Estimating body composition in children with Duchenne muscular dystrophy: comparison of bioelectrical impedance analysis and skinfold-thickness measurement

Elise Mok, Laurent Béghin, Pierre Gachon, Christel Daubrosse, Jean-Eudes Fontan, Jean-Marie Cuisset, Frédéric Gottrand, and Régis Hankard

ABSTRACT

Background: Duchenne muscular dystrophy (DMD) is often associated with obesity, which worsens the handicap early in the course of the disease. Nutritional assessment, however, can be difficult and often misleading in DMD.

Objective: Two methods of estimating body composition in DMD, skinfold-thickness (ST) measurement and bioelectrical impedance analysis (BIA), were compared with a reference method, labeled water dilution (WD).

Design: Body composition was estimated by using ST measurements and BIA (50 kHz, 800 mAmp), as well as the WD method (1 mL H218O/kg) in 11 DMD patients with a mean (±SD) age of 10.0 ± 2.5 y.

Results: When compared with the WD method, ST measurement significantly (P < 0.01) overestimated fat-free mass (FFM) (i.e., ± SD ST: 24.5 ± 5.9 kg; 95% CI: 0.8, 4.9 kg) than for ST (6.3 kg; 2.2, 8.6 kg). WD and BIA defined 73% and 55%, respectively, of the children as obese (%FM associated with body index cut-offs for obesity), whereas SD measurements defined 9% as obese (P < 0.01).

Conclusions: Body-composition estimates by BIA are closer to those by WD than are those by ST measurement. Early detection of fat accumulation and longitudinal monitoring of nutritional care are 2 relevant applications of BIA to prevent obesity and hence lessen the burden of DMD.

KEY WORDS Obesity, Duchenne muscular dystrophy, bioelectrical impedance, body composition, iso- tope labeling, children, fat-free mass, percentage fat mass, nutritional assessment, handicap

INTRODUCTION

As in many chronic diseases of childhood, nutritional support has become an important part of the care of children with Duchenne muscular dystrophy (DMD). DMD is a progressive genetic disease that is characterized by a dramatic loss of muscle mass and function. Obesity occurs early in the course of the disease and aggravates the burden of the weakened muscles. Malnutrition further exacerbates disease progression in the latter stages of DMD, when handicap impairs oral intake and complications increase nutritional needs. In a large cohort of patients with DMD, 44% of patients were obese by the age of 12 y, and 44% of patients had malnutrition by the age of 18 y (1). It is possible that weight control may delay the onset of wheelchair dependency in DMD. Moreover, maintenance of fat-free mass (FFM) is a key issue in nutritional support, whether the goal is to prevent or limit increased adiposity or to maintain body weight.

Methods for evaluating nutritional status can be difficult and often misleading in DMD. For instance, body composition can be estimated from measurements of skinfold thickness (ST), but the method can be uncomfortable, particularly in children. Moreover, ST measurement requires an experienced observer and has poor interobserver reliability. Bioelectrical impedance analysis (BIA) can serve as an alternative method for estimating body composition because it is easy to administer and does not cause discomfort. BIA is also less dependent on the observer’s skills. In contrast to normal subjects, BIA in patients with DMD provides lower estimates of FFM (i.e., a higher percentage of fat mass (%FM)) than does ST measurement when the 2 methods are performed simultaneously (R Hankard, unpublished data, 2002).

1 From INSERM Centre D’Investigation Clinique 9202, Assistance Publique-Hôpitaux de Paris, Hôpital Robert Debré, Paris, France (EM, CD, and RH); Laboratoire Adaptation Physiologiue aux Activités Physiques EA3813, Université de Poitiers, Poitiers, France (EM and RH); EA3925 INSERM Centre D’Investigation Clinique 9301, Centre Hospitalier Régional Universitaire de Lille, Lille, France (LB); EA3925 Clinique de Pédiatrie, Centre Hospitalier Régionale Universitaire de Lille, Hôpital Jeanne de Flandre, Lille, France (FG and LB); Unité du métabolisme protéino-énergétique, UMR INRA 1019 Laboratoire de Nutrition Humaine, Clermont-Ferrand, France (PG); the Pharmacy, Assistance Publique-Hôpitaux de Paris, Hôpital Jean Verdier, Paris, France (J-EF); and the Service de Neuphropédiatrie, Centre Hospitalier Universitaire Lille, Hôpital Roger-Salengro, Lille, France (J-MC).

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3 Reprints not available. Address correspondence to R Hankard, Pédiatrie, Centre Hospitalier Universitaire de Poitiers, 2 rue de la Milétrie, 86021 Poitiers Cedex, France. E-mail: r.hankard@chu-poitiers.fr.

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However, neither of these 2 methods has been validated in patients with DMD. We hypothesize that the BIA method will provide body-composition estimates closer to those of the reference method than will ST measurements in children with DMD. Hence, the aim of the study was to compare body-composition estimates from BIA and ST measurement with those from a reference method (WD method) in children with DMD.

SUBJECTS AND METHODS

Subjects

Patients were recruited among those followed in multidisciplinary outpatient facilities from university hospitals in Paris and Lille, France. All patients were diagnosed with DMD by muscle biopsy, molecular biology, or both. Children were admitted the night before the study to the Clinical Investigation Centre of Robert Debré Hospital in Paris and of Lille University Hospital in Lille. The sequence of events for the experiment was as follows: After voiding and while in the postabsorptive state, patients were asked to drink labeled water. Physical exam including BIA measurement was then performed. Urine collection was done 3–4 h after ingestion of labeled water. Urine samples collected for labeled water technique were analyzed in a single laboratory, eliminating any potential site differences. Routine urinalysis was conducted at the individual hospitals. Both laboratories adhered to the French national standards for quality control for biological and medical analyses.

All families gave written informed consent after the investigator thoroughly explained the study protocol to both the parents and the children. The protocol was approved by the Paris-Bichat Ethics Committee (Comité Consultatif pour la Protection de la Personne dans la Recherche Biomédicale) and conducted according to the principles of the Declaration of Helsinki.

Methods

z Scores (weight-for-age, weight-for-height, and height-for-age) were calculated by using reference values from French growth charts (2). Body mass index (BMI; in kg/m²) was expressed in z scores by using reference data for a French population (3). Obesity cutoffs were BMI > 30, according to the growth charts of Cole et al (4)—i.e., an age-specific BMI equivalent to a BMI > 30 in an 18-y-old person, as established by the International Obesity Task Force (5)—and %FM associated with BMI cutoffs for obesity—i.e., age-specific BMI equivalent to a BMI of 30 in an 18-y-old (5).

BIA measurements were performed using a monofrequency (50 kHz, 800 mAmp) unit (101Q; RJL Systems, Clinton Township, MI). FFM was calculated from the resistance index (RI) by the calculation $RI = \frac{H^2}{R}$, where $H$ = height in cm and $R$ = resistance in $\Omega$, and by using the equation of Houtkooper et al (6):

$$\text{FFM (kg)} = 0.61 \times RI + 0.25 \times X + 1.31 \quad (I)$$

where $X = \text{reactance in } \Omega$.

ST measurements were performed at 4 sites (prebicipital, retrotrocratic, suprailiac, and subscapular) by using a Harpenden Caliper (John Bull; British Indicators Ltd, St Albans, UK). ST measurements were carried out by 2 different observers. At the Paris site, measurements were taken by the principal investigator, and, at the Lille site, they were made by a researcher (trained by the principal investigator). Both observers were experienced in taking ST measurements. In the first group of children studied at the site in Lille, measurements were carried out by both observers on the same subject and skinfold site, to ensure reproducibility.

Body density (BD) was calculated by using Broca’s equation for boys aged < 12 y (7):

$$BD = 1.1533 - 0.0643 \times \log (\Sigma 4ST) \quad (2)$$

and the equation of Durnin and Rahaman (8) for boys aged > 12 y:

$$BD = 1.1690 - 0.0788 \times \log (\Sigma 4ST) \quad (3)$$

in both of which $\Sigma 4ST$ = the sum of the 4 ST measurements. Fat mass expressed as a percentage of body weight (%FM) was obtained from Siri’s equation (9):

$$%FM = \frac{(4.95/BD - 4.5)}{100} \quad (4)$$

Thus, the method for estimating body composition provides FFM estimates as in BIA or %FM estimates as in ST measurements, with the use of the following equations:

$$\text{Body weight (BW)} = \text{FFM} + \text{FM} \quad (5)$$

or

$$%FM = \frac{(BM/FM)}{100} \quad (6)$$

Labeled water ($H_2^{18}O$ 2%; Euriso-top, CEA Group, Saint-Aubin, France) was prepared according to good pharmaceutical practices in the pharmacy of each hospital. The dose given was 1 mL/kg. $^{18}O$ enrichments in the urine were measured by using an isotope ratio–mass spectrometer ($\mu$Gas-Optima; MICRO-MASS, Manchester, United Kingdom) according to the $H_2O$–$CO_2$ equilibration method described by Vaché et al (10). FFM was calculated from total body water (TBW) by assuming a 75% water content of FFM at this age (i.e., 10 y) (11, 12). Expected TBW was calculated as 64% of total body weight (11, 12). Muscle mass was estimated from creatinine excretion by assuming that the excretion of 1 g urinary creatinine/d represents 20 kg muscle mass (13).

Statistical analysis

BIA and ST measurement methods were compared with the reference method as described by Bland and Altman (14). Limits of agreement were defined as the mean (± 2 SDs) for the difference between methods. 95% CIs were defined as the mean ± 2.23 SEMs for the difference between methods with $t$ equal to 2.23 for 10 df and a significance level of 0.05. The effect of method was tested for significance by using a one-way analysis of variance, followed by post hoc comparisons of means by using Tukey’s test. Differences in proportions were tested for significance by using the chi-square test. Data are presented as means ± SD and as proportions (percentages) for continuous and categorical variables, respectively. Statistical analysis was performed using Statview software (version 5.0; Abacus Concepts, Berkeley, CA).

RESULTS

Eleven children with DMD were included in the study ($n = 2$ at Robert Debré Hospital and $n = 9$ at Lille University Hospital). The children had a mean age of 10.0 ± 2.5 y. The anthropometric and body-composition data of the children are shown in Table 1.
Obesity was present in 2 (18%) of 11 children using BMI > 30 (International Obesity Task Force) calculated according to Cole’s reference curves.

The effect of the method used on estimates of both FFM and %FM was significant. Compared with the reference method, ST measurement provided significantly higher estimates of FFM (ST: 24.5 ± 5.9; WD: 18.2 ± 2.5 kg) (Figure 1) and lower estimates of %FM (ST: 23.3 ± 10.4; WD: 40.1 ± 17.1%) (Figure 1). In contrast, FFM and %FM estimates from BIA method (FFM: 21.5 ± 4.5 kg; %FM: 31.3 ± 13.9%) did not significantly differ from those from the reference method (Figure 1). In addition, fat mass was 8.9 ± 6.6, 11.8 ± 8.2, and 15.1 ± 10.8 kg, respectively, for ST, BIA, and WD methods. According to Bland and Altman, the limits of agreement for the difference in FFM between BIA and WD was 3.3 ± 6.0 kg—ie, −2.7–9.3 kg—and the 95% CI was 0.79, 4.93 kg (Figure 2). This difference in FFM was larger when ST measurements were compared with WD measurements (limits of agreement for the difference in FFM between ST and WD: 6.3 ± 9.9 kg—ie, −3.6–16.2 kg and 95% CI: 2.16, 8.62 kg) than when BIA was compared with WD. A similar trend was observed when the methods were compared with respect to obesity diagnosis. Specifically, obesity defined by %FM associated with BMI cutoffs for obesity (eg, %FM > 35% for a 10-y-old) was present in 8 (73%) and 6 (55%) of 11 children for WD and BIA methods, respectively, compared with 1 (9%) of 11 children for ST measurements ($P < 0.01$).

**DISCUSSION**

The BIA method provided estimates of body composition closer to those of the reference method than to those of ST measurement. Specifically, ST measurement overestimated FFM and underestimated %FM. Furthermore, BIA differed from the reference method less than did ST. Although clinicians must be warned of its limitations, the BIA method provides a more appropriate tool for assessing body composition than does ST measurement, particularly for early detection of fat accumulation and for longitudinal monitoring in DMD patients.

TBW estimates were 66% of expected values obtained from reference data in boys (11, 12) and consistent with those from other studies (15, 16). Previous results showed that muscle mass estimations accounted for a 25% decrease from normal values (ie, an 8.5-kg muscle deficit; 17). Although reduced muscle mass may contribute to decreased TBW (75% muscle water content), the correlation between these 2 variables was reported to be weak (15, 16). In fact, TBW is made of intracellular and extracellular water. Muscle mass correlates with intracellular water and total body potassium and declines at a rate of 4%/y, which reflects the progression of the disease (18–20). At variance, exchangeable sodium and extracellular water grow with age, which suggests the replacement of muscle by connective tissue, as observed by histologic experiments in DMD (21). In clinical practice, BIA is
a better method than is ST measurement to estimate FFM (TBW) and %FM, but it cannot provide estimates of muscle mass.

Because children with DMD had less TBW, the apparent normal weight observed in these children can be misleading, as it reflects excess body fat. Whichever method used, %FM exceeded normal values, which average 16% at this age. The physical exam is hence misleading in patients with DMD. To some extent, muscle mass loss masks FM accumulation. Moreover, in this population, fat accumulation cannot be detected by using nutritional indexes, such as BMI-for-age. This latter point was highlighted by Griffiths and Edwards (22), who adapted weight-for-age charts from those of Tanner and Whitehouse (23) and took into account muscle mass loss in DMD. The prevalence of obesity in patients with DMD is >50% by the age of 13 y (1). And, as do other obese populations, obese boys with DMD show a centralized body fat distribution (1). Furthermore, the higher total FM observed in boys with DMD than in healthy boys is mostly due to increased intramuscular fat deposition in both the central and the peripheral regions (24). A simple method for estimating body composition is therefore mandatory to estimate body fat and to monitor nutritional care in patients with DMD.

Our study was not designed to validate a specific equation for children with DMD. Such studies require a large population, which is unrealistic with respect to rare diseases. In the current study, we compared the 2 most frequently used methods—i.e., ST measurement and BIA—with a reference method and observed that ST measurements overestimated FFM, which led to an underestimation of %FM in these children. Similar findings were reported using magnetic resonance imaging as the reference method. Specifically, anthropometric measurements such as ST measurement underestimated the body fat percentage of children with DMD in comparison to measures by magnetic resonance imaging (24, 25).

The ST method estimated the size of the subcutaneous fat depot to predict body composition as a whole with the use of equations validated against underwater densitometry as the reference technique (7, 8). The assumption that the fat distribution between peripheral and central regions is normal may not be borne out in DMD patients (24). As a consequence, FM estimated from ST measurement does not take into account fatty infiltration of muscles (intramuscular fat deposition) that occurs in DMD, and, hence, total-body FM is underestimated and, in turn, FFM is overestimated. This discrepancy highlights the importance of population-specific equations, particularly when body compartments are known to differ from normal, which could also occur in other diseases associated with increased muscle mass loss.

At variance, BIA estimates body composition from a variable that encompasses the whole body—i.e., TBW. BIA also has its own limitations, namely, the shape of the electrical model, cell membrane characteristics, and fraction of the current entering the intracellular space at different frequencies. However, these limitations do not prevent longitudinal comparisons, because errors cancel one another.

Obesity aggravates handicap and complicates surgery in DMD children. Weight control is therefore crucial to limit the burden of the disease. Clinical evaluation of FM can, however, be misleading in patients with DMD. BIA is a simple and reliable technique, which can provide estimates of FFM and %FM closer to those obtained with the reference method. Hence, the BIA method can enable early detection of FM accumulation, begin dietary counseling as well as monitor progress and perhaps reduce excess adiposity in DMD patients. Moreover, in DMD, as in other situations it is usually preferable to prevent rather than correct obesity. Finally, the BIA method may serve to evaluate the effect of new treatments on body composition (26). For instance, in an effort to preserve muscle mass and reduce overweight in obese DMD patients, an intervention study could test the effect of a specific diet therapy on body composition.

BIA is therefore an easy and simple tool that provides useful indicators in nutritional follow-up of DMD patients as well as in clinical research. Furthermore, it would be worthwhile to test its use as a method of assessing body composition in other diseases associated with increased muscle protein catabolism, eg, cystic fibrosis (27), wherein body compartments may differ from normal.

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