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Accuracy of anthropometric measurements in estimating fat mass in individuals with 21-hydroxylase deficiency

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ABSTRACT

Objective: The use of anthropometric measurements to estimate the percentage of body fat (%BF) is easy and inexpensive. However, the accuracy of these methods in patients with 21-hydroxylase deficiency (21OHD) has not been explored. The objective of this study was to evaluate the accuracy of skinfold-based models, body mass index (BMI), and waist circumference (WC) in estimations of %BF using dual-energy X-ray absorptiometry (DXA) as the reference method in individuals with 21OHD.**Methods:** Fifty-four 21OHD patients (32 women and 22 men), aged 7 to 20 y, were recruited for the study. DXA was used to determine %BF; four predictive skinfold equations, BMI, and WC were assessed for accuracy in determining %BF.**Results:** All predictive skinfold equations were highly associated (R , range: 0.82–0.89) with DXA %BF values. In women, BMI and WC showed moderate correlations ($R = 0.69$ for both BMI and WC) with DXA values. In contrast, among men there was a low explanatory power for BMI (13%) and WC (4%) and high errors (BMI, 6.9%; WC, 7.4%). All predictive equations significantly underestimated %BF (range of differences, -4.1 to -8.9) compared with DXA (women, 31.3 ± 6.1 ; men, 24.4 ± 7.3), and large limits of agreement were observed (range, -15.3 to 1.7 and -15.5 to 4.2 for women and men, respectively).**Conclusion:** In children and adolescents with 21OHD, %BF as estimated by skinfold measurements was associated more strongly with DXA-assessed %BF than both BMI and WC. However, still, the skinfold-based assessment underestimated DXA %BF and showed moderate agreement.© 2012 Elsevier Inc. Open access under the [Elsevier OA license](http://www.elsevier.com/locate/elsevier/oa).

Introduction

The most common enzyme impairment in congenital adrenal hyperplasia (CAH) is 21-hydroxylase deficiency (21OHD), accounting for more than 90% of cases [1]. The classic form of 21OHD is divided into two variants: simple-virilizing (SV), characterized by deficient cortisol production and increased androgen production, and salt-wasting (SW). In the SW form,

a deficiency in aldosterone production can occur, in addition to the same symptoms observed in SV [2]. The treatment of the classic form of 21OHD uses the lowest possible glucocorticoid dose to replace cortisol and aldosterone effectively and control the symptoms of androgen excess. However, if this replacement is not adequate, then patients can present with states of hyperandrogenism or hypercortisolism. The former can cause early puberty, infertility, and increases in lean mass; the latter can lead to insulin resistance, osteoporosis, and obesity [3–5].

The measurement of body composition is an important tool for pediatric research and clinical settings, because obesity is

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associated with an increased risk of several health problems in children and adolescents [6]. Several methods have been used to assess body composition in children and adolescents, and anthropometry [e.g., body mass index (BMI), waist circumference (WC), and skinfold thickness] is commonly used because it is a simple, noninvasive, and inexpensive technique compared with other laboratory-based methods. However, the selection of the best anthropometric measurement for the identification and control of excess adiposity is not without controversy [7–11]. BMI is important and useful at a population level, but it does not discriminate between lean mass and fat mass in an individual. WC is an important indicator of childhood obesity related to visceral fat rather than total body fat [12]. This may be especially important in patients with CAH who could develop increased trunk fat caused by glucocorticoid treatment [13].

Skinfold thickness is accepted as a predictor of body fatness because subcutaneous fat (40%–60% of total body fat) can be directly measured with a caliper. However, these measurements only provide an estimate of subcutaneous fat and cannot be used reliably to measure fat stored internally, such as visceral fat. Additionally, fat measurement using skinfolds is associated with many factors that can affect its accuracy and precision [7,14]. The use of a standardized method increases the reliability of skinfold thickness measurements, and the selection of equations that properly predict body fat mass can increase accuracy [11,14]. Skinfold equations used to predict total body fat from subcutaneous skinfold measurements in children and adolescents are generally based on samples of healthy individuals [11,15,16], and the accuracy in CAH patients has not yet been explored.

Dual-energy X-ray absorptiometry (DXA) is a technique that measures whole and segmental body fat and lean body mass. DXA is considered a valid and reliable method of assessing body composition, and it is commonly used as a reference technique in pediatric populations [11,14,17,18].

Because CAH 21OHD can alter body composition and distribution (fat trunk increment more particularly), mainly due to glucocorticoid treatment, the purpose of this study was to determine the accuracy of BMI, WC, and skinfold-based models in the estimation of the percentage of body fat (%BF) using DXA as the reference method in individuals with classic CAH 21OHD.

Materials and methods

Patients

We included 54 patients (32 women and 22 men), aged 7 to 20 y. All subjects were diagnosed with classic CAH 21OHD (16 SV and 38 SW), confirmed by clinical, hormonal, and molecular analyses [19–22]. These patients were diagnosed and followed at the Outpatient Pediatric Endocrinology Clinic of the Clinical Hospital of the University of Campinas (UNICAMP), Brazil, for at least 3 y [treatment duration (mean \pm SD), 12.5 \pm 4.4 y].

The patients were classified according to the criteria of Marshall and Tanner [23,24] for pubertal development by a pediatric endocrinologist as prepubertal ($n = 18$, stages I and II), pubertal ($n = 9$, stage III), and postpubertal ($n = 27$, stage IV or above and/or menarche in girls).

Experimental design

This was a cross-sectional study. All evaluations were performed on the day of the outpatient clinic visit. The study was approved by the Research Ethics Committee of UNICAMP and conducted in accordance with the declaration of Helsinki for human studies. Written informed consents were provided by all individuals or their legal guardians.

Anthropometric measurements

Anthropometric measurements (body weight in kilograms, and height and WC in centimeters) were performed by a skilled researcher using standardized procedures and conditions [25]. These data were used to calculate BMI (kg/m²),

and the absolute values were transformed into z-scores using the 2000 publication by the National Center of Health Statistics as a reference [26]. The skinfold measurements were made on the right side of the body at appropriately marked sites using a Lange caliper (Cambridge Scientific Instruments, Cambridge, MA, USA). The skinfold measurements were made at the triceps, calf, subscapular, biceps, and suprailiac sites according to standardized anatomic locations and methods [25]. On the basis of test-retest reliability using eight subjects, the technical error of measurement values for the triceps, calf, subscapular, biceps, and suprailiac skinfold measurements were 0.50 mm (3.3%), 0.43 mm (2.5%), 0.43 mm (4.3%), 0.35 mm (4.0%), and 0.56 mm (2.4%), respectively.

Four pediatric skinfold prediction equations were used to estimate %BF. Two equations were developed by Slaughter et al. [15]: Slaughter 1 = sum of triceps and medial calf skinfolds; and Slaughter 2 = sum of triceps and subscapular skinfolds. Two equations were developed by Deurenberg et al. [16]: Deurenberg 1 = log of sum of biceps and triceps skinfolds; and Deurenberg 2 = log of sum of biceps, triceps, suprailiac, and subscapular skinfolds. The equations used in the present study were selected for their validity before being applied to a clinical setting and met two criteria. First, the equations were recommended for children and adolescents (Slaughter et al. [15] equations: 8–18 y old; Deurenberg et al. [16] equations: 7–20 y old). Second, the equations included both sexes, but considered the influence of differences between the sexes and pubertal development, because the quantity of body fat and its distribution pattern are influenced by sex and pubertal development stage more than by age [14].

Dual energy X-ray absorptiometry

The %BF reference values were obtained by DXA. Whole-body DXA exams were performed according to the procedures recommended by the manufacturer on a fan beam Hologic model Discovery Wi densitometer, software version 12.7 (Hologic, Bedford, MA, USA). The densitometer was calibrated daily according to the manufacturer's recommendations.

Statistical analysis

For database and statistical analyses, SPSS version 18.0 (Statistical Package for the Social Sciences, Chicago, IL, USA) was used. The normal distribution of the data was tested using the Shapiro-Wilk test. The data were described using the mean and \pm SD for variables with a normal distribution (i.e., age, weight, BMI, triceps skinfold, suprailiac skinfold, and calf skinfold) and median and range (minimum and maximum values) for variables without a normal distribution (i.e., height, BMI z-score, biceps skinfold, and subscapular skinfold). Differences between the reference method (DXA) and each predictive equation (Slaughter 1 and 2 and Deurenberg 1 and 2) were calculated using paired-sample *t* tests. Independent-sample *t* tests were used to compare variables between sexes. Mann-Whitney *U*-tests were used as the alternative to the independent-sample *t* test, if the data did not present a normal distribution. Linear regression analysis was performed to assess the accuracy of each predictive equation to estimate %BF compared with DXA. The models were developed separately for women and men. To test whether the regression line differed from the line of identity, the slope and intercept were tested. If the slope was not different from 1, and the intercept was not different from 0, then the regression would not differ from the line of identity. Additionally, the standard error of estimate (SEE), coefficient of determination adjusted (R^{2adj}), and the coefficient of correlation (*R*) were analyzed. Agreement between the predictive equations and the reference method was assessed using the Bland-Altman method [27]. Pearson's bivariate correlations (*R*) were conducted to determine whether the difference between each predictive equation and the reference method was related to the mean of the two measurements (trends) in men and women. For all tests, statistical significance was established at $P < 0.05$.

Results

The general characteristics and body composition results of the 21OHD patients are presented in Table 1. Women had significantly higher values for biceps, triceps, and calf skinfold measurements ($P < 0.05$) for %BF measured by DXA compared with the four predictive equations ($P < 0.001$). All predictive equations demonstrated lower %BF values ($P < 0.001$) compared with DXA for both sexes (Table 1).

Figure 1 illustrates the relationship between %BF measured by DXA and the predictive skinfold equations, BMI, and WC. The %BF values estimated by four predictive skinfold equations demonstrated a significantly high correlation ($P < 0.001$) with the reference method for both sexes (women and men, respectively):

Table 1
General characteristics and body composition of the 21-hydroxylase deficiency patients

	Women	Men	Total
N	32	22	54
Age (y)	13.9 ± 4	13.2 ± 4.2	13.7 ± 4.1
Weight (kg)	48.5 ± 16.0	50.8 ± 15.5	49.5 ± 15.7
Height (cm)	150.3 (116.0, 172.0)	155.7 (119.0, 179.5)	151.2 (116.0, 179.5)
Body mass index (kg/m ²)	21.7 ± 4.5	21.5 ± 3.1	21.6 ± 3.9
BMIZ (z-scores)	0.67 (−1.49, 1.94)	0.75 (−0.60, 2.27)	0.71 (−1.49, 2.27)
Waist circumference (cm)	66.5 ± 9.6	68.8 ± 7.7	67.5 ± 8.9
Biceps SKF (mm)	8.5 (3, 19) [†]	5 (3, 14)	7 (3, 19)
Triceps SKF (mm)	15.9 ± 5.2 [†]	12.8 ± 4.5	14.6 ± 5.1
Suprailiac SKF (mm)	25.2 ± 12.3	20.2 ± 9.1	23.1 ± 11.3
Subscapular SKF (mm)	11 (5, 33)	10 (5, 24)	10.5 (5, 33)
Calf SKF (mm)	18.3 ± 6.8 [*]	14.0 ± 5.2	16.6 ± 6.5
%BF DXA (%)	31.3 ± 6.1 [*]	24.4 ± 7.3	28.5 ± 7.4
%BF Slaughter 1 (%)	25.7 ± 6.2 ^{*‡}	20.8 ± 7.0 [‡]	23.7 ± 6.9 [‡]
%BF Slaughter 2 (%)	24.4 ± 7.2 ^{*‡}	20.3 ± 7.2 [‡]	22.7 ± 7.5 [‡]
%BF Deurenberg 1 (%)	22.4 ± 4.8 ^{*‡}	16.9 ± 4.7 [‡]	20.1 ± 5.4 [‡]
%BF Deurenberg 2 (%)	25.7 ± 6.1 ^{*‡}	18.5 ± 4.7 [‡]	22.8 ± 6.6 [‡]

BF, body fat; BMIZ, body mass index z-scores; DXA, dual-energy X-ray absorptiometry; SKF, skinfold thickness
The data are expressed as mean ± SD or median (range)

* Significantly different from men (*t* test for independent samples, $P < 0.05$).

[†] Significantly different from men (Mann-Whitney *U*-test, $P < 0.05$).

[‡] Significantly different from the reference method (*t* test for paired samples, $P < 0.001$).

Slaughter equation 1, $R = 0.82$ and 0.87 ; Slaughter equation 2, $R = 0.85$ and 0.83 ; Deurenberg equation 1, $R = 0.85$ and 0.86 ; Deurenberg equation 2, $R = 0.88$ and 0.89 (Fig. 1A–D). BMI and WC were not significantly associated with %BF assessed by DXA among men (BMI: $R = 0.41$, $P = 0.06$; WC: $R = 0.20$, $P = 0.36$) and only moderately among women ($R = 0.69$ for both BMI and WC, $P < 0.001$) (Fig. 1E and 1F).

The regression analysis demonstrated that Slaughter equation 1 explained 66% and 74% and Slaughter equation 2 explained 72% and 69% of the variance in DXA values for women and men, respectively. The %BF estimated by the Deurenberg equations explained between 72% and 78% of the variance in DXA %BF values. Among men, there was a low explanatory power for BMI (13%) and WC (4%), and among women the BMI and WC explained 46% of the variance in DXA values.

The SEE for the predictive skinfold equations ranged from 3.0% to 3.6% among women and from 3.5% to 4.2% among men. BMI and WC showed high values for SEE (6.89% and 7.39% for BMI and WC, respectively). WC, BMI of women, BMI of men, and skinfolds of men for all equations, except Deurenberg equation 1, differed significantly from the regression line of identity (intercept and/or slope) (Fig. 1A–F).

The results of the Bland-Altman analysis in women and men are presented in Figure 2. The 95% limits of agreement (95% LOA) indicate large individual variability between these two measurements in 21OHD patients using Slaughter equation 1 (range, −12.8 to 1.7 and −10.9 to 3.6 for women and men, respectively) and Slaughter equation 2 (range, −14.4 to 0.6 and −12.4 to 4.2 for women and men, respectively) and significantly underestimated %BF determined by DXA (Slaughter equation 1 mean bias, −5.6 and −3.6 for women and men, respectively; Slaughter equation 2 mean bias, −6.9 and −4.1 for women and men, respectively). No significant trends (R) were found between the difference and the mean of both methods using the two Slaughter equations (Fig. 2A and 2B).

The Deurenberg equations exhibited large 95% LOA, ranging from −15.3 to −2.6 for women and −15.5 to 0.6 for men using Deurenberg equation 1 and from −11.6 to 0.4 for women and −13.4 to 1.6 for men using Deurenberg equation 2. The means of bias were −8.9 for women and −7.5 for men using Deurenberg

equation 1 and −5.6 for women and −5.9 for men using Deurenberg equation 2. A significant association was found between the difference in %BF using Deurenberg equation 1 and DXA and the mean of the two methods for women ($R = -0.42$, $P < 0.05$) and men ($R = -0.67$, $P < 0.01$) and Deurenberg equation 2 for men ($R = -0.70$, $P < 0.001$) (Fig. 2C and 2D).

Discussion

Our data demonstrated that in this sample, the %BF calculated by the four predictive skinfold equations was highly associated with the reference method. Furthermore, BMI and WC were moderately associated with DXA-assessed %BF among women and were not significantly associated among men. Although the skinfold equations systematically underestimated the %BF values obtained by DXA, at an individual level, the equations presented poor accuracy and, in some cases, depended on the level of body fat, indicating that %BF is overestimated in lean subjects and underestimated in obese subjects (Fig. 2C and 2D).

To our knowledge, this is the first study that addressed the validity of anthropometric measurements in children and adolescents with 21OHD. The accuracy of the predictive skinfold equations, BMI, and WC in assessing %BF was determined at the group level, and our results obtained from the four predictive equations for both sexes were significantly lower than the reference method. Similar results were reported previously [17, 18,28] in studies that attempted to validate Slaughter's equation in prepubertal children and in a multiethnic, representative sample of adolescents girls, although no significant differences were observed in a male sample aged 8 to 26 y [28]. The predictive equations were strongly associated with the reference method. These high associations were similar to the observed correlations in a sample of healthy male and female children and adolescents [28] and young children (aged 3 to 8 y) [17] that evaluated the Slaughter equation. In our study, BMI and WC showed moderate correlations among women, but were not significantly associated with DXA measurements of %BF among men. Recent studies in a representative pediatric sample suggested that skinfold-based models are more accurate than BMI and WC at estimating %BF in children [11].

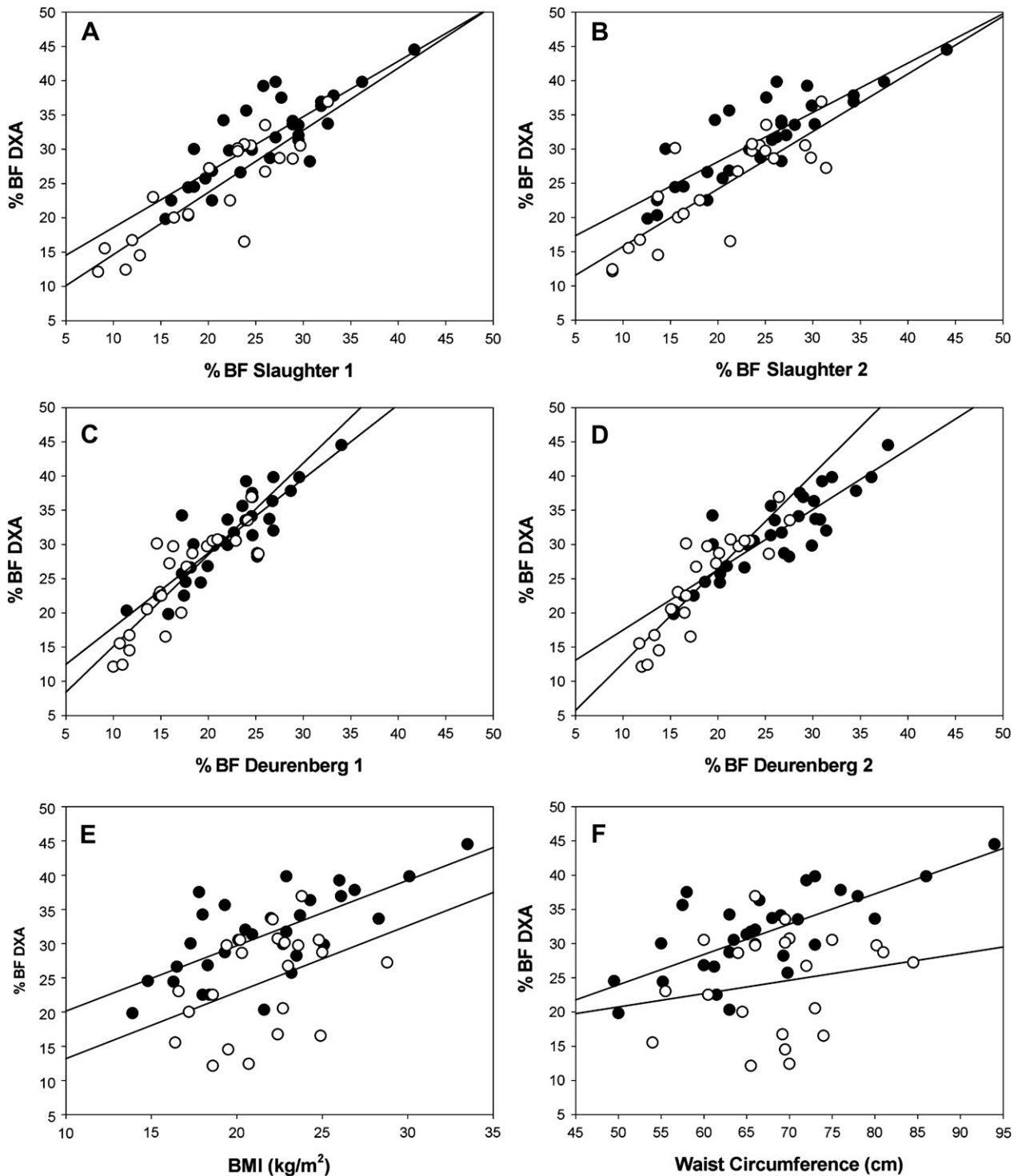


Fig. 1. Relationship between (●) female and (○) male body fat percentage using dual-energy X-ray absorptiometry (%BF DXA). (A) Slaughter skinfold equation 1 (%BF; women: $y = 10.8 + 0.8x$, coefficient of correlation [R] = 0.82, coefficient of determination adjusted [R^2_{adj}] = 0.66, standard error of estimation [SEE] = 3.6%; men: $y = 5.6 + 0.9x$, $R = 0.87$, $R^2_{adj} = 0.74$, SEE = 3.7%). (B) Slaughter skinfold equation 2 (%BF; women: $y = 13.7 + 0.7x$, $R = 0.85$, $R^2_{adj} = 0.72$, SEE = 3.3%; men: $y = 7.4 + 0.8x$, $R = 0.83$, $R^2_{adj} = 0.69$, SEE = 4.2%). (C) Deurenberg skinfold equation 1 (%BF; women: $y = 7.1 + 1.1x$, $R = 0.85$, $R^2_{adj} = 0.72$, SEE = 3.3%; men: $y = 1.7 + 1.3x$, $R = 0.86$, $R^2_{adj} = 0.73$, SEE = 3.9%). (D) Deurenberg skinfold equation 2 (%BF; women: $y = 8.7 + 0.9x$, $R = 0.88$, $R^2_{adj} = 0.76$, SEE = 3.0%; men: $y = -1.15 + 1.38x$, $R = 0.89$, $R^2_{adj} = 0.78$, SEE = 3.5%). (E) Body mass index (BMI; women: $y = 10.6 + 1.0x$, $R = 0.69$, $R^2_{adj} = 0.46$, SEE = 4.5%; men: $y = 3.5 + 1.0x$, $R = 0.41$, $R^2_{adj} = 0.13$, SEE = 6.8%). (F) Waist circumference (women: $y = 1.8 + 0.4x$, $R = 0.69$, $R^2_{adj} = 0.46$, SEE = 4.5%; men: $y = 11.0 + 0.2x$, $R = 0.20$, $R^2_{adj} = 0.04$, SEE = 7.3%). (—) Transversal solid line represents linear line of best fit.

Previous studies also demonstrated that BMI was more correlated with %BF than skinfolds in obese [8,9] and stunted children [29]. In obese children, this is partially attributable to

the higher error of measurement of skinfolds at high levels of adiposity [11], and BMI does not provide an accurate indication of body fat distribution [30]. Therefore, WC has been recognized

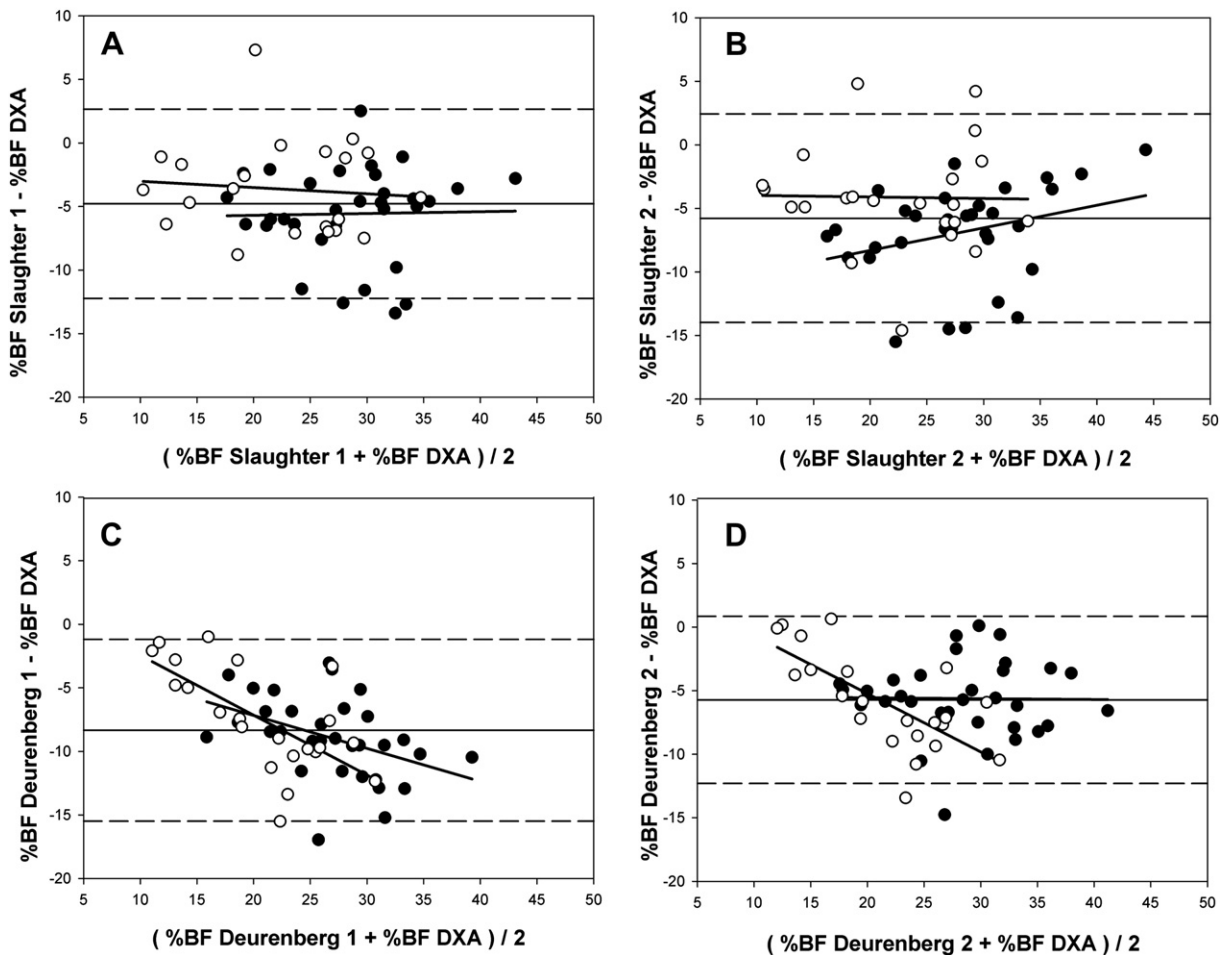


Fig. 2. Bland-Altman analysis of the agreement between the percentage of body fat (%BF) estimations using predictive equations and dual-energy X-ray absorptiometry (DXA) in (●) female and (○) male. (A) Slaughter skinfold equation 1 (women: mean differences between two methods [Bias] = -5.6 , 95% limits of agreement [95%LOA] = -12.8 : 1.7 , Pearson's bivariate correlations between the difference for each predictive equation and the reference method, and the mean of the two measurements [R] = 0.02 , $P = 0.90$; men: Bias = -3.6 , 95%LOA = -10.9 : 3.6 , $R = -0.09$, $P = 0.69$). (B) Slaughter skinfold equation 2 (women: Bias = -6.9 , 95%LOA = -14.4 : 0.6 , $R = 0.30$, $P = 0.10$; men: Bias = -4.1 , 95%LOA = -12.4 : 4.2 , $R = -0.02$, $P = 0.93$). (C) Deurenberg skinfold equation 1 (women: Bias = -8.9 , 95%LOA = -15.3 : -2.6 , $R = -0.42$, $P = 0.02$; men: Bias = -7.5 , 95%LOA = -15.5 : 0.6 , $R = -0.67$, $P = 0.001$). (D) Deurenberg skinfold equation 2 (women: Bias = -5.6 , 95%LOA = -11.6 : 0.4 , $R = -0.01$, $P = 0.94$; men: Bias = -5.9 , 95%LOA = -13.4 : 1.6 , $R = -0.70$, $P < 0.000$). The middle solid lines represent the mean differences between two methods. The dashed lines represent 95% limits of agreement (± 1.96 SD from mean). Trend line (solids line) represents the association between the differences of methods.

an important indicator of childhood obesity related to visceral fat, rather than total body fat, and a good predictor of cardiovascular risk in children and adolescents [12].

The results of the present study showed that the SEE estimations of the skinfold equations were approximately 3.3%BF for women and 3.8%BF for men. These SEE results are similar to (Slaughter equation 1: 3.8%; Slaughter equation 2: 3.7%) and lower than (Deurenberg prepubertal boys and girls, range: 4.5% to 5.6%; Deurenberg postpubertal girls: 4.5%) the results found by the researchers who developed these original equations [15,16]. For BMI and WC, the SEE was considered acceptable [31] among women but high among men (BMI: 6.9%; WC: 7.4%). Despite these results, the majority of the anthropometric measurements differed from the line of identity in the present study, demonstrating that adjustments might be necessary to calibrate the estimated values to the levels of adiposity in this population.

The lack of accuracy in the anthropometric measurements, primarily using BMI, in estimating the fat mass of these patients may be related to the fact that, although the literature shows that individuals with CAH present a higher risk of obesity [32], the complexity of the factors involved in the appearance and

development of CAH and its treatment may lead to different body composition in these patients. According to Isguven et al., children with CAH may have a BMI that is higher than control subjects because of an increase in fat mass [33], but this has not been confirmed by other authors, who, despite having observed higher values of fat mass, found no difference in BMI between CAH patients and controls [5]. These results suggest that a higher level of body fat could reflect the chronic effects of glucocorticoid therapy, and the higher lean mass may be an indication of the adverse effects of exposure to androgens excess [5]. Adults with CAH present higher BMI levels and higher fat mass compared with control subjects [34,35], but older patients (age >30 y) had a higher BMI and similar body fat, but higher lean mass, than controls [36]. One of the possible effects of excess glucocorticoid is the accumulation of abdominal fat [13], which may be reflected by an increase in WC, but this was not observed in the present study, which is a positive finding for these patients, because a high WC is strongly associated with cardiovascular disease [30].

At the individual level, our results revealed large differences, reflected by the wide 95% LOAs for each equation, with a clear

underestimation of %BF in individuals with 21OHD. These analyses suggest that individual estimations of %BF in patients with 21OHD, when taken alone, should be interpreted cautiously, as the skinfold equations tended to underestimate considerably the %BF values. Furthermore, mainly using the equations developed by Deurenberg et al. [16], the differences observed relative to the DXA criterion depended on the subjects' levels of adiposity, as reported in similar studies [14]. These results indicate that, in patients with lower %BF values, the %BF calculated using the Deurenberg skinfold equations tended to overestimate considerably the DXA results and, in patients with higher %BF values, the %BF calculated using the skinfold equations tended to underestimate considerably the DXA results. This finding could be critical in the clinical evaluation of these patients whose risk of obesity is elevated [32]. The large 95% LOAs observed in the present study indicate underestimations of approximately 12%–15%BF in women and 11%–16%BF in men.

Rodriguez et al. [14] observed that the accuracy of most of the skinfold-thickness equations for assessment of %BF in adolescents was poor at the individual level, but these authors recommend equations by Slaughter et al. for both male and female adolescents aged 13 to 17.9 y.

Nevertheless, another factor that must be considered is that Slaughter et al. developed the equations using a four-compartment (4C) model. Deurenberg et al. used hydrostatic weighing as the reference method, which is based on a two-compartment (2C) model. Although the density of fat-free mass (FFM_D) was considered to increase with age (1.08–1.10 g/cm³), no differences between the sexes were considered. Moreover, given that growth is not a linear process and might vary with sex and associated pathologies, 2C models can be inaccurate and cause clinically significant bias when estimating %BF [37]. The paucity of investigations does not allow us to know the relative contribution of fat-free mass components in children and adolescents with CAH.

One limitation of the present study is that, although DXA has been used as a reference method in body composition assessments for the last decade, it can present significant bias in pediatric populations compared with a 4C model [37]. The 4C model is currently recommended in research, but its complexity, length, elevated costs, and requirement for specialized staff make it less appropriate for use in large samples, young children, and other patients. Additionally, the 4C model is available in only a few research centers and is not error free. A propagation measurement error is associated with the number of components and respective techniques necessary for its application (e.g., body density, bone mineral, and total body water) [38]. Other methods (e.g., bioimpedance) and predictive skinfold equations should be tested and validated in children and adolescents with CAH to estimate body composition accurately in contexts in which the availability of more valid methods, such other reference methods, is limited.

Although the skinfold-based models were associated more strongly with %BF than WC, previous studies showed that WC is linked to several cardiometabolic parameters, including blood pressure, blood lipids, blood glucose, and insulin [12,39,40]. Unfortunately, the present study did not evaluate the correlation between anthropometric measurements and cardiometabolic parameters. It is important to stress that our results were obtained in children and adolescents with CAH 21OHD and diverge from the general recommendations of using BMI for assessing adiposity in children and adolescents and the importance of these simple and suitable measurements should not be overlooked. Future prospective studies should analyze the use of

anthropometric measurements in predicting cardiometabolic disease risk in these patients.

Conclusion

In this sample of patients with CAH 21OHD, the anthropometric measurements did not demonstrate accuracy in estimating %BF. Skinfold-based models had a stronger association with DXA than BMI and WC. However, the skinfold-based models underestimated %BF and showed a large limits of agreement, which may limit their application in clinical settings.

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References

- [1] Merke DP, Bornstein SR. Congenital adrenal hyperplasia. *Lancet* 2005; 365:2125–36.
- [2] Nimkarn S, Lin-Su K, New MI. Steroid 21 hydroxylase deficiency congenital adrenal hyperplasia. *Endocrinol Metab Clin North Am* 2009;38:699–718.
- [3] Merke DP. Approach to the adult with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *J Clin Endocrinol Metab* 2008;93:653–60.
- [4] Cameron FJ, Kaymakci B, Byrt EA, Ebeling PR, Warne GL, Wark JD. Bone mineral density and body composition in congenital adrenal hyperplasia. *J Clin Endocrinol Metab* 1995;80:2238–43.
- [5] Williams RM, Deeb A, Ong KK, Bich W, Murgatroyd PR, Hughes IA, et al. Insulin sensitivity and body composition in children with classical and nonclassical congenital adrenal hyperplasia. *Clin Endocrinol (Oxf)* 2010; 72:155–60.
- [6] Daniels SR, Arnett DK, Eckel RH, Gidding SS, Hayman LL, Kumanyika S, et al. Overweight in children and adolescents—Pathophysiology, consequences, prevention, and treatment. *Circulation* 2005;111:1999–2012.
- [7] Ellis KJ. Selected body composition methods can be used in field studies. *J Nutr* 2001;131:1589S–95S.
- [8] Watts K, Naylor LH, Davis EA, Jones TW, Beeson B, Bettenay F, et al. Do skinfolds accurately assess changes in body fat in obese children and adolescents? *Med Sci Sports Exerc* 2006;38:439–44.
- [9] Semiz S, Ozgoren E, Sabir N. Comparison of ultrasonographic and anthropometric methods to assess body fat in childhood obesity. *Int J Obes (Lond)* 2007;31:53–8.
- [10] Nooyens AC, Koppes LL, Visscher TL, Twisk JW, Kemper HC, Schuit AJ, et al. Adolescent skinfold thickness is a better predictor of high body fatness in adults than is body mass index: the Amsterdam Growth and Health Longitudinal Study. *Am J Clin Nutr* 2007;85:1533–9.
- [11] Kriemler S, Puder J, Zahner L, Roth R, Meyer U, Bedogni G. Estimation of percentage body fat in 6- to 13-year-old children by skinfold thickness, body mass index and waist circumference. *Br J Nutr* 2010;104:1565–72.
- [12] Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR, et al. Crossvalidation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. *Int J Obes (Lond)* 2006;30:23–30.
- [13] Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. *Endocr Rev* 2000;21:697–738.
- [14] Rodriguez G, Moreno LA, Blay MG, Blay VA, Fleta J, Sarria A, et al. Body fat measurement in adolescents: comparison of skinfold thickness equations with dual-energy X-ray absorptiometry. *Eur J Clin Nutr* 2005;59:1158–66.
- [15] Slaughter MH, Lohman TG, Boileau RA, Horswill CA, Stillman RJ, Van Loan MD, et al. Skinfold equation for estimation of body fatness in children and youth. *Human Biol* 1988;60:709–23.
- [16] Deurenberg P, Pieters JJJ, Hautvast JGAJ. The assessment of the body fat percentage by skinfold thickness measurements in childhood and young adolescence. *Br J Nutr* 1990;63:293–303.
- [17] Eisenmann JC, Heelan KA, Welk GJ. Assessing body composition among 3- to 8-year-old children: anthropometry, BIA, and DXA. *Obes Res* 2004; 12:1633–40.
- [18] Loftin M, Nichols J, Going S, Sothern M, Schmitz KH, Ring K, et al. Comparison of the validity of anthropometric and bioelectric impedance equations to assess body composition in adolescent girls. *Int J Body Compos Res* 2007;5:1–8.

- [19] Araujo M, Sanches MR, Suzuki LA, Guerra-Junior G, Farah SB, Mello MP. Molecular analysis of CYP21 and C4 genes in Brazilian families with the classical form of steroid 21-hydroxylase deficiency. *Braz J Med Biol Res* 1996;29:1–13.
- [20] Paulino LC, Araujo M, Guerra-Junior G, Lemos-Marini SHV, Mello MP. Mutation distribution and CYP21/C4 locus variability in Brazilian families with the classical form of the 21-hydroxylase deficiency. *Acta Paediatr* 1999;88:275–83.
- [21] Lau IF, Soardi FC, Lemos-Marini SHV, Guerra-Junior G, Baptista MTM, Mello MP. H28+C insertion in the CYP21 gene: a novel frame shift mutation in a Brazilian patient with the classical form of 21-hydroxylase deficiency. *J Clin Endocrinol Metab* 2001;86:5877–80.
- [22] Soardi FC, Barbaro M, Lau IF, Lemos-Marini SH, Baptista MT, Guerra-Junior G, et al. Inhibition of CYP21A2 enzyme activity caused by novel missense mutations identified in Brazilian and Scandinavian patients. *J Clin Endocrinol Metab* 2008;93:2416–20.
- [23] Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. *Arch Dis Child* 1969;44:291–303.
- [24] Marshall WA, Tanner JM. Variations in pattern of pubertal changes in boys. *Arch Dis Child* 1970;45:13–23.
- [25] Lohman TG, Roche AF, Martorell R, editors. *Anthropometric Standardization Reference Manual*. Champaign: Human Kinetics; 1988.
- [26] Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, Flegal KM, Guo SS, Wei R, et al. *CDC growth charts: United States. Adv Data* 2000;1–27.
- [27] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–10.
- [28] Ogle GD, Allen JR, Humphries IR, Lu PW, Briody JN, Morley K, et al. Body-composition assessment by dual-energy x-ray absorptiometry in subjects aged 4–26 y. *Am J Clin Nutr* 1995;61:746–53.
- [29] Hoffman DJ, Sawaya AL, Martins PA, McCrory MA, Roberts SB. Comparison of techniques to evaluate adiposity in stunted and nonstunted children. *Pediatrics* 2006;117:e725–32.
- [30] McCarthy HD. Body fat measurements in children as predictors for the metabolic syndrome: focus on waist circumference. *Proc Nutr Soc* 2006;65:385–92.
- [31] Lohman TG, editor. *Advances in body composition assessment*. Champaign, Illinois: Human Kinetics; 1992.
- [32] Volkl TM, Simm D, Beier C, Dorr HG. Obesity among children and adolescents with classic congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Pediatrics* 2006;117:e98–105.
- [33] Isguven P, Arslanoglu I, Mesutoglu N, Yildiz M, Erguven M. Bioelectrical impedance analysis of body fatness in childhood congenital adrenal hyperplasia and its metabolic correlates. *Eur J Pediatr* 2008;167:1263–8.
- [34] Stikkelbroeck NM, Oyen WJ, van der Wilt GJ, Hermus AR, Otten BJ. Normal bone mineral density and lean body mass, but increased fat mass, in young adult patients with congenital adrenal hyperplasia. *J Clin Endocrinol Metab* 2003;88:1036–42.
- [35] Hagenfeldt K, Martin Ritzen E, Ringertz H, Helleday J, Carlstrom K. Bone mass and body composition of adult women with congenital virilizing 21-hydroxylase deficiency after glucocorticoid treatment since infancy. *Eur J Endocrinol* 2000;143:667–71.
- [36] Falhammar H, Filipsson H, Holmdahl G, Janson PO, Nordenskjold A, Hagenfeldt K, et al. Metabolic profile and body composition in adult women with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *J Clin Endocrinol Metab* 2007;92:110–6.
- [37] Wells JC, Williams JE, Chomtho S, Darch T, Grijalva-Eternod C, Kennedy K, et al. Pediatric reference data for lean tissue properties: density and hydration from age 5 to 20 y. *Am J Clin Nutr* 2010;91:610–8.
- [38] Sopher AB, Thornton JC, Wang J, Pierson RN Jr, Heymsfield SB, Horlick M. Measurement of percentage of body fat in 411 children and adolescents: a comparison of dual-energy X-ray absorptiometry with a four-compartment model. *Pediatrics* 2004;113:1285–90.
- [39] Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. *Pediatrics* 2004;114:e198–205.
- [40] Moreira C, Santos R, Vale S, Santos PC, Abreu S, Marques AI, et al. Ability of different measures of adiposity to identify high metabolic risk in adolescents. *J Obes* 2011;2011:578106.