A novel indicator, relative children’s lipid accumulation product (RCLAP) for metabolic syndrome

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Research

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Abstract

Background

The children's lipid accumulation product (CLAP) was associated with MS in Chinese children and adolescents. The study was to develop a more effective indicator, relative children's lipid accumulation product RCLAP associated with MS reflect the density of lipid accumulation among Chinese children and adolescents.

Methods

A stratified cluster sampling method was used to recruit 683 students aged 8-15 years in this study. The presence of MS was defined according to the NCEP-ATP III criteria. The t-test, chi-square test, logistic regression models were used to analyze the associations of SBMI, SWHtR, SlnCLAP, SRCLAP-H, SRCLAP-SH, RCLAP-W with MS. Receiver Operating Characteristic (ROC) curves was used to evaluate the predictive efficiency of above indexes for predicting MS.

Results

The overall prevalence of MS was 4.8% (boys 6.6%, girls 2.8%). In girls, after adjusting for sedentary activity time, WHtR, BMI, CLAP, RCLAP-H, RCLAP-SH and RCLAP-W significantly increased risk of MS (OR(95%CI): 15.79 (3.15-79.21), 3.73 (0.87-15.95), Null, 96.13 (11.11-831.97), 96.13 (11.11-831.97), 18.28 (4.24-78.87), respectively). In boys, after adjusting for ages and moderate-to-vigorous physical activity time, WHtR, BMI, CLAP, RCLAP-H, RCLAP-SH and SRCLAP-W significantly increased risk of MS (OR(95%CI): 37.43(11.67-120.10), 68.33(18.51-252.20), 105.86(21.99-509.68), 171.75(33.60-878.00), 133.18(27.65-641.39), 50.13(15.48-162.37, respectively). The AUCs of RCLAP-H and RCLAP-SH for predicting MS were 0.950, 0.948 in girls, and 0.952, 0.952 in boys, which were higher than these of BMI, WHtR, CLAP and RCLAP-W.

Conclusion

The relative children's lipid accumulation products RCLAP-H and RCLAP-SH ) were more effective indicators for predicting MS than BMI, WHtR and CLAP in Chinese children and adolescents.

Introduction

Over the past two decades, there has been a striking increase in the number of people with metabolic syndrome (MS) [1]. In 2009, the overall age-standardized estimates prevalence of the MS was 21.3% based on the criteria of revised National Cholesterol Education Program—Third Adult Treatment Panel (NCEP-ATPIII) [2]. A meta-analysis showed that the MS increased the risk of type 2 diabetes and cardiovascular diseases (CVD) [3]. Concomitantly with the increasing prevalence of childhood obesity, the prevalence of metabolic syndrome is rising among children and adolescents [4]. According to the International Diabetes Federation (IDF), NCEP-ATPIII and Chinese children metabolic syndrome
righteousness and prevention advice (CHN2012) criteria, the prevalence of MS among Chinese children was 1.8%, 2.6% and 2.0%, respectively. In addition, the MS prevalence in children with overweight and obese was 4.7% and 17.3% based on IDF criteria in 2004–2014, respectively [5]. Childhood MS are associated with hypertension, hyperlipidemia, insulin resistance and type 2 diabetes, which can also lead to cardiometabolic diseases during adulthood. The MS was defined as the presence of ≥3 components: central obesity, hypertriglyceridemia, high fasting glucose, low high-density lipoprotein (HDL) and hypertension [6]. Many factors may induce MS, including unhealthy eating habits and lack of exercise [7, 8], the etiology and pathogenesis of MS are very complex [9, 10]. Thus, the more effective indicators to predict MS are very important in children and adolescents.

Some researches had reported that body mass index (BMI), waist circumference (WC), abdominal skinfold thickness (AST), Waist-to-height ratio (WHtR) and triglycerides (TG) were effectively related with MS [11–14]. However, the above indicator is limited to distinguishing adipose tissue from lean mass and showing circulating lipid accumulation. The lipid excess is along with expansion of visceral adipocytes and elevating blood concentrations of certain lipids, which was referred to as lipid overaccumulation and could lead to ectopic deposition of lipids in non-adipose tissues, insulin resistance and other metabolic dysfunctions [15–17]. Kahn et al [15] proposed a new marker the lipid accumulation product (LAP), reflected the total lipid accumulation in the body to predict MS in adults. The LAP that was product of waist circumference (WC) and fasting triglycerides (TG) concentration. The studies had showed LAP was a powerful marker for predicting MS and was better than BMI, WC and WHtR in adults. However, LAP may not directly reflect lipid accumulation in children and adolescents. Zhang et al [18] developed a novel indicator, the children's lipid accumulation product (CLAP), associated with MS in Chinese children and adolescents. The CLAP that was product of WC, AST, and TG concentration (CLAP = WC (cm) \times AST (mm) \times TG (mmol/L)/100). They reported that CLAP was an effective indicator associated with MS and was better than BMI and WHtR. Wang et al [19] showed that CLAP was significantly associated with hypertension in children and adolescents, and can more effectively predict childhood hypertension than WC, WHtR, BMI, AST, and TG. Yuan et al [20] showed that the CLAP was significantly associated with impaired fasting glucose (IFG) in Chinese boys, and it performed better than WC, WHtR, AST and TG. From the formula of CLAP, we know that AST shows the accumulation of skin fat at a point on the abdomen, multiplying by WC shows the accumulation of whole abdominal fat and then multiplying by TG to a certain extent shows the accumulation of body lipid. However, CLAP could not reflect the density of lipid accumulation in body.

It was well known that there are multifarious types of obesity, different obesity types have different locations where fat accumulates. The relative CLAP at per unit body height, sitting height and weight may reflect the density of lipid accumulation among children and adolescents. However, it has been not cleared whether the relative CLAP at per unit body height, sitting height and weight were more effective indicators related to MS than CLAP, BMI and WHtR. The purpose of this study was to develop more effective relative CLAP indicators for predicting MS.
Materials And Methods

Subjects

In this study, a total of 683 students aged 8-15 years were selected from two nine-year schools via the stratified cluster sampling methods, including 317 girls (46.4%) aged at (10.98±1.83 years) and 366 boys (53.6%) aged at (10.77±1.80 years).

Measurement

The medical staff who received standardized training measured the participants’ body weight, height, sitting height (SH), Diastolic blood pressure (DBP), Systolic blood pressure (SBP), WC and AST. The participants kept have an empty stomach when they were measured, and were requested barefoot, dressed in light clothes and stood straight. An electronic scale was used to measure weight, and the reading was accurate to 0.1 kg. Height and SH were measured using Mechanical height measure, and the readings were accurate to 0.1 cm. Blood pressure was measured on the right arm with an appropriately sized cuff using mercury sphygmomanometer after having a rest for at least 10 min. DBP was defined as the fifth Korotkoff sound (K5), SBP was defined as the onset of the Korotkoff sound (K1). The blood pressure was measured twice at interval of 2 min. Waist circumference (WC) was measured along a horizontal line at 1 cm above the belly button using a Nylon tapes, the reading was accurate to 0.1 cm. Abdominal skinfold thickness (AST) was measured at the intersection of the horizontal umbilicus and the right midclavicular line, the reading was accurate to 0.1 mm.

The children and adolescents after at least 8 h of overnight fasting were collected 3 mL venous blood samples by nurses received standardized training. The enzyme-linked immunoassay method was used to detect HDL-C. Enzymatic methods were used to detected TG and FBG levels.

Definition of Metabolic Syndrome (MS)

In this study, MS was diagnosed according to the amended NCEP-ATP III criteria [21]. high fasting blood glucose (FBG) ≥110mg/dL; abdominal obesity: WC ≥ 90th age-and sex-specific percentile for Chinese children [22]; high blood pressure: SBP and/or DBP ≥90th percentile for gender and age [23]; low high-density lipoprotein cholesterol (HDL-C) ≤40 mg/dL; high triglycerides (TG) ≥110mg/dL; when three or more of the five components were present that MS was identified.

Calculation of the Derivative Variables

Children’s lipid accumulation product (CLAP) = WC (cm) × AST (mm) × TG (mmol/L) / 100; BMI=weight (kg)/ height² (m²); WHtR = waist circumference (cm) / height (cm); Relative children’s lipid accumulation product per height (RCLAP-H) = WC (cm) × AST (mm) × TG (mmol/L) / height (cm); Relative children’s lipid accumulation product per sitting height (RCLAP-SH) = WC (cm) × AST (mm) × TG (mmol/L) / sitting height (cm); Relative children’s lipid accumulation product per weight (RCLAP-W) = WC (cm) × AST (mm) × TG (mmol/L) / weight (kg).
Surveys of Behavioral Indexes

We investigated dietary behaviors which included the frequency of breakfast, milk, fresh vegetables, fruits, nuts, fried foods, carbonated drinks, eating out, western-style fast food, high-energy snacks. Each of the dietary behavior items was assigned 6 grades including never (0 points), 1 time per month (0.25 points), 2 time per month (0.5 points), 1–3 times per week (2 points), 4–6 times per week (5 points), and 1 time per day (7 points). The total scores of healthy dietary behaviors (including breakfast, milk, fruits, nuts, fresh vegetables) and risk dietary behaviors (including fried foods, eating out, carbonated drinks, high-energy snacks, western-style fast food) were defined as ≥ the 75th percentile (P75) and < 75th percentile (P75) two grades. Children’s Leisure Activities Study Survey (CLASS) questionnaire was used to investigate Physical activities [24]. The moderate-to-vigorous physical activity was defined as <60min and ≥60min two grades, and sedentary activity time was defined as <120min and ≥120min two grades [25].

Statistical Analysis

Data were analyzed using the SPSS 23.0 software. The data were described using rate (or proportion) or mean ± standard deviation. The height, siting height, weight, WC, AST, BMI, WHtR, logarithmic CLAP, RCLAP-H, RCLAP-SH, RCLAP-W, SBP, and DBP was standardized for genders and ages using Z-score method (Abbreviations of above standardized indexes: SH, SSH, SW, WC, SAST, SBMI, SWHtR, SlnCLAP, SRCLAP-H, SRCLAP-SH, SRCLAP-W, SSBP, SDBP, respectively). The t-test, chi-square test and logistic regression models were used to analyze the associations of SBMI, SWHtR, SlnCLAP, SRCLAP-H, SRCLAP-SH, SRCLAP-W with MS, respectively. Receiver Operating Characteristic (ROC) curves were used to evaluate the predictive efficiency of above indexes for predicting MS. \( P < 0.05 \) was considered statistically significant.

Results

A total of 683 children aged 8–15 years (366 boys and 317 girls) were included in this study. The overall prevalence of MS was 4.8%, 2.8% for girls and 6.6% for boys. As shown in Table 1. The results showed that weight, WC, AST, BMI, WHtR, CLAP, RCLAP-H, RCLAP-SH, RCLAP-W, SBP, DBP, TG among girls with MS were significantly higher than those without MS; the boys with MS had higher values of height, sitting height, weight, WC, AST, BMI, WHtR, CLAP, RCLAP-H, RCLAP-SH, RCLAP-W, SBP, DBP, TG, compared to those without MS (\( P < 0.05 \)). On the contrary, girls and boys with MS had lower values of HDL-C than those without MS, respectively (\( P < 0.05 \)). The prevalence of MS among boys aged 12–15 years was significantly higher than that aged 8–11 years (\( P < 0.05 \)). The proportion of moderate-to-vigorous physical activity time (≥ 60 min) among boys with MS was significantly lower than those without MS (\( P < 0.05 \)).
Table 1
The comparison of anthropometric characteristics, dietary behaviors, physical activities, CLAP, RCLAP among children of different genders with Non-MS and MS

| Variables | Girls (317) |  | Boys (366) |  |
|-----------|-------------|----------------|-------------|----------------|
|           | Non-MS (97.2%) | MS (2.8%) | P | Non-MS (93.4%) | MS (6.6%) |
|           | τ/χ² |  | τ/χ² |  |
| SH | -0.01 ± 0.99 | 0.32 ± 1.04 | -0.98 | 0.329 | -0.03 ± 0.97 | 0.40 ± 1.17 | -2.05 | 0.041 |
| SSH | -0.01 ± 0.98 | 0.41 ± 1.19 | -1.27 | 0.204 | -0.04 ± 0.96 | 0.58 ± 1.24 | -2.99 | 0.003 |
| SW | -0.02 ± 0.99 | 0.83 ± 0.67 | -2.59 | 0.010 | -0.10 ± 0.91 | 1.45 ± 0.91 | -8.07 | < 0.001 |
| SWC | -0.05 ± 0.95 | 1.74 ± 0.73 | -5.61 | < 0.001 | -0.11 ± 0.91 | 1.58 ± 0.65 | -8.90 | < 0.001 |
| SAST | -0.03 ± 0.98 | 0.96 ± 0.72 | -3.00 | 0.003 | -0.10 ± 0.92 | 1.48 ± 0.72 | -10.22 | < 0.001 |
| SBMI | -0.02 ± 0.99 | 0.76 ± 0.52 | -2.36 | 0.019 | -0.11 ± 0.91 | 1.56 ± 0.69 | -11.26 | < 0.001 |
| SWHtR | -0.05 ± 0.95 | 1.79 ± 0.79 | -5.77 | < 0.001 | -0.11 ± 0.91 | 1.55 ± 0.65 | -11.82 | < 0.001 |
| SlnCLAP | -0.04 ± 0.97 | 1.43 ± 0.23 | -15.42 | < 0.001 | -0.11 ± 0.92 | 1.60 ± 0.51 | -14.91 | < 0.001 |
| SRCLAP-H | -0.05 ± 0.94 | 1.85 ± 0.67 | -6.01 | < 0.001 | -0.15 ± 0.78 | 2.20 ± 1.13 | -10.03 | < 0.001 |
| SRCLAP-SH | -0.05 ± 0.94 | 1.85 ± 0.66 | -5.98 | < 0.001 | -0.15 ± 0.79 | 2.19 ± 1.11 | -10.14 | < 0.001 |
| SRCLAP-W | -0.05 ± 0.96 | 1.57 ± 0.80 | -5.01 | < 0.001 | -0.14 ± 0.80 | 2.02 ± 1.19 | -8.76 | < 0.001 |
| SSBP | -0.04 ± 0.97 | 1.32 ± 0.87 | -4.18 | < 0.001 | -0.08 ± 0.96 | 1.09 ± 0.84 | -5.84 | < 0.001 |
| SDBP | -0.04 ± 0.96 | 1.34 ± 1.02 | -4.22 | < 0.001 | -0.06 ± 0.97 | 0.86 ± 0.91 | -4.46 | < 0.001 |
| HDL-C | 1.51 ± 0.29 | 1.18 ± 0.27 | 3.32 | 0.001 | 1.56 ± 0.30 | 1.20 ± 0.24 | 5.81 | < 0.001 |
| TG | 0.94 ± 0.38 | 1.39 ± 0.27 | -3.47 | 0.001 | 0.83 ± 0.34 | 1.50 ± 0.39 | -9.24 | < 0.001 |
| FBG | 5.09 ± 0.45 | 5.26 ± 0.34 | -1.08 | 0.283 | 5.18 ± 0.42 | 5.30 ± 0.44 | -1.36 | 0.176 |
| Variables                                      | Girls (317) | τ/χ² | P  | Boys (366) | τχ² | P  |
|-----------------------------------------------|-------------|------|----|-------------|-----|----|
| Non-MS (97.2%)                               | MS (2.8%)   |      |    | Non-MS (93.4%) | MS (6.6%) |      |
| Ages(years)                                   |             | 0.47 | 0.491 |             | 7.06 | 0.008 |
| 8-                                            | 187(96.4)   | 7(3.6) |       | 221(96.1)   | 9(3.9) |       |
| 12–15                                         | 121(98.4)   | 2(1.6) |       | 121(89.0)   | 15(11.0) |       |
| Healthy dietary behaviors                     |             | 0.13 | 0.723 |             | 0.08 | 0.769 |
| <P⁷⁵                                          | 241(96.8)   | 8(3.2) |       | 247(93.2)   | 18(6.8) |       |
| ≥P⁷⁵                                         | 67(98.5)    | 1(1.5) |       | 95(94.1)    | 6(5.9)  |       |
| Risk dietary behaviors                        |             | 0.00 | 1.00  |             | 1.33 | 0.250 |
| <P⁷⁵                                          | 256(97.3)   | 7(2.7) |       | 238(94.4)   | 14(5.6) |       |
| ≥P⁷⁵                                         | 52(96.3)    | 2(3.7) |       | 104(91.2)   | 10(8.8) |       |
| Moderate-to-vigorous physical activity time   |             | 0.61 | 0.434 |             | 4.46 | 0.035 |
| < 60 min                                      | 182(96.3)   | 7(3.7) |       | 166(90.7)   | 17(9.3) |       |
| ≥ 60 min                                      | 126(98.4)   | 2(1.6) |       | 176(96.2)   | 7(3.8)  |       |
| Sedentary activity time                       |             | 3.65 | 0.056 |             | 0.38 | 0.537 |
| < 120 min                                     | 124(94.7)   | 7(5.3) |       | 179(94.2)   | 11(5.8) |       |
| ≥ 120 min                                     | 184(98.9)   | 2(1.1) |       | 163(92.6)   | 13(7.4) |       |

The results of chi-square test showed that WHtR, CLAP, RCLAP-H, RCLAP-SH and RCLAP-W were significantly associated with MS among boys and girls. (Table 2). In girls, after adjusting for sedentary activity time factor, SWHtR ≥ 1, SBMI ≥ 1, SRCLAP-H ≥ 1, SRCLAP-SH ≥ 1 and SRCLAP-W ≥ 1 were significantly increased the risk of MS comparing with SWHtR < 1, SBMI < 1, SRCLAP-H < 1, SRCLAP-SH < 1 and SRCLAP-W < 1 (OR(95%CI): 15.79 (3.15–79.21), 3.73 (0.87–15.95), 96.13 (11.11-831.97), 96.13 (11.11-831.97), 18.28 (4.24–78.87), respectively). In boys, after adjusting for ages and moderate-to-vigorous physical activity time factors, SWHtR ≥ 1, SBMI ≥ 1, SlnCLAP ≥ 1, SRCLAP-H ≥ 1, SRCLAP-SH ≥ 1 and SRCLAP-W ≥ 1 were significantly increased the risk of MS comparing with SWHtR < 1, SBMI < 1, SlnCLAP < 1, SRCLAP-H < 1, SRCLAP-SH < 1 and SRCLAP-W < 1 (OR(95%CI): 37.43 (11.67–120.10), 68.33 (18.51–252.20), 105.86 (21.99-509.68), 171.75 (33.60–878.00), 133.18 (27.65-641.39), 50.13 (15.48-162.37), respectively). (Table 3).
Table 2
The association between WHtR, BMI, CLAP, RCLAP and MS among children in different genders

| Variables | Girls |       |       | Boys |       |       |
|-----------|-------|-------|-------|------|-------|-------|
|           |       | \(\chi^2\) | \(P\) |       | \(\chi^2\) | \(P\) |
| WHtR      |       |       |       | \(\chi^2\) |       |       |
| < 1       | 258(99.2) | 2(0.8) | 293(98.3) | 5(1.7) |      |      |
| ≥ 1       | 50(87.7)  | 7(12.3)| 49(72.1)  | 19(27.9)|      |      |
| SBMI      |       | 2.48  | 0.115 |      | 72.38 | < 0.001|
| < 1       | 275(97.9) | 6(2.1) | 298(98.7) | 8(1.3) |      |      |
| ≥ 1       | 33(91.7)  | 3(8.3) | 44(68.8)  | 20(31.3)|      |      |
| lnCLAP    |       | 44.22 | < 0.001|      | 90.72 | < 0.001|
| < 1       | 268(100.0) | 0(0.0) | 299(99.3) | 2(0.7) |      |      |
| ≥ 1       | 40(81.6)  | 9(18.4)| 43(66.2)  | 22(33.8)|      |      |
| RCLAP-H   |       | 47.67 | < 0.001|      | 116.98| < 0.001|
| < 1       | 280(99.6) | 1(0.4) | 311(99.4) | 2(0.6) |      |      |
| ≥ 1       | 28(77.8)  | 8(22.2)| 31(58.5)  | 22(41.5)|      |      |
| RCLAP-SH  |       | 47.67 | < 0.001|      | 111.81| < 0.001|
| < 1       | 280(99.6) | 1(0.4) | 309(99.4) | 2(0.6) |      |      |
| ≥ 1       | 28(77.8)  | 8(22.2)| 33(60.0)  | 22(40.0)|      |      |
| RCLAP-W   |       | 22.78 | < 0.001|      | 92.46 | < 0.001|
| < 1       | 278(98.9) | 3(1.1) | 309(98.7) | 4(1.3) |      |      |
| ≥ 1       | 30(83.3)  | 6(16.7)| 33(62.3)  | 20(36.7)|      |      |
Table 3
The adjusted association between WHtR, BMI, CLAP and RCLAP on MS using logistic regression model

| Variables | β(S.E.) | Wald  | P     | OR (95%CI)   |
|-----------|---------|-------|-------|--------------|
| **Girls** |         |       |       |              |
| SWHtR     |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 2.76(0.82) | 11.24 | 0.001 | 15.79(3.15–79.21) |
| SBMI      |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 1.32(0.74) | 3.14  | 0.076 | 3.73(0.87–15.95) |
| SlnCLAP   |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 19.74(2358.36) | 0.00  | 0.993 | -           |
| SCLAP-H   |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 4.57(1.10) | 17.19 | <0.001 | 96.13(11.11–831.97) |
| SCLAP-SH  |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 4.57(1.10) | 17.19 | <0.001 | 96.13(11.11–831.97) |
| SCLAP-W   |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 2.91(0.75) | 15.18 | <0.001 | 18.28(4.24–78.87) |
| **Boys**  |         |       |       |              |
| SWHtR     |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 3.62(0.60) | 37.09 | <0.001 | 37.43(11.67–120.10) |
| SBMI      |         |       |       |              |
| < 1       | 0       |       | 1     |              |
| ≥ 1       | 4.22(0.67) | 40.20 | <0.001 | 68.33(18.51–252.20) |
| Variables  | $\beta$($S.E.$) | $Wald$ | $P$ | $OR$ (95%CI)          |
|-----------|-----------------|-------|-----|-----------------------|
| SlnCLAP   |                 |       |     |                       |
| < 1       | 0               |       | 1   |                       |
| $\geq 1$  | 4.66(0.80)      | 32.80 | < 0.001 | 105.86(21.99-509.68) |
| SCLAP-H   |                 |       |     |                       |
| < 1       | 0               |       | 1   |                       |
| $\geq 1$  | 5.15(0.83)      | 38.21 | < 0.001 | 171.75(33.60–878.00) |
| SCLAP-SH  |                 |       |     |                       |
| < 1       | 0               |       | 1   |                       |
| $\geq 1$  | 4.89(0.80)      | 37.20 | < 0.001 | 133.18(27.65-641.39) |
| SCLAP-W   |                 |       |     |                       |
| < 1       | 0               |       | 1   |                       |
| $\geq 1$  | 3.92(0.60)      | 42.63 | < 0.001 | 50.13(15.48-162.37) |

As shown in Table 4 and Fig. 1, the AUCs of SBMI, SWHtR, SCLAP, SRCLAP-H, SRCLAP-SH, SRCLAP-W for predicting MS among girls were 0.827 (95%CI:0.766–0.888), 0.925 (95%CI:0.870–0.980), 0.946 (95%CI:0.919–0.973), 0.950 (95%CI:0.922–0.977), 0.948 (95%CI:0.921–0.975), 0.920 (95%CI:0.869–0.972). The AUCs of above indicators for predicting MS among boys were 0.916 (95%CI: 0.877–0.956), 0.916 (95%CI: 0.879–0.952), 0.946 (95%CI: 0.906–0.985), 0.952 (95%CI: 0.913–0.990), 0.952 (95%CI: 0.914–0.990), 0.929 (95%CI: 0.877–0.982), respectively.
Table 4
The areas under ROC curves of SBMI, SWHtR, SlnCLAP, SRCLAP-H, SRCLAP-SH, SRCLAP-W for predicting MS among girls and boys

| Variables | AUC  | S.E. | P      | 95% CI of AUC  |
|-----------|------|------|--------|----------------|
| Girls     |      |      |        |                |
| SBMI      | 0.827| 0.031| 0.001  | 0.766–0.888    |
| SWHtR     | 0.925| 0.028| < 0.001| 0.870–0.980    |
| SlnCLAP   | 0.946| 0.014| < 0.001| 0.919–0.973    |
| SRCLAP-H  | 0.950| 0.014| < 0.001| 0.922–0.977    |
| SRCLAP-SH | 0.948| 0.014| < 0.001| 0.921–0.975    |
| SRCLAP-W  | 0.920| 0.026| < 0.001| 0.869–0.972    |
| Boys      |      |      |        |                |
| SBMI      | 0.916| 0.020| < 0.001| 0.877–0.956    |
| SWHtR     | 0.916| 0.019| < 0.001| 0.879–0.952    |
| SlnCLAP   | 0.946| 0.020| < 0.001| 0.906–0.985    |
| SRCLAP-H  | 0.952| 0.020| < 0.001| 0.913–0.990    |
| SRCLAP-SH | 0.952| 0.019| < 0.001| 0.914–0.990    |
| SRCLAP-W  | 0.929| 0.027| < 0.001| 0.877–0.982    |

Discussion

Metabolic syndrome (MS) has become a major public health issue worldwide [26]. This study showed that the overall prevalence of MS was 4.8% (boys 6.6%, girls 2.8%) in children and adolescents aged 8–15 years. The similar prevalence of MS was reported among Indian studies aged 12–17 years (4.2%) [27] and US adolescents (4.5%) [28]. Rodríguezmorán et al [29] reported that there was higher prevalence of MS among Mexico adolescents (6.5%) and Esmailzadeh et al [30] reported that there was 10.1% of Iranian adolescents with MS. The present study showed that prevalence of MS among girls (2.8%) was lower than that in boys (6.6%), which was consistent with the results of most previous studies [21, 31, 32]. The reasons might be due to the fact that the boys had lower levels of moderate-to-vigorous physical activity and higher levels of risk dietary behaviors, so there has higher prevalence of overweight or obesity among boys than girls. However, other studies had also reported there was no significant difference of prevalence of MS between sex [9]. The current study showed that the prevalence of MS among boys aged 12–15 years was significantly higher than that aged 8–11 years, which was in line with the result of study from Gooty et al [33]. This may be associated with an increased exposure of risk factors for MS as
boys age [34]. It was reported that the ability to regulate glucose was progressively lost with age [35]. Moreover, in the present study we found that moderate-to-vigorous physical activity time < 60 min was a risk factor for MS in boys, which was consistent with previous studies [36, 37]. Styne et al [38] also showed that at least 20 min of vigorous short bursts of physical activity a day, for 3 to 5 days per week can improve metabolic measures in children and adolescents. Physical activity is helpful in improving lipid profile by increasing HDL concentration and decreasing both LDL and triglycerides concentrations [39].

The additional findings of this cross-sectional study were that the children with MS demonstrated higher BMI, WHtR, and CLAP levels compared to children without MS, which was in line with previous studies [11, 13, 14, 18]. However, these indexes were limited to showing the accumulation of lipids. BMI can't show indication of body fat distribution, and it is not only related to fat mass, but also related to fat-free mass [40]. WHtR were limited to showing the accumulation of lipids in blood circulation. CLAP is a better marker to predicting MS than BMI and WHtR in Chinese children and adolescents, however, it only reflects the state of lipids accumulation, but not the density of lipid accumulation. Now our results suggested SRCLAP-H and SRCLAP-SH were significantly associated with MS (in girls, the OR values (95%CI) were 96.13 (11.11-831.97) and 96.13 (11.11-831.97), respectively; in boys, the OR value (95%CI) were 171.75 (33.60–878.00) and 133.18 (27.65-641.39), respectively) and the abilities of RCLAP-H and RCLAP-SH for predicting MS were all higher than BMI, WHtR and CLAP. RCLAP-H reflected the lipids accumulation at per unit height which could reflect different metabolic risks based on children's height, for example, the children with the same CLAP have a greater risk of MS with shorter heights. RCLAP-SH reflected the lipid accumulation at per upper half of body. There had study showed that an upper body or centralised deposition of excess body fat carries an increased risk for obesity-associated metabolic complications [41, 42]. In our study population, the effect of SRCLAP-W was not obvious, which may be that WC and AST reflect weight to some extent, so the effect of CLAP divided by weight will be weakened.

We all know that excess lipid material will increasingly be deposited in nonadipose tissues (e.g. liver, kidneys, skeletal muscle, heart, blood vessels and pancreas) where it may adversely modify cellular metabolism, accelerate apoptosis [43, 44]. Commonly adopted predictive indicators of abdominal obesity include WC and related indices such as the waist-to-height and waist-to-hip ratios [45, 46]. Ectopic lipid deposition is difficult to quantify directly in children and adolescents, but an increased RCLAP value may indicate that various tissues or organs have become more vulnerable to injury from lipid overaccumulation. The metabolically obese normal-weight (MONW) [47] individuals who having normal body weight but with obesity, are characterized by the presence of a cluster of cardiovascular risk factors. Janssen [48] proposed who also fulfill the criteria for the MS be classified as MONW. Du et al [49] had showed LAP and visceral adiposity index (VAI) are effective markers for identifying the Chinese adults with MONW phenotype, we speculate that that RCLAP-H or RCLAP-SH may be applicable to identifying MONW in children and adolescents.

There were also some limitations in this study. Firstly, it was a cross sectional study, the causality between RCLAP and MS cannot be inferred. Secondly, we only studied Chinese children and adolescents,
the generalizability to other ethnic groups is limited. Finally, the sample size in our study is limited, so we cannot provide a representative cut-off values in different ages and gender for the time being. Therefore, the results need to be confirmed by other studies.

**Conclusion**

The present study developed relative children’s lipid accumulation products (RCLAP). The RCLAP at per unit body height (RCLAP-H), sitting height (RCLAP-SH) were accurate and simple method, and were more effective indicators for predicting MS than BMI, WHtR and CLAP in Chinese children and adolescents. The AUCs of RCLAP-H and RCLAP-SH for predicting MS were 0.950, 0.948 in girls, and were 0.952, 0.952 in boys, which were more powerful than BMI, WHtR and CLAP can.

**Abbreviations**

**CLAP**

children's lipid accumulation product

**RCLAP-H**

relative children’s lipid accumulation product per height

**RCLAP-SH**

relative children's lipid accumulation product per sitting height

**RCLAP-W**

relative children's lipid accumulation product per weight

**BMI**

body mass index

**WC**

waist circumference;

**WHtR**

waist-height ratio;

**SBP**

systolic blood pressure;
DBP

diastolic blood pressure;

AST

abdominal skinfold thickness;

HDL-C

high-density lipoprotein cholesterol;

TG

triacylglycerol;

FBG

fasting blood glucose.

Declarations

Ethics approval and consent to participate

The participants’ guardians signed informed consent before the medical examination. This study was approved by the Medical Ethics Committee of the Bengbu Medical College ([2015] 100 No.003) and was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

LZ conceptualized and designed the study, analyzed and interpreted the data, drafted the initial manuscript, reviewed and revised the manuscript.

ZZZ, BXW, YTY and LLS collected data, analyzed and interpreted the data, and critically reviewed the manuscript for important intellectual content.

LGF conceptualized and designed the study, coordinated and supervised data collection, analyzed and interpreted the data, reviewed and revised the manuscript.

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References

1. Basit A, Shera AS. Prevalence of metabolic syndrome in Pakistan. Metab Syndr Relat Disord. 2008;6:171–5.

2. Xi B, He D, Hu Y, Zhou D. Prevalence of metabolic syndrome and its influencing factors among the Chinese adults: The China Health and Nutrition Survey in 2009. Prev Med. 2013;57:867–71.

3. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am J Med. 2006;119:812–9.

4. Pacifico L, Anania C, Martino F, Poggiogalle E, Chiarelli F, Arca M, et al. Management of metabolic syndrome in children and adolescents. Nutr Metab Cardiovasc Dis. 2011;21:455–66.

5. Ye P, Yan Y, Ding W, Dong H, Liu Q, Huang G, et al. [Prevalence of metabolic syndrome in Chinese children and adolescents: A Meta-analysis]. Zhonghua Liu Xing Bing Xue Za Zhi. 2015;36:884–8.

6. Weiss R, Bremer AA, Lustig RH. What is metabolic syndrome, and why are children getting it? Ann N Y Acad Sci. 2013;1281:123–40.

7. Roopchand DE, Carmody RN, Kuhn P, Moskal K, Rojas-Silva P, Turnbaugh PJ, et al. Dietary Polyphenols Promote Growth of the Gut Bacterium Akkermansia muciniphila and Attenuate High-Fat Diet-Induced Metabolic Syndrome. Diabetes. 2015;64:2847–58.

8. Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Compr Physiol. 2012;2:1143–211.

9. Lambert M, Paradis G, O'Loughlin J, Delvin EE, Hanley JA, Levy E. Insulin resistance syndrome in a representative sample of children and adolescents from Quebec, Canada. Int J Obes Relat Metab Disord. 2004;28:833–41.

10. Duncan GE, Li SM, Zhou XH. Prevalence and trends of a metabolic syndrome phenotype among u.s. Adolescents, 1999–2000. Diabetes Care. 2004;27:2438–43.
11. Rodea-Montero ER, Evia-Viscarra ML, Apolinar-Jimenez E. Waist-to-Height Ratio Is a Better Anthropometric Index than Waist Circumference and BMI in Predicting Metabolic Syndrome among Obese Mexican Adolescents. Int J Endocrinol. 2014;2014:195407.

12. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006;444:881–7.

13. Al-Hamad D, Raman V. Metabolic syndrome in children and adolescents. Transl Pediatr. 2017;6:397–407.

14. Gray DS, Bray GA, Bauer M, Kaplan K, Gemayel N, Wood R, et al. Skinfold thickness measurements in obese subjects. Am J Clin Nutr. 1990;51:571–7.

15. Kahn HS. The "lipid accumulation product" performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. BMC Cardiovasc Disord. 2005;5:26.

16. Kahn HS, Valdez R. Metabolic risks identified by the combination of enlarged waist and elevated triacylglycerol concentration. Am J Clin Nutr. 2003;78:928–34.

17. Kahn HS. The lipid accumulation product is better than BMI for identifying diabetes: a population-based comparison. Diabetes Care. 2006;29:151–3.

18. Zhang Y, Hu J, Li Z, Li T, Chen M, Wu L, et al. A Novel Indicator of Lipid Accumulation Product Associated With Metabolic Syndrome In Chinese Children And Adolescents. Diabetes Metab Syndr Obes. 2019;12:2075–83.

19. Wang Y, Liu W, Sun L, Zhang Y, Wang B, Yuan Y, et al. A novel indicator, childhood lipid accumulation product, is associated with hypertension in Chinese children and adolescents. Hypertens Res. 2020;43:305–12.

20. Yuan Y, Xie H, Sun L, Wang B, Zhang L, Han H, et al. A Novel Indicator of Children's Lipid Accumulation Product Associated with Impaired Fasting Glucose in Chinese Children and Adolescents. Diabetes Metab Syndr Obes. 2020;13:1653–60.

21. Cook S, Weitzman M, Auinger P, Nguyen M, Dietz WH. Prevalence of a metabolic syndrome phenotype in adolescents: findings from the third National Health and Nutrition Examination Survey, 1988–1994. Arch Pediatr Adolesc Med. 2003;157:821–7.

22. Xi B, Zong X, Kelishadi R, Litwin M, Hong YM, Poh BK, et al. International Waist Circumference Percentile Cutoffs for Central Obesity in Children and Adolescents Aged 6 to 18 Years. J Clin Endocrinol Metab. 2020;105:e1569–83.

23. Mi J, Wang TY, Meng LH. Development of blood pressure reference standards for Chinese children and adolescents. Chinese Journal of Evidence-Based Pediatrics. 2010;5:4–14.

24. Huang YJ, Wong SH, Salmon J. Reliability and validity of the modified Chinese version of the Children's Leisure Activities Study Survey (CLASS) questionnaire in assessing physical activity among Hong Kong children. Pediatr Exerc Sci. 2009;21:339–53.

25. Villagran PS, Novalbos-Ruiz JP, Rodriguez-Martin A, Martinez-Nieto JM, Lechuga-Sancho AM. Implications of family socioeconomic level on risk behaviors in child-youth obesity. Nutr Hosp. 2013;28:1951–60.
26. Kassi E, Pervanidou P, Kaltsas G, Chrousos G. Metabolic syndrome: definitions and controversies. Bmc Med. 2011;9:48.

27. Marwaha RK, Khadgawat R, Tandon N, Kanwar R, Narang A, Sastry A, et al. Reference intervals of serum lipid profile in healthy Indian school children and adolescents. Clin Biochem. 2011;44:760–6.

28. Ford ES, Li C, Zhao G, Pearson WS, Mokdad AH. Prevalence of the metabolic syndrome among U.S. adolescents using the definition from the International Diabetes Federation. Diabetes Care. 2008;31:587–9.

29. Rodriguez-Moran M, Salazar-Vazquez B, Violante R, Guerrero-Romero F. Metabolic syndrome among children and adolescents aged 10–18 years. Diabetes Care. 2004;27:2516–7.

30. Esmailzadeh A, Mirmiran P, Azadbakht L, Etemadi A, Azizi F. High prevalence of the metabolic syndrome in Iranian adolescents. Obesity (Silver Spring). 2006;14:377–82.

31. Narayanan P, Meng OL, Mahanim O. Do the prevalence and components of metabolic syndrome differ among different ethnic groups? A cross-sectional study among obese Malaysian adolescents. Metab Syndr Relat Disord. 2011;9:389–95.

32. Tandon N, Garg MK, Singh Y, Marwaha RK. Prevalence of metabolic syndrome among urban Indian adolescents and its relation with insulin resistance (HOMA-IR). J Pediatr Endocrinol Metab. 2013;26:1123–30.

33. Gooty VD, Sinaiko AR, Ryder JR, Dengel DR, Jacobs DJ, Steinberger J. Association Between Carotid Intima Media Thickness, Age, and Cardiovascular Risk Factors in Children and Adolescents. Metab Syndr Relat Disord. 2018;16:122–6.

34. Dobbelsteyn CJ, Joffres MR, MacLean DR, Flowerdew G. A comparative evaluation of waist circumference, waist-to-hip ratio and body mass index as indicators of cardiovascular risk factors. The Canadian Heart Health Surveys. Int J Obes Relat Metab Disord. 2001;25:652–61.

35. Andres R. Aging and diabetes. Med Clin North Am. 1971;55:835–46.

36. Kelishadi R, Hovsepian S, Djalalinia S, Jamshidi F, Qorbani M. A systematic review on the prevalence of metabolic syndrome in Iranian children and adolescents. J Res Med Sci. 2016;21:90.

37. Chastin SF, Palarea-Albaladejo J, Dontje ML, Skelton DA. Combined Effects of Time Spent in Physical Activity, Sedentary Behaviors and Sleep on Obesity and Cardio-Metabolic Health Markers: A Novel Compositional Data Analysis Approach. Plos One. 2015;10:e139984.

38. Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, et al. Response to Letter: "Pediatric Obesity-Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline". J Clin Endocrinol Metab. 2017;102:2123–4.

39. Bremer AA, Auinger P, Byrd RS. Relationship between insulin resistance-associated metabolic parameters and anthropometric measurements with sugar-sweetened beverage intake and physical activity levels in US adolescents: findings from the 1999–2004 National Health and Nutrition Examination Survey. Arch Pediatr Adolesc Med. 2009;163:328–35.

40. Maynard LM, Wisemandle W, Roche AF, Chumlea WC, Guo SS, Siervogel RM. Childhood body composition in relation to body mass index. Pediatrics. 2001;107:344–50.
41. Ito H, Nakasuga K, Ohshima A, Sakai Y, Maruyama T, Kaji Y, et al. Excess accumulation of body fat is related to dyslipidemia in normal-weight subjects. Int J Obes Relat Metab Disord. 2004;28:242–7.

42. Frank AP, de Souza SR, Palmer BF, Clegg DJ. Determinants of body fat distribution in humans may provide insight about obesity-related health risks. J Lipid Res. 2019;60:1710–9.

43. Schaffer JE. Lipotoxicity: when tissues overeat. Curr Opin Lipidol. 2003;14:281–7.

44. Unger RH. Minireview: weapons of lean body mass destruction: the role of ectopic lipids in the metabolic syndrome. Endocrinology. 2003;144:5159–65.

45. Li C, Ford ES, Mokdad AH, Cook S. Recent trends in waist circumference and waist-height ratio among US children and adolescents. Pediatrics. 2006;118:e1390–8.

46. Fernandez JR, Redden DT, Pietrobelli A, Allison DB. Waist circumference percentiles in nationally representative samples of African-American, European-American, and Mexican-American children and adolescents. J Pediatr. 2004;145:439–44.

47. Ruderman NB, Schneider SH, Berchtold P. The "metabolically-obese," normal-weight individual. Am J Clin Nutr. 1981;34:1617–21.

48. St-Onge MP, Janssen I, Heymsfield SB. Metabolic syndrome in normal-weight Americans: new definition of the metabolically obese, normal-weight individual. Diabetes Care. 2004;27:2222–8.

49. Du T, Yu X, Zhang J, Sun X. Lipid accumulation product and visceral adiposity index are effective markers for identifying the metabolically obese normal-weight phenotype. Acta Diabetol. 2015;52:855–63.