with that between blood pressure and WC. After adjustment of confounding factors, overweight and obesity were the major risk factors of elevated blood pressure level. The blood pressure level was positively correlated with BMI.

The incidence of hypertension-induced stroke, myocardial infarction and alternative cardiovascular diseases is ever increasing, which is intimately correlated with the abnormal platelet and coagulation function in hypertension patients [14]. MPV is an indicator reflecting the platelet volume. The platelet with high MPV contains a large quantity of granules which are capable of releasing 5-hydroxy tryptamine and B thrombosis protein. Consequently, the adhesion function of the platelet is enhanced, which probably provokes the incidence of platelet aggregation and thrombosis formation. Previous investigations have demonstrated that the MPV in patients with early-stage hypertension was slightly high, whereas it was decreased to normal range after proper adjustment of life style, weight loss and reduction in Na+ intake after 20 w. They concluded that the decline in MPV is potentially associated with the lower incidence of thrombosis formation in individuals diagnosed with early-stage hypertension [15]. In this study, the MPV was statistically compared among the patients with advanced-stage hypertension and early-stage hypertension and healthy controls. However, no statistical significance was documented in terms of the MPV among different populations, which probably results from the race disparity between two studies. In addition, complex variations probably occur in patients diagnosed with hypertension, which cannot be comprehensively reflected by the MPV alone.

In terms of WBC parameter, the WBC in the advanced-stage hypertension group was significantly higher compared with that in the control group. The hs-CRP levels in both the early-stage and advanced-stage hypertension groups were considerably higher than that in the control counterparts. Among all inflammatory parameters, hs-CRP level is more sensitive compared with WBC since the hs-CRP level rather than the WBC tends to elevate in patients diagnosed with early-stage hypertension. Similarly, previous investigations demonstrated that hs-CRP level is a stable and accurate indicator reflecting the clinical prognosis of cardiovascular diseases and mortality rate in hypertensive individuals. The elevation in hs-CRP level prompts the higher risk of cardiovascular diseases in hypertensive patients, which is considered to be associated with chronic and mild inflammation responses.

In addition, logistic regression analysis revealed that FPG and uA are risk factors of the incidence of hypertension, whereas these two parameters are not associated with the early-stage hypertension. Approximately 52.0% of patients diagnosed with early-stage hypertension are complicated with at least one metabolic disorder. Logistic regression analysis hinted that BMI is the risk factor of the occurrence of early-stage hypertension. Therefore, patients diagnosed with early-stage hypertension have a relatively high risk of cardiac metabolic abnormality. Previous studies also reported that approximately 31.3% of early-stage hypertension is likely to progress into hypertension within 5 y, especially for those complicated with high levels of TC and LDL-C levels. Moreover, the elderly patients are also a high risk population. Previous investigations have demonstrated that the inner membrane of radial artery in patients diagnosed with early-stage hypertension is thicker compared with that of healthy counterparts [16]. Consequently, the incidence of the thickening of inner membrane of carotid artery is regarded as a clinical parameter for the incidence of early-stage hypertension, especially in those with a blood pressure between 130-139/80-89 mmHg. In addition, patients diagnosed with early-stage hypertension present with pathological enlargement of the left ventricular volume, prompting that early-stage hypertension can also lead to target organ injuries [17]. These findings collective demonstrated that patients diagnosed with early-stage hypertension have a risk of cardiac metabolic abnormality, even suffering from target organ damage. Consequently, effective and active interventions, such as weight loss and healthy life style, should be taken to prevent and control the incidence of cardiac metabolic abnormality for patients with early-stage hypertension. In China, the overall prevalence of hypertension rose substantially between 2002 and 2010 from 20% to 34%. Unfortunately, the management of hypertension in China has been ineffective for many years. In 2010, only 35.7% of hypertensive individuals were aware of their condition and fewer than 18% of such individuals were effectively controlling their hypertension [16,17]. It has been estimated that hypertension was associated with 20% of the deaths recorded in China in 2005, including 2.33 million-nearly 80% of the deaths from cardiovascular diseases. Hypertension not only causes premature death, but also adds to household costs. Consequently, potential risk factors should be considered and glucose level control and physical exercise contribute to prevent the risk of early-stage population, especially for the senior population with high BMI.

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