Diagnostic performance of anthropometric measurements in detecting elevated serum alanine aminotransferase: a school-based screening of 7271 Shenzhen adolescents

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Abstract

Background Screening for elevated serum alanine aminotransferase (ALT) can help identifying individuals at the risks of chronic and metabolic diseases, but blood collection is invasive and cannot be widely used for investigations. Considered as simple and inexpensive screening indices, anthropometric measurements can be measured in a large crowd and may be important surrogate markers for ALT levels. Among adolescents, few studies focused on the diagnostic performance of anthropometric parameters such as body mass index (BMI) and BMI z-score as predictive factors for discerning an elevated ALT activity. We sought to fill this knowledge gap among Shenzhen adolescents.

Methods A school-based study was performed from 9 high schools in Shenzhen during February 2017 and June 2018. Receiver operating characteristic curve was used to examine the diagnostic performance of each measurement.

Results Altogether 7271 adolescents aged 9–17 years were involved. The proportion of elevated ALT greatly increased with increasing classification of BMI-z. By the sex-specific cut-offs for elevated ALT (30 U/L boys; 19 U/L girls), BMI showed the highest area under the curve of 0.789 (95% CI 0.765-0.812) and followed by weight (0.779 [0.755-0.802]), BMI-z (0.747 [0.722-0.772]), height (0.622 [0.597-0.647]), and age (0.608 [0.584-0.632]), while height-z was not capable. With the cut-off of 67.8 kg for weight and 22.6 kg/m2 for BMI, the accuracy was 87.1% for weight and 82.9% for BMI.

Conclusions The presence of elevated ALT was more common in overweight or obese adolescents. BMI and weight had the superiority of detecting elevated ALT, followed by BMI-z, height, and age.

1. Background

The liver enzyme of serum alanine aminotransferase (ALT) is commonly used to assess potential liver dysfunction and clinically as a screening tool for the detection of probable nonalcoholic fatty liver disease (NAFLD)[1–4]. An elevation of serum ALT concentration is a key feature of NAFLD, and liver biopsy is the gold standard to confirm the diagnosis of NAFLD, characterized by pathological changes to liver structure and function such as fat accumulation, hepatocyte dysfunction, and fibrosis[4]. The elevation of ALT has also been recorded by published evidence to be strongly linked to, or to predict, the developing of type 2 diabetes mellitus, insulin resistance, and cardiovascular diseases (e.g. atherogenesis and coronary heart disease)[2, 3, 5–11].

Screening for the concentration of serum ALT and verifying an elevated ALT activity could assist in determining individuals at risk for the above chronic conditions and reducing the possibility of future liver diseases[12, 13]. However, the measurement of ALT levels requires blood collection, which is invasive and could be impractical in large-scale investigations. In contrast, measurements of anthropometric indices such as height, weight, and BMI are relatively simple, cheap, quick, and non-invasive, and therefore can be applied to a great number of people and easily conducted during common health examinations, especially for non-adults[12, 14, 15]. If these anthropometric indices showed a close correlation with serum ALT levels or had sufficient ability to detect an ALT elevation, they could be a useful surrogate for ALT levels.

Two multi-center, population-based epidemiological researches conducted in the mainland of China have consistently demonstrated that the higher values of body mass index (BMI), hip circumference, waist circumference, waist-to-hip ratio (WHpR), and waist-to-height ratio (WHtR) were able to predict an elevated ALT activity among adolescents and adults[14, 16]. Recently, the nontraditional index of BMI z-score has also been put forward as another important anthropometric indicator of ALT elevation[4, 17]. However, whether the potential of the z-score of height, a novel body index, for predicting elevated ALT was comparable or superior to the abovementioned parameters was still unclear up to now. In addition, although most previous studies on the relations of anthropometric measurements with ALT elevation were conducted among adults[14, 18–20], few investigations focused on the performance predication of those predictors for diagnosing elevated ALT among adolescents[12, 17, 21].

Considering such a negotiable knowledge gap, we aimed to examine the diagnostic performance of individual characteristics (i.e. age and gender) and several anthropometric parameters (i.e. height, weight, BMI, BMI-z, and height-z) as predictive factors of an elevated ALT activity in Shenzhen adolescents, and to determine the optimal cut-off points for these parameters that would identify an adolescent with an elevation of serum ALT level. Assessing anthropometric measurements is crucial for early detection and prevention of an activity of elevated ALT or the subsequent development of NAFLD among children and adolescents.

2. Methods

2.1 Study sitting and population

Situated approximately 1° south of the Tropic of Cancer, within the Pearl River Delta region of Guangdong province, and bordered Hong Kong, Shenzhen is one of the 4 first-tier cities in mainland China, the first Special Economic Zone of China (established in 1980), and a major financial centre and the worldly largest manufacturing base[22, 23]. The population and economy have grown rapidly, with a total gross domestic product (GDP) of 255 billion USD and approximate 25,000 USD per capita in 2015[22, 24]. The municipality covers an area of 1997.3 km^2 and the population is around 11.37 million; Bao'an District is the first largest area among 10 district-level jurisdictions of Shenzhen, with a total population of 2.86 million accounting for over a quarter of Shenzhen's total population at the end of 2016[22].

2.2 Data collections and measures

Involved freshmen from 9 junior and senior high schools of Bao'an District, a cross-sectional study organized with the assistance of the Bao'an Government of Shenzhen was officially carried out[25]. Data collection activities were completed during February 2017 and June 2018. This school-based study was approved by the Institutional Review Board of Baoan Central Hospital of Shenzhen, and written informed consents for each student and their parents were obtained.

Individual characteristic data such as gender and date of birth were taken from each participant, and anthropometric parameters of weight and standing-height were respectively measured to the nearest 0.1 kg and 0.5 cm by trained physicians using a standard weighing machine. At each high school, blood samples were drawn in the morning after participants fasting for at least 10 hours by trained nurses. ALT was measured with the fully automatic biochemical analyzer (Model AU5821, Tokyo, Japan). We restricted our analysis to adolescents but not adults, and a student aged between 9.0 and 17.9 years was regarded as an adolescent. Finally, a total of 7271 adolescents who had complete anthropometric and clinical data participated in the current investigation.

For each participant, age with 1 decimal was transformed based on the date of birth and BMI (kg/m^2) was calculated in weight divided by the square of height to set up a database. Based on an international norm from the World Health Organization (WHO) growth reference (i.e. the 2007 WHO reference) for school-aged children and adolescents aged 5 – 19 years, anthropometric indicators of z-score values of height-for-age (height-z) and BMI-for-age (BMI-z) for both boys and girls were calculated by the R macro, provided on the WHO website (https://www.who.int/growthref/en/)[26, 27]. Moreover, according to the z-score of BMI-for-age, we defined BMI-z > 2SD as obesity, 1SD < BMI-z ≤ 2SD as overweight, -2SD ≤ BMI-z ≤ 1SD as normal-weight, and BMI-z < -2SD as underweight; where SD was standard deviation of the BMI z-scores.

2.3 Definition of elevated serum ALT levels

The thresholds of elevated ALT needed to be determined consistent with previously reported levels, as there was no consensus on what level constituted an elevated serum ALT concentration for adolescents. For the most commonly use of definitions among adolescents, an activity of elevated serum ALT was defined as > 30 U/L for boys and > 19 U/L for girls (diagnostic criterion I)[2, 3, 8, 28]. Main analysis was undertaken using these sex-specific cut-offs, and a secondary analysis for the sake of comparison was also reported, defining with higher thresholds (> 40 U/L for both boys and girls; diagnostic criterion II) that have been proposed in previous observational literatures[7, 13, 29] to explore whether higher thresholds led to the same or different results.

2.4 Statistical analyses

The normal distribution of each continuous anthropometric measurement was determined by the one-sample Kolmogorov-Smirnov test. The non-normally distributed measurements were described as median with inter-quartile range (25th percentile – 75th percentile; IQR); significance for differences between elevated and normal serum ALT was evaluated by the Mann–Whitney U test. Stratified by the classification of BMI z-score, the crude prevalence along with 95% confidence interval (CI) of elevated ALT was quantitatively estimated, and the trend of the proportion of elevated ALT based on BMI-z was carried out with a chi-square test. The Spearman's rank correlation analyses among the skewed parameters were also performed.

Extensively used in clinical epidemiology for evaluation of diagnostic ability of biomarkers (e.g. serum markers) or a diagnostic test with dichotomous outcome (i.e. positive or negative result) in classification of the diseased from healthy population, the receiver operating characteristic (ROC) curve, defined as a plot of the sensitivity of a test as y-axis versus 1-specificity as x-axis, is an effective method and graphical technique to describe the accuracy of a prediction model or diagnostic test[30, 31]. Sensitivity and specificity, the basic measures of accuracy of a diagnostic test, vary with different cut-off thresholds, and sensitivity is inversely related to specificity[15, 31]. Positive predictive value (PPV) is defined as the probability of disease for positive test results, and negative predictive value (NPV) is defined as the probability of being healthy for negative test results. However, influenced by the prior prevalence of disease in a population, PPV rises while NPV decreases with an increased prevalence of disease[30].

In the current study, we utilized the ROC curve analysis to find out the optimal cut-off points and to examine the diagnostic performance of each anthropometric measurement as indicators of ALT elevation. An anthropometric parameter value with the highest Youden index was chosen as the optimal cut-off point[15]. The observed agreement and the area under the curve (AUC) were also determined. Statistical analyses were processed in R 3.5.1 (http://www.R-project.org) and SPSS for Windows 16.0, with two-tailed P-value < 0.05 considered statistically significant.

3. Results

3.1 Characteristics of participants

Altogether 7,271 adolescents aged 9–17 years were recruited in the present study for the operative statistical analysis, involving 4,014 (55.2%) boys and 3,257 (44.8%) girls. Characteristics of study subjects with and without elevated serum ALT activity are listed in Table 1. The indices of age, weight, height, BMI, height-z, and BMI-*z* were non-normal distribution (all P<0.001). Overall, the median (IQR) level was 14.7 (12.4–15.7) years for age, 53.0 (46.7–61.0) kg for weight, 1.65 (1.59–1.72) meter for height, 19.31 (17.63–21.66) kg/m^2 for BMI, 0.59 (-0.18 to 1.41) for height-z, and -0.01 (-0.77 to 0.83) for BMI-z. Each anthropometric index but not height-*z* was significantly greater among adolescents with an elevated ALT activity than those with a normal ALT level, regardless of the use of definitions (most P<0.001).

3.2 Crude prevalence of elevated ALT by the BMI-*z* classification

On the basis of ALT activity thresholds of diagnostic criterion I, an elevated ALT activity was present in 2.48% (6/242) of underweight, 3.79% (208/5493) of normal-weight, 12.58% (137/1089) of overweight, and 36.91% (165/447) of obese adolescents; based on the criterion II, the proportion of elevated ALT was 0.83% (2/242), 0.89% (49/5493), 4.96% (54/1089), and 20.58% (92/447) for the corresponding subgroups (Table S1). Regardless of the use of diagnostic criteria, the abnormality prevalence rate of ALT greatly increased with increasing classification of BMI z-score and peaked in the obesity group for all participants, boys, and girls (all P_{trend}<0.001). Overweight or obese adolescents were much more likely to obtain increased ALT concentrations than normal-weight or underweight adolescents.

3.3 Univariate ROC curve analyses

Figure S1 illustrates the diagnostic performance of anthropometric indices for identifying elevated serum ALT by ROC curves, and Table 2 presents the information about the AUCs of the curves. The anthropometric parameter of BMI showed the highest AUC (95% CI) for elevated ALT (0.789 [0.765–0.812] by criterion I; 0.850 [0.818–0.882] by criterion II), and followed by weight (0.779 [0.755–0.802]; 0.850 [0.817–0.882]) and the z-score of BMI (0.747 [0.722–0.772]; 0.822 [0.787–0.858]). As compared to the above 3 obesity indices, age and height had a poorer diagnostic efficiency in detecting abnormal ALT. The discriminatory power of height z-score in the prediction of elevated ALT was null (both P > 0.1), and gender also had no ability to evaluate elevated ALT by the same upper limit of normal (ULN) between boys and girls for ALT of the diagnostic criterion I (P = 0.435). In the stratification analyses by gender, similar outcomes were also provided in Table S2.

Table 3 elucidates the optimal cut-off points and the probability of meaningful and significant parameters in diagnosing abnormal ALT, based on the ROC analyses. The suggested cut-off points of were 67.8 & 68.9 kg for weight and 22.6 & 22.3 kg/m^2 for BMI, separately by the criteria I and II. Based on the cut-offs, the parameter of weight achieved the highest ability to correctly classify subjects as elevated ALT, with an accuracy of 87.1% by criterion I and 88.9% by criterion II. However, BMI took control of a larger Youden index (46.1%) than other parameters with criterion I. BMI and weight had an approximate diagnostic performance in diagnosing elevated ALT among Shenzhen adolescents of ages 9–17 years.

3.4 Correlation analyses and combined anthropometric measurements for detecting elevated ALT in multivariate analysis

Table S3 displays the Spearman's correlation coefficients between anthropometric indices and ALT levels. BMI had a very high positive correlation with BMI *z*-score (r = 0.891) and weight (r = 0.829), suggesting a multicollinearity among each obesity parameter. Weight was also quite strongly and positively correlated with height (r = 0.673) and BMI-*z* (r = 0.657).

Table 4 shows the capability of combined anthropometric indices to diagnose the presence of elevated ALT in multivariate models. The combined indices of "age+gender+height+weight" showed the strongest capability to indicate the levels of ALT, with an AUC (95% CI) of 0.816 (0.795–0.836) for criterion I and 0.858 (0.826–0.891) for criterion II. In particular, a very slight increase of 0.037 (0.816 *vs* 0.779) for criterion I and 0.008 (0.858 *vs* 0.850) for criterion II in accuracy was demonstrated, as compared with the univariable weight model. The multivariate combined BMI model also fitted well with an analogous good accuracy (AUC = 0.813 for criterion I and 0.858 for II). Compared to the univariable models of obesity indices (i.e. weight, BMI, or BMI-*z*), the combined models did not markedly improve the prediction of elevated ALT for adolescents.

4. Discussion

Screening for increased ALT levels is conducive to identifying individuals at the risks of some chronic and metabolic diseases, but blood collection of serum ALT is invasive and cannot be widely used for a massive epidemiological survey among children and adolescents because of subject burden and cost. Considered as a simple, easily obtained, inexpensive, and convenient screening measure, anthropometry can be monitored in a large crowd and might be an important surrogate marker for ALT concentrations, if the discriminative accuracy of the anthropometric parameters is very high for diagnosing abnormal ALT. Primary focused on the diagnostic performance, anthropometric data for Shenzhen adolescents aged 9–17 years were used to detect elevated serum ALT in our present survey, and we confirmed the belief that anthropometric measurements were important predictors of elevated ALT among Shenzhen adolescents. An elevated ALT activity was more common in overweight or obese adolescents than those with a normal or relatively low BMI z-score. BMI and weight showed an approximate diagnostic performance for predicting the presence of elevated ALT, followed by the z-score of BMI, height, and age.

Consistent findings that the proportion of elevated ALT greatly increased with increasing degree of obesity (e.g. the percentile or z-score of BMI), and higher proportion among overweight or obese adolescents than normal-weight ones were shown in previous studies and our research, regardless of the use of diagnostic criteria for an elevated ALT activity[7, 13, 18, 32]. Based on the thresholds of ALT activity (40 U/L for boys and girls), nearly 6.6% of the Mexican youths (9.8% of boys and 3.8% of girls) had elevated ALT levels by using the baseline data from 1262 participants of 8–19 years in the Mexican Health Worker Cohort Study (MHWCS); elevated ALT concentration was also observed in 2.7% of normal-BMI, 14.2% of overweight, and 28.9% of the obese children and adolescents[13]. According to the same thresholds (i.e. criterion II), the percentage of elevated ALT among Shenzhen adolescents of 9 – 17 years was 0.89% for normal-weight, 4.96% for overweight, and 20.58% for obese participants. Mexican youths had a slightly higher crude proportion of elevated ALT than Shenzhen adolescents, without adjusting for age and gender based on the distribution of the world population. Likewise, using a sample of 1591 youths from the 2008 – 2009 Korea National Health and Nutrition Examination Survey (KNHANES), another study conducted by Seung Park and cooperators also found a close prevalence of elevated ALT (> 33 U/L for boys and > 25 U/L for girls) among Korean youths of 12 – 18 years — 5.9% (95%CI 4.9%–7.2%) for the overall study population, 15.7% (11.3%–21.5%) for overweight adolescents (85th ≤ BM < 95th percentile), and 34.9% (25.6%–45.4%) for subjects with a BMI ≥ 95th percentile[32]. The odds ratios (ORs) for elevated ALT also sharply increased with the greater levels of obesity, with an OR (95% CI) of 7.23 (4.33–12.10) for overweight and 23.62 (12.98–42.98) for obese adolescents, comparing to normal-weight adolescents (BMI < 85th percentile) in an unadjusted analysis[32].

Screening for school-adolescents, it is clearly more convenient to collect anthropometric measures than biochemical measures, but the abilities of several individual characteristics and anthropometric indices to correctly predict elevated serum ALT in Shenzhen children are questionable and need to be assessed. Determined by the univariate ROC curves, our results showed that the anthropometric parameter of BMI had the best superiority of discerning the presence of elevated ALT (AUC = 0.789 for criterion I and 0.850 for II), weight and BMI-z displayed the second and third highest detection accuracy (AUC range from 0.747 to 0.850), and followed by height, age, and gender (from 0.490 to 0.695). As such, we believed that the single variable of height, age, or gender was not reliable surrogate measure of an activity of elevated ALT among Shenzhen adolescents of 9 – 17 years. Further, age, gender, and height were considered as covariates together with each predictor of obesity indices (i.e. weight, BMI, or BMI-z) to predict elevated ALT in the subsequent multivariate model analyses, although the diagnostic accuracy of the combined models did not markedly improve. On the other hand, the current study firstly, as far as we known, investigated the association of height z-score with serum ALT in adolescents and estimated the usefulness of height-z as a predictive index of elevated ALT. Nevertheless, the present result showed a null discriminative power of height z-score for predicting an elevated ALT serum activity.

For BMI, several studies had pointed out that BMI was able to determine the presence of elevated ALT among adults, although the accuracy was not very high in absolute term — the AUC (95% CI) was 0.658 (0.633–0.683) for men and 0.651 (0.616–0.685) for women in the rural areas of China[14] and 0.64 (0.60–0.68) for Italian general population[19]. Focused on adolescents, a representative study with a sample of 454 youths of 11–17 years from 2 northern Italian cities also found a similar diagnostic performance of dichotomized BMI for elevated ALT, with an AUC of 0.64 (0.50–0.77)[17]. Compared to the dichotomized BMI model, the Italian adolescents study also indicated a more accurate univariable model of BMI-z (AUC = 0.71 [0.59–0.81]), and the predictive ability was increased substantially by considering gender together with BMI-z (AUC = 0.80 [0.71–0.89])[17]. In addition, based on the data from the National Health and Nutrition Examination Survey (NHANES) during 1999 to 2014, an United States study consisted of 5019 adolescents of 12–19 years suggested a significant correlation between BMI z-score and serum ALT levels ($r = 0.29$, $P < 0.0001$)[4]. Significant positive associations of ALT with obesity indices (e.g. BMI, body fat percentage, truncal fat mass, total fat mass, waist circumference, and WHtR) were further confirmed in Korean male adolescents[21].

Several potential limitations of our research should be recognized. First, participants were only from a single city of China, and it might be therefore difficult to generalize these findings to other adolescent populations. Second, our cross-sectional study omitted to measure some important individual anthropometric parameters — hip circumference, waist circumference, neck circumference, and the subsequent indicators of WHpR, WHtR, and A Body Shape Index (ABSI), which might achieve a better diagnostic performance and to be more sensitive predictive indicates for diagnosing an elevated ALT activity among the indigenous adolescents. For predicting the ALT levels, WHtR and to some extent BMI were congruously shown to be the best body indices in some Asians, as compares to waist circumference, hip circumference, WHpR, and the useless index of ABSI[12, 14, 16]. Another limitation was our inability to consider the potential confounders of ethyl alcohol intake and hepatitis B virus (HBV) and C virus (HCV) infections, which were well-known risk factors for increases in ALT[4, 12, 17, 19]. However, alcohol consumption and HBV and HCV infections were less prevalent in school-adolescents of China[33, 34], and we hypothesized that the obesity indices could be even more important predictors of elevated ALT among the adolescents of Shenzhen, and the above potential confounders were not likely to have a substantial impact on current results.

5. Conclusions

An elevated ALT activity was more frequent in overweight or obese adolescents than normal-weight subjects. Anthropometric obesity indices of BMI, weight, and BMI-z achieved a very high diagnostic performance for predicting elevated ALT among Shenzhen adolescents and followed by height and age, while height-z was not capable.

Declarations

Ethics approval and consent to participate: This school-based study was approved by the Institutional Review Board of Baoan Central Hospital of Shenzhen, and written informed consents for each student and their parents were obtained.

Consent for publication: All of the authors have read and approved the paper.

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Abbreviations: alanine aminotransferase, ALT; area under the curve, AUC; body mass index, BMI; confidence interval, CI; hepatitis B virus, HBV; hepatitis C virus, HCV; negative predictive value, NPV; nonalcoholic fatty liver disease, NAFLD; positive predictive value, PPV; receiver operating characteristic, ROC; standard deviation, SD; waist-to-hip ratio, WHpR; waist-to-height ratio, WHtR.

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: Y.L.O. and Z.D. conceived and designed the experiments. Y.L.O., Y.R.L., C.N.J., and J.Z. collected and cleaned the data. Y.L.O. drafted the manuscript. Z.D. guided statistical analysis, revised the manuscript, and interpreted the results. All authors read and approved the final manuscript.

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Tables

Table 1. Baseline descriptive statistics for anthropometric measurements stratified by gender among Shenzhen adolescents (aged 9−17 years), separately based on the diagnostic criteria I and II for elevated ALT.

Group	Total adolescents	Criterion I (> 30 U/L for boys and > 19 U/L for girls)			Criterion II (> 40 U/L for boys and girls)		
		Normal ALT	Elevated ALT	*P*-value*	Normal ALT	Elevated ALT	*P* *
Overall (n = 7271)							
Age, years	14.7 (12.4−15.7)	14.7 (12.3−15.7)	15.3 (13.8−16.1)	<0.001	14.7 (12.3−15.7)	15.3 (14.3−16.1)	<0.001
Height, m	1.65 (1.59−1.72)	1.64 (1.59−1.71)	1.69 (1.63−1.75)	<0.001	1.65 (1.59−1.72)	1.73 (1.65−1.78)	<0.001
Weight, kg	53.0 (46.7−61.0)	52.2 (46.2−59.8)	70.0 (56.1−83.6)	<0.001	52.6 (46.5−60.2)	77.7 (63.1−90.1)	<0.001
BMI, kg/m^2	19.31 (17.63−21.66)	19.15 (17.55−21.23)	24.51 (20.38−27.95)	<0.001	19.25 (17.59−21.45)	26.39 (22.40−30.22)	<0.001
Height-*z*	0.59 (-0.18−1.41)	0.58 (-0.18−1.41)	0.71 (-0.12−1.47)	0.104	0.59 (-0.18−1.41)	0.65 (-0.13−1.48)	0.526
BMI-*z*	-0.01 (-0.77−0.83)	-0.06 (-0.81−0.74)	1.40 (0.16−2.27)	<0.001	-0.04 (-0.79−0.79)	1.89 (0.85−2.54)	<0.001
Boys (n = 4014)							
Age, years	14.7 (12.4−15.7)	14.7 (12.3−15.7)	15.4 (14.4−16.1)	<0.001	14.7 (12.4−15.7)	15.4 (14.6−16.2)	<0.001
Height, m	1.69 (1.61−1.75)	1.69 (1.61−1.75)	1.74 (1.68−1.78)	<0.001	1.69 (1.61−1.75)	1.74 (1.68−1.79)	<0.001
Weight, kg	55.4 (48.1−64.7)	54.7 (47.9−63.0)	79.0 (66.9−88.6)	<0.001	55.0 (48.0−63.7)	81.4 (69.5−92.4)	<0.001
BMI, kg/m^2	19.37 (17.64−22.04)	19.16 (17.55−21.47)	26.42 (22.98−30.06)	<0.001	19.26 (17.59−21.70)	27.20 (23.92−30.61)	<0.001
Height-*z*	0.65 (-0.16−1.55)	0.65 (-0.16−1.55)	0.66 (-0.16−1.42)	0.086	0.65 (-0.16−1.55)	0.66 (-0.12−1.50)	0.857
BMI-*z*	0.12 (-0.74−1.06)	0.04 (-0.78−0.90)	1.98 (0.99−2.55)	<0.001	0.07 (-0.77−0.95)	2.14 (1.27−2.67)	<0.001
Girls (n = 3257)							
Age, years	14.7 (12.3−15.7)	14.7 (12.3−15.7)	15.0 (13.3−16.0)	<0.001	14.7 (12.3−15.7)	14.6 (13.3−15.4)	0.557
Height, m	1.62 (1.57−1.67)	1.61 (1.57−1.66)	1.64 (1.58−1.71)	<0.001	1.62 (1.57−1.66)	1.62 (1.58−1.69)	0.270
Weight, kg	50.6 (45.2−57.0)	50.1 (45.0−56.0)	58.5 (50.6−71.1)	<0.001	50.5 (45.2−56.8)	59.0 (48.7−75.6)	<0.001
BMI, kg/m^2	19.26 (17.60−21.26)	19.13 (17.54−20.98)	21.60 (19.05−25.59)	<0.001	19.23 (17.60−21.19)	22.01 (18.86−27.12)	<0.001
Height-*z*	0.51 (-0.20−1.32)	0.50 (-0.20−1.31)	0.82 (-0.09−1.52)	0.006	0.51 (-0.20−1.32)	0.40 (-0.20−1.37)	0.857
BMI-*z*	-0.13 (-0.82−0.61)	-0.16 (-0.84−0.54)	0.64 (-0.39−1.60)	<0.001	-0.14 (-0.82−0.60)	0.73 (-0.53−1.80)	<0.001

Data are expressed as median (interquartile range [IQR]) for the anthropometric measurements with skewed distributions.

* Comparing elevated ALT to normal ALT by the Mann–Whitney U test.

Table 2. The AUC (95% CI) of the ROC curve to judge the discrimination ability of various anthropometric measurements for detecting elevated ALT (separately by the criteria I and II) in univariate analyses.

Variable	Criterion I (> 30 U/L for boys and > 19 U/L for girls)				Criterion II (> 40 U/L for boys and girls)			
	AUC	95% CI	SE	*P**	AUC	95% CI	SE	*P**
Age	0.608	0.584–0.632	0.012	<0.001	0.613	0.577–0.649	0.018	<0.001
Gender	0.490	0.464–0.516	0.013	0.435	0.628	0.593–0.664	0.018	<0.001
Height	0.622	0.597–0.647	0.013	<0.001	0.695	0.658–0.732	0.019	<0.001
Weight	**0.779**	**0.755–0.802**	**0.012**	**<0.001**	**0.850**	**0.817–0.882**	**0.016**	**<0.001**
BMI	**0.789**	**0.765–0.812**	**0.012**	**<0.001**	**0.850**	**0.818–0.882**	**0.016**	**<0.001**
Height-*z*	0.522	0.496–0.547	0.013	0.102	0.514	0.473–0.554	0.021	0.517
BMI-*z*	**0.747**	**0.722–0.772**	**0.013**	**<0.001**	**0.822**	**0.787–0.858**	**0.018**	**<0.001**

AUC, area under curve; ALT, alanine aminotransferase; CI, confidence interval; ROC, receiver operating characteristic; SE, standard error.

* Null hypothesis: true area = 0.5.

Table 3. The optimal cut-off points and the probability of significant anthropometric parameters for identifying elevated ALT, separately based on the diagnostic criteria I and II.

Parameter	Criterion I (> 30 U/L for boys and > 19 U/L for girls)							Criterion II (> 40 U/L for boys and girls)						
	Cut-off	Accuracy	Sen	Spe	Youden index	PPV	NPV	Cut-off	Accuracy	Sen	Spe	Youden index	PPV	NPV
Age	13.7 years	44.0	76.2#	41.5	17.7	9.0	95.8	13.7 years	41.8	78.7#	40.8	19.5	3.6	98.6
Height	164.0 cm	49.0	72.3	47.3	19.5	9.5	95.7	169.5 cm	67.3	61.9	67.5	29.4	5.0	98.5
Weight	67.8 kg	87.1#	55.0	89.5#	44.6	28.6#	96.3	68.9 kg	88.9#	69.5	89.5#	59.0#	15.6#	99.1
BMI	22.6 kg/m^2	82.9	61.6	84.5	46.1#	23.3	96.6#	22.3 kg/m^2	80.8	77.2	80.9	58.0	10.1	99.2#
BMI-*z*	0.95	79.1	60.1	80.5	40.6	19.1	96.4	1.25	84.3	70.1	84.7	54.7	11.3	99.0

Sen, sensitivity; Spe, specificity; PPV, positive predictive value; NPV, negative predictive value.

The optimal cut-off points were based on the maximum Youden index for each parameter; the probability of parameters for identifying elevated ALT is expressed as %.

The best performance for each conventional diagnostic test index.

Table 4. The AUC (95% CI) of the ROC curve to express the diagnostic performance of combined anthropometric measurements for detecting elevated ALT (separately by the diagnostic criteria I and II) in multivariate analyses.

Combined measurements	Criterion I (> 30 U/L for boys and > 19 U/L for girls)				Criterion II (> 40 U/L for boys and girls)			
	AUC	95% CI	SE	P*	AUC	95% CI	SE	P*
Age+gender+height	0.643	0.619–0.668	0.012	<0.001	0.716	0.679–0.753	0.019	<0.001
Age+gender+height+weight	0.816	0.795–0.836	0.011	<0.001	0.858	0.826–0.891	0.016	<0.001
Age+gender+height+BMI	0.813	0.792–0.834	0.011	<0.001	0.858	0.826–0.890	0.016	<0.001
Age+gender+height+BMI-*z*	0.807	0.785–0.829	0.011	<0.001	0.856	0.823–0.889	0.017	<0.001

AUC, area under curve; ALT, alanine aminotransferase; CI, confidence interval; ROC, receiver operating characteristic; SE, standard error.

* Null hypothesis: true area = 0.5.

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