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Assessment of body composition in children with chronic renal failure

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Abstract In children with chronic renal failure treated conservatively by dialysis or by transplantation, various alterations of the nutritional, metabolic and fluid homeostasis may occur that may critically affect the patients' acute and chronic well-being. In the past, the assessment of body composition in children was hampered by insufficient precision, standardization and/or availability of appropriate anthropometric tools. Recently, there have been several methodological advances that may facilitate close and precise monitoring of body composition in this population. Specifically, the use of body mass index (BMI) data in children has become possible by the introduction of pediatric reference values processed for the calculation of standard deviation scores accounting for the skewed distribution of BMI. Skewness-adapted reference data have also been provided for percentage fat mass as assessed by multisite skinfold measurements. In addition, bioelectrical impedance analysis has been validated in healthy children as well as in pediatric dialysis and renal transplant populations. This novel auxological technique provides a highly reproducible, non-invasive and inexpensive way of assessing changes in total body water content in dialysed patients, as well as changes in fat and fat-free mass prior to dialysis and after renal transplantation.

Key words Anthropometry · Body mass index · Skinfold · Bioimpedance · Dialysis · Transplantation · Chronic renal failure

Introduction

Children with chronic renal failure are a population at risk from various acute and chronic alterations of body composition. In infancy, uremic anorexia inevitably leads to malnutrition and wasting. This complication can be prevented or corrected by consequent tube feeding; however, monitoring of the nutritional state by weight alone is difficult due to fluid imbalances resulting from renal salt and water loss or, in advanced renal failure, insufficient fluid elimination. Also, while infants on forced feeding regimens tend to become obese, it is usually unclear whether a normalization of lean body mass is in fact achieved.

In children on dialysis, wasting of fat-free mass is frequently masked by occult water retention. The estimation of "dry weight" in a constantly growing organism is one of the most difficult challenges for the pediatric nephrologist.

After renal transplantation, the assessment of body composition remains an important albeit frequently neglected part of patient care. Corticosteroid treatment for maintenance of immunosuppression causes a variable cushingoid appearance. In the absence of routine tools to assess body composition, it is frequently difficult to differentiate changes in body fat from those in metabolically active fat-free tissue.

In this article, several recent methodological advances facilitating the routine assessment of body composition will be discussed, which may be particularly useful in the pediatric chronic renal failure population.

Body mass index

The body mass index (BMI), i.e., body weight divided by the square of the height, has gained wide acceptance as a marker of the cardiovascular risk incurred by obesity in adults. The rationale for favoring BMI over a simple weight to height ratio lies in the assumption that fat-free mass is directly proportional to height squared, and the weight at a given height squared should be a linear function of the relative fat mass of an individual. An individual's position within his/her gender-specific BMI distribution appears to be rather stable; subjects with low

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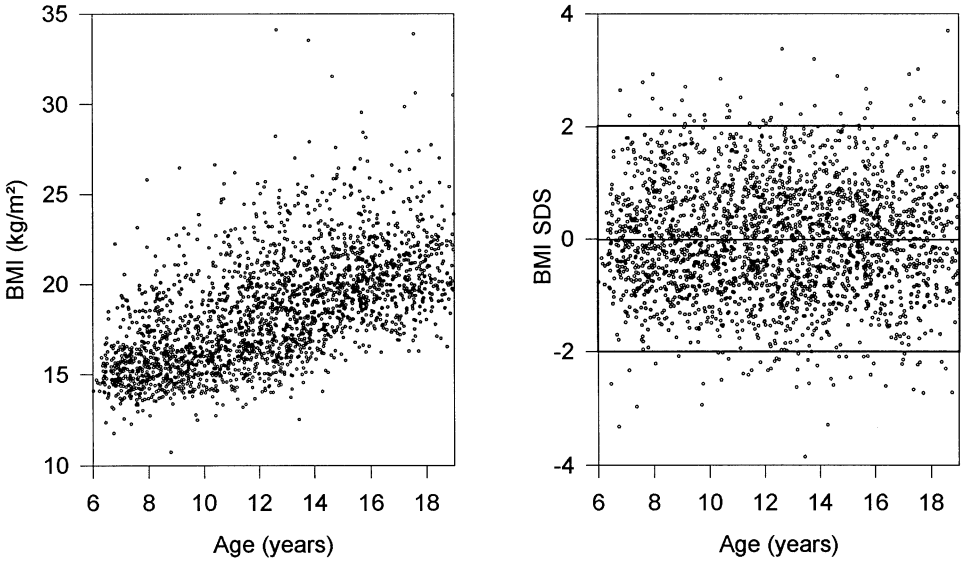

Fig. 1 Transformation of skewed BMI data to normally distributed standard deviation scores by the LMS method in 2554 healthy schoolchildren and adolescents aged 6–19 years. Data were taken from a cross-sectional anthropometric survey performed in Heidelberg in 1989/1990 [22]. The *L*, *M*, and *S* reference values derived from and reapplied in this population were published in ref. [6]

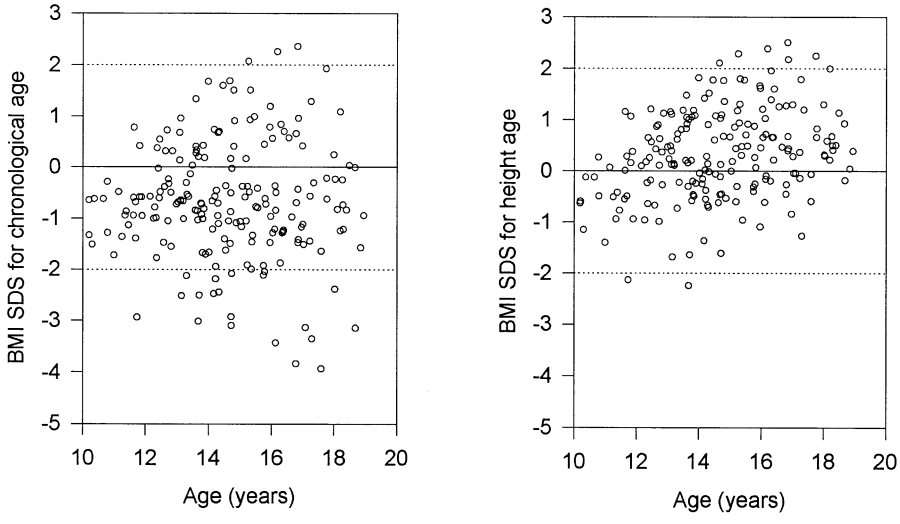

Fig. 2 Effect of BMI normalization for chronological vs height age in peripubertal renal allograft recipients. Growth retardation erroneously suggests normal or even reduced BMI SDS despite a cushingoid appearance when referring to chronological age (*left panel*). Correction for growth retardation by normalization to height age reveals mild obesity in this population (*right panel*)

or high BMI values show "tracking" of their percentile channel even from childhood to adult life [1]. In contrast to its common use in adults, BMI is rarely applied in pediatric populations. This is mainly because BMI is strongly age dependent, necessitating standardization of the index according to the age of the child.

Age-dependent parameters in children are usually normalized by transformation to standard deviation scores (SDS), relating an individual value to the mean and SD value of a reference population matched for gender and age. This normalization procedure is only valid for data where a Gaussian distribution can be assumed. Body weight and all indicators of body fat content are characterized by skewed distributions. Recently, Cole and Green proposed a technique to standardize skewed data by calculating a skewness factor (*L*) in addition to the median (*M*) and variance (*S*) of reference distributions [2]. Interpolation of the *L*, *M* and *S* values of the reference population at a given age enables normally distributed SDS values to be calculated for any parameter with a skewed distribution by the following formula:

$$SDS=[(Y/M(t))^{L(t)}-1]/(L(t)*S(t))$$

where *Y* represents the individual value, and *M*, *L* and *S* the respective reference values at the interpolated age (*t*). The efficacy of this technique in normalizing skewed BMI data is illustrated in Fig. 1.

BMI reference data processed for application of the LMS method have been provided for pediatric populations in England, Sweden, France, Italy and Germany [3–7]. Thus, it has become possible to calculate mathematically valid BMI SDS values in children, which can be used for cross-sectional and longitudinal analyses of childhood obesity whenever only weight and height are available.

It should be noted that due to the highly dynamic changes in BMI during childhood, the use of chronological age in standardized BMI data becomes questionable

in patients with growth disorders. Although this has not been formally proven, intuitive evidence suggests that the body composition of growth-retarded children should be in concordance with height age rather than chronological age. For example, in a 5-year-old child with the size of a 3-year-old infant, the BMI reference values of the 3-year age group are likely to be more appropriate than those of 5 years. Hence, we propose to use height age rather than chronological age for standardization in populations suffering from growth disorders.

An application of this principle in a group of renal allograft recipients with a mean height SDS of –2 yielded apparently normal BMI SDS values (0.1±1.2) when related to chronological age, despite a typical, moderately cushingoid appearance of the patients. Upon standardization for height age, an apparently more appropriate mean BMI SDS of 1±1.25 was obtained (Fig. 2).

Using the same procedure, we were also able to show an increase in mean BMI SDS by more than one SD unit in 16 children followed over 4 years after renal transplantation, and a gradual decline in BMI SDS, illustrating the loss of cushingoid appearance, during a 3-year period after switching from prednisolone to the less-cushingogenic alternative corticosteroid deflazacort [8]. Recently, we also applied BMI SDS for the first time in a retrospective analysis of 25 infants on long-term tube feeding. We demonstrated a rapid normalization of BMI by tube feeding. This finding is particularly important from a methodological aspect, since absolute weight or raw BMI data are not suitable for even short-term monitoring of the nutritional state in this age group due to their highly dynamic spontaneous changes with age [9].

Skinfold thickness measurements

In the past, the assessment of skinfold thicknesses has been the main tool for assessing body fat in children. However, few and outdated reference data were available for comparison, mainly in the form of percentile tables unsuitable for further statistical analysis. Moreover, the reproducibility of single skinfold measurements is poor, with 3%–7% intraobserver and 8%–20% interobserver coefficients of variation (CV) [10]. However, we previously demonstrated that despite the limited precision of a single skinfold thickness assessment, acceptable reproducibility can be achieved when multisite skinfold thickness assessments are integrated in estimations of whole-body percentage fat mass (PFM) using validated prediction equations [10]. A specific problem concerning the accuracy of PFM estimations in children is the changing density of the fat-free mass during childhood [11]. Previous PFM prediction equations validated under the assumption of an invariable density of the fat-free tissue introduced systematic estimation errors. Slaughter et al. [12] published a set of equations to estimate PFM from triceps and subscapular skinfold measurements in children of various age groups, accounting for the increasing body density during childhood by use of a multicompartment validation model.

We used the Slaughter equations to produce a set of pediatric reference values for PFM (Fig. 3) [7]. Moderately experienced caliper users should be able to achieve FM estimates within an intraobserver CV of 2%, corresponding to 0.4% of fractional fat mass [10]. Our reference tables also include *L*, *M*, and *S* reference values, allowing the calculation of SDS values for further parametric statistical analysis of the markedly skewed PFM.

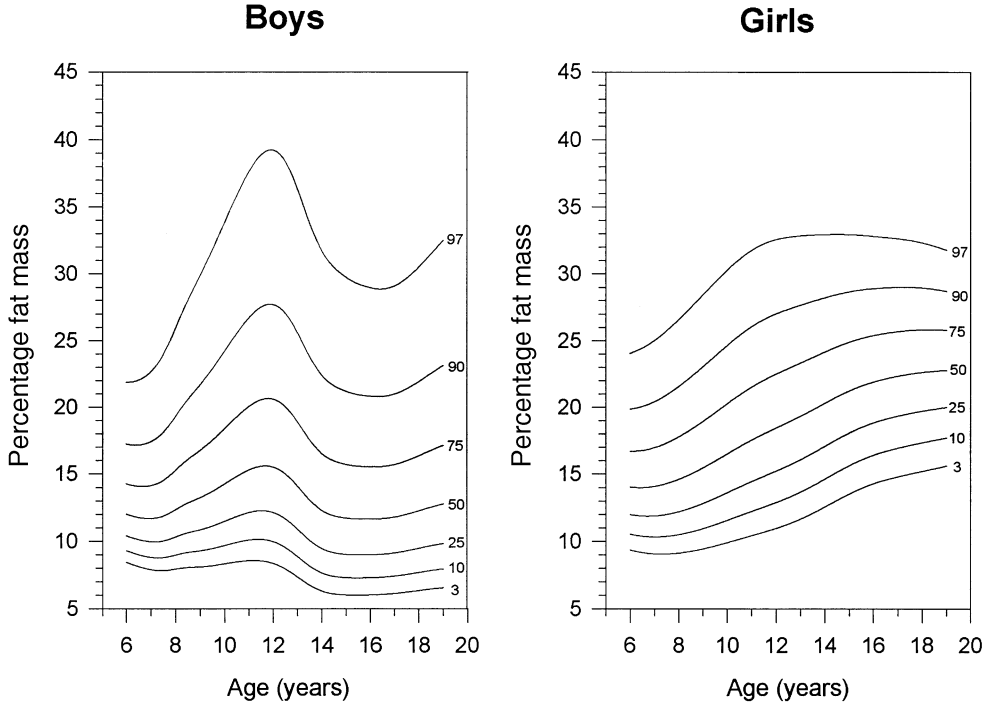

Fig. 3 Reference values for skinfold-derived percentage fat mass estimates in boys and girls aged 6–19 years (from [6] with permission)

Bioelectrical impedance analysis

Bioelectrical impedance (BI) is defined as the conductive resistance of a biological tissue exposed to an alternating electrical current. Since only electrolyte-containing fluids but not adipocytes conduct electrical currents, whole-body BI is inversely related to the total body water (TBW) content. The measured impedance value can be transformed to a "resistance index" (RI=height^2/impedance) in order to normalize for the length and volume of the measured subject. The RI displays a close linear relationship with TBW. Since in normohydrated subjects TBW is a constant fraction of the fat-free mass (FFM), the RI can be used to estimate both TBW and FFM. The validity of the RI concept has been confirmed in children [10, 13].

The high technical precision, lack of invasiveness and low cost of the method, together with its minimal requirements concerning observer experience and patient cooperation, make it a very attractive tool for the routine assessment of the state of hydration and fat/FFM distribution in clinical practice. BI is of particular interest in children with chronic renal failure, where a precise estimate of the dry weight has been a long sought after target. However, several potential problems require consideration: first of all, the electrolyte content of the fat-free fluids changes with age during childhood, necessitating the use of specific TBW and FFM prediction equations for children [10]. Secondly, the experience with BI analysis in other acute and chronic disease states suggests that the hydration of the fat-free tissues as well as the size of the interstitial fluid compartment may be altered in a disease-specific manner [14]. Therefore, estimations of TBW and FFM from BI in children on dialysis or after renal transplantation may only be valid using prediction equations developed for these particular populations. Thirdly, as outlined above, children with chronic renal failure may exhibit marked alterations and variability of their TBW contents. While TBW itself may be measured correctly by use of appropriate prediction equations, the large individual variability of the TBW-FFM relationship renders FFM prediction extremely problematic in this patient group. During the past decade, we have made efforts to validate and evaluate the usefulness of BI analysis in healthy children as well as in patients with renal disease.

In 112 normal children and adolescents aged 5–18 years, we validated BI against an independent assessment of FFM using the gold standard technique of ^{40}K spectrometry, which provides a measure of body cell mass via the total body potassium content [10]. A best-fitting formula was developed to predict FFM from BI; this equation includes age in order to correct for the developmental changes in body composition during childhood (Fig. 4).

The final, cross-validated equation:

$$\text{FFM [kg]} = 0.65 \times (\text{height}^2/\text{impedance})[\text{ohms/cm}^2] + 0.68 \times \text{age [years]} + 0.15$$

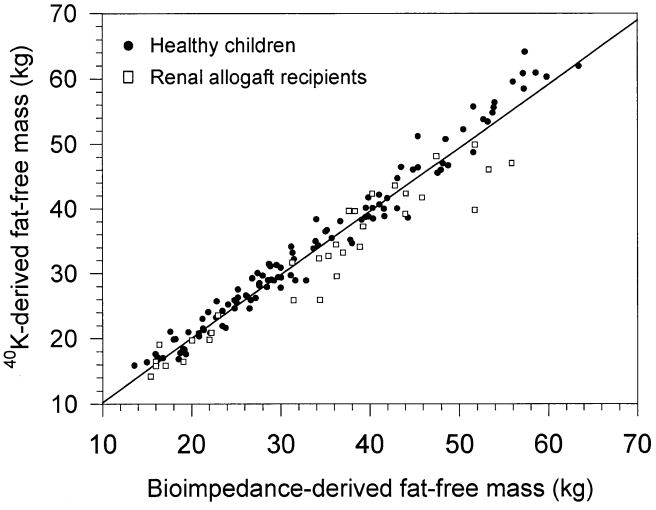

Fig. 4 Cross-validation of bioimpedance-derived FFM prediction equation in renal allograft recipients by comparison with direct FFM assessment utilizing 40K spectrometry (*dots* 112 healthy children, *squares* 32 pediatric renal transplant recipients)

predicted FFM with a residual error of 5.8% or 1.98 kg (Fig. 4). This degree of precision is comparable to findings in several other validation studies in children [13, 15, 16].

Subsequently, we evaluated the usefulness of BI in the assessment of TBW by comparison with direct TBW measurements using the deuterium oxide dilution technique in 23 children on hemo- or peritoneal dialysis [17]. Again, an optimized prediction equation for TBW in dialysed children was developed, which reads as follows:

$$\text{TBW [liter]} = 0.144 \times (\text{impedance/height}^2)\ [\text{ohms/cm}^2] + 0.40 \times \text{weight [kg]} + 1.99$$

By this equation, TBW was estimated with a residual error of 1.67l (CV 8.5%). The validity of the prediction equation was later confirmed by a cross-validation study using a different bioimpedance device in a different cohort of pediatric dialysis patients, where excellent accuracy and precision of the estimates based on the published formula were achieved [18]. In contrast, previous prediction equations established in healthy children proved to be unreliable in our pediatric dialysis population, with systematic under- or overestimations of true TBW by up to 10% and an unacceptable residual error of 2.8l (CV 14%) [17].

Notably, BI measurements are almost completely unaffected by the presence of dialysis fluid in the abdomen [19]. With the tetrapolar whole body measurement, resistance is apparently mainly determined by the hydration of the arm and leg where the electrodes are placed rather than by the tissue composition of the trunk. Due to this phenomenon, drainage of the peritoneal dialysis fluid is not required prior to assessment in daily practice.

The good reproducibility of BI-based TBW predictions makes this technology an interesting tool for the

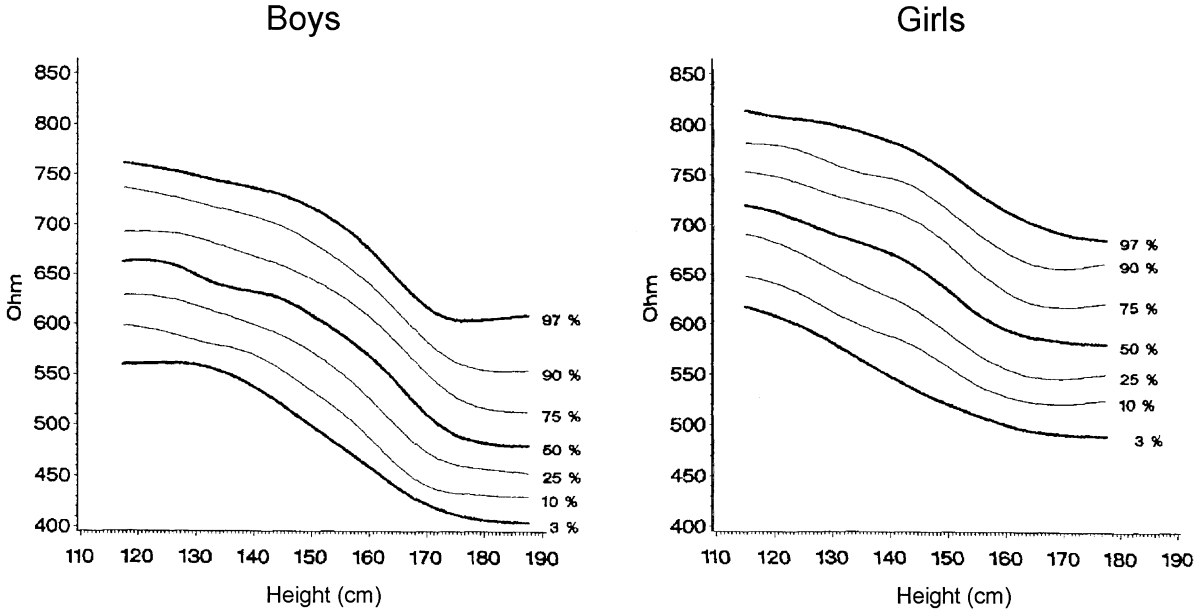

Fig. 5 Reference percentiles for bioimpedance values relative to height, derived in 1276 boys (*left panel*) and 1278 girls (*right panel*) (from [23] with permission)

calculation of the urea distribution volume (=TBW), a parameter required to calculate the urea clearance (*Kt/V*) as part of the monitoring of dialysis adequacy [20]. Furthermore, we feel that regular (i.e., monthly) documentation of the native, non-transformed BI values is a useful adjunct to clinical assessment and blood pressure recording in the interpretation of weight changes in an individual. Impedance values are rather stable over time, and any increase in body weight associated with a decrease in BI values is highly suspicious of increasing fluid retention. In contrast, a weight gain in the presence of stable or rising impedance values indicates an increase in body solids. Having utilized this concept in clinical practice over the last 8 years, we strongly advocate the routine use of BI measurements in the monitoring of dry weight in dialysed children. For orientation, reference values for BI values relative to body height are given in Fig. 5.

We also assessed the usefulness of BI in the prediction of fat-free mass in renal allograft recipients, in whom hydration is usually stable in the postacute state, but corticosteroid-induced cushingoid changes of body composition occur that may be due to changes in lean body mass, fat mass or both. In a cohort of 32 pediatric allograft recipients we demonstrated that, using the FFM prediction equation derived in healthy children, FFM was estimated with a slightly lower precision and with a trend towards systematic overestimation particularly in very obese children [21] (Fig. 4). Hence, the degree of adiposity tends to be somewhat underrated by BI analysis. Nonetheless, in the absence of other inexpensive and non-invasive tools for the assessment of fat and fat-free mass, BI analysis may have a place in the longitudinal monitoring of changes in body composition after renal transplantation, both in routine and in research settings. In 15 patients studied longitudinally during the 1st year after transplantation we were able to demonstrate that the weight gain beyond the third post-transplant month is not only due to increased fat deposition, but in part also to an increase in fat-free mass [22].

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