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An effective indicator in predicting cardiovascular events: urine albumin to creatinine ratio

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Abstract. – OBJECTIVE: To study elderly hypertensive patients with trace albuminuria (urine albumin to creatinine ratio (UACR)) and the relationship between the occurrence of new cardiovascular events, to provide a basis for early prevention in elderly patients with high blood pressure.

PATIENTS AND METHODS: A total of 3564 elderly patients with high blood pressure were enrolled in the study. Based on UACR, patients were divided into four groups (group A: 0.05-3.20 mg/g; group B:3.21-10.04 mg/g; group C: 10.05-19.33 and group D: 19.34-30.00 mg/g). All patients underwent follow-up for an average period of 3.8 years. Four groups were compared for new cardiovascular events and they were correlated with UACR.

RESULTS: Through multivariate Cox proportional hazards regression analysis, the relative risk of cardiocerebrovascular events, cerebral infarction, and acute myocardial infarction (mi), in group D was 1.74 times ($p < 0.05$), 1.66 times ($p < 0.05$), and 2.48 times ($p < 0.05$), respectively. UACR level in females and those with higher age, body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C levels and lower HDL-C were higher. During follow-up, patients from group D with sudden cardiac death, acute myocardial infarction, cerebral hemorrhage, cerebral infarction occurrence was significantly higher than group A ($\chi^2 = 79.3$, $p = 79.3$)

CONCLUSIONS: According to UACR level, we can perform early prevention for elderly patients with high blood pressure, thus reducing the occurrence of cerebral infarction and myocardial infarction.

Key Words:
Elderly hypertension crowd, urine trace albumin, Urine creatinine, New cardiovascular events.

Introduction

Hypertension (high blood pressure) in the elderly population is one of the most common diseases seen in cardiovascular medicine, and is also one of the main diseases threatening human health. High blood pressure can also increase the incidence of coronary heart disease and cerebrovascular disease[1]. According to a 1991 survey in China[2], the prevalence of high blood pressure was 11.98% among 950,356 people from 30 provinces and cities in the nation. The prevalence in the elderly population is as high as 34.4%. One study[3] showed that by the end of 2015, the number of patients with hypertension in China had reached 1.6 million, meaning that one out of 9 people has high blood pressure in China. The rate of patients with hypertension is still rising and there are 360 million new cases of hypertensive patients every year in our country. High blood pressure can seriously affect the patient's heart, brain and blood vessel function, which can seriously affect the patient's quality of life. Three major complications (stroke, heart failure, or myocardial infarction) in patients with essential hypertension (EH) are the main conditions that can threaten a patient's life and the leading causes of death in patients with hypertension. The mortality caused by hypertension and its complications is the leading cause of human mortality[4]. In recent years, the treatment and prevention of hypertension have gradually become an area of intense research due to the development of pharmaceuticals. Payab et al[5] showed that hypertensive patients in the early stage of disease could be well controlled, but so far there are no effective treatments for hypertension. At present, it is only possible to maintain control of the disease. Early and long-term prevention of hypertension is therefore very important, and can reduce the occurrence of cardiovascular and

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cerebrovascular events, improving the quality of life and reducing the mortality rate of patients. It was reported that the urinary albumin to creatinine ratio (UACR) in elderly patients with hypertension is closely associated with new cardiovascular events[6]. The higher the UACR, the higher the occurrence of new cardiovascular events. At present, the study of UACR in hypertensive patients is low in our country. Therefore, we studied the relationship between UACR level and new cardiovascular events in elderly patients with hypertension, so as to improve the effective basis for early prevention and treatment of hypertension. 3564 elderly hypertensive patients were selected and divided into four groups (A, B, C, D) according to the level of UACR to compare the occurrence rate of new cardiovascular events, proportion of males, average age, body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C and HDL-C levels of patients in each group.

Patients and Methods

Patients

We selected 3564 elderly patients with hypertension in our hospital from June 2008 to June 2010, and all met the diagnostic criteria of hypertension outlined in the Chinese hypertension prevention guide[7]: 1. Patients with systolic blood pressure ≥140 mmHg (1 mmHg = 0.133kPa) and diastolic pressure ≥90 mmHg; 2. Patients with systolic blood pressure ≥140 mmHg; 3. Patients with diastolic pressure ≥90 mmHg. Exclusion criteria include[7]: 1. Patients with myocardial infarction. 2. Patients who had a stroke. 3. Patients with liver or renal function damage, alanine aminotransferase (ALT) and Creatinine levels higher than normal than >2 fold. 4. Patients with kidney disease, infectious diseases, cancer, blood diseases or autoimmune diseases. Patients were divided into 4 groups: A, B, C or D according to the level of UACR detected. There were 901 patients in group A, with UACR levels between 0.05-3.20 mg/g, 884 patients in group B, with UACR levels between 3.21-10.04 mg/g, 889 patients in group C, with UACR levels between 10.05-19.33 mg/g and 890 patients in group D with UACR levels between 19.34-30.00 mg/g. This study was approved by the Ethics Committee of Shanghai TCM Integrated Hospital. Signed written informed consents were obtained from the patients and/or guardians.

Detection Methods

Urine samples were collected in the early morning and the urinary albumin and creatinine values were measured. We then calculated the urinary albumin to creatinine ratio (UACR). The TG, TC, LDL-C, HDL-C, fasting plasma glucose, uric acid and liver and renal function indexes were calculated by laboratory tests[8]. Measurements of blood pressure, height and body mass were noted. Information about previous cardiovascular disease history in patients and relevant diagnoses and treatments were collected. Patients who smoked at least one cigarette per day with a continuous smoking history of more than one year were defined as smoking patients.

Observation Index

The patients were followed up and analyzed for the occurrence of sudden cardiac death, acute myocardial infarction, cerebral hemorrhage and cerebral infarction in the different groups and we made comparisons on the ratio of males to females, age, body weight index, smoking, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C levels and HDL-C level of patients in the different groups at the same time.

Follow-up

All patients were followed up from June 2010 to June 2015 and the average time of follow-up was 3.8 ± 1.2 years. Specific follow-up steps were as follows: patient received a telephone inquiry or clinical inquiry every six months. The occurrence of new cardio cerebral vascular events was recorded, including non-fatal events and mortality events. If a patient died, the family was asked for pertinent information. Cardiac events include acute myocardial infarction and sudden cardiac death. The diagnostic criteria for acute myocardial infarction were based on the diagnostic criteria developed by the Chinese Medical Association of Cardiovascular Disease[9,10]. Diagnostic criteria for sudden cardiac death were based on the diagnostic criteria developed by ACC/AHA/ESC in 2006[11]. The diagnosis criteria of cerebral vascular events were mainly based on the diagnostic criteria of the Fourth Academic Conference of cerebrovascular disease, mainly including cerebral hemorrhage and cerebral infarction[12].

Statistical Analysis

The data in this study were mainly analyzed by using SPSS statistical analysis software (SPSS Inc., Chicago, IL, USA), using χ^2-test for comparisons of the prevalence of sudden cardiac death, acute myocardial infarction, cerebral hemorrhage and cere-

Table I. Comparison of general information and biochemical indexes of patients in the four groups.

Index	Group A (n=901)	Group B (n=884)	Group C (n=889)	Group D (n=890)	*p*-value
Male/female (No.)	689/212	654/230	636/253	604/286	<0.05
Age (years)	67.4±7.3	69.8±8.4	72.5±6.6	76.9±4.9	<0.05
Body mass index (kg/m^2)	24.7±3.3	25.0±3.6	25.4±3.7	26.1±4.0	<0.05
Smoking [No. (%)]	147 (16.3)	156 (17.6)	161 (18.1)	158 (17.8)	>0.05
Systolic blood pressure (mmHg)	136.2±20.1	138.4±21.3	139.6±22.6	143.2±23.8	<0.05
Diastolic pressure (mmHg)	84.7±13.1	85.1±13.5	85.4±13.8	85.5±14.1	<0.05
Fasting blood glucose (mmol/L)	4.6±2.5	5.1±3.1	5.3±3.2	6.0±3.5	<0.05
TC (mmol/L)	4.7±1.3	5.1±1.5	5.4±1.6	5.9±1.7	<0.05
TG (mmol/L)	2.0±1.1	2.3±1.4	2.5±1.3	2.9±1.5	<0.05
LDL-C (mmol/L)	2.5±0.8	2.8±1.0	3.4±1.3	3.9±1.6	<0.05
HDL-C (mmol/L)	1.7±0.5	1.5±0.4	1.2±0.2	0.9±0.4	<0.05

bral infarction for patients in the four groups, using *t*-test for the age, body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C and HDL-C levels of the four groups of patients and it was set that at α=0.05 indicates the standard for significant difference and when $p < 0.05$, there was a statistically significant difference.

Results

Comparison of General Information and Biochemical Indexes of Patients in Four Groups

The UACR levels in females and those with higher age, body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C levels and lower HDL-C were higher. The differences between each group were statistically significant ($p < 0.05$) (Table I).

Comparison of Occurrence of new Cardiovascular Events During Follow-up of patients in the four Groups

During follow-up, sudden cardiac death, acute myocardial infarction, cerebral hemorrhage, and cerebral infarction occurrence in patients of group D were significantly higher than those in group A ($\chi^2 = 79.3$, $p < 0.001$). The differences were statistically significant.

Multivariate Cox Proportional Hazard Regression Analysis

Sudden cardiac death, acute myocardial infarction, cerebral hemorrhage and cerebral infarction of patients, as dependent variables, were compared between the four groups, and group A was set as the control group. The general information (age, gender, body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C, HDL-C) with statistical differences among the four groups were used as the independent variables to carry on the single factor analysis. The Enter method was used to put these variables into the equation, and the variables in the three groups B, C, and D were listed. The results showed that the age, gender, systolic blood pressure and other factors were related to the total cardiovascular events and cerebral infarction in patients of group D. The age and gender of patients in group D were related to myocardial infarction. Through the correction of the above factors, the results show that the total

Table II. Comparison of occurrence of new cardiovascular events during follow-up of patients in the four groups.

New cardiovascular events	Group A (n=901)	Group B (n=884)	Group C (n=889)	Group D (n=890)
Sudden cardiac death	0 (0.0)	1 (0.1)	3 (0.4)	7 (7.9)*
Acute myocardial infarction	4 (0.4)	9 (1.0)	22 (2.5)	34 (3.8)*
Cerebral hemorrhage	3 (0.3)	6 (0.7)	11 (1.2)	22 (2.5)*
Cerebral infarction	18 (2.0)	27 (3.1)	48 (5.4)	67 (7.5)*
Total occurrence rate of cardiovascular events	25 (2.7)	43 (4.9)	84 (9.5)	130 (14.7)*

Note: Comparison of group A and D (*$p < 0.05$, $\chi^2 = 79.3$.

Table III. Multivariate Cox proportional hazard regression analysis.

Index	B value	Wald	R value	95%CI	*p*-value
Total cerebral vascular events					
Group B	0.06	0.41	1.12	0.71-1.86	0.639
Group C	0.17	1.13	1.20	0.62-1.79	0.342
Group D	0.54	9.49	1.75	1.31-2.56	0.001
Gender	0.29	6.18	1.41	1.01-1.96	0.002
Age	0.07	75.7	1.04	1.03-1.06	0.001
Systolic blood pressure	0.13	14.9	1.05	1.00-1.02	0.015
Cerebral infarction					
Group B	0.14	0.68	0.88	0.51-1.43	0.362
Group C	0.09	0.17	1.16	0.85-1.87	0.508
Group D	0.46	5.24	1.63	1.16-2.56	0.004
Gender	0.51	5.71	1.54	1.21-2.42	0.021
Age	0.06	50.2	1.10	1.10-1.12	0.003
Systolic blood pressure	0.04	29.3	1.06	1.01-1.04	0.002
Acute myocardial infarction					
Group B	0.41	1.44	1.51	0.91-2.85	0.318
Group C	0.18	1.27	1.08	0.31-2.07	0.538
Group D	0.89	8.19	2.54	1.31-3.52	0.005
Gender	0.68	3.53	1.99	1.05-3.88	0.029
Age	0.05	32.08	1.13	1.02-1.10	0.001

cardiovascular events, the relative risk factors for cerebral infarction and acute myocardial infarction in patients of group D, were 1.74 times ($p < 0.05$), 1.66 times ($p < 0.05$) and 2.48 times ($p < 0.05$) that of group A respectively (Table III).

Discussion

With the improvement of living standards, people's lifestyles and diet structure have changed. The incidence of hypertension in China has increased year by year[13]. Hypertension is a common clinical chronic disease, which is the main risk factor for cardiovascular and cerebrovascular diseases[14-16]. Stroke, myocardial infarction, heart failure and chronic kidney disease are the main complications and the leading causes of death in patients with hypertension[17], accounting for the number one cause of mortality among human diseases. The clinical definition of hypertension is systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg without the use of antihypertensive drugs. It can be divided into grade 1, 2 or 3 according to the level of blood pressure of the patient. At the same time, the state of the patient will determine the progression of disease severity, including benign hypertension and malignant hypertension. Benign hypertension is the main type seen in clinic[18]. Patients with benign hypertension show no symptoms in the early stage. Physical examinations occasionally cause increased blood pressure, dizziness, vertigo, tinnitus, insomnia, and lack of adverse reactions after fatigue or emotional agitation. The blood pressure of hypertensive patients only has a transient increase in the early stage[19]. With the progression of hypertension, the blood pressure will continue to rise, affecting organ function. Hypertensive patients in the latter stage will appear with headache, dizziness and excessive labor, climate temperature stimuli and disease rebound caused by discontinuation of drugs will cause the patient discomfort[20]. The patient's blood pressure will rise sharply, and there will be a severe headache, nausea and visual impairment among other symptoms. Severe patients will present with convulsions, coma and a transient paralysis[21]. Early cardiac performance is not charactetistic in patients with hypertension. Cardiac function still has normal compensatory ability. Loss of compensation in cardiac function will appear in the latter stage and lead to heart failure[22]. Patients with hypertension will have renal dysfunction due to chronic renal hypertension, leading to renal arteriosclerosis, nocturia, polyuria, and urine containing large amounts of protein. Urinary concentrating ability will be impaired, resulting in azotemia and uremia[23]. The occurrence of cardiovascular events was

significantly increased in elderly patients with hypertension due to the effect of aging on various organs and tissues[24]. Elderly patients with hypertension are prone to stroke, heart failure and myocardial infarction as well as other complications[25], which seriously endangers the lives of these patients. Because the clinical symptoms of patients with hypertension at early stage are not evident, there is a lack of early prevention and treatment in elderly hypertensive patients, making morbidity associated with hypertension more acute, and predisposes them to severe cardiovascular events. Therefore, early diagnosis and prevention of hypertension in elderly patients is very important. Jones and Viberti[26] found that UACR levels can directly predict the risk of cardiovascular events in patients with diabetes. Also, the HOPE (Hearth Outcomes Prevention Evaluation Trial) study[27] found that microalbuminuria is closely linked to cardiovascular events in patients with hypertension, independent of blood pressure. UACR can effectively predict prevalence and mortality of patients with cardiovascular events by detecting microalbuminuria. Ding et al[28] found that urinary albumin levels can be independent of the occurrence of cardiovascular events in the normal human. The current point of view of UACR as an independent predictive factor of cardiovascular events has been recognized. UACR levels can be effective measurement in elderly hypertensive patients with a probability of having cardiovascular events, therefore it provides an effective basis for clinical prevention and treatment, and can effectively prevent sudden cardiac death, acute myocardial infarction, cerebral hemorrhage, cerebral infarction and other complications. In the present study, we also show that, among patients in groups A, B, C and D , with increased UACR, sudden cardiac death, acute myocardial infarction, cerebral hemorrhage, and cerebral infarction in patients from group D were significantly higher than those in group A (χ^2 =79.3, p = 0.00). The occurrence rate of complications in patients of group B and C were higher than those of group A. Koga et al[29] found that UACR levels are linked to patient gender, weight, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C levels and HDL-C levels[29]. We observed that with increased UACR, the proportion of males in groups A, B, C and D decreased significantly. At the same time, the average age of the patients increased and body mass index, systolic blood pressure, fasting blood glucose, TG, TC, LDL-C levels were significantly higher compared to those with lower UACR. However, HDL-C levels decreased. The differences were statistically significant ($p < 0.05$). At the same time, using the Enter method, variables in group B, C, D were listed. The data show that the age, gender, systolic blood pressure and other factors in patients of D group is related to total cardiovascular events and cerebral infarction. Myocardial infarction is related to the age and gender of patients in group D. Through the correction of the above factors, the results show that the relative risk factors of total cardiovascular events, cerebral infarction and acute myocardial infarction of patients in D group were 1.74 times ($p < 0.05$), 1.66 times ($p < 0.05$ and 2.48 times ($p < 0.05$) those of patients in A group, respectively. Therefore, predicting the occurrence rate of cardiovascular disease in elderly patients with hypertension according to the level of UACR is very important for the prevention and treatment of hypertension.

Conclusions

The UACR levels can predict the probability of new cardiovascular events in elderly patients with hypertension. The risk of occurrence of cardiovascular events is higher in patients with high levels of UACR compared to those with low levels of UACR. Therefore, early prevention can be applied in elderly patients with hypertension according to UACR levels, which will effectively reduce the occurrence of cerebral and myocardial infarction. Therefore, UACR levels can predict new onset cardiovascular events in hypertensive patients, and is worth applying clinically.

Conflict of interest

The authors declare no conflicts of interest.

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