Association between leg length-to-height ratio and metabolic syndrome in Chinese children aged 3 to 6 years

Gongshu Liu a, Jian Liu b,*, Nan Li a, Zheying Tang a, Fengrong Lan a, Lei Pan a, Xilin Yang c, Gang Hu d, Zhijie Yu b,e,**,1

a Tianjin Women and Children’s Health Center, Tianjin, China
b Department of Community Health Sciences, Brock University, St. Catharines, ON, Canada, L2S 3A1
c Department of Epidemiology and Biostatistics, School of Public Health, Tianjin Medical University, Tianjin, China
d Chronic Disease Epidemiology Laboratory, Pennington Biomedical Research Center, Baton Rouge, LA, USA
e Population Cancer Research Program and Department of Pediatrics, Dalhousie University, Halifax, NS, B3H 4R2, Canada

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ABSTRACT
Objective. The aim of this study is to investigate the association between leg-length-to-height ratio (LLHR) and metabolic syndrome (MetS) among Chinese children.

Methods. 1236 children (619 obese and 617 nonobese children) aged 3–6 years participated in a cross-sectional survey in 2005 in Tianjin, China. Information on body adiposity, metabolic traits, and related covariates was obtained using a standardized protocol. LLHR was calculated as the ratio of leg length to stature.

Results. In the multivariable logistic regression analyses, compared with those in the lowest quartile, odds ratios (OR) and 95% confidence intervals (CI) of MetS among children in the second through the highest quartiles of LLHR Z-score were 0.89 (95% CI, 0.64–1.25), 0.45 (95% CI, 0.32–0.63), and 0.37 (95% CI, 0.26–0.53), respectively. Compared with children with both higher levels of LLHR and lower levels of adipose indices, the corresponding ORs of MetS for those with both lower levels of LLHR and higher levels of anthropometric indices were 4.51 (95% CI, 3.08–6.62) for BMI Z-score, 3.86 (95% CI, 2.60–5.73) for waist circumference, and 2.75 (95% CI, 1.85–4.10) for waist-to-hip ratio, respectively.

Conclusions. Greater LLHR is inversely associated with MetS in Chinese children.

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Introduction
A growing body of evidence suggests that pediatric obesity and related metabolic abnormalities have profound implications on risk of cardiometabolic disease in adulthood (Gunnell et al., 1998; Guo et al., 2002; Magnussen et al., 2010). Sinha et al. (2002) reported that there is a significant correlation between obesity and metabolic abnormalities in American children and adolescents. A longitudinal study further revealed that pediatric metabolic syndrome (MetS) was related to severe adult atherosclerosis and an increased risk of type 2 diabetes (T2D) (Magnussen et al., 2010).

Prenatal and postnatal development has been shown to be associated with risk of cardiometabolic disease in adulthood (Barker, 1995). Low birth weight, an indicator of attenuated intrauterine development, has been found to be related to an increased risk of T2D (Kajiser et al., 2009) and CVD (Barker et al., 2005). A recent systematic review (Paajanen et al., 2010) reported that shorter stature in adults is associated with increased risks of CVD morbidity and mortality compared with those with relatively greater stature. There is some evidence suggesting an inverse relation of body height to both insulin resistance (Brown et al., 1991; Davey Smith et al., 2001) and risk of T2D (Njolstad et al., 1998; Sayeed et al., 1997). Several studies (Gunnell et al., 1999; Li et al., 2007; Wadsworth et al., 2002) have shown that leg length, but not trunk length, is the height component that is more sensitive to postpartum environmental exposures during infancy. In contrast, birth weight, a proxy of intrauterine development, has an identical impact on both leg and trunk length growth (Gunnell et al., 1999; Wadsworth et al., 2002). Some studies, including ours, have shown that relatively longer leg length...
seek clarification from the parents. After anthropometry and other measurements were taken approximately 0.5-mL sample of peripheral blood was taken from the child’s middle finger.

Characteristics of the sample and anthropometric measurements

During the physical examination, weight was measured with a beam-balance scale with subjects wearing light indoor clothing without shoes. Height and sitting height were measured by a stadiometer. Sitting height was measured as the child sitting on the seat straight against the wall of the stadiometer and recorded as the distance between the head piece that was touching the child’s head firmly and the seat of the stadiometer. Waist circumference was measured at the level of the umbilicus and hip circumference was measured at the widest point around the left and right greater trochanters. The values of height, sitting height, waist circumference and hip circumference were recorded to 0.1 cm and weight was recorded to 0.1 kg.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Ponderal index (PI) was calculated as birth weight in kilograms divided by birth length in meters cubed. Waist-to-hip ratio (WHR) was calculated by dividing waist circumference by hip circumference. Leg-length was determined as the difference between body height and sitting height (Bogin and Varela-Silva, 2010). LLHR was computed as the ratio of leg length to body height: (leg-length / height) × 100.

Measurements of metabolic traits

Blood pressure was measured using a standardized mercury sphygmomanometer with an appropriate cuff bladder for children. The fourth Korotkoff sound was adopted for diastolic blood pressure recording. The measurement was taken on the right arm of the participant in a comfortable sitting position after at least 5 minutes’ rest. Mean blood pressure was calculated from 2 readings unless the difference between these readings was greater than 10 mm Hg, in which case a third measurement was taken and the mean of the last 2 measurements was used.

Serum fasting glucose, total cholesterol, high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol, and triglycerides were measured on an automatic analyzer (RX Daytona; Randox Laboratories Ltd, Antrim, Ireland) with reagents purchased from the manufacturer.

Definition of metabolic syndrome

In this analysis, the pediatric MetS was defined as having three or more of the following components: 1) waist circumference ≥75 percentile of age- and sex-specific waist circumference distribution (Fernandez et al., 2004); 2) triglycerides ≥0.85 mmol/L; 3) HDL cholesterol <1.55 mmol/L (Jolliffe and Janssen, 2006); 4) either systolic or diastolic blood pressure ≥75 percentile age- and sex-specific blood pressure distribution (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, 2004); and 5) fasting glucose ≥5.6 mmol/L (Magnussen et al., 2010).

Assessment of covariates

Parents’ educational attainment was categorized into three groups: 9 years or less, 10 to 12 years, and 13 years or more. Both mother’s and father’s BMI were derived from information of height and weight collected in the self-administered questionnaire. Based on the responses to relevant questions from the questionnaire, the following categorical variables were created and dichotomized as yes or no: breast-feeding at age of 12 months, complementary food introduction before age of 6 months, sleep duration less than 9 h, sweetened beverage consumption more than 500 ml/week, high-fat meat intake defined as if fat content was more than half of total meat, everyday intake of vegetables and fruits, duration of television viewing 60 minutes/day or more, and duration of any type of physical activity 30 min/day or less. Disease status was classified as yes for 13 participants who reported having pneumonia, cold, or fever during the past 30 days (Tian et al., 2010).

Statistical analysis

In order to account for age and sex differences in LLHR, we computed age- and sex-specific standard deviation scores (Z-score) of LLHR for
each child. Differences in the variables across LLHR Z-score quartiles were assessed by either a general linear regression model for continuous variables or the Chi-square test for categorical variables. Multivariable logistic regression models were utilized to assess the associations of LLHR with the prevalence of MetS. The analyses were performed with adjustment for age and sex (Model one) and then further controlling for other potential confounders (Model two) that we have previously reported to be associated with obesity and metabolic disorders in Chinese children (Bowers et al., 2011; Tian et al., 2010; Yu et al., 2008; Zhang et al., 2009). To examine whether the association between LLRH and MetS was affected by different measurements used to describe adiposity, i.e., BMI, Z-score, waist circumference, and WHR, we redefined modified MetS as having two or more MetS components excluding enlarged waist circumference. Levels of LLRH were classified as low and high by the median of LLHR Z-score and the anthropometric indices were grouped into tertiles. In addition, we evaluated the associations of LLHR Z-score with MetS components by using multivariable linear regression models. When appropriate, natural log-transformation was performed to improve the normality of data on MetS components. The statistical significance was defined as \( P < 0.05 \) (2-sided). All statistical analyses were performed with SAS version 9.2 (SAS Institute, Cary, North Carolina).

### Results

#### General characteristics of study participants

The general characteristics of participants by quartiles of LLHR Z-score are listed in Table 1. In general, compared with children with lower levels of LLHR, those with higher levels of LLHR were more likely to be girls and nonobesity and consume high fat meat. A higher percentage reported high levels of mother's educational attainment. Meanwhile, they had lower levels of body weight, BMI, waist and hip circumference, WHR, blood pressure, triglycerides, and mother's BMI and higher levels of body height, leg length, and HDL-cholesterol.

#### Associations of leg length-to-height ratio with metabolic syndrome

When adjusting for age and sex, results from logistic regression analyses indicated that greater LLHR was associated with decreased odds of having MetS in children aged 3 to 6 years \( (P_{\text{for trend}} < 0.0001) \) across LLHR Z-score quartiles, Table 2. In the multivariable adjusted model, the odds ratios (OR, 95% confidence interval [CI]) of having MetS for children in the second through top quartiles were 0.89 (95% CI, 0.64–1.25), 0.45 (95% CI, 0.32–0.63), and 0.37 (95% CI, 0.23–0.58) compared to the lowest quartile.

![Table 1](image)

| Characteristics | Quartiles of age- and sex-specific leg length-to-height ratio Z-score | \( P \) |
|-----------------|---------------------------------------------------------------|------|
| Age (yr)        | Q1 (lowest) \( n = 309 \) | 5.2 (0.9) | 5.3 (0.9) | 5.3 (0.8) | 5.4 (0.9) | 0.22 |
| (n)             | Q2 (n = 309) | 114 (36.9) | 152 (49.2) | 125 (40.5) | 135 (43.7) | 0.016 |
| n (%)           | Q3 (n = 309) | 207 (67.0) | 178 (57.6) | 143 (46.3) | 91 (29.5) | <0.0001 |
| Birth weight (g) | Q4 (highest) \( n = 309 \) | 3530 (464) | 3552 (567) | 3550 (625) | 3503 (446) | 0.63 |
| Birth length (cm) | Q1 | 54.4 (12.3) | 53.5 (10.9) | 52.9 (10.1) | 54.2 (11.5) | 0.32 |
| Ponderal Index (kg/m\(^3\)) | Q2 | 25.2 (7.7) | 25.5 (6.3) | 26.3 (7.6) | 24.8 (6.9) | 0.071 |
| Q3 | 39.2 (1.2) | 39.5 (3.6) | 39.3 (3.7) | 39.5 (3.6) | 0.63 |
| Q4 | 25.7 (6.4) | 25.2 (6.0) | 24.2 (5.8) | 22.9 (4.9) | <0.0001 |
| Body height (cm) | Q1 | 114.7 (7.3) | 115.9 (7.1) | 116.3 (6.9) | 116.6 (6.8) | 0.004 |
| Q2 | 48.5 (3.8) | 50.4 (3.6) | 51.4 (3.5) | 52.7 (3.6) | <0.0001 |
| Q3 | 19.3 (1.3) | 18.5 (3.0) | 17.7 (2.9) | 16.7 (2.4) | <0.0001 |
| Q4 | 61.4 (8.5) | 60.9 (8.2) | 59.2 (8.0) | 57.6 (7.0) | <0.0001 |
| Body mass index (kg/m\(^2\)) | Q1 | 66.2 (7.7) | 65.6 (7.2) | 64.2 (7.0) | 62.6 (6.3) | <0.0001 |
| Q2 | 0.93 (0.04) | 0.93 (0.05) | 0.92 (0.04) | 0.92 (0.04) | 0.25 |
| Q3 | 99.2 (11.1) | 98.0 (10.6) | 96.5 (9.9) | 94.6 (9.3) | <0.0001 |
| Q4 | 63.8 (8.2) | 63.7 (8.3) | 62.6 (7.6) | 61.4 (6.7) | 0.0003 |
| Glucose (mg/dL) | Q1 | 5.02 (0.47) | 4.97 (0.58) | 5.00 (0.51) | 4.95 (0.57) | 0.38 |
| Q2 | 4.01 (0.64) | 4.07 (0.64) | 4.05 (0.66) | 4.14 (0.69) | 0.10 |
| Q3 | 1.47 (0.30) | 1.47 (0.27) | 1.52 (0.34) | 1.52 (0.31) | 0.022 |
| Q4 | 0.91 (0.47) | 0.88 (0.38) | 0.84 (0.43) | 0.82 (0.36) | 0.046 |
| HDL cholesterol (mg/dL) | Q1 | 2.33 (0.58) | 2.38 (0.56) | 2.32 (0.52) | 2.38 (0.61) | 0.38 |
| Q2 | 22.8 (3.3) | 22.7 (3.7) | 22.5 (2.9) | 22.1 (3.0) | 0.013 |
| Q3 | 4.49 (0.40) | 25.1 (4.3) | 25.0 (3.6) | 24.5 (3.9) | 0.25 |
| Q4 | 115 (37.2) | 115 (43.9) | 145 (46.9) | 147 (47.6) | 0.033 |
| Fathers' education (yr, n, %) | Q1 | 86 (27.8) | 94 (25.2) | 78 (22.7) | 69 (22.3) | 0.84 |
| Q2 | 108 (35.0) | 80 (28.7) | 86 (27.8) | 93 (30.1) | 0.94 |
| Q3 | 115 (37.2) | 115 (43.9) | 145 (46.9) | 147 (47.6) | 0.033 |
| Q4 | 5 (1.6) | 4 (1.3) | 5 (1.0) | 1 (0.3) | 0.51 |
| Sweetened beverage drinking >500 ml/week (yes, n, %) | Q1 | 101 (32.7) | 104 (33.7) | 120 (38.8) | 104 (33.7) | 0.36 |
| Q2 | 137 (44.3) | 138 (44.7) | 147 (47.6) | 157 (48.9) | 0.73 |
| Q3 | 140 (44.7) | 127 (41.1) | 136 (44.0) | 133 (41.0) | 0.82 |
| Q4 | 149 (48.2) | 123 (39.8) | 137 (44.3) | 131 (42.4) | 0.19 |
| Mothers' body mass index (kg/m\(^2\)) | Q1 | 45.6 (36.1) | 203 (65.7) | 207 (67.0) | 210 (68.0) | 0.009 |
| Q2 | 174 (56.3) | 140 (45.3) | 132 (42.7) | 120 (38.8) | 0.15 |
| Q3 | 147 (47.6) | 67 (21.7) | 83 (26.9) | 86 (27.8) | 0.20 |

\( ^a \) Data are mean (standard deviation) and number of participants (percentage); percentages do not total 100 due to rounding.

\( ^b \) Parent-reported pneumonia, cold or fever during past month.
Discussion

In this large-scale cross-sectional analysis, we found that the ratio of leg length to body stature was inversely associated with MetS in Chinese children as young as three to six years of age. This association appeared to be independent of a number of both parental and postnatal factors known to be related to obesity and metabolic disorders in Chinese children (Bowers et al., 2011; Tian et al., 2010; Yu et al., 2008; Zhang et al., 2009). Importantly, we observed an additive effect of shorter leg length and all dimensions of adiposity on MetS risk, suggesting that LLHR might be a marker for pathogenesis of cardiometabolic disorders in children (Grundy et al., 2005; Savva et al., 2000).

Many studies have repeatedly observed stature components in adults, particularly leg length, to be associated with cardiometabolic disorders, including obesity (Gunnell et al., 2003; Lawlor et al., 2004), insulin resistance (Asao et al., 2006; Davey Smith et al., 2001; Lawlor et al., 2004), dyslipidemia (Gunnell et al., 2003; Han et al., 1997; Lawlor et al., 2002), elevated blood pressure (Langenberg et al., 2005), T2D (Asao et al., 2006; Lawlor et al., 2002; Liu et al., 2009), and CVD (Davey Smith et al., 2001; Ferrie et al., 2006; Lawlor et al., 2004). Although the underlying mechanism of the stature–disease risk association is not fully understood, it is generally believed that it reflects an impaired nutrition status in early life (Leitch, 1951), which may modify the metabolic pathway and influence risk of disease development. Recently, some studies reported that LLHR was negatively associated with the risk of childhood overweight and obesity (Frisancho, 2007; Liu et al., 2012; Pliakas and McCarthy, 2009). To our knowledge, this is the first analysis investigating the association of relative leg length with MetS in relation to obesity status—the known cardiometabolic risk factors in children.

It is commonly believed that the relatively shorter stature or leg length may indicate an adverse environmental exposure before prepubescence, but the actual mechanism is unclear. Several hypotheses have been proposed for the possible explanations of this observed stature–disease relationship (Bogin et al., 2007). It is pointed out that human growth is highly sensitive during the prepubertal growth and development in responding to the overall quality of living conditions and the legs are growing faster relative to other body parts from birth to age 7 years (Bogin and Varela-Silva, 2010). A relatively shorter leg length may indicate the occurrence of adversity during infancy and childhood leading to competition between body parts. The vital organs of head, thorax, and abdomen of the body will be protected from any adversity at the expense of the less vital tissues including the limbs. Therefore, the cost of the competition may not just lead to shorter limbs, but may also change the metabolic patterns that may influence the risk of developing cardiometabolic disease (Varela-Silva et al., 2007). This observation has been supported by data from several experimental studies (Ferron et al., 2010; Fulzele et al., 2010) suggesting that some proteins, e.g., osteocalcin) produced during bone turn over might have endocrine function that were involved in the regulation of glucose metabolism and might play an important role in the development of T2D.
investigate factors related to parental SES that may influence children's body growth.

Our study has some limitations. Firstly, the cross-sectional design of the study did not allow us to make inferences based on temporal sequence. Secondly, there is no consensus on the definition of pediatric MetS (Paul et al., 2007). The cut-offs adopted in our study could only indicate elevated levels of these measurements. Further studies are warranted to evaluate the long-term health effects of childhood clustering of multiple metabolic abnormalities. Thirdly, the assessment of covariables was based on the parents' responses to questionnaires. This might be subject to recall bias, which might lead to underestimation of the observed associations. Finally, our study participants were from a case–control study that may limit the generalizability of our findings. Notwithstanding these limitations, the population-based larger sample size and actual anthropometric and laboratory measurements were the strengths of the study.

Conclusions

We find that LLHR is inversely associated with MetS in Chinese children as young as 3 to 6 years of age. LLHR and adiposity may have an additive effect in relation to pediatric MetS. These findings may suggest that further investigations are warranted to delineate the biological pathways underlying the observed association and to identify appropriate means toward enhancing prepubertal LLHR for reducing individual risk of developing cardiometabolic disease.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.pmedr.2014.11.002.

Disclosure

The authors have full access to the data in this study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

The sponsors were not involved in the study design, data collection, analysis, or interpretation.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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