Liver Enzymes, Type 2 Diabetes, and Metabolic Syndrome in Middle-Aged, Urban Chinese Men

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Abstract

Background: We examined associations between elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) with physical activity and obesity measures in middle-aged urban Chinese men. The associations between elevated aminotransferases with impaired fasting glucose, newly diagnosed type 2 diabetes (T2D), and metabolic syndrome were also evaluated in this population.

Methods: The study included 3,978 urban Chinese men 40–74 years of age from a population-based cohort study, the Shanghai Men's Health Study, who were free of T2D at baseline and had provided fasting blood samples. Elevated AST and ALT levels were defined as >40 U/L. Anthropometric measurements and information on lifestyle factors and disease history were collected by in-person interviews.

Results: A total of 11.13% and 5.85% study participants had elevated serum ALT and AST levels, respectively. Both body mass index (BMI) and waist-to-hip ratio (WHR) were positively associated with elevated ALT and AST. We found stronger associations between ALT and BMI/WHR than between AST and BMI/WHR. Physical activity was inversely associated with ALT and AST, but the association was attenuated after adjustment for BMI and WHR. Elevated serum aminotransferase levels were associated with T2D and metabolic syndrome.

Conclusions: In this representative sample of middle-aged Chinese men, elevated ALT and AST were associated with a prevalence of metabolic syndrome and T2D. These findings suggest that the relationship between obesity and T2D might involve liver injury. Physical activity might reduce the levels of ALT and AST, probably mediated through weight reduction.

Introduction

SERUM AMINOTRANSFERASE LEVELS, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) are commonly measured as indirect markers of liver inflammation or injury.¹ Because ALT is closely related to liver fat accumulation,² ALT has also been used as a surrogate marker for nonalcoholic fatty liver disease (NAFLD) in some epidemiologic studies.^{3–5} NAFLD affects 10% to 24% of the general population in United States.⁶ NAFLD is frequently observed among obese subjects³ and may be involved in the pathogenesis of type 2 diabetes (T2D).

Associations between elevations in ALT^{8–13} and AST^{2,8,10,14,15} with T2D have been reported. Data linking

elevated serum aminotransferase levels with metabolic syndrome are also available.^{3,4,9,15} Thus, elevated ALT values might be a risk factor for T2D and metabolic syndrome. Identification of factors associated with the elevated aminotransferases could help in the prevention of metabolic syndrome and T2D. There is some data linking obesity and elevated aminotransferases^{5,7,16}; however, data on the associations between serum aminotransferase levels and physical activity are limited.^{17,18}

Using data collected in the Shanghai Men's Health Study (SMHS), a population-based study of middle-aged men living in urban Shanghai, China, we evaluated associations between elevated ALT and AST levels and measures of overall obesity, central obesity, and physical activity in a

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subset of SMHS participants who provided fasting blood samples and were free of T2D at baseline. We also evaluated associations between elevated liver enzymes and prevalence of T2D and metabolic syndrome.

Methods

The Shanghai Men's Health Study

The SMHS is a population-based cohort study of 61,500 Chinese men aged 40–74 years, living in urban Shanghai, China. Recruitment for the SMHS was between April, 2002, and June, 2006. A total of 83,058 eligible male residents of eight communities in urban Shanghai were invited to participate by trained interviewers through in-person contact, and 61,500 men who had no prior history of cancer were enrolled in the study (response rate, 74.0%). Reasons for nonparticipation were refusal (21.1%), out of area during enrollment (3.1%), and other miscellaneous reasons including poor health or hearing problems (1.8%). The study protocols were approved by the Institutional Review Boards of participating institutes, and all participants provided written informed consent. Through in-person interviews, information was collected on demographic characteristics, disease history, and lifestyle factors, including dietary intake and physical activity. Participants were measured for weight and circumferences of the waist and hips according to a standard protocol. Participants were asked to provide biological samples, including a blood or cheek cell sample and a spot urine sample. In a subcohort of 3,978 participants who had no history of diabetes at baseline and who had provided a fasting blood sample, we measured levels of ALT, AST and other disease-related biomarkers. This subcohort forms the basis of the current study.

Blood glucose, lipid, and aminotransferases measurements

At the time of the interview, a 10-mL blood sample was drawn into an ethylenediaminetetraacetic acid (EDTA) vacutainer tube. The samples were kept in a portable Styrofoam box with ice packs (0–4°C) and were processed within 6 h. All samples were stored at –70°C immediately after processing. Among participants who donated a blood sample at baseline ($n=46,169$), 12.5% reported having had their last meal at least 8 h prior to the blood draw. For this study, we included the first 3,978 participants who were free of T2D at baseline and who had provided a fasting blood sample. The activities of AST and ALT were measured by using ACE AST (ASTNEW) and ALT (ALTNEW) reagents, respectively, on an ACE Clinical Chemistry System (Alfa Wassermann, Inc, West Caldwell, NJ). Blood glucose level and lipid profiles were also measured using an ACE clinical chemistry system.

High liver enzymes definition

Elevation in serum AST or ALT activity was defined as greater than 40 U/L.

Physical activity

Information about physical activity was obtained using a validated physical activity questionnaire.¹⁹ The question-

naire evaluated physical activity during the 5 years preceding the interview, including exercise; daily living activities, including walking, stair climbing, cycling, and household activities; and commuting journey to/from work. Summary energy expenditure values [metabolic equivalent task (MET)-h/day] for these activities were estimated using a compendium of physical activity values.²⁰ We calculated total physical activity (total METs) by combining the three types of physical activity—exercise, daily living, and commuting.

Anthropometric measurements

Weight, height, and waist and hip circumferences were taken twice, according to a standard protocol. If the difference between the first two measurements was larger than 1 cm for circumferences or 1 kg for weight, a third measurement was taken. The average of the two closest measurements was applied in the present study. From these measurements, the following variables were created: body mass index (BMI), weight in kilograms divided by the square of height in meters, and waist-to-hip ratio (WHR; waist circumference divided by hip circumference).

Other confounding factors

Usual dietary intake was assessed using a validated food frequency questionnaire.²¹ The Chinese Food Composition Tables²² were used to estimate total energy intake (kcal/day). Sociodemographic factors, including age, education (none, elementary school, high school, college), income (<500, 500–999, 1,000–1,999, >1,999 yuan/year), occupation (professional, clerical, manual), smoking status, alcohol intake (nondrinkers, drinking ≤ 2 drinks/day and drinking ≥ 2 drinks/day), and cardiovascular disease (CVD) at baseline (yes/no) were collected by questionnaire.

Metabolic syndrome criteria

Participants were classified as having metabolic syndrome according to the Adult Treatment Panel III (ATP III)-modified criteria, which uses waist circumference cut points that are ethnicity-specific for Chinese men (≥ 90 cm instead of 102 cm) and a fasting glucose cut point of ≥ 5.6 mmol/L.²³ Other criteria for metabolic syndrome were serum triglyceride levels >1.70 mmol/L, high-density lipoprotein cholesterol (HDL-C) <1.04 mmol/L, and blood pressure $\geq 85/130$ mmHg or taking medication for hypertension.

T2D criteria

Normal glucose tolerance, fasting glucose cut point of <5.6 mmol/L, impaired fasting glucose, fasting glucose between 5.6 mmol/L and 6.9 mmol/L, and T2D fasting glucose >7 mmol/L.²³

Statistical analysis

Participants with chronic hepatitis ($n=97$) were excluded, leaving 3,881 participants for the analyses. Associations between high ALT and AST levels with population characteristics were evaluated using analysis of variance (ANOVA) for continuous variables (with the exception of age which was nonnormally distributed, and thus a Kruskal–Wallis test was used instead) and chi-squared test for categorical variables.

Associations between high ALT and AST levels with BMI quintiles, WHR quintiles, physical activity categories, and the prevalence of T2D, metabolic syndrome, and impaired fasting glucose were investigated by unconditional logistic regression analysis. Tests for trend were performed by entering the categorical variables as continuous parameters in the models. All statistical analyses were performed using SAS (version 9.1). All tests of statistical significance were based on two-sided probability.

Results

The prevalence of elevated ALT and AST levels in this population was 11.83% and 5.85%, respectively. Participants with elevated serum ALT levels had higher BMI, WHR, and daily energy intake and were less likely to smoke or participate in sports than those without the condition (Table 1). The prevalence of elevated serum ALT levels was positively associated with each individual component of metabolic syndrome, the number of metabolic syndrome components

present, and the prevalence of metabolic syndrome. Participants with elevated serum AST levels had higher BMI and WHR and were more likely to drink alcohol than those without the condition. Positive associations between elevated AST and T2D and metabolic syndrome were also found. AST was associated with the individual components of the metabolic syndrome with the exception of low HDL-C.

Elevated ALT and AST levels were associated with higher BMI and WHR (Tables 2 and 3). However, the positive association between BMI and WHR with high ALT was much stronger than that for high AST. The multivariate adjusted odds ratios (ORs) for high ALT across quintiles of BMI were 1.00, 1.20, 2.70, 4.34, and 10.19, whereas ORs for high AST were 1.00, 0.56, 0.89, 1.41, and 2.87. We also investigated associations between having high ALT and AST with weight gain since 20 years (data not shown). Compared with men with no weight gain, men who gained 2.8 kg or more per 5-year period had an OR of 11.6 [95% confidence interval (CI) 6.71–20.0] for high ALT and 3.70 (95% CI 2.04–6.70) for high AST.

TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION BY HIGH ALT AND HIGH AST PREVALENCE

	<i>All</i>	<i>Normal ALT</i>	<i>High ALT</i>	<i>P value</i>	<i>Normal AST</i>	<i>High AST</i>	<i>P value</i>
Age (median)	48.0	49.0	47.0	<0.01	49.0	47	<0.01
kcal/day (mean)	1931.5	1923.5	1995.7	<0.01	1929.2	1972.11	0.24
BMI (mean)	23.3	23.0	25.5	<0.01	23.2	24.9	<0.01
WHR (mean)	0.89	0.89	0.93	<0.01	0.89	0.92	<0.01
Current smoker (%)	75.73	76.3	71.3	0.02	75.9	73.1	0.35
Alcohol (%)	37.85	38.3	36.2	0.08	37.3	47.6	<0.01
Exercise (%)	21.67	22.3	16.7	<0.01	21.6	22.1	0.87
Education (%)				0.04			0.54
None	3.12	3.4	1.4		3.1	3.4	
Elementary	38.2	38.3	36.2		38.1	39.7	
Up to high school	40.7	40.3	43.0		40.5	42.6	
College	18.0	17.9	19.4		18.2	14.2	
Income level (%)				0.71			0.02
<500	19.1	19.1	19.7		18.8	25.5	
500–999	41.9	42.2	39.3		41.8	43.3	
1,000–1,999	29.6	29.5	30.8		29.8	26.0	
>1,999	9.4	9.3	10.2		9.6	5.3	
Occupation (%)				0.22			0.04
Professional	20.2	20.1	20.9		20.2	19.9	
Clerical	23.1	22.8	26.0		22.7	30.1	
Manual workers	56.7	57.1	53.0		57.0	50.0	
CVD (%)	4.1	4.2	3.0	0.22	4.1	4.3	0.86
T2D prevalence (%)	6.1	5.1	13.7	<0.01	5.5	14.9	<0.01
Family history T2D (%)	19.2	18.6	24.1	<0.01	18.9	24.3	0.06
Metabolic syndrome prevalence (%)	29.5	25.8	59.3	<0.01	27.8	58.6	<0.01
Metabolic syndrome components (%)							
High waist	25.7	22.3	53.0	<0.01	24.4	48.1	<0.01
Glucose intolerance	39.1	36.9	56.9	<0.01	37.9	60.6	<0.01
High triglycerides	40.9	37.8	67.8	<0.01	39.2	71.1	<0.01
Low HDL	26.1	24.9	35.6	<0.01	25.9	28.4	0.43
Hypertension	48.6	47.3	58.3	<0.01	47.7	63.9	<0.01
Metabolic syndrome components (%)				<0.01			<0.01
None	18.1	19.4	7.4		18.6	8.2	
1 component	27.8	29.6	13.7		28.6	13.9	
2 components	24.6	25.2	19.7		24.9	19.2	
3 components	17.1	15.9	26.2		16.7	23.6	
4 components	10.0	8.1	25.2		9.1	26.4	
5 components	2.4	1.7	7.9		2.1	8.6	

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; WHR, waist-to-hip ratio; CVD, cardiovascular disease; T2D, type 2 diabetes; HDL, high-density lipoprotein.

TABLE 2. ASSOCIATIONS OF HIGH ALT^a WITH BMI, WHR, AND PHYSICAL ACTIVITY

	OR1 ^b	(95% CI)	OR2 ^c	(95% CI)
BMI				
Quintile 1	1.00		1.00	
Quintile 2	1.20	0.71–2.02	0.91	0.54–1.55
Quintile 3	2.70	1.69–4.29	1.71	1.06–2.78
Quintile 4	4.34	2.78–6.78	2.47	1.53–3.96
Quintile 5	10.19	6.66–15.59	4.84	300–7.78
<i>P</i> trend	0.001		0.001	
WHR				
Quintile 1	1.00		1.00	
Quintile 2	1.68	0.97–2.89	1.10	0.63–1.91
Quintile 3	4.12	2.51–6.76	2.12	1.26–3.55
Quintile 4	6.03	3.68–9.89	2.73	1.62–4.60
Quintile 5	10.10	6.22–16.33	3.54	2.09–6.02
<i>P</i> trend	0.001		0.001	
Exercise participation				
No	1.00		1.00	
Yes	0.74	0.56–0.97	0.74	0.55–0.99
<i>P</i> trend	0.03		0.04	
Daily living activity METs				
≤3	1.00		1.00	
>3–6	0.86	0.66–1.11	0.97	0.74–1.28
>6–9	0.63	0.46–0.86	0.76	0.55–1.05
>9–12	0.75	0.52–1.10	0.98	0.66–1.46
>12	0.61	0.38–0.96	0.73	0.45–1.19
<i>P</i> trend	<0.01		0.18	
Commuting activity METs				
None	1.00		1.00	
<3	1.00	0.80–1.24	1.10	0.87–1.39
≥3	0.73	0.52–1.02	0.86	0.61–1.22
<i>P</i> trend	0.13		0.73	
Total PA METs^d				
≤3	1.00		1.00	
>3–6	0.83	0.61–1.14	0.96	0.69–1.34
>6–9	0.66	0.48–0.92	0.84	0.60–1.19
>9–12	0.59	0.41–0.85	0.72	0.49–1.06
>12	0.52	0.35–0.77	0.73	0.49–1.10
<i>P</i> trend	0.001		0.03	

^aHigh ALT (>40 U/L).^bOR1: Adjusted for age, kcal/day, alcohol consumption, smoking, education, income, occupation, pre-existing cardiovascular disease. In addition, BMI and WHR analysis were adjusted for total physical activity.^cOR2: As above plus WHR for BMI analysis, BMI for WHR analysis, and BMI and WHR for physical activity analysis.^dTotal physical activity METs: Exercise, daily living, and commuting METs combined.

ALT, alanine aminotransferase; BMI, body mass index; WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; METs, metabolic equivalents.

Exercise, daily living, commuting physical activity, and total physical activity (which included leisure time, daily living, and commuting to work physical activity) were inversely related to elevated ALT (Table 2). Exercise and daily living physical activity were not associated with elevated AST, and inverse associations between commuting to and from work and total physical activity with elevated AST were observed (Table 3). The ORs for ≤3, >3–6, >6–9, >9–12, and >12 total physical activity METs were 1.00, 0.83, 0.66, 0.59, and 0.52 for high ALT and 1.00, 1.04, 0.83, 0.90, and 0.63 for AST, respectively. The associations were attenuated after adjustment for BMI and WHR. We repeated the analysis after stratification for BMI and WHR categories

TABLE 3. ASSOCIATIONS OF HIGH AST^a WITH BMI, WHR, AND PHYSICAL ACTIVITY

	OR1 ^b	(95% CI)	OR2 ^c	(95% CI)
BMI^a				
Quintile 1	1.00		1.00	
Quintile 2	0.56	0.31–1.00	0.42	0.24–0.77
Quintile 3	0.89	0.53–1.52	0.53	0.31–0.94
Quintile 4	1.41	0.86–2.29	0.77	0.45–1.31
Quintile 5	2.87	1.89–4.43	1.30	0.76–2.21
<i>P</i> trend	0.01		0.01	
WHR^a				
Quintile 1	1.00		1.00	
Quintile 2	0.58	0.30–1.13	0.47	0.24–0.91
Quintile 3	1.72	1.01–2.93	1.20	0.69–2.12
Quintile 4	2.12	1.24–3.62	1.38	0.77–2.47
Quintile 5	3.49	2.11–5.77	1.94	1.08–3.49
<i>P</i> trend	0.001		0.001	
Exercise participation				
No	1.00		1.00	
Yes	1.16	0.81–1.67	1.17	0.81–1.70
<i>P</i> trend	0.42		0.39	
Daily living activity METs				
≤3	1.00		1.00	
>3–6	1.00	0.68–1.46	1.10	0.75–1.63
>6–9	0.83	0.54–1.23	0.97	0.62–1.52
>9–12	0.90	0.53–1.57	1.10	0.65–1.88
>12	0.69	0.36–1.30	0.78	0.41–1.50
<i>P</i> trend			0.55	
Commuting activity METs				
None	1.00		1.00	
<3	0.94	.69–1.28	0.99	0.72–1.35
≥3	0.50	0.29–0.85		0.32–0.95
<i>P</i> trend	0.03		0.08	
Total PA METs^d				
≤3	1.00		1.00	
>3–6	1.04	0.65–1.66	1.20	0.74–1.93
>6–9	0.83	0.51–1.36	1.01	0.61–1.66
>9–12	0.90	0.53–1.53	1.01	0.64–1.86
>12	0.63	0.35–1.11	0.80	0.45–1.44
<i>P</i> trend	0.06		0.31	

^aHigh AST (>40 U/L).^bOR1: Adjusted for age, kcal/day, alcohol consumption, smoking, education, income, occupation, pre-existing cardiovascular disease. In addition, BMI and WHR analysis were adjusted for total physical activity.^cOR2: As above plus WHR for BMI analysis, BMI for WHR analysis, and BMI and WHR for physical activity analysis.^dTotal PA METs: Exercise, daily living, and commuting metabolic equivalents combined.

AST, aspartate aminotransferase; BMI, body mass index; WHR, waist-to-hip ratio; OR, odds ratio; CI, confidence interval; METs, metabolic equivalents.

and found similar inverse trends (data not shown). To address the potentially confounding effects of alcohol consumption on hepatic steatosis and liver injury, we repeated the analysis after exclusion of participants with an alcohol intake of two or more drinks per day; we found similar trends (data not shown).

We found a positive graded association between quintiles of ALT and AST levels with metabolic syndrome (Table 4). The association was stronger for ALT than for AST. Further adjustment for BMI attenuated the results in particular for ALT association with metabolic syndrome.

Both ALT and AST were positively associated with impaired fasting glucose and undiagnosed T2D (Tables 5 and

TABLE 4. LOGISTIC REGRESSION ANALYSIS WITH METABOLIC SYNDROME AS THE DEPENDENT VARIABLE AND ALT AND AST AS THE INDEPENDENT VARIABLES

	OR1 ^a	(95% CI)	OR2 ^b	(95% CI)
ALT				
Quintile 1	1.00		1.00	
Quintile 2	2.17	1.60–2.94	1.52	1.10–2.12
Quintile 3	2.98	2.20–4.04	1.71	1.23–3.38
Quintile 4	5.66	4.26–7.54	2.69	1.97–3.69
Quintile 5	11.39	8.56–15.16	3.85	2.80–5.29
High ALT ^c	4.25	3.43–5.26	2.21	1.73–2.82
AST				
Quintile 1	1.00		1.00	
Quintile 2	0.67	0.54–0.82	0.90	0.72–1.13
Quintile 3	1.83	1.47–2.28	1.62	1.27–2.08
Quintile 4	2.63	2.16–3.22	2.22	1.77–2.78
Quintile 5	4.72	3.84–5.82	3.62	2.84–4.59
High AST ^c	3.67	2.73–4.94	2.73	1.91–3.91

^aOR1: Adjusted for age, kcal/day, physical activity, smoking, education level, income level, occupation, pre-existing cardiovascular disease.

^bOR2: All of the above, plus BMI.

^cHigh ALT (>40 U/L) and high AST (>40 U/L).

ALT, alanine aminotransferase; AST, aspartate aminotransferase; OR, odds ratio; CI, confidence interval.

6). The ORs of undiagnosed T2D for quintiles of ALT were 1.00, 1.89, 2.30, 3.39, and 7.39 and 1.00, 0.79, 1.29, 2.06, and 4.22 for AST. Further adjustment for BMI and WHR attenuated the results, in particular for the association between ALT quintiles and T2D.

Discussion

In this sample of middle-aged men, elevated ALT and AST were positively associated with obesity and inversely asso-

TABLE 5. LOGISTIC REGRESSION ANALYSIS WITH IMPAIRED FASTING GLUCOSE VERSUS NORMAL GLUCOSE TOLERANCE AND ALT AND AST AS THE INDEPENDENT VARIABLES

	OR1 ^a	(95% CI)	OR2 ^b	(95% CI)
ALT				
Quintile 1	1.00		1.00	
Quintile 2	1.41	1.12–1.77	1.29	1.02–1.63
Quintile 3	1.64	1.29–2.08	1.44	1.13–1.83
Quintile 4	2.11	1.69–2.65	1.75	1.38–2.21
Quintile 5	2.72	2.17–3.42	2.07	1.61–2.65
High ALT	2.00	1.61–2.49	1.61	1.28–2.02
AST				
Quintile 1	1.00		1.00	
Quintile 2	1.01	0.84–1.21	1.07	0.89–1.29
Quintile 3	1.63	1.33–2.00	1.57	1.28–1.93
Quintile 4	2.48	2.06–2.99	2.32	1.92–2.80
Quintile 5	3.43	2.80–4.20	3.12	2.53–3.83
High AST	2.20	1.61–3.00	1.92	1.40–2.64

^aOR1: Adjusted for age, kcal/day, alcohol consumption, smoking, physical activity, education level, income level, occupation established cardiovascular disease, family history of diabetes.

^bOR2: As above plus BMI and WHR.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; OR, odds ratio; CI, confidence interval; BMI, body mass index; WHR, waist-to-hip ratio.

TABLE 6. LOGISTIC REGRESSION ANALYSIS WITH T2D VERSUS NORMAL GLUCOSE TOLERANCE AND ALT AND AST AS THE INDEPENDENT VARIABLES

	OR1 ^a	(95% CI)	OR2 ^b	(95% CI)
ALT				
Quintile 1	1.00		1.00	
Quintile 2	1.89	1.06–3.36	1.53	0.85–2.74
Quintile 3	2.30	1.28–4.14	1.60	0.88–2.92
Quintile 4	3.39	1.96–5.88	1.98	1.11–3.51
Quintile 5	7.39	4.37–12.50	3.61	2.05–6.34
High ALT	3.91	2.76–5.55	2.43	1.68–3.53
AST				
Quintile 1	1.00		1.00	
Quintile 2	0.79	0.54–1.17	1.00	0.67–1.49
Quintile 3	1.29	0.83–2.02	1.13	0.72–1.78
Quintile 4	2.06	1.40–3.04	1.70	1.14–2.54
Quintile 5	4.22	2.90–6.16	3.15	2.12–4.67
High AST	4.03	2.54–6.41	2.81	1.72–4.61

^aOR1: Adjusted for age, kcal/day, alcohol consumption, smoking, physical activity, education level, income level, occupation established cardiovascular disease, family history of diabetes.

^bOR2: As above plus BMI and WHR.

T2D, type 2 diabetes; ALT, alanine aminotransferase; AST, aspartate aminotransferase; OR, odds ratio; CI, confidence interval; BMI, body mass index; WHR, waist-to-hip ratio.

ciated with physical activity. Having high ALT and AST was associated with a higher prevalence of metabolic syndrome and T2D. Our findings on the direct associations between BMI and WHR and elevated ALT and AST are in agreement with other studies.^{5,16} Serum ALT levels have a strong association with visceral fat accumulation. Visceral adipose tissue was the main predictor of elevated ALT concentrations in the context of NAFLD among nondiabetic overweight Korean women.⁷

We found an inverse association between physical activity and ALT and AST. Adjustment for BMI and or WHR attenuated the association. Data on associations between physical activity with ALT and AST levels are limited. Physical activity was inversely associated with serum aminotransferase levels among obese children²⁴ and among middle-aged British women.¹⁸ An inverse association between physical fitness and NAFLD has been reported.¹⁷ Physical activity was inversely associated with intrahepatic fat content.²⁵ ALT levels have been associated with decreased hepatic insulin sensitivity.¹² Thus, physical activity may reduce the risk of T2D via increasing the insulin sensitivity in muscle²⁶ and also via a decrease of intrahepatic fat content.²⁵

Other studies have found similar associations between elevated ALT levels and metabolic syndrome, including a study done in Korean adolescents²⁷ and a Japanese population older than 40 years,²⁸ among others. In a population-based cross-sectional survey in three rural communities in South Korea, the ORs for the metabolic syndrome in the highest quintiles of ALT were 7.1-fold higher than the lowest quintile in men, similar to our results.⁴ Elevation in both AST and ALT levels was associated with metabolic syndrome and its components in an Italian study.²⁹ NAFLD is a common explanation for abnormal liver test results in blood donors⁶ and a cause of asymptomatic elevation of aminotransferases levels in up to 90% of cases once other causes of liver disease have been excluded.³⁰ NAFLD has been described as the hepatic component of metabolic syndrome.³¹

Our results of an association between elevated ALT and T2D agreed with those from other studies. ALT has been associated with T2D in most,^{8–13} but not all, studies.¹⁵ ALT has been associated with the incidence of T2D.^{11–13} The association between elevated AST and T2D is less clear. Although associations between AST and T2D have been reported in some studies,^{2,8,10,14,15} AST levels were not associated with T2D in two studies,^{12,14} and in another study conducted in Japan, an association between AST and T2D was observed in men but not women.⁸ In a different study, AST was associated with impaired glucose tolerance only, but not with T2D.¹⁵

Alcohol consumption is associated with increased serum levels of ALT and AST.¹⁶ Therefore, we conducted sensitivity analysis and reran the analyses after exclusion of participants consuming more than two alcoholic drinks per day. We did not observe a major change in our findings.

The strengths of this study are the population-based design, the extensive information on confounders, and the validated physical activity questionnaire that collected data on different types of physical activity. The main limitation of this study is the cross-sectional design, which prevented us from making any causal inferences based on our results.

In conclusion, obesity, metabolic syndrome and undiagnosed T2D were associated with a higher prevalence of elevated serum aminotransferase levels among middle-aged Chinese men. Because elevated serum aminotransferase levels may be an early risk marker for chronic disease development, they might have value as a risk marker for T2D and may be useful in strategies for the prevention of these disorders. Physical activity is inversely associated with ATL and AST and thus should be promoted.

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Author Disclosure Statement

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