Research Article

Association between ALT/AST and Muscle Mass in Patients with Type 2 Diabetes Mellitus

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Objective. The alanine aminotransferase/aspartate aminotransferase (ALT/AST) ratio is thought to be related to metabolic disorders and insulin resistance. Type 2 diabetes mellitus (T2DM) is a high-risk population for low muscle mass. This study was performed to evaluate the association between ALT/AST and muscle mass in subjects with T2DM.

Method. This cross-sectional study enrolled 1068 subjects (566 males and 502 females) with T2DM. General information, medical history, and blood samples were collected. Skeletal muscle index (SMI) was detected using dual-energy X-ray absorptiometry. Logistic regression analysis was utilized to determine the correlation of ALT/AST and low muscle mass in subjects with T2DM. Multiple linear regression analysis was utilized to evaluate the association between ALT/AST, SMI and other metabolic characteristics.

Result. Of all subjects, 115 men (20.3%) and 71 women (14.1%) presented low muscle mass. ALT/AST was related to an increased risk for low muscle mass in both genders. Multiple linear regression analysis displayed that SMI was negatively associated with ALT/AST, age, glycosylated hemoglobin (HbA1c), and high-density lipoprotein cholesterol (HDL) in male group. While in female group, SMI was positively associated with systolic blood pressure (SBP) and negatively associated with ALT/AST and age. Furthermore, ALT/AST was associated with age and BMI in both genders. Conclusion. ALT/AST was negatively associated with muscle mass in subjects with T2DM.

1. Introduction

Sarcopenia is a syndrome featured with the gradual and widespread decline in skeletal muscle mass and function [1]. Skeletal muscle plays a vital role in posture and movement. It is also essential for glucose uptake and energy metabolism. Skeletal muscle mass gradually decreases with aging, resulting in impaired muscle strength and mobility [2]. Sarcopenia has been demonstrated to be related to movement disorders, falls, fractures, disabilities, and metabolic disorders [3]. Type 2 diabetes mellitus (T2DM) is a very common metabolic disease, which is widely distributed all over the world. In 2021, the number of adults with diabetes worldwide reached 537 million. Earlier studies have shown that T2DM is associated with an increased risk for sarcopenia [4–6]. The risk of sarcopenia in subjects with T2DM was obviously elevated compared to subjects with normal blood glucose. According to a Korean study, the risk of sarcopenia in diabetic patients was two to four times compared with that in nondiabetic patients [7]. The incidence of sarcopenia was 28.4% in T2DM group and 18.7% in control group reported by Veronese et al. [8]. In view of the adverse impact of low muscle mass or sarcopenia on patients, timely identification and intervention is especially important. One potential approach is to look for probable risk factors or biomarkers for sarcopenia.

Serum alanine aminotransferase/aspartate aminotransferase (ALT/AST) ratio has been commonly used as an indicator for liver damage. Over the past few years, several researches showed that ALT/AST was associated with insulin resistance and metabolic disorders [9–12]. Zou et al. showed that ALT/AST was associated with new-onset nonalcoholic fatty liver disease [13]. Song et al. reported that ALT/AST levels in early pregnancy were correlated with the incidence of gestational diabetes [14]. A large study in western China showed that elevated serum AST/ALT was...
related to an increased prevalence of sarcopenia among people over 50 years of age [15].

So far, the studies about the association between ALT/AST and muscle mass in people with T2DM are limited. The present study was performed to analyze the correlation between ALT/AST and muscle mass in T2DM patients.

2. Materials and Methods

2.1. Subjects. This cross-sectional study was performed in the Endocrinology department of Qilu Hospital (Qingdao) from September 2017 to September 2019. A total of 1068 patients with T2DM were included in our study. All selected participants are ≥20 years old. Exclusion criteria include patients with pregnancy, severe liver, kidney or cardiovascular diseases, malignant tumor, and disability. This research was approved by the hospital ethics committee and carried out according to the Declaration of Helsinki.

2.2. The Criterion of Low Muscle Mass. Skeletal muscle index (SMI) was detected by the dual-energy X-ray absorptiometry (Hologic Discovery A). All subjects were operated by the same technician. SMI is equal to the skeletal muscle mass of limbs in kilograms divided by the square of height in meters (kg/m²). According to the consensus of Asian Working Group for Sarcopenia, the standard of low muscle mass is SMI less than 7.0 kg/m² for men or 5.4 kg/m² for women [16].

2.3. Measurements. The anthropometry, clinical, and laboratory analysis were carried out. Height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured in all subjects. Body mass index (BMI) was computed according to the formula of weight in kilograms divided by the square of height in meters (kg/m²). After fasting overnight, blood specimens were collected from all participants. ALT, AST, fasting blood glucose (FPG), glycosylated hemoglobin (HbA1c), triglyceride (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), and total cholesterol (TC) were detected in all subjects.

2.4. Statistical Analysis. Make use of Statistical Products and Service Solutions (SPSS for Windows, 22nd edition, Chicago, Illinois) for analysis. Continuous variables were tested for normality of distribution. Variables with approximately normal distributions were described by mean ± standard deviation (SD) and those with skewed distributions were described by median and 25 to 75th percentile. Categorical variables were described by number and proportion. The unpaired t-test or Mann–Whitney test was used for continuous variables and chi-square test was used for categorical variables to analyze the difference between patients with and without low muscle mass in T2DM. Logistic regression analysis was used to evaluate the relationship between ALT/AST and low muscle mass. Multiple regression analysis was used to explore the correlation between ALT/AST, SMI, and other metabolic variables. P < 0.05 was considered to be statistically significant.

3. Results

3.1. Population Characteristics. The characteristics of subjects were shown in Table 1. The current study included 1068 adult patients with T2DM. Among all patients, 115 male patients (20.3%) and 71 female patients (14.1%) presented low muscle mass.

Subjects with low muscle mass had higher age, duration of diabetes, ALT/AST, HbA1c, and HDL, but lower BMI, DBP, ALT, AST, and TG compared with those with normal muscle mass in men. Low muscle mass group presented increased age, ALT/AST, and decreased BMI, FPG, and TG compared with normal muscle mass group in women.

3.2. The Correlation between ALT/AST and Low Muscle Mass. As shown in Table 2, ALT/AST showed an increased risk for low muscle mass in male (OR = 3.804) and female (OR = 3.320) patients with T2DM. After adjusting for age, smoking, drinking, and duration of diabetes, ALT/AST was still positively related to low muscle mass (OR = 2.763 for male and OR = 3.116 for female). Moreover, after adjusting age, duration of diabetes, drinking, smoking, SBP, DBP, FPG, HbA1c, TC, TG, HDL, and LDL, ALT/AST was still positively correlated with low muscle mass (OR = 2.179 for men and OR = 2.594 for women).

3.3. The Correlation between SMI and Clinical Variables. The correlation between SMI and clinical variables was shown in Table 3. SMI was negatively associated with age, ALT/AST, HbA1c, and HDL in men with T2DM. While in women with T2DM, SMI was positively related to SBP, and negatively related to age and ALT/AST.

3.4. The Correlation between ALT/AST and Other Characteristics. Table 4 showed the correlation of ALT/AST and other clinical variables. In male subjects, ALT/AST was positively related to age, but negatively related to BMI and TG. While in female subjects, ALT/AST was positively related to age whereas negatively related to BMI.

4. Discussion

Our research is aimed at investigating the relationship between ALT/AST and muscle mass in subjects with T2DM. The present results showed that ALT/AST was associated with an increased risk for low muscle mass in T2DM. ALT/AST was negatively correlated with SMI. In addition, ALT/AST was positively correlated with age and negatively correlated with BMI.

Age, physical inactivity, malnutrition, insulin resistance, and chronic inflammations are considered as main underlying mechanisms of low muscle mass or sarcopenia [17]. The present study showed that the age of the low muscle mass group was increased compared with the normal muscle mass group, which was in line with our expectation. Meanwhile, compared with subjects with normal muscle mass, the low muscle mass group showed lower BMI and TG in both genders. In the traditional view, obesity was regarded as a risk factor for low muscle mass or sarcopenia. Du et al. reported that several metabolic variables including BMI were
### Table 1: The characteristics of patients with and without low muscle mass.

| Characteristics     | Normal muscle mass (n = 451) | Male (n = 566) | Female (n = 502) | P value | Male (n = 431) | Female (n = 71) | P value |
|---------------------|------------------------------|----------------|------------------|---------|----------------|-----------------|---------|
| Age (years)         | 54.78 ± 11.95                | 54.78 ± 12.60  | 54.78 ± 11.95    | <0.001  | 60.69 ± 13.37  | 65.45 ± 11.36  | 0.002   |
| Smoking             |                              | 0.640          |                  |         |                |                 | 0.999   |
| No (n)              | 211                          | 51             | 426              |         | 2             | 1               |         |
| Yes (n)             | 240                          | 64             | 5                |         |                |                 |         |
| Drinking            | 0.932                        |                |                  |         |                |                 | 0.999   |
| No (n)              | 253                          | 64             | 429              |         |                |                 |         |
| Yes (n)             | 198                          | 51             | 2                |         |                |                 |         |
| Duration (years)    | 7.0 (4.0,10.0)               | 8.0 (6.0,12.0)  | 8.0 (5.0,10.0)   | 0.006   | 7.0 (4.0,10.0)  | 8.0 (5.0,10.0)  | 0.932   |
| BMI (kg/m²)         | 27.53 ± 4.05                 | 23.68 ± 4.89   | 27.39 ± 4.59     | <0.001  | 23.68 ± 4.89   | 22.33 ± 2.90    | <0.001  |
| SMI (kg/m²)         | 8.16 ± 1.50                  | 6.45 ± 0.48    | 6.50 ± 0.86      | <0.001  | 6.45 ± 0.48    | 5.06 ± 0.33     | <0.001  |
| SBP (mmHg)          | 140.60 ± 18.54               | 137.31 ± 21.63 | 143.52 ± 20.83   | 0.137   | 137.31 ± 21.63 | 142.76 ± 21.95  | 0.779   |
| DBP (mmHg)          | 82.15 ± 12.47                | 78.54 ± 13.13  | 76.59 ± 12.63    | 0.006   | 78.54 ± 13.13  | 76.58 ± 11.22   | 0.994   |
| TG (mmol/L)         | 1.63 (1.05,2.46)             | 1.10 (0.85,1.83)| 1.47 (1.03,2.15) | <0.001  | 1.10 (0.85,1.83)| 1.32 (0.86,1.62)| 0.002   |
| TC (mmol/L)         | 4.49 ± 1.13                  | 4.45 ± 1.08    | 4.70 ± 1.35      | 0.724   | 4.45 ± 1.08    | 4.61 ± 1.16     | 0.624   |
| LDL (mmol/L)        | 2.96 ± 0.89                  | 2.95 ± 0.95    | 2.99 ± 0.93      | 0.958   | 2.95 ± 0.95    | 2.90 ± 0.99     | 0.445   |
| HDL (mmol/L)        | 1.14 ± 0.27                  | 1.23 ± 0.34    | 1.29 ± 0.37      | 0.011   | 1.23 ± 0.34    | 1.36 ± 0.35     | 0.136   |
| FPG (mmol/L)        | 8.11 ± 2.78                  | 7.96 ± 3.16    | 7.76 ± 2.89      | 0.604   | 7.96 ± 3.16    | 6.99 ± 2.74     | 0.037   |
| HbA1c (%)           | 8.39 ± 2.09                  | 8.90 ± 2.16    | 8.33 ± 2.02      | 0.028   | 8.90 ± 2.16    | 8.16 ± 2.15     | 0.528   |
| ALT (U/L)           | 19.0 (14.0,28.0)             | 15.0 (11.0,21.0)| 16.0 (12.0,22.0) | <0.001  | 15.0 (11.0,21.0)| 14.0 (11.0,20.0)| 0.066   |
| AST (U/L)           | 17.0 (14.0,22.0)             | 16.0 (13.0,20.0)| 16.0 (13.0,20.0) | 0.003   | 16.0 (13.0,20.0)| 18.0 (14.0,20.0)| 0.402   |
| ALT/AST             | 0.87 (0.68,1.07)             | 1.00 (0.82,1.26)| 1.00 (0.80,1.20) | <0.001  | 1.00 (0.82,1.26)| 1.09 (0.96,1.38)| <0.001  |

### Table 2: The correlation between ALT/AST and low muscle mass.

| Model | Male Model 2 | Male Model 3 | Female Model 2 | Female Model 3 |
|-------|--------------|--------------|----------------|----------------|
| OR (95% CI) | 3.804 (2.105-6.875) | 2.763 (1.455-5.250) | 2.179 (1.077-4.407) | 1.146 (0.510-2.594) |
| P value | <0.001 | 0.002 | 0.030 | 0.001 |

Model 1 was crude model; model 2 was adjusted for age, duration of diabetes, drinking, smoking; model 3 was adjusted for age, duration of diabetes, drinking, smoking, SBP, DBP, FPG, HbA1c, TC, TG, HDL, and LDL.

### Table 3: The correlation between SMI and clinical characteristics.

| Characteristics | Male β (95% CI) | P value | Female β (95% CI) | P value |
|-----------------|-----------------|---------|-------------------|---------|
| Age (years)     | -0.021 (-0.029, -0.013) | <0.001 | -0.024 (-0.033, -0.015) | <0.001 |
| Duration (years)| -0.002 (-0.017, 0.013) | 0.784 | 0.005 (-0.009, 0.019) | 0.475 |
| SBP (mmHg)      | 0.004 (-0.001, 0.010) | 0.094 | 0.006 (0.000, 0.011) | 0.031 |
| DBP (mmHg)      | 0.005 (-0.003, 0.013) | 0.197 | -0.001 (-0.010, 0.007) | 0.754 |
| ALT/AST         | -0.270 (-0.534, -0.006) | 0.045 | -0.396 (-0.467, -0.146) | 0.002 |
| FPG (mmol/L)    | 0.024 (-0.010, 0.058) | 0.164 | -0.010 (-0.046, 0.026) | 0.597 |
| HbA1c (%)       | -0.067 (-0.111, -0.023) | 0.003 | -0.016 (-0.065, 0.033) | 0.520 |
| TG (mmol/L)     | 0.016 (-0.048, 0.080) | 0.621 | 0.009 (-0.071, 0.088) | 0.833 |
| TC (mmol/L)     | 0.035 (-0.255, 0.324) | 0.814 | 0.028 (-0.175, 0.321) | 0.787 |
| LDL (mmol/L)    | -0.015 (-0.307, 0.278) | 0.921 | -0.027 (-0.246, 0.192) | 0.807 |
| HDL (mmol/L)    | -0.533 (-0.982, -0.084) | 0.020 | -0.266 (-0.662, 0.131) | 0.189 |
ALT and AST are important serum biomarkers of human body which could be detected quickly, cheaply, and repeatedly worldwide. ALT mainly exists in heart, liver, skeletal muscle, kidney, erythrocyte, and brain. One study from Italy indicated that lower levels of ALT and AST were obviously lower than subjects without sarcopenia [24, 25]. We got similar results in our study. The precise mechanism underlying this association is unclear. Decreased TG levels perhaps implied a status of poor health accompanied with low muscle mass or sarcopenia [26].

In short, ALT/AST is negatively associated with muscle mass among patients with T2DM.

Data Availability
Data are available upon reasonable request.

Ethical Approval
This study was approved by the Ethics Committee of Qilu Hospital of Shandong University (Qingdao).

### Table 4: The correlation between ALT/AST and clinical characteristics.

|                     | Male (β (95% CI)) | Male P value | Female (β (95% CI)) | Female P value |
|---------------------|-------------------|--------------|---------------------|---------------|
| Age (years)         | 0.008 (-0.005, 0.010) | <0.001       | 0.003 (-0.000, 0.007) | 0.031         |
| Duration (years)    | 0.002 (-0.003, 0.007) | 0.469        | 0.002 (-0.003, 0.007) | 0.483         |
| BMI (kg/m²)         | -0.007 (-0.014, -0.001) | 0.028        | -0.010 (-0.016, -0.003) | 0.002         |
| SBP (mmHg)          | 0.000 (-0.001, 0.002) | 0.675        | -0.001 (-0.003, 0.001) | 0.292         |
| DBP (mmHg)          | 0.000 (-0.003, 0.002) | 0.876        | -0.001 (-0.004, 0.002) | 0.487         |
| FPG (mmol/L)        | -0.005 (-0.016, 0.006) | 0.382        | -0.002 (-0.015, 0.011) | 0.725         |
| HbA1c (%)           | 0.004 (-0.010, 0.019) | 0.566        | -0.008 (-0.025, 0.010) | 0.403         |
| TG (mmol/L)         | -0.027 (-0.048, -0.006) | 0.013        | -0.002 (-0.030, 0.027) | 0.916         |
| TC (mmol/L)         | 0.045 (-0.049, 0.140) | 0.348        | -0.072 (-0.145, 0.002) | 0.055         |
| LDL (mmol/L)        | -0.044 (-0.139, 0.052) | 0.372        | 0.040 (-0.039, 0.119) | 0.322         |
| HDL (mmol/L)        | 0.088 (-0.059, 0.235) | 0.243        | 0.132 (-0.011, 0.275) | 0.070         |
Mediators of Inflammation

Conflicts of Interest
All authors declare that there are no conflicts of interest in the publication of this article.

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