How to Simplify the Diagnostic Criteria of Metabolic Syndrome in Adolescents

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Key Words: adolescents; blood pressure-to-height ratio; diagnosis; metabolic syndrome; waist-to-height ratio

Background: This study evaluated the feasibility and accuracy of the height-corrected definition for identifying metabolic syndrome (MS).

Methods: In 2006, anthropometric and biochemical measurements were assessed in a cross-sectional population-based study of 3136 Han adolescents, aged 13–17 years. MS was defined according to the definitions of Cook et al., International Diabetes Federation, and the Society of Pediatrics, Chinese Medical Association. Waist-to-height and blood pressure-to-height ratios were alternatives to waist circumference and blood pressure in the height-corrected definition.

Results: According to the MS definition and the height-corrected MS definition, this agreement would be classified as “very good” (National Cholesterol Education Program kappa coefficients: 0.850 in boys and 0.816 in girls; International Diabetes Federation kappa coefficients: 0.953 in boys and 0.807 in girls; Society of Pediatrics, Chinese Medical Association kappa coefficients: 0.932 in boys; p < 0.001) and “good” (Society of Pediatrics, Chinese Medical Association kappa coefficients: 0.737 in girls; p < 0.001).

Conclusion: The present study demonstrates that the height-corrected definition of MS is a simple, inexpensive, and accurate tool for identifying MS in Han adolescents.

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1. Introduction

Metabolic syndrome (MS) is defined as a cluster of glucose intolerance, hypertension, dyslipidemia, and central obesity, and insulin resistance is the pathogenesis. MS represents a significant risk for the development of cardiovascular disease, type 2 diabetes mellitus, and all-cause mortality.1–3

Owing to changes in childhood lifestyle, which are characterized by the lack of physical activity and an energy-dense diet, MS is highly prevalent among adolescents in China.4 The Bogalusa Heart Study indicated that the progression of atherosclerotic disease starts in children and young adults, and the severity of atherosclerosis is related to multiple cardiovascular risk factors, such as obesity, hypertension, and dyslipidemia.5 Patient motivation leading to multiple cardiovascular risk factors, such as obesity, hyperlipidemia, and young adults, and the severity of atherosclerosis is related to multiple cardiovascular risk factors, such as obesity, hypertension, and dyslipidemia.6

2. Methods and procedures

2.1. Participants

After obtaining informed consent from adolescents and their parents, a cross-sectional, population-based study was conducted. The study population was determined according to two-stage cluster sampling. In the first stage, samples of middle schools in Qinhuangdao, China, were randomly obtained; in the second stage, adolescents (aged 13–17 years) in these schools were invited to participate in 2006. A total of 3136 Han adolescents (1601 boys and 1535 girls) were included in the study population. All participants were required to be healthy. For this purpose, both a detailed medical history and a complete physical examination were performed prior to the study. This study was approved by the Ethics Committee of the First Hospital of Qinhuangdao.

2.2. Measurements

Anthropometric measurements, including those of height, weight, and WC, were obtained while the participants were in light clothing and were barefoot. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. WC was measured at a level midway between the lowest rib and the top of the iliac crest. All measurements were taken twice, and the two measurements were averaged for analysis. The body mass index was calculated by dividing weight (kg) by height squared (m²). WHtR was calculated by dividing the WC by height. Blood pressure was measured three times with a mercury sphygmonanometer while the participants were seated after 10 minutes of rest, and the three measurements were averaged for analysis. Blood pressure cuff width was 40–50% of the arm circumference. Systolic blood pressure (SBP) was determined by the onset of the "tapping" Korotkoff sounds (K1). The fifth Korotkoff sound (K5) was defined as the diastolic blood pressure (DBP). Only when a very low K5 persisted, K4 (muffling of the sounds) was recorded as the DBP. The following equations for BPHR were used: SBP-to-height ratio = SBP (mmHg)/height (cm) and DBP-to-height ratio = DBP (mmHg)/height (cm). All research staff received technical training for anthropometric measurements.

After a 10-hour overnight fast, blood samples were collected from an antecubital vein into heparinized tubes. Fasting plasma glucose concentration was measured using the glucose oxidase method. Lipid analyses were conducted using enzymatic procedures with an autoanalyzer (model 7170A; Hitachi, Tokyo, Japan). Nonhigh-density lipoprotein cholesterol (non-HDL-C) was calculated by subtracting HDL-C from total cholesterol; non-HDL-C = total cholesterol − HDL-C.

2.3. Definition of MS

We applied three commonly used definitions of pediatric MS. Each definition included the following five major components: (1) central obesity; (2) blood pressure; (3) blood glucose; (4) triglycerides; and (5) HDL-C. The definition by Cook et al10 corresponds to the National Cholesterol Education Program (MS-NCEP) definition adapted for adolescents. According to this definition, an adolescent is diagnosed with MS if a predefined critical value is exceeded for three or more of these components. In the MS definition by the International Diabetes Federation (MS-IDF), the diagnosis of MS requires the presence of central obesity plus any two of the other four factors.11 The definition of MS in children and adolescents developed by the Society of Pediatrics, Chinese Medical Association in 2012 (MS-CHN) was also used. In MS-CHN, the fifth component was defined as HDL-C <1.03 mmol/L or non-HDL-C ≥ 2.76 mmol/L.12 All definitions are summarized in Table 1.

In the height-corrected definition of MS, central obesity was defined as WHtR ≥ 0.48 for boys and ≥ 0.46 for girls.12 The data involved 21,858 children and adolescents aged 7–16 years who were randomly surveyed from six representative geographical areas, including Beijing, Tianjin, Hangzhou, Shanghai, Chongqing, and Nanning. SBP/DBP ≥ 90th percentile.
was defined as SBP-to-height ratio/DBP-to-height ratio $\geq 0.75/0.46$, and SBP/DBP $\geq 95^{th}$ percentile was defined as SBP-to-height ratio/DBP-to-height ratio $\geq 0.76/0.49$. Data were obtained from a Chinese national survey conducted in 2010, and 197,191 children aged 7–17 years were included. All height-corrected definitions are also summarized in Table 1.

2.5. Statistical analyses

All analyses were performed using the SPSS 11.5 statistical software (SPSS 11.5 for Windows; SPSS, Inc., Chicago, IL, USA). Sensitivity, specificity, and predictive values for the height-corrected definition were calculated and compared with the gold standard. We also used the kappa coefficient to assess the level of agreement between the height-corrected definition and the gold standard. Agreement strength was based on the following criteria: 0.00–0.20 = poor; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.80 = good; 0.81–1.00 = very good. A p value of $<0.05$ was considered statistically significant.

3. Results

The prevalence of MS diagnosed by MS-NCEP, MS-IDF, and MS-CHN in 13–17-year-old adolescents was 3.8%, 2.3%, and 2.6%, respectively. The distribution of each component of MS is shown in Figure 1. Overall, central obesity and abnormal blood pressure were most common.

Accuracy levels of WHtR for identifying central obesity (defined as WC) are shown in Table 2. For MS-NCEP and MS-CHN (defined as WC), the sensitivities were 90.4% in boys and 95.5% in girls. For MS-IDF (defined as WC), the sensitivities were 95.6% in boys and 95.3% in girls. The specificity was 95.7% in boys and 95.3% in girls. The specificity was 97.9% in girls and 95.2% in girls. For MS-IDF (defined as WC), the sensitivities were 95.6% in boys and 95.3% in girls. The specificity was 95.7% in boys and 93.3% in girls.

For MS-CHN, the sensitivities were 90.4% in boys and 95.5% in girls. The specificity was 95.2% in boys and 95.3% in girls. For MS-IDF (defined as WC), the sensitivities were 95.6% in boys and 95.3% in girls. The specificity was 95.7% in boys and 93.3% in girls. For MS-IDF (defined as WC), the sensitivities were 95.6% in boys and 95.3% in girls. The specificity was 95.7% in boys and 93.3% in girls. For MS-IDF (defined as WC), the sensitivities were 95.6% in boys and 95.3% in girls. The specificity was 95.7% in boys and 93.3% in girls.
4. Discussion

MS is present in a significant proportion of Han adolescents. According to the different definitions of MS, we found that the prevalence of MS among Han adolescents was 2.3–3.8%. This result was similar to that of the survey of six Chinese cities (MS-IDF 1.4% and MS-CHN 2.4%). The definition of MS and the height-corrected definition of MS achieved a high level of agreement. In our study, we found that WHtR and BPHR accurately identified central obesity and abnormal blood pressure in Han adolescents, respectively. This is why height-corrected definition has good performance for screening MS.

Visceral fat contributes to the adverse health consequences of obesity. One hypothesis is that visceral fat directly produces substances that cause the metabolic derangements associated with an increased cardiovascular disease risk in obesity. Another hypothesis is that visceral fat is largely a marker for excess free fatty acid release. It has been shown that WHtR correctly discriminates between low...
and high levels of trunk fat mass index, measured by dual-energy X-ray absorptiometry, in children and adolescents.\textsuperscript{19} Magnetic resonance imaging is considered to be the most accurate approach for quantification of fat distribution.\textsuperscript{20} WHtR was also strongly correlated with visceral adipose tissue assessed by magnetic resonance imaging.\textsuperscript{21} Furthermore, as a measure of abdominal fat accumulation, WHtR is regarded as a better predictor of insulin resistance.\textsuperscript{22}

An epidemiologic study found that WHtR was a simple, effective, and practical tool for mass screening of childhood MS in China. However, the sensitivity and specificity were only 80%.\textsuperscript{23} Bailey et al.\textsuperscript{24} found that the hypertriglyceridemic waist phenotype might be a better simple marker than WHtR for identifying children and adolescents at risk for cardiometabolic disorders. Our recent study found that the hypertriglyceridemic WHtR phenotype was a simple marker for identifying adolescents with an atherogenic lipid profile.\textsuperscript{25} This means that a combination of WHtR and other metabolic risk factors can improve the power of WHtR for identifying cardiometabolic disorders.

<table>
<thead>
<tr>
<th>Gold standard (WC)</th>
<th>Screening method (WHtR)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive cases</td>
<td>Negative cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS-NCEP and MS-CHN Boys Positive cases</td>
<td>209</td>
<td>22</td>
<td>90.4</td>
<td>97.9</td>
<td>88.1</td>
</tr>
<tr>
<td>Girls Positive cases</td>
<td>172</td>
<td>8</td>
<td>95.5</td>
<td>95.2</td>
<td>72.5</td>
</tr>
<tr>
<td>MS-IDF Boys Positive cases</td>
<td>177</td>
<td>8</td>
<td>95.6</td>
<td>95.7</td>
<td>74.6</td>
</tr>
<tr>
<td>Girls Positive cases</td>
<td>145</td>
<td>7</td>
<td>95.3</td>
<td>93.3</td>
<td>61.1</td>
</tr>
</tbody>
</table>

Gold standard: MS-NCEP and MS-CHN WC ≥90th percentile; MS-IDF WC ≥90th percentile (13–15 years), WC ≥90 cm for boys and ≥80 cm for girls (16–17 years). Screening method: WHtR ≥0.48 for boys and ≥0.46 for girls.

MS-CHN = metabolic syndrome defined by the Society of Pediatrics, Chinese Medical Association; MS-IDF = metabolic syndrome defined by the International Diabetes Federation; MS-NCEP = metabolic syndrome defined by the National Cholesterol Education Program; NPV = negative predictive value; PPV = positive predictive value.

An epidemiologic study found that WHtR was a simple, effective, and practical tool for mass screening of childhood MS in China. However, the sensitivity and specificity were only 80%.\textsuperscript{23} Bailey et al.\textsuperscript{24} found that the hypertriglyceridemic waist phenotype might be a better simple marker than WHtR for identifying children and adolescents at risk for cardiometabolic disorders. Our recent study found that the hypertriglyceridemic WHtR phenotype was a simple marker for identifying adolescents with an atherogenic lipid profile.\textsuperscript{25} This means that a combination of WHtR and other metabolic risk factors can improve the power of WHtR for identifying cardiometabolic disorders.

<table>
<thead>
<tr>
<th>Gold standard (BP)</th>
<th>Screening method (BPHR)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive cases</td>
<td>Negative cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS-NCEP Boys Positive cases</td>
<td>262</td>
<td>32</td>
<td>89.1</td>
<td>91.5</td>
<td>70.2</td>
</tr>
<tr>
<td>Girls Positive cases</td>
<td>303</td>
<td>2</td>
<td>99.3</td>
<td>86.3</td>
<td>64.3</td>
</tr>
<tr>
<td>MS-CHN Boys Positive cases</td>
<td>101</td>
<td>7</td>
<td>93.5</td>
<td>94.8</td>
<td>56.7</td>
</tr>
<tr>
<td>Girls Positive cases</td>
<td>89</td>
<td>0</td>
<td>100.0</td>
<td>84.2</td>
<td>28.0</td>
</tr>
</tbody>
</table>

Gold standard: MS-NCEP BP ≥90th percentile; MS-CHN BP ≥95th percentile. Screening method: MS-NCEP SBPHR/DBPHR ≥0.75/0.46; MS-CHN SBPHR/DBPHR ≥0.76/0.49.

DBPHR = diastolic blood pressure-to-height ratio; MS-CHN = metabolic syndrome defined by the Society of Pediatrics, Chinese Medical Association; MS-NCEP = metabolic syndrome defined by the National Cholesterol Education Program; NPV = negative predictive value; PPV = positive predictive value; SBPHR = systolic blood pressure-to-height ratio.

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Abnormal blood pressure is another component of MS. Childhood hypertension has become a widely investigated topic due to its increasing prevalence. Childhood hypertension is often asymptomatic. However, hypertension in childhood and adolescence is not benign and causes significant target organ damage, which is already present at diagnosis. Hypertension and prehypertension were frequently undiagnosed in this pediatric population because diagnosis was based on a set of age-, sex-, and height-specific references of SBP and DBP. Several studies suggested that BPHR was a good screening method in Chinese children and adolescents, which could greatly reduce the workload of pediatric clinicians.

The diagnostic criteria of MS are varied. In pediatric studies, as many as 40 different definitions of MS have been applied. MS-NCEP is the most widely used definition in pediatric practice. MS-IDF is the first consensus-based definition of MS in children, but whether it is also suitable for the Chinese population remains uncertain. Therefore, the Chinese Medical Association created the Chinese definition of MS based upon the MS-IDF framework. In our study, central obesity and abnormal blood pressure were defined as WHtR and BPHR, respectively. The performance of the height-corrected definition for identifying MS was good among these definitions. Both sensitivities and specificities were much higher.

<table>
<thead>
<tr>
<th>Gold standard (MS definition)</th>
<th>Screening method (height-corrected MS definition)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive cases</td>
<td>Negative cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MS-NCEP</td>
<td>Boys</td>
<td>Positive cases</td>
<td>63</td>
<td>9</td>
<td>87.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>12</td>
<td>1517</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>Positive cases</td>
<td>44</td>
<td>2</td>
<td>95.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>17</td>
<td>1472</td>
<td></td>
</tr>
<tr>
<td>MS-IDF</td>
<td>Boys</td>
<td>Positive cases</td>
<td>42</td>
<td>0</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>4</td>
<td>1555</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>Positive cases</td>
<td>28</td>
<td>1</td>
<td>96.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>12</td>
<td>1494</td>
<td></td>
</tr>
<tr>
<td>MS-CHN</td>
<td>Boys</td>
<td>Positive cases</td>
<td>50</td>
<td>1</td>
<td>98.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>6</td>
<td>1544</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>Positive cases</td>
<td>29</td>
<td>1</td>
<td>96.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative cases</td>
<td>19</td>
<td>1486</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Accuracy of height-corrected metabolic syndrome (MS) definition for screening MS defined as the gold standard (MS definition).

MS-CHN = metabolic syndrome defined by the Society of Pediatrics, Chinese Medical Association; MS-IDF = metabolic syndrome defined by the International Diabetes Federation; MS-NCEP = metabolic syndrome defined by the National Cholesterol Education Program; NPV = negative predictive value; PPV = positive predictive value.

There are two limitations in our study. First, it included children of only the Han ethnicity, limiting the applicability of the study results to other ethnic groups. At present, several studies have confirmed high performance levels of WHtR and BPHR to identify obesity and elevated blood pressure in different ethnic groups. Thus, we speculate that this method could be applied to other ethnic groups. Second, this study was a cross-sectional, population-based study, but the relationship between the height-corrected definition of MS and the risk of future cardiovascular disease in adults is not clear.

We conclude that the height-corrected definition of MS is a simple, easy, inexpensive, and accurate tool for identifying MS in Han adolescents. Compared with the definition of MS, the height-corrected definition of MS is a non-age-dependent method with higher applicability to screening of cardiovascular risk factors in adolescents.

Conflicts of interest

The authors have no relevant conflicts of interest to disclose. This study was self-financed.

References


