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Original Article

Serum potassium levels are associated with coronary artery lesion severity in coronary artery disease

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Abstract: Objectives: The present study is to investigate the relation between serum potassium levels and the severity of coronary artery lesions in coronary artery disease (CAD). Methods: We selected 799 patients who underwent coronary angiography. Serum potassium levels were measured, and Gensini scores were calculated to evaluate the severity of coronary artery lesions in CAD. The correlation between serum potassium level and Gensini scores was examined by Pearson correlation analysis. Results: Serum potassium levels were significantly increased in patients with lower (≤ 39 points; 3.90 ± 0.02 mmol/L, n = 453) and higher (> 39 points; 3.97 ± 0.02, n = 194) Gensini scores compared with normal controls (3.82 ± 0.03 mmol/L; $P < 0.05$). Furthermore, serum potassium level of the high-score group was also significantly higher than that of the low-score group ($P < 0.05$). Positive correlation between serum potassium level and Gensini scores in patients with CAD was observed ($r = 0.093$, $P < 0.05$). In addition, the levels of serum potassium in the single-vessel (3.95 ± 0.03 mmol/L, n = 214), dual-vessel (3.95 ± 0.03 mmol/L, n = 202), and multiple-vessel (3.94 ± 0.03 mmol/L, n = 231) groups were significantly higher than that in the normal control group (3.82 ± 0.03 mmol/L, n = 152; $P < 0.05$). Conclusions: The present study demonstrates that elevated levels of serum potassium are closely associated with the severity of coronary artery lesions and the number of disease vessels in CAD patients.

Keywords: Coronary artery disease, serum potassium, coronary artery lesion

Introduction

As a result of improved living standards, increased social pressure, decreased physical activity, increasingly high-fat diets, and an aging population, the incidence and number of deaths from coronary artery disease (CAD) have been continuously increasing in China over the past decades, and this condition now poses a serious threat to the health of the population [1-4]. CAD is a type of cardiac disease that involves myocardial ischemia and hypoxia or myocardial necrosis resulted from coronary artery stenosis or occlusion. In recent years, several studies have demonstrated that increased serum potassium ion concentration (< 10 mmol/L) induces relaxation of the arterial smooth muscle cells and promotes vasodilatation that is known as K^+-induced vasodilatation [5, 6]. K^+-induced vasodilatation is widely observed in small arteries in various tissues (e.g., myocardial muscle and brain) and explained by two cellular mechanisms: increase in the conductance of inwardly rectifying K^+ channels, and facilitation of electrogenic Na^+/K^+-ATPase [5-8].

In addition, high-potassium diet has been shown to play a role in maintaining normal blood pressure and preventing coronary atherosclerosis [9-11]. Potential mechanisms for this action include the following: i) potassium elevation inhibits free radical formation from vascular endothelial cells and macrophages; ii) increases in potassium inhibit vascular smooth muscle cell proliferation; iii) potassium induces suppression of reactive oxygen species overproduction; iv) potassium elevation inhibits platelet aggregation and arterial thrombosis; and v) potassium elevation reduces renal vascular resistance and increases glomerular filtration rate [9-14]. However, few studies on the correlation between serum potassium levels and the severity of coronary artery lesions have been reported. In this study, we measure serum potassium levels of 799 patients who under-

Table 1. General clinical data of patients with coronary artery disease

Variables	Control group (n = 152)	CAD group (n = 647)	*P* value
Demographic characteristics			
Age (years)	56 ± 0.8	61 ± 0.4	< 0.001
Sex, male, n (%)	100 (66)	401 (62)	> 0.05
Body mass index (kg/m^2)	24.65 ± 0.31	24.53 ± 0.21	0.31
Cardiac or coexisting conditions			
Smoking, n (%)	42 (28)	317 (49)	< 0.01
Alcohol consumption, n (%)	32 (21)	284 (44)	< 0.01
Hypertension, n (%)	86 (67)	351 (54)	> 0.05
Diabetes, n (%)	24 (16)	110 (17)	> 0.05
Dyslipidemia, n (%)	60 (39)	449 (69)	< 0.01
Previous myocardial infarction	0	38 (5)	
Previous angioplasty	0	61 (9)	
Previous bypass surgery	0	7 (1)	
Biological parameters			
TG (mmol/L)	1.75 ± 0.09	2.28 ± 0.06	< 0.001
T-CHO (mmol/L)	4.58 ± 0.08	5.02 ± 0.05	< 0.001
HDL-C (mmol/L)	1.15 ± 0.02	1.13 ± 0.01	0.58
LDL-C (mmol/L)	2.71 ± 0.06	2.81 ± 0.04	0.19
Creatinine (mmol/L)	70.01 ± 1.51	70.44 ± 0.87	0.6
Blood urea nitrogen (mmol/L)	5.58 ± 0.14	5.97 ± 0.14	0.17
Medications			
ARBs or ACEIs	42 (27)	195 (30)	> 0.05
CCBs	32 (21)	168 (26)	> 0.05
β-blockers	68 (45)	419 (65)	< 0.01
Anti-lipids	138 (90)	624 (96)	< 0.01
Aspirin	142 (93)	647 (100)	< 0.01
Insulin	12 (7)	77 (12)	> 0.05

went coronary angiography, in order to determine the relationship between serum potassium levels in patients with CAD and the severity of coronary artery lesions.

Materials and methods

Patients

A total of 799 patients who underwent coronary angiography in the Department of Cardiology at Yanbian University Hospital between August 2012 and July 2014 were selected for this study. Within 24 hours after admission to the hospital, medical histories, sex, age, body mass index, smoking, alcohol consumption, diabetes, hypertension, and medication use were recorded for each patient. Within 24 hours after admission and before coronary angiography, fasting venous blood was drawn from all patients for the measurements of potassium, triglyceride (TG), total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, and blood urea nitrogen levels. After coronary angiography, cases with normal results were included in the normal control group (152 cases: 100 men and 52 women) and cases with coronary artery stenosis ≥ 50% of the vessel diameter were included in the CAD group (647 cases: 401 men and 246 women). Gensini scoring system was used to divide the 647 CAD patients into two groups [14]: 453 and 194 cases were classified as low (≤ 39 points) and high (> 39 points) Genisini score groups, respectively. Patients with acute myocardial infarction, severe renal insufficiency, unstable vital signs (including severe chronic heart failure [left ventricular ejection fraction < 45%], acute pulmonary edema, and cardiogenic shock), severe arrhythmia or myocardial bridging, previous cerebrovascular diseases, or intake of diuretics for hypertension were excluded from the study. All procedures were approved by the Ethics Committee of Yanbian University. Written informed consents were obtained from all patients or their families.

Gensini scoring

Coronary angiography was performed using Judkin's method. The projection position was routinely selected and selective coronary angiography was conducted. Angiography showing the maximal degree of stenosis was adapted for the quantitative coronary angiogram analysis, which was performed using a contour detection minimum cost algorithm (DSA Artis Zee Biplane; Siemens, Erlangen, Germany) [2]. The severity of the coronary artery lesions was determined using the Gensini scoring system [10] as follows: ≤ 25% vascular stenosis (1 point), 26-50% (2 points), 51-75% (4 points), 76-90% (8 points), 91-99% (16 points), and

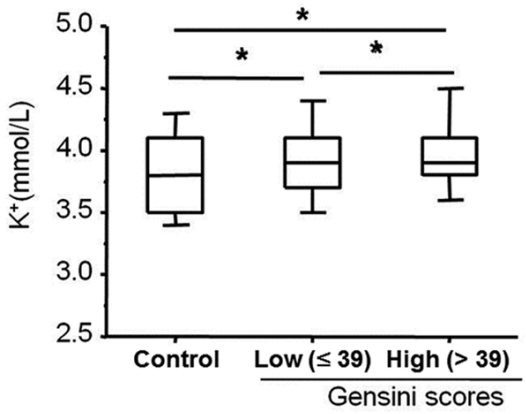

Figure 1. Correlation between serum potassium levels and severity of coronary artery disease. Gensini scoring system was used to divide the 647 CAD patients into two groups: 453 and 194 cases were classified as low (≤ 39 points) and high (> 39 points) Genisini score groups, respectively. Cases with normal results were included in the normal control group (152 cases). Boxes show interquartile ranges. The lower and upper boundaries of the boxes indicate the 25th and 75th percentile levels, respectively, and the horizontal lines within the boxes indicate the median levels.

100% (32 points). The coefficients for each lesion segment were as follows: left main coronary artery (5 points); proximal, mid, and distal segments of the left anterior descending coronary artery (2.5, 1.5, and 1 point, respectively); first and second diagonal branches (1 and 0.5 point, respectively); proximal and distal portions of the circumflex artery (2.5 and 1 point, respectively); obtuse marginal branch (1 point); and proximal, mid, and distal segments of the right coronary artery, posterior descending artery, and posterior left ventricular branch (1 point each). The coefficient of each segment and the corresponding degree of stenosis were multiplied, and the final score for the coronary artery lesions of each patient was the sum of the points of all segments. Based on the extent of the lesions, CAD patients were divided into 3 groups: lesions in a single vessel, dual vessels, and multiple vessels.

Statistical analysis

Continuous data are presented as means ± SEM. Between-group comparisons were performed using *t*-test. Categorical data were presented as percentages and analyzed using χ^2 test. The correlation between serum potassium level and Gensini scores was examined by Pearson correlation analysis. Differences with *P* values < 0.05 were considered statistically significant.

Results

General clinical data comparison

To evaluate risk factors for CAD, we measured general clinical parameters of CAD patients. Mean age, triglycerides (TG), and total cholesterol as well as the percentages of smoking, alcohol consumption, and dyslipidemia in CAD patients were significantly higher than those in normal control group (P < 0.05). There were no significant differences in sex, body mass index, percentages of hypertension and diabetes, or mean values for low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, creatinine, and blood urea nitrogen between CAD patients and controll group (P > 0.05) (**Table 1**). Patients with CAD were more likely to have myocardial infarction or coronary bypass graft or angioplasty. Frequencies of CAD patients undergoing treatment with anti-hypertensive, anti-lipid, or anti-platelet medications were higher than those in normal control group (**Table 1**).

Serum potassium levels in patients with CAD are positively correalted with the severity of coronary artery lesions

To investigate the association between the severity of coronary artery lesions and serum potassium concentration, Gensini scoring was performed. To further explore the relationship between serum potassium level and Gensini scores, we performed Pearson correlation analysis. For patients with coronary stenosis, Gensini scores ranged from 1 to 178 (median 22). Serum potassium levels were significantly increased in patients with lower (≤ 39 points; 3.90 ± 0.02 mmol/L, n = 453) and higher (> 39 points; 3.97 ± 0.02, n = 194) Gensini scores compared with normal patients (3.82 ± 0.03 mmol/L; P < 0.05). Furthermore, serum potassium level of the high-score group was also significantly higher than that of the low-score group (P < 0.05) (**Figure 1**). In addition, Pearson correlation analysis showed positive correlation between serum potassium levels and Gensini scores in patients with CAD (r = 0.093, P < 0.05). The results indicate that serum potassium levels in patients with CAD are positively correalted with the severity of coronary artery lesions.

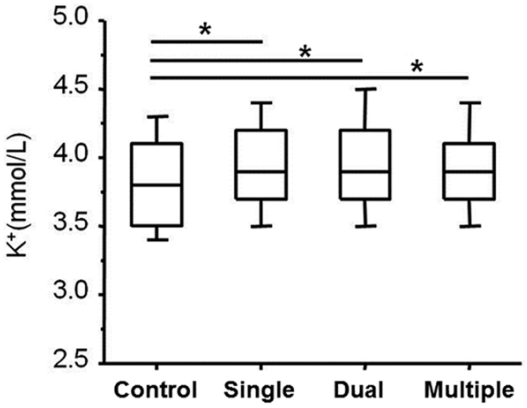

Figure 2. Correlation between serum potassium levels and multivessel disease. Cases with normal results were included in the normal control group (152 cases). Patients with single-, dual-, and multiple-vessel involvement were included in the experimental groups (n = 214, 202, and 231, respectively). Boxes show interquartile ranges. The lower and upper boundaries of the boxes indicate the 25th and 75th percentile levels, respectively, and the horizontal lines within the boxes indicate the median levels.

Degree of potassium increase in CAD patients is not significantly correlated with coronary artery lesion extent

To study the association between coronary artery lesion extent and serum potassium concentration, Gensini scores were recorded and Pearson correlation analysis was performed. Compared with the normal control group, the serum potassium concentration in all CAD patients was found to be increased, independent of the extent of the lesions. Of note, the serum potassium concentrations in patients with single-, dual-, and multiple-vessel involvement (3.95 ± 0.03, 3.95 ± 0.03, and 3.94 ± 0.03 mmol/L; n = 214, 202, and 231, respectively) were significantly higher than that in normal control group (3.82 ± 0.03, n = 152) ($P < 0.05$; **Figure 2**). The result suggests that the degree of potassium increase in CAD patients is not significantly correlated with coronary artery lesion extent.

Discussion

Potassium is an important electrolyte in human body and a basic component required for maintaining the resting membrane potential. Changes in serum potassium ion concentration not only result in changes in the heart rate and myocardial contractility, but also significantly affect vasodilatation and atherosclerosis formation [5, 13]. The results of this study indicate that the higher the severity of coronary artery lesions is, the higher the serum potassium concentration is. In the present study, Gensini scoring system was used to quantify the severity of coronary artery lesions. This method takes into account not only the differences in myocardial blood supply from different branches and locations, but also the degree of stenosis of each lesioned vessel. Therefore, its evaluation of the severity of coronary artery lesions is highly accurate and comprehensive. For this reason, Gensini scoring system is one of the most commonly used methods in the world.

In this study, CAD patients were divided into low-score and high-score groups according to the Gensini scoring system. Compared with the normal control group, the serum potassium concentrations in the low- and high-score groups were significantly increased. In addition, the serum potassium concentration of the high-score group was higher than that of the low-score group. In previous studies, the effects of potassium on blood vessels have been found to be mainly related to the activity of inwardly rectifying potassium channels. Increased extracellular potassium concentrations activate the inwardly rectifying potassium channels [5, 6], thereby resulting in hyperpolarization of the vascular smooth muscle cells and inhibition of L-type calcium channels, consequently triggering vasodilatation. Ando et al. show that high-potassium diets can reduce the production of reactive oxygen species and improve insulin resistance, and thus conclude that potassium plays a role in vessel protection in oxidative stress-induced blood vessel damages [9]. In addition, elevated serum potassium levels inhibit platelet aggregation and arterial thrombus formation [13, 15], and have been demonstrated to play a role in preventing coronary atherosclerosis [11, 16]. Accordingly in the present study, serum potassium concentrations were found to increase along with Gensini scores, suggesting a compensatory mechanism of the body in response to coronary artery lesions and insufficient blood supply to myocardium. However, the exact mechanism of this compensatory response remains unclear. We speculate that the compensatory response may be mediated by the renin-angiotensin system or result from the pathophysiologic process of myocardial ischemia [12].

Furthermore, it has been suggested that serum potassium level is related to the extent of coronary artery lesions [12]. The results of the present study indicate that, although serum potassium levels are increased in CAD patients with different extents of lesions, the degree of increase is not significantly correlated with the extent of the lesions. This observation suggests that changes in serum potassium levels are related to the severity of coronary artery stenosis, but not significantly associated with the extent of coronary artery lesions.

However, there are certain limitations in the present study. Related studies have suggested that patients with acute myocardial infarction have a higher incidence of hypokalemia, as a result of either i) increased myocardial necrosis resulting in more significant activation of the aldosterone system, thereby promoting potassium excretion; or ii) enhanced stimulation of the sympathetic-adrenal medullary system under stress conditions, which leads to increased activation of β_2-adrenergic receptors and consequently of the cell membrane sodium-potassium pumps, which in turn allows potassium translocation into skeletal muscles, thereby resulting in reduced serum potassium levels [17-19]. Therefore, under acute stress conditions, serum potassium levels will decrease, which is contradictory with the results of chronic coronary artery lesions. Due to this reason, patients with acute myocardial infarction were excluded in the present study. However, changes in serum potassium levels in patients with acute myocardial infarction and different physiological and pathological processes in acute and chronic lesions require further investigations. Taken together, we demonstrate for the first time that serum potassium levels increase with increasing severity of coronary artery lesions, which may represent a compensatory response of the body in response to coronary artery lesions and inadequate myocardial blood supply. In the future, serum potassium level may be used as a reference for the severity of coronary artery lesions and as a risk stratification tool to determine the optimal clinical treatment and the prognosis of patients.

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Disclosure of conflict of interest

None.

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