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Waist Circumference and Body Mass Index in Children with Chronic Kidney Disease and Metabolic, Cardiovascular, and Renal Outcomes

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Abstract

Objective—To describe the prevalence of obesity as estimated by waist circumference (WC) and body mass index (BMI) and compare associations of WC and BMI with indicators of metabolic, cardiovascular and renal health in children with chronic kidney disease (CKD).

Study design—Cross-sectional analysis stratified by CKD etiology (non-glomerular or glomerular) of 737 subjects. The Kappa statistic was used to assess agreement between the two measures of obesity. Linear regression models were performed using WC and BMI as separate independent variables. Dependent variables included lipid measures, insulin resistance, blood pressure, left ventricular mass index (LVMI), proteinuria and estimated glomerular filtration rate (eGFR). Associations were scaled to standard deviations (SDs) and interpreted as the change in dependent variable associated with a one SD change in WC or BMI.

Results—There was good agreement (Kappa statistic = 0.68) between WC and BMI in identifying obesity. Approximately 10 percent of subjects had obesity by one measure but not the other. BMI was more strongly associated with eGFR compared with WC. BMI was more strongly associated with LVMI in the non-glomerular CKD group compared with WC, but both had significant associations. The associations between WC and BMI with the remainder of the dependent variables were not significantly different.

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The authors declare no conflicts of interest.

Conclusions—Measurement of waist circumference added limited information to BMI in this cohort. Further longitudinal study is needed to determine how WC and BMI compare in predicting outcomes, particularly for children with CKD identified as having obesity by one measure but not the other.

Keywords

Obesity; dyslipidemia; metabolic syndrome; blood pressure; pediatric

Children with end-stage renal disease have an increased risk of cardiovascular mortality¹ and subclinical manifestations of early cardiovascular disease are found in children with earlier stages of chronic kidney disease (CKD). There are multiple traditional and nontraditional risk factors that contribute to cardiovascular risk in CKD^{2,3}. One traditional risk factor is obesity, a modifiable clinical target. Despite issues with growth and malnutrition in some children with CKD, obesity is commonly observed, with approximately 15 percent having a body mass index (BMI) >95th percentile⁴ and 24 percent having a BMI >90th percentile⁵.

BMI is the most commonly used estimate of obesity in children, but it measures both lean body mass and total fat (ie, general adiposity) and limitations include moderate sensitivity in detecting excess adiposity in children⁶. What is not clear is which estimate of obesity is the most appropriate to use in children with CKD. In CKD, BMI may underestimate the prevalence of obesity given that some patients have reduced muscle mass. BMI also shows a conflicting relationship with adverse outcomes in both the general population and a CKD population⁷ and therefore BMI may not be the most appropriate measure. Waist circumference (WC) is an estimate of central obesity which reflects visceral fat, the most relevant type in terms of cardiovascular risk and insulin resistance. As such, it may be a more appropriate indicator of obesity. Despite the appeal of WC, it is frequently not found to provide additional benefit to the use of BMI percentile in the general pediatric population⁸. However, because WC is height-independent, it may be a more suitable instrument in the pediatric CKD population which has substantial height deficits and growth abnormalities.

There are no data on the utility of WC or other central obesity estimates in a pediatric CKD population. The purposes of this study were to a) describe the prevalence of central obesity in children with CKD by WC and BMI percentile and to b) compare and contrast the relationships between markers of metabolic, cardiovascular and renal health with WC and BMI z-scores.

Methods

The Chronic Kidney in Children (CKiD) cohort study is a longitudinal, observational study designed to investigate the natural and treated history of pediatric CKD. This multicenter study spans 54 sites in the US and Canada and has enrolled 891 children between the ages of 1 and 16 years from 2005 to 2014. Eligibility for enrollment included an estimated glomerular filtration rate (eGFR) 30 to 90 ml/min/1.73m² and a diagnosis of CKD. CKD diagnoses were broadly grouped into two categories of underlying pathology: glomerular and non-glomerular forms of CKD. These families of CKD diagnoses were previously

described⁹ and have been shown to have distinct patterns of comorbidities and disease trajectories. Annual study visits collected anthropometric, clinical and renal health data. Full details of the study have been previously reported¹⁰. The study was approved by each participating center's Institutional Review Board and written informed consent was obtained from the parents or guardians of subjects. Written assent was obtained from the subjects when applicable.

The primary exposures were WC and BMI. WC measurement was added to the CKiD protocol in June 2008 (approximately 3 years after study inception), and was summarized as the average of two or three measurements using a Gulick tape measure (Jansen Medical Supply, Houston, TX). Specifically, WC was measured on a standing participant from the horizontal plane 1 cm above the navel with the child instructed to gently breathe out at the time of measurements without holding their abdomen or breath. WC was measured at least twice, with a third measurement taken if the first two differed by more than 0.1 cm. WC z-scores and percentiles were calculated by previously published methods based on normal children, specifically, methods that determine continuous (i.e., smoothed) functions of percentiles based on least mean squares (LMS) tables¹¹. Because these tables were based on children between ages 5 and 19, we restricted our analytic sample to participants within that age range. BMI was calculated from the average of three height and weight measurements and converted to age- and sex-specific z-scores according to LMS tables¹².

Obesity defined by WC percentiles was determined as being higher than the 94th percentile for boys and 84th percentile for girls, which were found to correspond to Adult Treatment Panel metabolic syndrome criteria for abnormal WC in adult men (102 cm) and women (88 cm) within a large group of children and adolescents with a similar age range to the CKiD population¹³. Obesity determined by age- and sex-specific BMI percentiles was based on a threshold of the 95th percentile for both boys and girls¹⁴. All analyses were stratified by underlying CKD diagnoses (glomerular vs non-glomerular) because these diagnoses were expected to have different relationships with metabolic, cardiovascular and renal biomarkers.

Dependent variables were indicators of metabolic, cardiovascular and renal health. Metabolic variables included fasting total cholesterol (mg/dL), high density lipoprotein (HDL) cholesterol (mg/dL), non-HDL cholesterol (mg/dL), triglycerides (mg/dL), fasting glucose (mg/dL) and homeostatic model assessment and insulin resistance (HOMA-IR); these variables were measured every other year with the exception of glucose (measured every year) and HOMA-IR (measured once in this population). Cardiovascular variables included systolic and diastolic blood pressure (BP) (mmHg) and were the average of three measurements taken at least 30 seconds apart, measured annually and converted to z-scores according to the normal population, adjusting for age, sex and height¹⁵. Left ventricular mass was measured as the average of three M-mode echocardiography dimensions and indexed to height^{2.7} (LVMI, g/m^{2.7}) and was measured every other year, per protocol. For indicators of CKD severity, variables measured annually included urine protein: creatinine ratio (mg protein/mg creatinine) and eGFR from the full 2012 CKiD equation¹⁶. This equation is expressed as: $eGFR (ml/min/1.73m^2) = 39.8 \times [ht/Cr]^{0.456} \times [1.8/CysC]^{0.418} \times [30/BUN]^{0.079} \times [1.076]^{male} \times [ht/1.4]^{0.179}$ where ht = height in meters, Cr = serum

creatinine in mg/dL, CysC = serum cystatin C in mg/dL, and BUN = blood urea nitrogen in mg/dL.

Statistical analyses

The agreement between obesity defined by WC and by BMI was assessed using the Kappa statistic. Because some variables were collected at different time points (eg, BP at all visits and lipids at every other visit), we present descriptive statistics of the first available visit and the number of observations for each outcome (i.e. data from repeat study visits for each subject were used if available). Separate linear regression models were fit for each outcome with the predictor being WC z-scores and BMI z-scores. Outcomes were log-transformed (with the exception of BP z-scores) and the slope from these regression models were presented as the percent change in outcome for a 1 SD change in WC or BMI (based on the normal population). Generalized estimating equations accounted for the repeated measurements within individuals. To compare whether the associations between the outcome with WC or BMI were different, bootstrap methods were used to determine statistically significant differences in the two slopes for each outcome and were based on 500 samples. Specifically, each bootstrapped sample was based on a random selection with replacement at the individual level of the same number of subjects as the original study sample. Each subject contributed his or her observed repeated measurements to preserve the within-person correlation. The test statistic was calculated as the ratio of the difference in slopes (in the numerator) to the SD of these differences (in the denominator). All analyses were conducted in SAS 9.4 (Cary, NC).

Results

Of 891 children enrolled, 737 children between 5 and 19 years of age contributed at least one visit with both WC and BMI. A total of 513 children with a non-glomerular diagnosis (mean age 11 years, 64% boys) and 224 children with a glomerular diagnosis (mean age 14 years, 52% boys) were included. Table I describes differences between children with non-glomerular and glomerular diagnoses. The duration of CKD at the time of study entry was significantly longer for children with non-glomerular CKD (mean time = 11 years) compared with those with glomerular CKD (mean time = 6 years), which reflects the presence of primarily congenital diseases among children with non-glomerular CKD. Children with non-glomerular diagnoses had substantial height deficits (mean height z-score = -0.58 SDs) and normal weight (mean weight z-score = -0.06 SDs). Given the low height and normal weight, the BMI (mean BMI z-score = 0.33 SDs) was greater than the general pediatric population. The WC (mean WC z-score = 0.23 SDs) was also greater than the expected population average (i.e., mean z-score = 0). In contrast, children with glomerular diagnoses did not have as severe height deficits (mean height z-score = -0.19 SDs), were substantially heavier (mean weight z-score = 0.59 SDs), and correspondingly had higher BMI (BMI z-score = 0.76 SDs). The WC in children with glomerular diagnoses were also higher (mean WC z-score = 0.59 SDs).

Table 2 presents agreement by obesity defined by WC percentiles (rows) and BMI percentiles (columns) at baseline and for all person-visits with corresponding Kappa

statistics. At baseline, there was agreement in the estimate of children as being with or without obesity by WC and BMI in 92% in the non-glomerular CKD group and 87% in the glomerular CKD group. Among children with non-glomerular CKD, 23 (4.5%) had obesity by WC criteria but not BMI criteria, and 19 (3.7%) had obesity by BMI criteria but not WC criteria. The Kappa statistic comparing the agreement of these 2 definitions of obesity was 0.68 (95% confidence interval [CI]: 0.59 – 0.77), indicating fair agreement¹⁷. Among children with glomerular CKD, 21 (9.4%) had obesity by WC criteria but not BMI criteria, and 8 (3.6%) had obesity by BMI criteria but not WC criteria. The corresponding Kappa statistic was 0.68 (95% CI: 0.57 – 0.78). The results were consistent when all person-visits were pooled: the proportion of misclassified children was similar and the kappa statistics were 0.67 and 0.72 for children with non-glomerular and glomerular CKD, respectively.

Table 3 presents descriptive statistics of metabolic, cardiovascular and renal outcome variables at baseline and the total number of person-visits contributing data, stratified by CKD diagnosis. By protocol, total cholesterol, HDL, non-HDL and triglyceride data were measured at every other annual visit while glucose was measured at each visit. The mean HDL, triglyceride and glucose levels were similar for children with non-glomerular and glomerular diagnoses. Children with glomerular CKD had higher levels of total cholesterol and non-HDL than children with non-glomerular CKD. HOMA-IR was measured once (n = 221 and 50 for the non-glomerular and glomerular groups, respectively) and was greater in the glomerular group than in the non-glomerular group. For cardiovascular outcomes, systolic and diastolic BP z-scores were determined at every study visit. At baseline, children with non-glomerular CKD had slightly elevated mean systolic BP z-scores (0.23 SDs), while those with glomerular CKD were closer to normal (0.12 SDs). Diastolic BP z-scores were elevated at baseline for both groups (0.37 for children with non-glomerular CKD and 0.29 for children with glomerular CKD). LVMI was measured at every other visit and mean levels at baseline were 30 g/m^{2.7} for both groups. Urine protein:creatinine ratio and eGFR were measured at each visit. Mean baseline levels of urine protein:creatinine were higher among those with a glomerular diagnosis (1.5 mg/mg Cr vs. 0.8 mg/mg Cr). These data were right skewed as the median levels were 0.6 and 0.3 mg/mg creatinine, respectively. Mean baseline levels of eGFR were also higher in the glomerular CKD group (63.8 vs. 52.1 ml/min/1.73m²).

To determine strength of relationships between WC and BMI z-scores and metabolic, cardiovascular and renal outcomes, separate linear regressions were performed within each CKD diagnosis group, with WC z-score as the sole independent variable and then BMI z-score as the sole independent variable. The slopes of these were converted to percent differences when the outcome was not a z-score and are interpreted as the difference associated with a 1 SD increase in WC or BMI. Table 4 describes these slopes, as well as the bootstrapped p values comparing whether the slope determined by WC z-score was different than that determined by BMI z-score.

Among children with non-glomerular CKD, WC z-score was significantly associated with HDL cholesterol, non-HDL cholesterol, triglycerides, glucose, HOMA-IR, systolic BP z-score, LVMI, and urine protein:creatinine ratio. In the same group of children, BMI was significantly associated with all the above markers except for urine protein:creatinine ratio,

but was additionally significantly associated with total cholesterol and diastolic BP z-score. BMI z-score was more strongly associated with LVMI than WC z-score ($p = 0.011$). Additionally, for each SD increase, BMI was associated with 1.68% higher eGFR, although WC was associated with 1.38% lower eGFR, and this difference was statistically significant (p value < 0.001). There were no significant differences in the relationships comparing WC z-score and BMI z-score for metabolic health outcomes, although BMI z-score was borderline significantly different than WC z-score for total cholesterol ($p = 0.081$).

Among children with glomerular CKD, WC z-scores were significantly associated with HDL cholesterol, triglycerides, HOMA-IR, systolic BP z-score, LVMI, and eGFR. BMI z-scores were significantly associated with all the above markers except for triglycerides. For each SD increase, BMI was associated with 6.81% higher eGFR, although WC was associated with 4.34% higher eGFR. The difference in the strength of association with eGFR between BMI and WC was statistically significant ($P = .039$). There were no significant differences in relationships by WC z-scores or BMI z-scores for the remaining eleven outcomes.

Discussion

This study compared WC and BMI in estimating obesity in children with CKD and compared associations between WC and BMI with markers of metabolic, cardiovascular and renal health. There was good agreement between WC and BMI in categorizing CKiD participants with obesity, indicating that both estimated the same underlying construct. For the most part, WC and BMI had similar direction and strength of univariate associations with markers of metabolic, cardiovascular and renal health, but BMI was more positively associated with eGFR.

In otherwise healthy children, measures of central adiposity including WC have been shown to predict independently both metabolic risk factors such as dyslipidemia and insulin resistance^{18,19} and cardiovascular risk factors including hypertension²⁰, higher carotid intima-media thickness²¹, and higher left ventricular mass and diastolic dysfunction²². However, other studies have reported no added benefit of central obesity measures to that provided by BMI in children^{8, 23–25} and our results in children with CKD are consistent with these findings.

In our study, children with glomerular causes of CKD had a higher WC and BMI z-score than children with non-glomerular causes of CKD. One potential explanation for this finding is that the non-glomerular CKD group had a longer period of time with CKD before entering the study (11 vs 6 years) which may have had a greater impact on nutrition and growth (as evidenced by the lower mean height z-score in the non-glomerular CKD group). Differences in WC and BMI by CKD diagnosis group may also be due to a higher prevalence of corticosteroid use among children with glomerular CKD (26% vs. <1%). Although edema was more common among children with glomerular CKD (6.7% vs. 1.0%), this low prevalence could not account for the higher WC and BMI z-scores.

Obesity estimated by WC and BMI was largely congruent among these children with CKD with kappa values between 0.67 and 0.72. However, approximately 10 percent of the study population was identified as obese by one measure but not the other. The discordance was highest in children with glomerular CKD who had obesity by WC but did not have obesity by BMI criteria (9.4%). This again may be explained by children with glomerular disease having a greater exposure to corticosteroids which results in redistribution of body fat to the abdomen. The discordance was less pronounced when the analysis included repeated measurements (6.6%) which may reflect discontinuation of steroid therapy allowing the body fat to redistribute again out of the abdomen. We used the suggested WC percentile cutoffs by Cook et al because these values were shown in a large population of children to correspond with adult definitions of obesity by WC and given the lack of a universally accepted definition of obesity using WC criteria in children.¹³ However, obesity thresholds were different between boys (94th percentile) and girls (84th percentile). This was a potential limitation to compare a single BMI-based threshold for obesity because BMI and WC z-score purport to measure the same construct. However, Kuhle et al found similar thresholds for defining obesity by WC in Canadian children²⁶. As a sensitivity analysis, we replicated the agreement analysis in Table 2 using the 95th percentile of WC as the threshold for both boys and girls and did not find substantially altered kappa statistics (range: 0.67 to 0.75). Further investigation for validating single or sex-specific obesity thresholds for WC in a normal population is needed.

For most of the univariate associations with metabolic variables, there were no differences between WC and BMI z-scores. Similar to the metabolic indicators, there was generally good agreement between WC z-scores and BMI z-scores and associations with cardiovascular markers. Among children with non-glomerular CKD, BMI z-scores had a stronger association with LVMI than WC z-scores and this difference was significant ($p = 0.011$). It is unclear if this stronger association was due to the height being a factor in the calculation of both BMI and LVMI or if there was an underlying biological mechanism to account for BMI z-scores being more strongly associated with LVMI relative to WC z-scores. The BP measurements were used regardless of whether or not subjects were taking anti-hypertensive medications, but because the primary aim was to compare the association of WC and BMI with BP rather than with hypertension category and given the same BP data were used in the univariate associations with WC and BMI, the results comparing how WC and BMI associated with BP were still valid.

For urine protein:creatinine ratio, there was a trend towards a stronger association with WC z-scores compared with BMI z-scores for both glomerular and non-glomerular CKD groups, although these results did not reach statistical significance. This trend was consistent with previous reports associating central adiposity with unfavorable renal hemodynamics and glomerular hyperfiltration after adjustment for BMI²⁷ and an increased risk for albuminuria has been reported in young adult populations with increased WC²⁸. Notably, among children with glomerular CKD, higher WC and BMI z-scores were associated with higher eGFR, with BMI z-scores being more strongly associated than WC z-scores ($p = 0.039$). Similarly, longitudinal studies of adult CKD patients found more favorable outcomes of CKD progression in the overweight and mildly obese BMI ranges although outcomes worsened with progressively higher BMI²⁹. The finding of higher WC and BMI being associated with

higher eGFR may reflect wasting and poor appetite associated with more severe CKD^{30,31} or potential non-linear relationships not captured by the model (as was noted in the study by Lu et al²⁹). Additionally, a higher (and healthier) lean body mass among those with a glomerular diagnosis and obesity may partially explain why higher z-scores of BMI and WC were associated with increased eGFR.

Among those with non-glomerular CKD, the direction of association of WC z-scores and eGFR was different than that of BMI z-score and eGFR ($p < 0.001$), although neither association was significantly different than 0. The reason for the incongruent relationship between WC and BMI and eGFR in the non-glomerular CKD group compared with both WC and BMI having the same direction of relationship with eGFR in the glomerular CKD group is not clear. One possible explanation is that given the longer duration of CKD before study entry in the non-glomerular CKD group, it is possible that chronic hyperfiltration associated with central obesity resulted in lower eGFR over time, but we cannot draw conclusions on this hypothesis given the cross-sectional nature of this study. It should also be noted that identifying glomerular hyperfiltration in those with CKD is largely theoretical and this hypothesis should be explored in other studies. In addition, there may be confounding by steroid use both causing increased WC/BMI and leading to higher eGFR by treating the underlying disease in children with glomerular CKD.

The strengths of this study included the use of a large, well-characterized cohort of children with CKD of diverse underlying cause and heterogeneity of body sizes. Additionally, the CKiD protocols ensured standardized procedures, including calculations of BMI and WC, across study sites. There were also several limitations to this study. First, the analyses of univariate associations (Table 4) were based on slope-intercept models and did not account for non-linearity. These comparisons were still valid as both WC and BMI had the same model constraints. However, it should be noted that these summaries of associations are simplified relationships that were used as metrics of agreement, rather than a comprehensive epidemiologic description of the relationships of WC and BMI with metabolic, cardiovascular and renal health parameters. Second, HOMA-IR was measured in a small subset of participants and we cautiously present inferences for this outcome due to the relatively small sample size. Nonetheless, this metabolic outcome was closely related to both WC and BMI z-scores. Third, although the process of measuring WC was standardized across sites, there may be more potential for measurement error in WC than BMI because measurement of WC may be more prone to variation in technique compared with measurement of BMI, which is done with calibrated instruments.

Because WC and BMI provide similar value in classification of obesity and associations with relevant biomarkers, BMI may be preferred to WC in clinical practice as it is may be easier to obtain and interpret. However, further study of these measures appears to be warranted, especially longitudinal assessment of how WC and BMI predict metabolic, cardiovascular and renal outcomes, particularly for children identified as obese by one measure but not the other.

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Abbreviations

BMI	Body mass index
BP	Blood pressure
CI	Confidence interval
CKD	Chronic kidney disease
CKiD	Chronic Kidney Disease in Children study
GFR	estimated glomerular filtration rate
HDL	High density lipoprotein
HOMA-IR	Homeostatic model assessment and insulin resistance
LMS	Least mean squares
LVMI	Left ventricular mass index
SD	Standard deviation
WC	Waist circumference

References

1. Parekh RS, Carroll CE, Wolfe RA, Port FK. Cardiovascular mortality in children and young adults with end-stage kidney disease. *J Pediatr*. 2002; 141:191–7. [PubMed: 12183713]
2. Wilson AC, Mitsnefes MM. Cardiovascular disease in CKD in children: update on risk factors, risk assessment, and management. *Am J Kidney Dis*. 2009; 54:345–60. [PubMed: 19619845]
3. Mitsnefes M. Cardiovascular disease in children with chronic kidney disease. *J Am Soc Nephrol*. 2012; 23:578–85. [PubMed: 22383696]
4. Wilson AC, Schneider MF, Cox C, Greenbaum LA, Saland J, White CT, et al. Prevalence and correlates of multiple cardiovascular risk factors in children with chronic kidney disease. *Clin J Am Soc Nephrol*. 2011; 6:2759–65. [PubMed: 21980183]
5. Furth SL, Abraham AG, Jerry-Fluker J, Schwartz GJ, Benfield M, Kaskel F, et al. Metabolic abnormalities, cardiovascular disease risk factors, and GFR decline in children with chronic kidney disease. *Clin J Am Soc Nephrol*. 2011; 6:2132–40. [PubMed: 21841064]
6. Javed A, Jumean M, Murad MH, Okorodudu D, Kumar S, Somers VK, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity in children and

- adolescents: a systematic review and meta-analysis. *Pediatr Obes.* 2015; 10:234–44. [PubMed: 24961794]
7. Zoccali C, Torino C, Tripepi G, Mallamaci F. Assessment of obesity in chronic kidney disease: what is the best measure? *Curr Opin Nephrol Hypertens.* 2012; 21:641–6. [PubMed: 23010758]
 8. Reilly JJ, Kelly J, Wilson DC. Accuracy of simple clinical and epidemiological definitions of childhood obesity: systematic review and evidence appraisal. *Obes Rev.* 2010; 11:645–55. [PubMed: 20059704]
 9. Flynn JT, Mitsnefes M, Pierce C, Cole SR, Parekh RS, Furth SL, et al. Blood pressure in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children study. *Hypertension.* 2008; 52:631–7. [PubMed: 18725579]
 10. Furth SL, Cole SR, Moxey-Mims M, Kaskel F, Mak R, Schwartz G, et al. Design and methods of the Chronic Kidney Disease in Children (CKiD) prospective cohort study. *Clin J Am Soc Nephrol.* 2006; 1:1006–15. [PubMed: 17699320]
 11. Sharma AK, Metzger DL, Daymont C, Hadjiyannakis S, Rodd CJ. LMS tables for waist-circumference and waist-height ratio Z-scores in children aged 5–19 y in NHANES III: association with cardio-metabolic risks. *Pediatr Res.* 2015; 78:723–9. [PubMed: 26331767]
 12. Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, Wei R, et al. Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. *Pediatrics.* 2002; 109:45–60. [PubMed: 11773541]
 13. Cook S, Auinger P, Huang TT. Growth curves for cardio-metabolic risk factors in children and adolescents. *J Pediatr.* 2009; 155:S6.e15–26.
 14. Barlow SE, the Expert Committee. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics.* 2007; 120:S164–S192. [PubMed: 18055651]
 15. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. *Pediatrics.* 2004; 114:555–576. [PubMed: 15286277]
 16. Schwartz GJ, Schneider MF, Maier PS, Moxey-Mims M, Dharnidharka V, Warady BA, et al. Improved equations estimating GFR in children with chronic kidney disease using an immunonephelometric determination of cystatin C. *Kidney Int.* 2012; 82:445–53. [PubMed: 22622496]
 17. Fleiss, JL. Statistical methods for rates and proportions. 2nd. New York: John Wiley; 1981.
 18. Watts K, Bell LM, Byrne SM, Jones TW, Davis EA. Waist circumference predicts cardiovascular risk in young Australian children. *J Paediatr Child Health.* 2008; 44:709–15. [PubMed: 19077071]
 19. Samouda H, de Beaufort C, Stranges S, Guinhouy BC, Gilson G, Hirsch M, et al. Adding anthropometric measures of regional adiposity to BMI improves prediction of cardiometabolic, inflammatory and adipokines profiles in youths: a cross-sectional study. *BMC Pediatr.* 2015; 15:168. [PubMed: 26497052]
 20. Genovesi S, Antolini L, Giussani M, Pieruzzi F, Galbiati S, Valsecchi MG, et al. Usefulness of waist circumference for the identification of childhood hypertension. *J Hypertens.* 2008; 26:1563–70. [PubMed: 18622233]
 21. Kollias A, Psilopatis I, Karagiaouri E, Glaraki M, Grammatikos E, Grammatikos EE, et al. Adiposity, blood pressure, and carotid intima-media thickness in Greek adolescents. *Obesity.* 2013; 21:1013–7. [PubMed: 23784905]
 22. Mehta SK, Richards N, Lorber R, Rosenthal GL. Abdominal obesity, waist circumference, body mass index, and echocardiographic measures in children and adolescents. *Congenit Heart Dis.* 2009; 4:338–47. [PubMed: 19740188]
 23. Huxley R, Mendis S, Zheleznyakov E, Reddy S, Chan J. Body mass index, waist circumference and waist:hip ratio as predictors of cardiovascular risk – a review of the literature. *Eur J Clin Nutr.* 2010; 64:16–22. [PubMed: 19654593]
 24. Lawlor DA, Benfield L, Logue J, Tilling K, Howe LD, Fraser A, et al. Association between general and central adiposity in childhood, and change in these, with cardiovascular risk factors in adolescence: prospective cohort study. *BMJ.* 2010; 341:c6224. [PubMed: 21109577]

25. Sardinha LB, Santos DA, Silva AM, Grontved A, Andersen LB, Ekelund U. A comparison between BMI, waist circumference, and waist-to-height ratio for identifying cardio-metabolic risk in children and adolescents. *PLoS One*. 2016; 11:e0149351. [PubMed: 26901828]
26. Kuhle S, Maguire B, Ata N, Hamilton D. Percentile curves for anthropometric measures for Canadian children and youth. *PLoS One*. 10:e0132891.
27. Kwakernaak AJ, Zelle DM, Bakker SJ, Navis G. Central body fat distribution associates with unfavorable renal hemodynamics independent of body mass index. *J Am Soc Nephrol*. 2013; 24:987–94. [PubMed: 23578944]
28. Sarathy H, Henriquez G, Abramowitz MK, Kramer H, Rosas SE, Johns T, et al. Abdominal obesity, race and chronic kidney disease in young adults: results from NHANES 1999–2010. *PLoS One*. 11:e0153588.
29. Lu JL, Kalantar-Zadeh K, Ma JZ, Quarles LD, Kovesdy CP. Association of body mass index with outcomes in patients with CKD. *J Am Soc Nephrol*. 2014; 25:2088–96. [PubMed: 24652789]
30. Abraham AG, Mak RH, Mitsnefes M, White C, Moxey-Mims M, Warady B, et al. Protein energy wasting in children with chronic kidney disease. *Pediatr Nephrol*. 2014; 29:1231–8. [PubMed: 24504731]
31. Ayestaran FW, Schneider MF, Kaskel FJ, Srivaths PR, Seo-Mayer PW, Moxey-Mims M, et al. Perceived appetite and clinical outcomes in children with chronic kidney disease. *Pediatr Nephrol*. 2016; 31:1121–7. [PubMed: 26857711]

Table 1

Demographic and clinical characteristics at study enrollment, stratified by underlying chronic kidney disease diagnosis. Mean (standard deviation) and N (%). P values based on t-test for continuous variables or Fisher's exact test for categorical variables.

Variable	CKD diagnosis		P Value
	Non-glomerular	Glomerular	
N	513	224	
Age at study visit, years	11.3 (4.0)	13.6 (3.6)	<0.001
Years since CKD onset	10.7 (4.2)	5.6 (4.7)	<0.001
Male sex	330 (64.3%)	117 (52.2%)	0.002
Race Category			<0.001
Caucasian	358 (69.8%)	121 (54.0%)	
Black	97 (18.9%)	67 (29.9%)	
Other	58 (11.3%)	36 (16.1%)	
Number of visits with available anthropometric data ^a	4 [3, 6]	4 [2, 5]	<0.001
Height, cm	140.4 (22.1)	154.4 (19.3)	<0.001
Weight, kg	41.2 (19.6)	58.3 (25.8)	<0.001
Body mass index, kg/m ²	19.7 (4.9)	23.3 (6.9)	<0.001
Mean waist circumference, cm	68.7 (13.9)	79.0 (18.2)	<0.001
Height/length z-score adjusted for age and gender	-0.58 (1.15)	-0.19 (1.21)	<0.001
Weight z-score adjusted for age and gender	-0.06 (1.34)	0.59 (1.42)	<0.001
Body mass index z-score adjusted for age and gender	0.33 (1.18)	0.76 (1.21)	<0.001
Waist circumference z score adjusted for age and gender	0.23 (1.01)	0.59 (1.01)	<0.001
Edema	5 (1.0%)	15 (6.7%)	<0.001

Abbreviations: CKD, chronic kidney disease

^aMedian and interquartile range presented for number of available visits.

Concordance of obesity defined by waist circumference (WC) z-scores and body mass index (BMI) z-scores, stratified by underlying chronic kidney disease (CKD) diagnosis at baseline. For BMI, obesity was defined as 95th percentile for all children. For WC, obesity was defined as 94th percentile for boys and 84th percentile for girls¹³.

Table 2

	Non-glomerular CKD		Glomerular CKD	
	BMI Without obesity	BMI With obesity	BMI Without obesity	BMI With obesity
Baseline	WC Without obesity	415 (80.9%)	19 (3.7%)	148 (66.1%)
	WC With obesity	23 (4.5%)	56 (10.9%)	21 (9.4%)
	Kappa (95%CI)	0.68 (0.59, 0.77)		0.68 (0.57, 0.78)
	WC Without obesity	1805 (81.5%)	88 (4.0%)	558 (69.8%)
All Visits	WC With obesity	94 (4.2%)	229 (10.3%)	53 (6.6%)
	Kappa (95%CI)	0.67 (0.62, 0.71)		0.72 (0.66, 0.78)

Abbreviations: BMI, body mass index; CKD, chronic kidney disease; WC, waist circumference

Table 3

Descriptive statistics of first available metabolic, cardiovascular and renal health data and number of available person visits, by underlying chronic kidney disease diagnosis. Mean (standard deviation) and total person-visits [n].

Variable	Non-glomerular	Glomerular
<i>Metabolic health</i>		
Total Cholesterol (mg/dL)	167.2 (35.0) [976]	178.4 (60.5) [285]
HDL cholesterol (mg/dL)	52.1 (14.0) [976]	53.2 (14.9) [285]
Non-HDL cholesterol (mg/dL)	115.1 (34.1) [975]	125.2 (57.9) [285]
Triglycerides (mg/dL)	119.3 (73.8) [976]	120.4 (75.3) [285]
Glucose (mg/dL)	92.0 (13.6) [2,020]	93.4 (19.6) [649]
HOMA-IR	2.2 (2.2) [221]	3.3 (3.3) [50]
<i>Cardiovascular health</i>		
Systolic BP z-score	0.23 (1.11) [2,165]	0.12 (1.23) [783]
Diastolic BP z-score	0.37 (0.93) [2,165]	0.29 (0.97) [782]
LVMI (units g/m ^{2.7})	30.3 (8.9) [742]	31.0 (9.7) [212]
<i>Renal health</i>		
Urine protein, mg/mg creatinine	0.8 (1.6) [2,041]	1.5 (2.7) [653]
eGFR, ml/min/1.73m ²	52.1 (18.4) [2,031]	63.8 (22.2) [648]

Abbreviations: HDL, high density lipoproteins; HOMA-IR, homeostatic model assessment-insulin resistance; BP, blood pressure; LVMI, left ventricular mass index; eGFR, estimated glomerular filtration rate based on 2012 equation¹⁶.

Table 4

Univariate associations of waist circumference (WC) z-scores and body mass index (BMI) z-scores with markers of metabolic, cardiovascular and renal health. The slope from the WC model was compared with the BMI model using bootstrapping methods. **Bold** indicates $p < 0.05$.

Dependent Variable	Non-Glomerular CKD diagnosis		Glomerular CKD diagnosis	
	Per 1 unit change in WC z-score	Per 1 unit change in BMI z-score	Per 1 unit change in WC z-score	Per 1 unit change in BMI z-score
Metabolic health				
Total Cholesterol (mg/dL) (95% CI)	1.03% (−0.51%, 2.59%)	2.41% (0.98%, 3.85%)	−1.70% (−4.86%, 1.56%)	−1.12% (−3.96%, 1.80%)
P for difference	0.081		0.705	
HDL cholesterol (mg/dL) (95% CI)	−5.84% (−7.68%, −3.96%)	−4.60% (−6.39%, −2.79%)	−8.11% (−10.64%, −5.50%)	−5.75% (−8.34%, −3.08%)
P for difference	0.232		0.143	
Non-HDL cholesterol (mg/dL) (95% CI)	4.16% (2.10%, 6.27%)	5.65% (3.59%, 7.75%)	1.61% (−2.73%, 6.15%)	1.37% (−2.60%, 5.51%)
P for difference	0.160		0.940	
Triglycerides (mg/dL) (95% CI)	13.30% (9.15%, 17.61%)	12.76% (8.82%, 16.85%)	8.51% (2.03%, 15.41%)	4.93% (−1.13%, 11.36%)
P for difference	0.773		0.667	
Glucose (mg/dL) (95% CI)	1.10% (0.31%, 1.89%)	0.96% (0.26%, 1.67%)	0.76% (−1.15%, 2.70%)	0.04% (−1.82%, 1.94%)
P for difference	0.670		0.319	
HOMA-IR (95% CI)	29.15% (15.91%, 43.91%)	27.66% (16.45%, 39.94%)	30.95% (9.60%, 56.47%)	29.24% (13.46%, 47.22%)
P for difference	0.957		0.981	
Cardiovascular health				
Systolic BP z-score (95% CI)	0.11 (0.06, 0.17)	0.15 (0.09, 0.20)	0.19 (0.09, 0.30)	0.24 (0.15, 0.33)
P for difference	0.205		0.310	
Diastolic BP z-score (95% CI)	0.03 (−0.01,0.08)	0.05 (0.00, 0.09)	−0.03 (−0.12, 0.05)	−0.01 (−0.08, 0.07)
P for difference	0.469		0.331	
LVMI (units g/m ^{2.7}) (95% CI)	5.79% (3.33%, 8.32%)	8.54% (6.47%, 10.65%)	11.44% (6.28%, 16.86%)	10.40% (6.42%, 14.53%)
P for difference	0.011		0.879	
Renal health				
Urine protein:creatinine (95% CI)	7.51% (0.45%, 15.06%)	3.68% (−3.51%, 11.40%)	10.46% (−2.32%, 24.91%)	2.41% (−9.35%, 15.69%)
P for difference	0.287		0.122	
eGFR, ml/min/1.73m ² (95% CI)	−1.38% (−3.29%, 0.55%)	1.68% (−0.60%, 4.02%)	4.34% (0.00%, 8.88%)	6.81% (2.67%, 11.12%)
P for difference	<.001		0.039	

Abbreviations: HDL, high density lipoproteins; HOMA-IR, homeostatic model assessment-insulin resistance; BP, blood pressure; LVMI, left ventricular mass index; eGFR, estimated glomerular filtration rate based on 2012 equation¹⁶.