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Appendicular muscle mass and fasting triglycerides predict serum liver aminotransferases in young female collegiate athletes

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ABSTRACT

Objective We test the hypothesis that aspartate aminotransferase (AST) may be associated inversely with serum triglycerides (TG) and positively with high density lipoprotein (HDL) cholesterol in young athletes because athletes have larger amounts of muscle mass.

Research design and methods Pearson's correlation coefficients were calculated between serum AST and alanine aminotransferase (ALT) and body composition identified by dual-energy X-ray absorptiometry, markers of insulin resistance, serum lipids, lipoproteins, apolipoproteins, adiponectin and leptin in 174 female collegiate athletes (18–22 years). Multivariate linear regression analyses were used to identify independent determinants of the aminotransferases.

Results AST and ALT showed positive correlation with appendicular skeletal muscle mass (ASM) and height-adjusted ASM. In addition, ALT as well as AST showed inverse, not positive, association with fasting TG. Further, both AST and ALT showed positive associations with HDL cholesterol and apolipoprotein AI, a major apolipoprotein of HDL particles. Multivariate analysis revealed that height-adjusted ASM and TG (inverse) were independent determinants for AST and ALT. Further, fat mass index (inverse) and resting heart rate (inverse) predicted AST and apolipoprotein AI predicted ALT.

Conclusions In young female collegiate athletes, both serum AST and ALT showed inverse association with fasting TG and positive association with apoAI, both of which may be mediated through positive association between the aminotransferases and ASM. The association between ALT and TG is opposite in direction in young athletes (inverse) and in the general population (positive).

Significance of this study

What is already known about this subject?

Mildly elevated serum aminotransferase concentrations

- are frequently observed in overweight and obese subjects with non-alcoholic fatty liver disease and
- show positive association with insulin resistance (IR).

What are the new findings?

Mild elevations in serum aminotransferases in athletes

- are markers of muscle training or muscle injury and
- show inverse, not positive, association with IR.

How might these results change the focus of research or clinical practice?

- Attention needs to be paid to the interpretation of associations between serum aminotransferases and IR-related variables in physically active people.

INTRODUCTION

Asymptomatic elevations in liver aminotransferases, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are found in many cases with non-alcoholic fatty liver disease, which is also known as the hepatic manifestation of the metabolic syndrome.[1] Liver aminotransferases, ALT in particular, have been reported to be associated with high triglycerides (TG) and low HDL cholesterol (atherogenic dyslipidemia) in overweight/obese children,[2] young healthy male students[3] and young adults (the Bogalusa Heart Study)[4] and in a general population (the Framingham Heart Study).[5] ALT as compared with AST appears to be a better marker of insulin resistance (IR) in muscle and the liver[6–8] and of accumulation of liver fat.[8]

Studies in the general population have shown clear correlation between ALT and AST and body weight and BMI.[9 10] Although ALT is found mainly in the liver, AST is present in considerable amounts in the muscle in addition to the liver and can be released in case of muscular training or muscle damage.[11] Prolonged daily training produces chronically elevated serum aminotransferase activities.[12] Although most athletes do not have significant biochemical abnormalities on prescreening evaluations, the most common abnormalities were increases in AST.[13] However, there are scant data on the relationship between aminotransferases and body composition and IR-related metabolic

variables in athletes. Singhal *et al*[14] studied body composition using whole-body dual-energy X-ray absorptiometry (DXA) and biochemical parameters, including AST and ALT, in young female normal-weight athletes and found that athletic activity was associated with elevated AST, lower body fat and heart rate. However, they did not report associations between body composition and the aminotransferase levels. Although the liver is well known to produce glucose and TG, skeletal muscle is a major site of insulin-mediated glucose disposal in the postprandial state.[15] In addition, in the fasting state, skeletal muscle is a site of clearance of TG in very-low density lipoprotein particles and production of HDL particles as well.[16] Therefore, we tested the hypothesis that serum AST may be associated with muscle mass, serum TG and HDL cholesterol in young endurance-trained college students, a population in which confounding factors are so scarce.[17–20]

METHODS

Participants were the same as in our previously reported cross-sectional study[20]: 174 female collegiate athletes aged 18–22 years. They were all Japanese and were recruited as volunteers. They were students of Department of Health and Sports Sciences and were also members of volleyball club, basketball club or track club (middle-distance runners) of the University. They had been training regularly for 2 years or longer prior to the study, 5 hours a day and 6 days a week and participated regularly in competitive events in their respective sport specialties. Subjects who reported that they were under treatment for clinically diagnosed acute or chronic inflammatory diseases, endocrine, cardiovascular, hepatic and renal diseases and those with hormonal contraception and unusual dietary habits were excluded. Nobody reported smoking and drinking alcohol every day. Nobody reported receiving any medications or having regular supplements. All subjects gave written consent after the experimental procedure had been explained.

After a 12 hours overnight fast, participants underwent blood sampling, measurements of anthropometric indices, body composition, blood pressure and pulse rate as previously described.[18–20] In fasted blood samples, plasma glucose, serum insulin, adiponectin and leptin were measured as previously reported.[18–20] Serum TG, cholesterol, HDL cholesterol, AST and ALT were measured using an autoanalyzer (AU5232, Olympus, Tokyo, Japan). Apolipoprotein AI (apoAI) and apolipoprotein B-100 (apoB) were measured by respective commercially available kits using an Olympus autoanalyzer (AU600, Mitsubishi Chemicals, Tokyo, Japan). IR was evaluated by fasting insulin and homeostasis model assessment-IR.[21]

Lean tissue mass, fat mass and bone mineral mass for arms, legs, trunk and the total body were measured using whole-body DXA (Hologic QDR-2000, software version 7.20D, Waltham, Massachusetts, USA) as previously reported.[18 19] Because lean mass in arms and legs represents skeletal muscle mass, a sum of the two was used as appendicular skeletal muscle mass (ASM). Skeletal muscle mass was also assessed by ASM index (ASMI) calculated as ASM in kilograms divided by squared height in meters. Lean mass in arms, legs, trunk and the total body was assessed by the absolute values and lean mass index calculated as described above. Fat mass in arms, legs, trunk and the total body was assessed by the absolute values and fat mass index (FMI) calculated as respective fat mass in kilograms divided by squared height in meters. Fat mass in the four regions was also evaluated as the percentage of body weight and expressed as respective percentage fat. Abdominal fat accumulation was assessed by the ratio of trunk to leg fat.[22]

Data were presented as mean ±SD unless otherwise stated. Due to deviation from normal distribution, the aminotransferases were logarithmically transformed for analysis. Correlations of the aminotransferases with body composition and cardiometabolic parameters were evaluated by Pearson's correlation analysis. In order to evaluate the most important determinants of aminotransferases, a stepwise multiple linear regression analysis was performed. Independent variables included were all variables that showed significant associations with AST and ALT in Pearson's analysis. A value of $P<0.05$ was considered significant. Statistics were performed with SPSS system 17.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

As previously reported in details[20] and shown in table 1, young collegiate athletes were normal weight and insulin-sensitive as indicated by low fasting insulin levels and had normal fasting levels of glucose, lipids and lipoproteins. Although majority of them had normal liver function, maximum AST and ALT were 113 and 48 U/L, respectively. They were characterized by bradycardia and optimal blood pressure.[20]

AST but not ALT showed inverse correlation with percentage fat and FMI in legs, trunk and total body and serum leptin (table 1). In addition, both AST and ALT showed positive correlation with a majority of indices of lean mass, including ASM and ASMI. Both AST and ALT were associated positively with HDL cholesterol and apoA1 and inversely with fasting TG and resting pulse rate. ASM showed positive associations with body fat mass but not with FMI (r: 0.20, $P<0.05$ and 0.03, respectively) and ASMI showed positive associations with both (r: 0.21 and 0.18, respectively, both $P<0.05$).

Multivariate linear regression analyses for AST and ALT as dependent variables were done (table 2). Independent variables included were variables which showed significant associations with AST and ALT shown in table 1. ASMI, FMI (inverse), resting pulse rate (inverse) and TG (inverse) emerged as independent determinants for AST and explained 12.6% of the variability of AST. Independent determinants for ALT were ASMI, apolipoprotein

Table 1 Features of female collegiate athletes and correlation coefficients of aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

	Mean±SD (n = 174)	Correlation coefficients	
		log AST	log ALT
Age (years)	19.9±1.3	−0.138	−0.005
Height (cm)	165.2±6.1	0.208**	0.237**
Weight (kg)	59.1±6.6	0.112	0.209**
BMI (kg/m^2)	21.6±1.9	−0.024	0.080
Waist circumference (cm)	74.8±5.0	−0.043	0.018
Arm fat mass (kg)	1.1±0.5	−0.034	0.061
Leg fat mass (kg)	5.5±1.6	−0.088	0.014
Trunk fat mass(kg)	6.5±2.1	−0.138	0.014
Total fat mass (kg)	13.7±4.1	−0.115	0.020
Arm FMI (kg/m^2)	7.1±2.8	−0.113	−0.047
Leg FMI (kg/m^2)	9.3±2.0	−0.265**	−0.185*
Trunk FMI (kg/m^2)	8.6±2.3	−0.248**	−0.132
Total FMI (kg/m^2)	5.0±1.5	−0.157*	−0.024
% Arm fat (%)	19.3±7.2	−0.080	−0.011
% Leg fat (%)	25.3±5.0	−0.224**	−0.132
% Trunk fat (%)	23.2±5.8	−0.209**	−0.081
% Total body fat (%)	22.8±5.1	−0.206**	−0.091
Trunk/leg fat ratio	1.17±0.21	−0.122	0.000
ASM (kg)	19.3±2.2	0.289**	0.313**
Arm lean mass (kg)	4.1±0.5	0.117	0.218**
Leg lean mass (kg)	15.2±1.8	0.321**	0.322**
Trunk lean mass (kg)	20.2±2.0	0.263**	0.284**
Total lean mass (kg)	42.9±4.3	0.285**	0.307**
ASMI (kg/m^2)	7.1±0.6	0.232**	0.241**
Arm LMI (kg/m^2)	1.51±0.16	0.000	0.097
Leg LMI (kg/m^2)	5.5±0.4	0.283**	0.260**
Trunk LMI (kg/m^2)	7.4±0.5	0.156*	0.162*
Total LMI (kg/m^2)	15.7±1.0	0.201**	0.206**
Fasting glucose (mg/dL)	86±6	−0.075	0.011
Fasting insulin (μU/mL)	5.8±4.6	−0.083	−0.076
HOMA-IR	1.26±1.44	−0.082	−0.046
Triglycerides (mg/dL)	56±21	−0.203**	−0.170*
Cholesterol (mg/dL)	181±26	−0.052	0.017
HDL cholesterol (mg/dL)	77±13	0.157*	0.174*
LDL cholesterol (mg/dL)	92±21	−0.124	−0.055
Apolipoprotein AI (mg/dL)	172±22	0.196**	0.223**
Apolipoprotein B (mg/dL)	69±13	−0.148	−0.087
Leptin (ng/mL)	6.4±2.9	−0.213**	−0.058
Adiponectin (μg/mL)	11.6±4.3	0.031	0.072
AST (U/L)	21±11	1	0.720**
ALT (U/L)	14±6	0.720**	1
Systolic BP (mm Hg)	106±10	0.025	0.065
Diastolic BP (mm Hg)	59±7	0.008	0.064
Resting pulse (bpm)	57±8	−0.208**	−0.153*

*P<0.05, **P<0.01, ***P<0.001.
ASM, appendicular skeletal muscle mass; ASMI, ASM index; BMI, body mass index; BP, blood pressure; FMI, fat mass index; HOMA-IR, homeostasis model assessment-insulin resistance; LMI, lean mass index.

AI and TG (inverse). However, these three variables explained only 8.7% of the ALT variability.

DISCUSSION

To the best of our knowledge, this is the first study to show the relationship between serum aminotransferases and sophisticated measures of body composition using DXA in athletes. The main finding is that in healthy, normal-weight Japanese female athletes in early adult life, AST and ALT were positively associated with ASMI, HDL cholesterol and apolipoprotein AI, a major apolipoprotein of HDL,[23] and inversely with TG and resting pulse rate, a marker that the exercise-trained state has been achieved.[24] Unexpectedly, AST showed inverse association with FMI and serum leptin. Among those variables, ASMI and TG (inverse) were independent determinants for both AST and ALT. Other independent determinants for AST were FMI (inverse) and resting heart rate (inverse) and for ALT apolipoprotein AI. It is noteworthy that these findings were observed in a young, normal- weight population in which confounding factors are so scarce.[20]

There are scant data on the relationship between AST and body composition and metabolic variables in athletes although aminotransferases, AST in particular, are present in considerable amounts in the muscle in addition to the liver and can be released in case of muscular training or muscle damage.[11] As far as we know, there is only one study by Singhal *et al*[14] who examined the relationship between body composition using DXA and biochemical parameters. including AST and ALT. in young female normal-weight athletes. They concluded that athletic activity was associated with elevated AST, lower body fat and heart rate. However, they did not report associations between body composition and the aminotransferase levels. The present study has demonstrated that serum AST and serum ALT predict skeletal muscle mass in athletes. We have no appropriate explanation for unexpected association of AST with fat mass. It was reported that AST levels and fat cell volume are influenced by common set of genes in baboons, a valuable non-human primate model for the study of obesity and its comorbidities.[25 26]

Table 2 Multivariate linear regression analyses for AST and ALT as dependent variables in young female collegiate athletes

		95% CI			
AST	**Standardized β**	**Lower**	**Upper**	**P values**	**Cumulative R^2**
ASMI	0.227	0.022	0.101	0.002	0.048
FMI	−0.181	−0.033	−0.004	0.014	0.084
Resting pulse rate	−0.172	−0.006	−0.001	0.017	0.110
Triglycerides (TG)	−0.147	−0.180	−0.002	0.044	0.126
ALT					
ASMI	0.179	0.358	3.742	0.018	0.048
Apolipoprotein AI	0.169	0.007	0.092	0.023	0.066
TG	−0.164	−8.138	−0.485	0.027	0.087

Independent variables included were variables which showed significant associations with AST and ALT shown in table 1. Common independent variables for AST and ALT: ASMI, triglycerides, apoAI, HDL cholesterol and resting pulse rate. Serum leptin was also included for AST.
ALT, alanine aminotransferase; ASMI, appendicular skeletal muscle mass index; AST , aspartate aminotransferase ; FMI, fat mass index.

In the fasting state, smooth muscle is a site of clearance of TG in very-low density lipoprotein particles and production of HDL particles.[16] Further, TG clearance and HDL production were both provoked by endurance exercise training.[16] These observations may be in line with our findings that fasting TG and apoAI, a major apolipoprotein of HDL,[23] were independent inverse determinants of AST and ALT, markers of skeletal muscle mass in young female athletes. Because high TG and low HDL-C concentrations are both significantly associated with IR,[27] it appears reasonable to assume that AST and ALT may be inverse markers of IR in young female athletes.

This study has several strengths, including homogeneous study population with scarce confounding factors, and accurate and reliable measures of body composition by DXA. The cross-sectional design of the present study complicates the drawing of causal inferences, and a single measurement of biochemical variables may be susceptible to short-term variation, which would bias the results toward the null. We used crude measures of IR, which may be less accurate. Information on the menstrual status was not obtained. As we studied young Japanese female college students only, the results may not be extrapolated to populations other than elite athletes. Finally, statistical power was not calculated.

In conclusion, both serum AST and ALT were associated inversely with fasting TG and positively with ASM and apoAI in young female collegiate athletes. The association between ALT and TG is opposite in direction in young athletes and in the general population; inverse in the former and positive in the latter.

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Data sharing statement The ethics committees of the University does not allow us to open data except for a manuscript.

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