Original Article
Possible association between serum alkaline phosphatase concentration and thoracicacute aortic dissection

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Abstract: *Objectives:* Alkaline phosphatase (ALP) is an enzyme that catalyzes the hydrolysis of organic pyrophosphate. Accumulating data have demonstrated that the concentration of increased ALP is associated with C-reactive protein (CRP) concentration, and inflammation was complicated in the pathogenesis of acute aortic dissection (ADD). Therefore, the aim of our study was to examine the relationship between serum ALP concentration and thoracic ADD. *Methods*: We retrieved demographic data and test results of biochemical data of 68 patients with thoracic ADD and 126 Non-thoracic ADD patients, retrospectively. *Results:* A total of 194 patients were divided into thoracic ADD groups and non-thoracic ADD groups. Age, creatinine(Cr) and high-density lipoprotein cholesterol (HDL-C) were found to be statistical significance between the two groups. The mean ALP level was significantly higher in patients with thoracic ADD compared with Non-thoracic ADD patients (80.6±23.02 Vs. 65.9±16.49, *P*=0.001). Stepwise multiple logistic regression analyses revealed a significantly association of ALP with thoracic ADD (OR=1.038, 95% CI: 1.015-1.062, *P*=0.001). In addition, HDL-C was negative associated with thoracic ADD in multiple logistic regression analyses after adjustment for age, sex and Cr (OR=-0.083, 95% CI: 0.012-0.560, *P*=0.011). *Conclusions*: The present study suggests that the level of serum ALP is associated with thoracic ADD, and serum ALP concentration may be apotential risk factor for thoracic ADD.

Keywords: Serum alkaline phosphatase, acute aortic dissection, high-density lipoprotein cholesterol

Introduction

Alkaline phosphatase (ALP) is an enzyme that catalyzes the hydrolysis of organic pyrophosphate [1], and that it widely exists varioustissues such as bone, liver and kidney. Pathological causes of increased serum ALP concentration is observed in patients with bone diseases and liver diseases. Several clinical and epidemiological investigation attest that elevated ALP concentration increases the risk of coronary artery calcification and coronary artery disease, as well as mortality of chronic kidney disease [2-4]. It has been demonstrated in previous trials that serum ALP concentration is associated with the risk of cardiovascular disease (CVD) in patients with subclinical atherosclerosis [5, 6]. Thoracic acute aortic dissection (ADD) is a clinically relevant disorder that requires rapid diagnosis and surgical intervention [7, 8]. Mee Kyoung Kim et al [9] reported that increased ALP level was a risk factor of metabolic syndrome in the middle-aged population. Accumulating data have demonstrated that the concentration of increased ALP is associated with C-reactive protein (CRP) concentration, which indicates serum ALP level may be a marker to reflect the low-grade chronic inflammation [10]. A study from Italy showed that inflammation factors are found to be a pathogenesis of ADD, and found that several inflammatory markers are increased in patients with ADD such as C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-8) and tumor necrosis factor (TNF) [11]. Obviously, inflammatory factors may be involved in the pathogenesis of ADD. Therefore, the aim of our study was to determine the relationship between serum ALP concentration and thoracic ADD.

Table 1. The results of baseline information between patients with thoracic acute aortic dissection and non-thoracic acute aortic dissection patients

Parameter	AD patients	Non-AD patients	p-value
	n=68	n=122	
Gander (Male)	22/46	40/82	0.951
Age (yr)	50.5±10.99	42.9±13.0	0.001
Alanine transaminase (U/L)	19.5±12.11	23.7±17.51	0.202
Aspartate aminotransferase (U/L)	17.6±7.74	18.7±6.99	0.451
random blood glucose (mmol/L)	4.8±0.57	4.8±0.58	0.631
cholesterol (mmol/L)	3.9±0.91	4.0±0.60	0.317
Low density lipoprotein (mmol /L)	2.4±0.76	2.5±0.50	0.473
High density lipoprotein (mmol/L)	0.9±0.22	1.2±0.33	0.003
Triglyceride (mmol/L)	1.2±0.28	1.1±0.34	0.653
Creatinine (μmol/L))	76.3±20.8	67.1±15.31	0.020
Serum Phosphorus (mmol/L)	1.1±0.15	1.1±0.16	0.266
Alkaline phosphatase (U/L)	80.6±23.02	65.9±16.49	0.001

Age, Creatinine (Cr) and high-density lipoprotein cholesterol (HDL-C) were found to be statistical significance between the two groups. The mean ALP level was significantly higher in those with thoracic ADD (80.6±23.02 VS. 65.9±16.49, P=0.001) (**Table 1**). Stepwise multiple logistic regression analyses revealed a significantly association of ALP with thoracic ADD (OR=1.038, 95% CI: 1.015-1.062, P=0.001). In addition, HDL-C was negative associated with thoracic ADD in multiple logistic regression analyses after adjustment for age, sex and Cr (OR=-0.083, 95% CI: 0.012-0.560, P=0.011) as shown in **Table 2**.

Patients and methods

We retrieved demographic data and test results of biochemical data of 68 patients with thoracicADD and 126 Non-thoracic ADD patients between January 2012 and January 2013, retrospectively. In the present study, we excluded patients with following disease and/or situation: dysfunction of liver and kidney, presence of cerebrovascular diseases and bone diseases, diabetes mellitus, infectious diseases, autoimmune diseases, malignant tumorand pregnant. The research related to human use has been complied with the tenets of the Helsinki Declaration, and has been approved by the institutional review board.

Statistical analysis

All data were analyzed using the SPSS statistical package. Continuous variable were showed as mean ± standard deviation. Normally distribution was examined using Kolmogorov-Smirnov test. Student's t-test, X^2 test and Mann-Whitney U test were used to compare the difference between thoracic ADD patients and those without. Stepwise Logistic regression analysis was also used to determine underling factors associated with thoracic ADD.

Results

A total of 194 patients were divided into thoracic ADD groups and non-thoracic ADD groups.

Discussion

Recent studies have shown that increased ALP concentration was a predictor of mortality in patients with stroke, and they found that it was associated with recurrent cardiovascular events in stroke patients [12]. A study from patients with maintenance hemodialysis in the US reported that patients on hemodialysis with higher ALP were found to have higher mortality both vascular and non-vascular causes of death [13]. Very recently, Xie Y et al [14] found the relationship between serum ALP concentration and nasopharyngeal carcinoma, the results suggest that serum ALP concent ration may be a marker to assess prognosis of patients with nasopharyngeal carcinoma. In the present study, we have found convincing interactions between increased ALP concentration and thoracic ADD, and serum ALP concentration was a potential risk factor in patients thoracic ADD. In fact, the association of serum ALP concentration and coronary heart disease (CHD) has been reported in previous studies, and serum ALP concentration is associated with the outcomes of various adverse events such asreduced lung function, inflammation, endothelial dysfunction and solidification [15]. It is then noteworthy that the relationship between serum ALP concentration and CVD should be interpreted by inflammation since atherosclerosis is associated with inflammatory processes [14], and the high expression of

Table 2. Stepwise Logistic regression analysis between biochemical parameters and aortic dissection patients in crude model and adjusted modle

	Crude model			Adjusted model		
	Bate	OR (CI 95%)	*P* value	Bate	OR (CI 95%)	*P-value*
High density lipoprotein (mmol/L)	-2.486	0.083 (0.012-0.560)	0.011	-2.034	0.132 (0.018-0.945)	0.044
Alkaline phosphatase (U/L)	0.038	1.038 (1.015-1.062)	0.001	0.055	1.055 (1.027-1.084)	<0.001

ALP is observed in the atherosclerotic plaque [16], whereas vascular inflammation is a promoter for the initiation and development of atherosclerosis [17]. Thus, inflammatory processes may contribute to increase serum ALP concentration in the presence of vessel inflammation. Indeed, both AMI and AAD are diseases of acute arterial wall origin with transient inflammation, however, they differ in pathophysiology, and the area of vascular damage is much larger in patients with AAD than in patients with AMI [18]. Tenascin-C (TN-C), as a matricellular protein, is not expressed and increased in normally tissues, whereas it is closely associated with tissue injury and inflammation in various pathologic conditions, of note, Toshihiro Nozato et al [19] reported an association of Tenascin-C and ADD, demonstrating the existence of acute vascular inflammation in patients with ADD. However, serum ALP has been considered to be an acute phase reactant [20]. Hence, the relationship between the concentration of serum ALP and thoracic ADD can be stressed acute vascular inflammation. In addition, a strong association between serum ALP leveland hypertension was observed in a rural Japanese population [21], therefore, the fluctuation of blood pressure before the outcomes of ADD is also a possibility that increases serum ALP level.

Our study had several limitations. First, the present study was limited by a number of patients. Second, the association between serum ALP concentration and acute phase reactant such as CRP was not evaluated in patients with thoracic ADD. However, the present study suggests that the level of serum ALP is associated with thoracic ADD, and serum ALP may be a risk factor for thoracic ADD.

Disclosure of conflict of interest

None.

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