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Original Article

The role of fructosamine and hemoglobin levels in non-diabetic patients with thoracica cute aortic dissection

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Abstract: Objectives: Recent investigations demonstrated that oxidative stress a crucial role in the etiology of acute aortic dissection (AAD). The levels of fructosamine and glycosylated hemoglobin (HbA1c) have been considered as marker to reflect oxidative stress in various diseases. Therefore, this study was planned to investigate the levels of fructosamine and HbA1c in patients with thoracic ADD. Methods: The study sample included 235 consecutive patients for suspected thoracic ADD, a definitive and reliable diagnosis of thoracic ADD was established in 70 of 235 suspected thoracic ADD patients. Results: The levels of serum fructosamine, HbA1c and random blood glucose were significantly higher in thoracic ADD than in those without. There were no statistically differences between the two groups with respect to age and gender, random blood glucose, creatine kinase (CK), creatine kinase isoenzyme (CK-MB), total protein (TP), low density lipoprotein-cholesterol (LDL-C), triglyceride (TG) and total cholesterol (TC). The correlation analysis showed no correlation between random blood glucose and fructosamine, HbA1c in patients with thoracic AAD. Of note, increased fructosamine and HbA1c levels were associated with thoracic ADD in logistic regression analysis (OR=1.251, P<0.001, 95% CI: 1.060-1.480; OR=2.330, P=0.005, 95% CI: 1.420-3.281). The receiver operating characteristics (ROC) curve analysis of fructosamine and HbA1c exhibited some significant results in estimating thoracic ADD patients. Conclusions: Our data suggest that the increased levels of fructosamine and HbA1c are associated with thoracic ADD, and the results indicate that increased levels of fructosamine and HbA1c may be risk factor of thoracic ADD.

Keywords: Serum fructosamine, glycosylated hemoglobin, acute aortic dissection, oxidative stress

Introduction

Acute aortic dissection (AAD) is an acute condition that requires rapid diagnosis and definite management, and that it is no doubting indication for emergent surgical intervention [1]. Reports showed the mortality rise of 1-2% for each hour in patients with AAD [2]. Rapid and accurate diagnosis for suspected AAD patients is extremely crucial in clinical practice. In the past decades, computed tomography (CT) clinically has been considered to be a main method to diagnose thoracic AAD [3], these methods however are limited by unavailable at bedside and time consuming. Very recently, recent investigations demonstrated that oxidative stress is a crucial role in the etiology of AAD and inflammation may result in dilation, dissection and rupture of the aortic wall [4]. The inflammatory conditions of the aortic wall have been demonstrated during the course of AD in previous studies [5, 6]. It has been reported that several inflammatory markers are increased in patients with AAD, such as interleukin-6 (IL-6), C-reactive protein (CRP) and tumor necrosis factor (TNF) [4].

Glycation of hemoglobin and protein is parameters in clinical practice to assess glycemic control in patients with diabetes [7]. Recently, evidence was provided on the interaction between serum fructosamine and acute traumatic fracture (ATF) [8]. Peng et al [9] reported that mild alteration of serum fructosamine concentration was associated with estimated glomerular filtration rate in nondiabetic individuals without chronic kidney disease. Serum fructosamine has been found to be a risk factor for

Table 1. The laboratory characteristics of thoracic ADD patients in suspected thoracic ADD patients

Variables	Thoracic ADD patients n=70	Non-ADD patients n=158	*P*-value
Creatine kinase (U/L)	67.0±33.99	80.7±35.80	0.068
Creatine kinase isoenzyme (U/L)	11.6±2.57	12.5±3.85	0.230
Total protein (mol/L)	66.6±6.38	67.0±5.45	0.739
High density lipoprotein-cholesterol (mmol/L)	1.0±0.26	1.2±0.38	0.013
Low density lipoprotein-cholesterol (mmol/L)	2.4±0.75	2.7±0.84	0.117
Triglyceride (mmol/L)	1.1±0.28	1.2±0.36	0.449
Total cholesterol (mmol/L)	3.9±0.90	4.2±0.98	0.122
Random blood glucose (mol/L)	5.2±0.74	4.8±0.57	0.602
Serum fructosamine (mol/L)	2.6±0.31	2.1±0.26	<0.001
Glycosylated hemoglobin (%)	5.8±0.46	5.0±0.47	<0.001

mortality and morbidity in hemodialysis patients [10]. In addition, higher glycosylated hemoglobin (HbA1c) levels are strong associated with risk of CVD in population without diabetes [11]. Advanced glycation end products (AGEs) belong to glycation products, which are able to induce immunomodulatory action, reactive oxygen species and inflammation [12]. In fact, serum fructosamine and glycosylated hemoglobin (HbA1c), as early glycation product, has been considered as serum marker to reflect oxidative stress and inflammation [13]. However, the useful assessment has not been previously investigated for fructosamine and HbA1c levels in patients with thoracic ADD to the best of our knowledge. Therefore, this study was planned to investigate the association of fructosamine and HbA1c levels with thoracic ADD.

Patients and methods

The study sample included 235 consecutive patients who admitted at the first affiliated hospital, Xinjiang medical university for suspected thoracic ADD, a definitive and reliable diagnosis of thoracic ADD was established in 70 of 235 suspected thoracic ADD patients according to the international diagnostic criteria, which divides all patients into thoracic ADD and non-ADD patients, and all patients had no a previous history of diabetes mellitus. Additional exclusion criteria included: Hematologic disorders, hyperproteinemia, hepatic or renal dysfunction, infectious disease, cerebrovascular disease, cancer, neuropsychiatric disease and known cardiovascular disease.

The samples of all patients were collected within 2 hours in suspected thoracic ADD patients. Whole blood was used for the measure of fructosamine, HbA1c, random blood glucose, creatine kinase (CK), creatine kinase isoenzyme (CK-MB), total protein (TP), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), triglyceride (TG), and total cholesterol (TC) by using Beckman DXC-800.

The research related to human use has been complied with the tenets of the Helsinki Declaration, and has been approved by the first affiliated hospital, Xinjiang medical university. Informed consent has been obtained from individuals in this study.

Statistical analysis

Our data were analyzed by using SPASS16.0 statistical software. Continuous variables are presented as mean ± SD. We used Kolmogorov-Smirnov test to identify data normality. Differences between thoracic ADD and those without were evaluated by using Student's t test or U test. Pearson correlation analysis was used to analyze correlations between serum fructosamine, HbA1c and related parameter. Logistic regression analysis was performed to identify laboratory parameters associated with thoracic ADD. A receiver operating characteristic (ROC) curve analysis was performed to estimate the value of serum fructosamine and HbA1c in thoracic ADD patients. Statistical significance was accepted at $P<0.05$

Results

Data of the thoracic ADD patients and non-ADD patients are shown in **Table 1**. The levels of serum fructosamine and HbA1c were significantly higher in thoracic ADD than in those without (2.6±0.31 Vs 2.1±0.26, $P<0.001$), as shown in **Figures 1**, **2**. A lower HDL-C was found

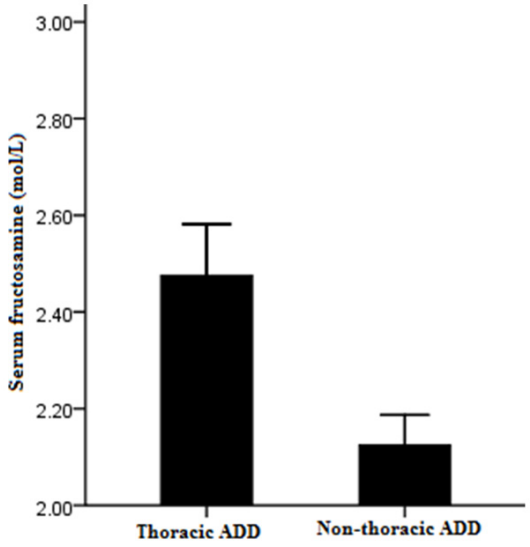

Figure 1. Increased serum fructosamine levels in thoracic ADD patients compared with non-thoracic patients.

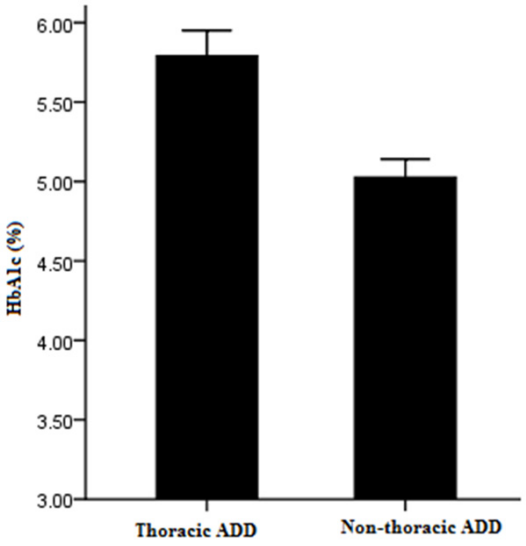

Figure 2. Increased HbA1 clevels in thoracic ADD patients compared with non-thoracic patients.

in thoracic ADD patients compared with non-ADD patients. There were no statistically differences between the two groups with respect to age and gender, random blood glucose, CK, CK-MB, TP, LDL-C, TG and TC. The correlation analysis showed no correlations between random blood glucose and fructosamine, HbA1c in patients with thoracic AAD.

Of note, increased fructosamine and HbA1c levels were associated with thoracic ADD in logistic regression analysis (OR=1.251, P< 0.001, 95% CI: 1.060-1.480; OR=2.330, P= 0.005, 95% CI: 1.420-3.281) (**Table 2**). The receiver operating characteristics (ROC) curve analysis of fructosamine and HbA1c exhibited some significant results in estimating thoracic ADD patients, as shown in **Table 3** and **Figure 3**.

Discussion

The levels of non-enzymatic glycation of hemoglobin and protein main depend on the concentration of blood glucose [14]. Increased levels of serum fructosamine have been reported in patients with retinopathy of prematurity, which may contribute to the development of retinopathy in prematurity [15]. It has been highlighted that increased fructosamine and HbA1c are associated with morbidity and mortality of cardiovascular disease (CVD) in the general population, as well as in diabetic and non-diabetic individuals [16, 17]. Increased fructosamine and HbA1c levels have been documented in some pathological conditions such as cancer, acute myocardial infarction and cardiovascular disease [13, 18-20]. Few studies, however, have investigated a possible association between biochemical markers and thoracic ADD in the clinical laboratory. To the best of our knowledge, this is the first study to investigate the relationship between fructosamine, HbA1c and thoracic ADD. In the present study, an increased fructosamine and HbA1c levels were observed in thoracic ADD who had no previous history of diabetes mellitus, and were associated with thoracic ADD in logistic regression analysis.

Increased plasma AGEs, a glycation product, were found to be significantly correlated with atherosclerosis, and that it could induce oxidative stress and promote inflammation invascular endothelial cell [21]. Indeed, the association between increased plasma AGEs and oxidative stress has been showed in previous studies [21]. Evidence in the literature has indicated that the process of AGEs production is involved with oxidative pathways, and glucose oxidation in the body is also related to AGE generation [22]. Other evidence also reported that antioxidants play a protective role in glycation [23]. In patients without diabetes mellitus, there is now growing evidence to suggest that AGEs are associated with reactive oxygen species and

Table 2. Stepwise logistic regression analysis between laboratory parameters and aortic dissection patients

Variables	*P*-value	OR	95% CI
Serum fructosamine (mol/L)	<0.001	1.251	1.060-1.480
Glycosylated hemoglobin (%)	0.005	2.330	1.420-3.281

Table 3. The results of the receiver operating characteristics curve analysis for fructosamine and HbA1c in thoracic ADD patients

Variables	Sensitivity	Specificity	Cut-off value	AUC	95% CI
Serum fructosamine (mol/L)	82.9%	70.1%	2.24	0.800	0.739-0.907
Glycosylated hemoglobin (%)	80.0%	73.9%	5.35	0.870	0.796-0.994

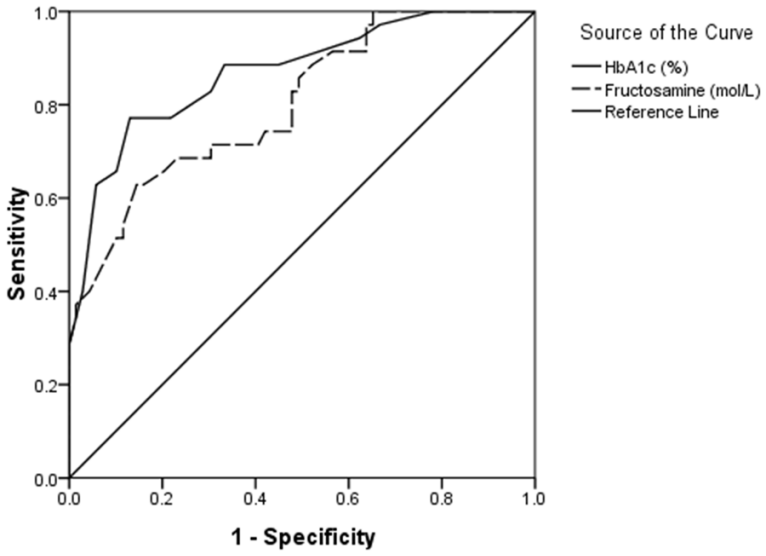

Figure 3. The receiver operating characteristics to evaluate performance of fructosamine and HbA1c in suspected thoracic ADD patients.

inflammation [12]. These results support the hypothesis that oxidative stress may involve with glycation product. In fact, fructosamine and HbA1c are early glycation products in diabetic and non-diabetic subjects [7]. In addition, a fluctuation of blood pressure also can enhance glycation of proteins and hemoglobin [24, 25]. A close linear relationship between glycation and oxidative stress has been suggested by Selvaraj N et al [26]. Nevertheless, excessive oxidative stress has being involved in the pathogenesis of ADD [26]. Thus, excessive oxidative stress may help to explain increased fructosamine and HbA1c in patients with thoracic ADD.

The major limitation of this study was represented by the limited number of patients. Additional, future prospective cohort studies are required to confirm whether increased fructosamine and HbA1c are useful in thoracic ADD patients. However, our data suggest that the increased levels of fructosamine and HbA1c are associated with thoracic ADD, and the results indicate that increased levels of fructosamine and HbA1c may be risk factor of thoracic ADD.

Disclosure of conflict of interest

None.

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