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The associations between liver enzymes and the risk of metabolic syndrome in the elderly

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ABSTRACT

Background: Studies have demonstrated that liver enzymes are associated with metabolic syndrome (MetS). However, little information is available regarding these relationships in elderly populations. Our present study aimed to explore the associations between liver enzymes and the risk of MetS in elderly populations.

Methods: This cross-sectional study included 1444 elder participants (970 men and 474 women) who attended annual physical examinations. Univariate and multivariate logistic regressions were performed to estimate the associations between liver enzymes and the risk of MetS and its components according to quartiles of the concentration of each liver enzyme.

Results: The prevalence of MetS and its components increased remarkably with increasing quartiles of alanine aminotransferase (ALT), gamma-glutamyltransferase (GGT) and alkaline phosphatase (ALP) but not with aspartate aminotransferase (AST) in the elderly. Compared with subjects in the bottom quartile, the adjusted odds ratio for MetS in the highest ALT, GGT and ALP quartiles were 1.78 (95% CI 1.21–2.61), 2.58 (95% CI 1.77–3.78) and 1.85 (95%CI 1.27–2.70) respectively. No statistically significant increases in the odds ratio for MetS according to increased quartiles of AST were found in either the univariate or multivariate logistic regression analyses.

Conclusions: Elevated liver enzymes levels (mainly ALT, GGT and ALP but not AST) are positively associated with the prevalence of MetS in elderly populations.

1. Background

Metabolic syndrome (MetS) is a complicated disorder characterized by several risk factors, including abdominal obesity, high blood pressure, hyperglycemia, and dyslipidemia (including hypertriglyceridemia and reduced lower high-density lipoprotein cholesterol). MetS is associated with significant increased risk of cardiovascular related diseases including diabetes, myocardial infarction, stroke, cardiovascular related mortality and all-cause mortality (Grundy, 2007; Mottillo et al., 2010). MetS has now become not only a clinical issue but also become an important global public health challenge with its significant increasing prevalence all over the world (Alberti et al., 2009). Hence, early detection and intervention against MetS are very important for preventing the progression of cardiovascular related diseases and reducing the public health burden.

Nonalcoholic fatty liver disease (NAFLD) is thought to be the hepatic manifestation of MetS (Adams et al., 2009; Kotronen and Yki-Jarvinen, 2008; Yki-Jarvinen, 2014). NAFLD is usually associated with elevated liver enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyltransferase (GGT) and alkaline phosphatase (ALP) (Clark et al., 2003; Hossain et al., 2016; Pantsari and Harrison, 2006; Salman et al., 2016; Schindhelm et al., 2006). To date, several epidemiological studies have explored the associations between liver enzymes and MetS in different populations (Hanley et al., 2005; Koskinen et al., 2012; Lee and Yang, 2013; Perera et al., 2008; Villegas et al., 2011). However, these results are not consistent, and little information is available regarding these relationships in elderly populations. Because the prevalence of MetS is closely related with age, and the incidence of MetS is much higher in elderly populations (Ford et al., 2002; Gu et al., 2005; Xi et al., 2013), we conducted a cross-sectional study to investigate the relationships of liver enzymes with MetS and its components in elderly people.

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2. Methods

2.1. Study populations

The present cross-sectional study enrolled 1680 Han Chinese elderly participants (aged 60–93 years) who visited the health examination center of Tongren hospital for annual physical check-ups from March 2016 to October 2016. All participants completed a health questionnaire and health check-up according to a standardized protocol. Because serum liver enzyme levels can be significantly affected by alcohol consumption and hepatitis viruses, those who were currently drinking and those who were currently suffering from viral hepatitis were excluded from our present study. Ultimately, 1444 elderly participants (970 men and 474 women) with complete data were included in our study. Written informed consent was obtained from all eligible participants, and this study was approved by the Ethics Committee of Tongren Hospital, Shanghai Jiao Tong University School of Medicine.

2.2. Data collection and laboratory measurements

A standardized questionnaire was used to obtain the general information of the subjects, including age, medical history, history of drug treatment, cigarette smoking, etc. Standing height and weight were measured without shoes to the nearest 0.1 cm and 0.1 kg, respectively. Waist circumference (WC) was measured to the nearest 0.1 cm between iliac crest and the rib cage with a non-elastic tape. The body mass index (BMI) was assessed by the formula weight (kg)/height^2 (m^2). Resting blood pressure was measured two times with an electronic sphygmomanometer (HEM-741C; Omron, Tokyo, Japan) in the seated position after at least 5 min of rest in a quiet room.

Venous blood samples after an overnight fast were obtained from the antecubital vein and were then sent to the laboratory center for analysis. Fasting plasma glucose (FPG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), creatinine, uric acid and liver enzymes were measured enzymatically on an automatic analyzer (Architect Ci8200, Abbott Co., Illinois, USA). All laboratory assays were measured without knowledge of the information of the participants.

2.3. Definition of MetS

In our present study, we chose the definition of MetS according to the 2009 harmonizing definition criteria as including three or more of the following factors (Alberti et al., 2009): abdominal obesity, i.e., WC ≥ 90 cm in Asian men or ≥80 cm in Asian women; systemic hypertension, i.e., a systolic blood pressure (SBP) ≥ 130 mm Hg, a diastolic blood pressure (DBP) ≥ 85 mm Hg, or the use of antihypertensive drugs; hypertriglyceridemia, i.e., TG ≥ 150 mg/dl; reduced HDL-C, i.e., HDL-C < 40 mg/dl in men or < 50 mg/dl in women; hyperglycemia, i.e., FPG ≥ 100 mg/dl or the use of antidiabetic agents.

2.4. Statistical analysis

Continuous variables are summarized as the means with the standard deviations (SDs), and categorical variables are expressed as the numbers and percentages. Independent *t*-tests and chi-square tests were used to compare the differences in characteristics difference between the MetS group and non-MetS group. To evaluate the odds ratio (ORs) for MetS according to varying levels of liver enzymes, the subjects were divided into quartiles according to their liver enzymes levels. Pearson's correlation coefficients were used to calculate the associations of liver enzyme levels with each component of MetS. Univariate and multivariate logistic regression were performed to evaluate the ORs of MetS and its components according to the quartiles of the liver enzymes levels. All statistical tests were two-sided, and a P-value < 0.05 was considered to be statistically significant. All statistical analyses were performed with SPSS software 18.0 (SPSS Inc., Chicago, IL, USA).

Table 1
Characteristics of the study populations.

	MetS(n = 524)	Non-MetS(n = 920)	P value
Sex (men, %)	358 (68.32%)	612 (66.52%)	0.484
Age (year)	69.58 ± 7.01	70.04 ± 7.65	0.255
BMI (kg/m^2)	26.81 ± 2.60	23.30 ± 2.83	< 0.001
WC (cm)	93.16 ± 10.62	80.81 ± 11.26	< 0.001
Current smoking (%)	26 (4.96%)	59 (6.41%)	0.616
SBP (mm Hg)	139.02 ± 16.23	130.67 ± 17.23	< 0.001
DBP (mm Hg)	82.51 ± 10.31	78.02 ± 9.66	< 0.001
TG (mg/dl)	217.75 ± 135.10	127.72 ± 83.10	< 0.001
TC (mg/dl)	201.11 ± 41.20	196.37 ± 36.78	0.024
HDL-C (mg/dl)	58.18 ± 15.92	69.35 ± 17.37	< 0.001
LDL-C (mg/dl)	102.81 ± 31.63	99.48 ± 27.93	0.039
FPG (mmol/L)	6.31 ± 1.97	5.35 ± 1.21	< 0.001
ALT (IU/L)	26.98 ± 15.51	22.01 ± 12.58	< 0.001
AST (IU/L)	23.37 ± 8.85	23.25 ± 8.66	0.796
GGT (IU/L)	29.80 ± 19.54	23.42 ± 18.93	< 0.001
ALP (IU/L)	86.25 ± 16.25	81.41 ± 12.80	< 0.001
Total bilirubin	14.50 ± 5.27	14.65 ± 5.53	0.617
Albumin	37.01 ± 4.31	36.98 ± 4.13	0.906
Uric acid (mg/dl)	6.26 ± 1.52	5.67 ± 1.36	< 0.001
Creatinine (umol/l)	81.48 ± 25.71	80.16 ± 24.25	0.331
No of MetS components	3.31 ± 0.46	1.38 ± 0.68	< 0.001

Abbreviation: BMI: body mass index; WC: waist circumference; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FPG: fasting plasma glucose; ALT: alanine aminotransferase; AST: aspartate aminotransferase; GGT: gamma-glutamyltransferase. ALP: alkaline phosphatase.

3. Results

3.1. Characteristics of the study populations

The main characteristics of subjects are presented in Table 1. Among the included 1444 participants, 524 subjects were diagnosed with MetS, and the prevalence of MetS was 36.3% across all subjects (35.0% of the women and 36.9% of the men). There were no significant differences in age, gender or smoking status between the MetS and non-MetS groups (P > 0.05). However, the subjects in MetS group had significantly higher WC, BMI, SBP, DBP, TC, TG, LDL-C, FPG, and uric acid levels but lower HDL-C values than the subjects in the non-MetS groups. Additionally, the mean number of MetS components was much higher in the MetS group than non-MetS group (3.31 ± 0.46 vs 1.38 ± 0.68; P < 0.01).

3.2. Correlations of liver enzyme levels and MetS components

Pearson's correlation coefficients were calculated to evaluate the correlations between liver enzyme levels and MetS components after adjustments for sex and age (Table 2). ALT was positively associated with WC, FPG and TG and negatively correlated with HDL-C. GGT was positively correlated with WC, FPG, TG, SBP and DBP. ALP was positively associated with WC, FPG and TG and negatively correlated with HDL-C. However, there were no statistically positive or negative correlations of AST with any MetS components.

3.3. Odds ratios for MetS according to the quartiles of the liver enzyme levels

Univariate and multivariate logistic regression analyses were conducted to evaluate the liver enzyme levels and the risk of MetS. As presented in Table 3, compared with the subjects in the bottom ALT