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Original Article

Correlation of serum alanine aminotransferase and aspartate aminotransferase with coronary heart disease

Jianying Shen, Jingying Zhang, Jing Wen, Qiang Ming, Ji Zhang, Yawei Xu

Department of Cardiology, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai 200072, China

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Abstract: Objective: This study aimed to explore the relationship between different risk factors (especially serum alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) and coronary heart disease (CHD). Methods: A total of 610 inpatients were recruited. Initial coronary angiography (CAG) was performed to evaluate the severity of coronary lesions. On the basis of findings from CAG, patients were divided into control group (n=260) and CHD group (n=350). Logistic regression analysis was employed for the evaluation of clinical characteristics and biochemical parameters, aiming to explore the relationship between risk factors (including AST and ALT) and CHD. Results: Results showed type 2 diabetes, hypertension, dyslipidemia, smoking and family history of CHD were clinical risk factors of CHD. Laboratory examinations showed the serum levels of triglycerides, low-density lipoprotein, AST and ALT in CHD group were significantly higher than those in control group ($P<0.05$). Of these parameters, the AST was 50.98±8.12 U/L in CHD group and 20.14±3.94 U/L in control group ($P<0.01$); the ALT was 42.31±8.34 U/L in CHD group and 18.25±6.38 U/L in control group ($P<0.01$). Conclusion: The serum levels of AST and ALT in CHD patients are higher than those in controls. High serum AST and ALT are biochemical markers which can be used to predict the severity of CHD and are also independent risk factors of CHD.

Keywords: Alanine aminotransferase, aspartate aminotransferase, coronary heart disease, risk

Introduction

Coronary atherosclerotic heart disease is a type of heart disease caused by myocardial ischemia and hypoxia due to coronary atherosclerosis (CA) induced vascular obstruction and, together with coronary functional change (spasm), are also known as coronary heart diseases (CHD) [1, 2]. CHD is a disease caused by different risk factors at distinct levels, of which type 2 diabetes, dyslipidemia, obesity and smoking are known important risk factors of CHD [3, 4]. A variety of studies have confirmed that type 2 diabetes in the presence of CHD not only deteriorates the coronary lesions, but hinders the formation of coronary collateral circulation, which significantly increases the mortality of CHD patients [5, 6]. CHD has been one of major diseases threatening human health and causing death [7].

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are intracellular enzymes responsible for the catalysis of transamination between amino acids and ketonic acid. Increased AST and ALT usually indicate liver injury. AST and ALT have been widely used in clinical practice to evaluate the liver function [8-10]. ALT is mainly distributed in the liver, and increased serum ALT is a marker of liver injury. The increase in serum ALT is mainly ascribed to disordered glucose metabolism and related nonalcoholic fatty liver disease (NAFLD) beside viral hepatitis and excessive drinking [11]. NAFLD and sustained abnormal ALT may serve as independent predictors of arteriosclerosis and CHD. It has been reported that the increase in serum ALT in subjects without viral hepatitis and excessive drinking is mainly attributed to NAFLD, and these patients have elevated risk for CHD [12]. AST is widely distributed in the heart, liver, lung, bone, muscle, kidney and pancreas, of which myocytes have the highest expression of AST, followed by hepatocytes [13]. X showed, in the presence of myocardial

Table 1. Demographics between control group and CHD group

Variable		Control (n=260)	CHD (n=350)	X^2	P
Age	<40	8	12	2.69	0.61
	40-50	25	40		
	50-60	106	152		
	60-70	90	100		
	>70	31	46		
Gender	M	140	185	2.31	0.89
	F	120	165		
Education level	Junior high school	98	140	4.76	0.21
	Senior middle school	73	109		
	University	89	101		
Type of occupation	Physical	145	187	1.59	1.01
	Mental	115	163		

Table 2. Clinical risk factors between CHD group and control group

Variables		Control (N=260)		CHD (N=350)		X^2	P
		N	%	N	%		
Type 2 diabetes	Yes	100	38.5	250	71.4	19.265	0.000
	No	160	61.5	200	28.6		
Hypertension	Yes	90	34.6	280	80.0	128.758	0.000
	No	170	65.4	70	20.0		
Dyslipidemia	Yes	115	44.2	263	75.1	60.485	0.000
	No	145	55.8	87	24.9		
History of smoking	Yes	126	48.5	240	68.6	25.137	0.000
	No	134	51.5	110	31.4		
History of drinking	Yes	120	46.2	180	51.4	1.66	0.198
	No	140	53.8	170	48.6		
BMI	Abnormal	122	46.9	189	54.0	2.99	0.084
	Normal	138	53.1	161	46.0		
Family history of CHD	Yes	90	34.6	285	81.4	138.04	0.000
	No	170	65.4	65	18.6		

injury or liver injury, mitochondrion related oxidative stress may cause injury to mitochondria, cell necrosis and mitochondrial disintegration and AST is released into blood. Thus, AST may serve as a parameter used to evaluate the extent of liver injury or myocardial injury, therapeutic efficacy, and prognosis of these diseases [14].

It has been widely accepted that ALT may be used as a parameter for the prediction of NAFLD and type 2 diabetes, but few studies have been conducted to investigate the relationship between sera ALT /AST and CHD. Increasing investigators propose that increased ALT is closely related to endothelial dysfunction induced atherosclerosis and inflammation [15]. This study aimed to investigate the relationship between serum AST/ALT and CHD.

Materials and methods

General information

Patients who received initial coronary angiography (CAG) due to chest pain were recruited from the Department of Cardiology of our hospital from July 2012 to July 2014. Patients with stent implanting after acute myocardial infarction, endocrine diseases, autoimmune diseases, secondary hypertension, myocarditis, rheumatic heart disease, tumors, viral hepatitis, hepatic cirrhosis, other liver diseases, acute or chronic infection and stroke were excluded. All the patients received CAG, and divided into two groups according to the findings from CAG and other routine examinations: control group (CAG failed to find evidence on CHD; and electrocardiography, echocardiography and CAG were performed due to chest pain and chest tightness; n=260) and CHD group (patients were diagnosed with newly onset CHD, had precordial pain of different extents and were not treated with lipid-lowering drugs within 1 month; n=350). There were no significant differences in the age, gender, education level and type of occupation between control group and CHD group (P>0.05).

Methods

General condition: The age, gender, type 2 diabetes, hypertension, dyslipidemia, smoking, drinking, body mass index (BMI) and family history of CHD were recorded and compared between two groups.

Table 3. Laboratory findings between CHD group and control group ($\bar{X}$±S)

Variables	Control (N=260)	CHD (N=350)	T	P
TC (mmol/L	4.23±1.81	5.72±1.42	1.89	0.21
TG (mmol/L)	1.56±0.71	2.86±1.31	2.99	0.02
HDL-C (mmol/L)	1.36±0.21	1.43±0.62	1.12	0.43
LDL-C (mmol/L)	2.15±0.92	3.76±1.21	2.83	0.03
Urea nitrogen (mmol/L)	5.05±1.12	5.62±0.97	1.56	0.32
Uric acid (umol/L)	331.22±89.73	351.26±101.34	1.09	0.52
Creatinine (umol/L)	65.05±20.92	67.36±18.51	0.98	0.62
Alkaline phosphatase (U/L)	60.16±15.42	62.44±16.22	0.79	0.72
Hemoglobin (g/L)	129.15±35.46	138.72±35.33	3.19	0.01
Total bilirubin (umol/L)	11.25±3.32	13.46±4.59	1.78	0.23
ALT (U/L)	18.25±6.38	42.31±8.34	7.12	0.001
AST (U/L)	20.14±3.94	50.98±8.12	5.65	0.001

Routine examinations: Patients were fasted for 12 h, and venous blood was collected in the morning. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), urea nitrogen, uric acid, creatinine, alkaline phosphatase, hemoglobin, total bilirubin, AST and ALT were detected.

Methods: The general condition and results of routine examinations were compared between control group and CHD group. Diagnostic criteria and detection of exposure related factors: hypertension was diagnosed according to the WHO/ISH criteria for hypertension [16]; diabetes was diagnosed according to the WHO diagnostic criteria [17]; dyslipidemia was diagnosed according to the Guideline for the Prevention and Therapy of Dyslipidemia in Chinese Adults; history of drinking was defined as at least 100 g of alcohol per day for at least 1 year; history of smoking was defined as at least 1 cigarette per day or a smoker for at least 5 years; family history of CHD was defined as at least one of relatives (parents, sisters and brothers) diagnosed with CHD.

Statistical analysis

Statistical analysis was performed with SPSS version 19.0. Quantitative data are expressed as mean ± standard deviation ($\bar{X}$±S) and compared with independent t test. Qualitative data were compared with chi square test. Multivariate variables were analyzed with logistic regression analysis.

Results

Demographics at baseline

There were no significant differences in the age, gender, education level and type of occupation between control group and CHD group, suggesting the demographics were balanced (**Table 1**).

Clinical information

The incidences of type 2 diabetes, hypertension, dyslipidemia, history of smoking, and family history of CHD were markedly different between control group and CHD group (P<0.01; **Table 2**).

Laboratory findings

In CHD group, the TC, TG, LDL-C, Hb, AST and ALT were significantly different from those in control group (P<0.05; **Table 3**; **Figure 1**). Marked differences were not observed in other parameters between two groups (P>0.05; **Table 3**).

Multivariate logistic regression analysis of risk factors for CHD

Forward stepwise logistic regression equation was used, and the standards for inclusion and exclusion were 0.05 and 0.1, respectively. The gender, age, education level, type of occupation, type 2 diabetes, hypertension, Dyslipidemia, smoking, drinking, BMI, family history of CHD, TC, TG, HDL-C, LDL-C, urea nitrogen, creatinine, uric acid, alkaline phosphatase, hemoglobin, total bilirubin, AST and ALT served as independent variables and CHD as a dependent variable. Non-conditional logistic regression equation was used. Finally, TC, LDL-C, Hb, ALT, AST, type 2 diabetes, hypertension, smoking and family history of CHD were found to be independent risk factors of CHD, and HDL-C was a protective factor of CHD (**Table 4**).

Discussion

CHD is caused by coronary atherosclerosis, but its etiology and pathogenesis are still poorly

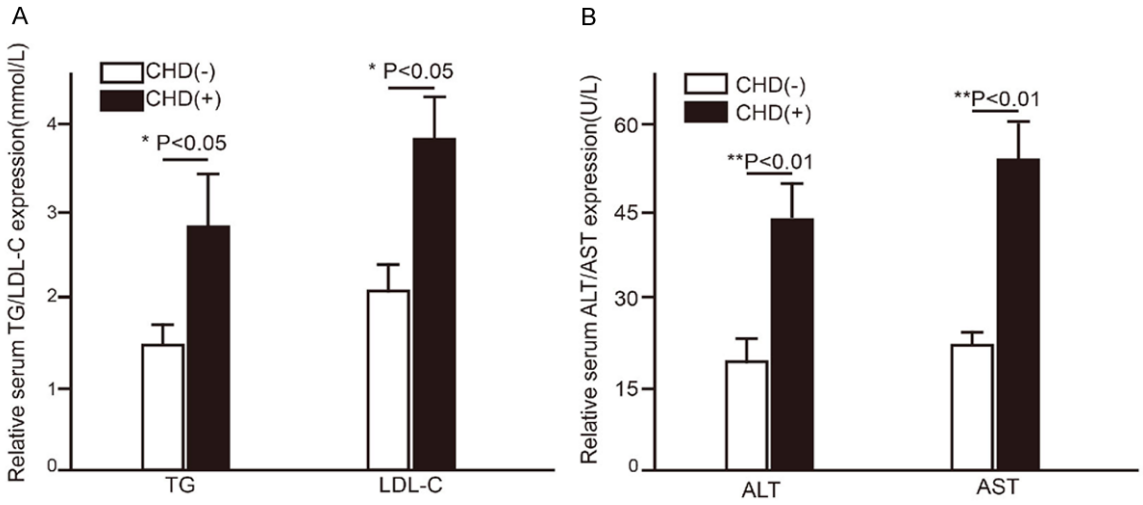

Figure 1. The serum level of TG/LDL-c and ALT/AST.

Table 4. Logistic regression analysis of risk factors of CHD

Variables	Regression coefficient B	Standard error	Wald X^2	P	OR
TC	0.93	0.361	3.25	0.05	2.58
HDL-C	-3.61	1.72	4.231	0.03	0.2
LDL-C	0.841	0.31	3.05	0.05	2.43
Hemoglobin	1.23	0.44	3.78	0.044	2.97
ALT	0.79	0.291	2.872	0.05	2.13
AST	1.176	0.412	3.992	0.03	3.56
Type 2 diabetes	2.31	1.121	4.126	0.01	9.74
Hypertension	2.24	1.092	4.11	0.019	8.761
History of smoking	4.562	2.11	7.65	0.001	15.34
Family history of CHD	4.126	1.993	6.74	0.008	13.25
Constant	-3.971	1.871	4.759	0.01	

understood [18, 19]. A large number of studies have shown that the pathogenesis of coronary atherosclerosis is closely related to arterial wall cells, extracellular matrix, blood components (especially monocytes, platelets and LDL-C), focal hemodynamics, environmental factors and genetic factors [3, 20]. It has been accepted that the risk factors of CHD include the increased TG, TC and LDL-C, reduced HDL-C, obesity, advanced age, male sex, type 2 diabetes, smoking, hypertension, and family history of CHD [20-22]. In this study, we aimed to explore the relationship between AST/ALT and CHD.

ALT is a marker of NAFLD and can be used to predict type 2 diabetes [11, 23, 24]. In recent years, some studies reported that ALT was associated with endothelial dysfunction and CHD [25]. There is evidence showing that NAFLD is an independent risk factor of CHD, which is independent of traditional risk factors of CHD. NAFLD patients have a shorter survival time and an increased CHD related mortality [26, 27]. Targher et al found ALT was independently related to CHD, independent of NAFLD and metabolic syndrome, and ALT could be used as an independent predictor of CHD [28, 29]. AST is mainly distributed in the myocytes, followed by hepatocytes. In myocytes, AST has two isoforms: ASTs in the cytoplasm and m-AST in the mitochondrion. About 80% of AST exists in the mitochondrion, and thus AST is a non-specific intracellular functional enzyme. The serum AST is at a low level [30, 31]. In the presence of myocardial injury, mitochondria are damaged, and serum m-AST increases significantly. Thus, serum m-AST may reflect the severity of myocyte injury.

In the present study, there were no marked differences in the age, gender, education level and type of occupation, suggesting that the demographics were comparable between two groups (**Table 1**). General information was col-

lected from these subjects, and results showed type 2 diabetes, hypertension, dyslipidemia, history of smoking and family history of CHD were markedly different between control group and CHD group (P<0.01), which was consistent with previous findings (**Table 2**). In addition, biochemical examinations showed the serum levels of TG, LDL-C, Hb, AST and ALT in CHD group were significantly higher than those in control group (P<0.05; **Table 3**; **Figure 1**). TG and LDL-C have been found to be risk factors of CHD [32], but few studies report that AST and ALT are risk factors of CHD. This study focused on the relationship between AST/ALT and CHD. Logistic regression analysis showed AST and ALT, besides TG, LDL-C, Hb, type 2 diabetes, hypertension, history of smoking and family history of CHD, were independent risk factors of CHD. In the present study, patients with other diseases were excluded (such as viral hepatitis, hepatic cirrhosis, acute/chronic infection, drug induced hepatitis, NAFLD and other systemic diseases). Results showed the serum levels of ALT and AST in CHD group were markedly higher than those in control group. These findings, together with those from logistic regression analysis, showed serum levels of ALT and AST could be used as independent predictors of CHD.

Taken together, our results reveal that the occurrence and development of CHD are related to multiple factors and caused via multiple steps. Classic risk factors of CHD including type 2 diabetes, hypertension, dyslipidemia, history of smoking, and family history of CHD, TG and LDL-C are also confirmed in the present study. Moreover, our results also indicate that AST and ALT are new risk factors of CHD. Thus, rational diet, controlling of intake of cholesterol and fat, intake of more fruits and vegetables, smoking cessation, drinking cessation, and reduction in passive smoking are helpful to prevent CHD. In addition, serum AST and ALT may serve as independent predictors of CHD and be used for the early diagnosis and prevention of CHD.

Disclosure of conflict of interest

None.

Address correspondence to: Yawei Xu, Department of Cardiology, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai 200072, China. E-mail: xuyawei@tongji.edu.cn

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