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Increased fat mass and high incidence of overweight despite low body mass index in patients with spinal muscular atrophy

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ABSTRACT

Body composition is sparsely described in spinal muscular atrophy (SMA). Body (BMI, mass/height in m^2), fat-free (FFMI, lean mass/height in m^2) and fat (FMI, fat mass/height in m^2) mass indexes were estimated in 25 children (aged 5–18) with SMA (2 type I, 13 type II, 10 type III) using dual-energy radiograph absorptiometry and anthropometric data referenced to gender and age-matched healthy children (NHANES III, New York Pediatric Rosetta Body Project). BMI was ⩾50th percentile in 11 (44%) and ⩾85th in 5 (20%). FFMI was reduced ($p < 0.005$) and FMI was increased ($p < 0.005$) in the overall study cohort. FMI was ⩾50th, ⩾85th and 95th percentiles in 19 (76%), 10 (40%) and 5 (20%) subjects, respectively. Using a receiver operator characteristic curve, BMI above 75th, 50th and 3rd percentiles maximized sensitivity and specificity for FMI ⩾95th, ⩾85th and ⩾50th percentiles, respectively. Children with SMA have reduced lean and increased fat mass compared to healthy children. Obesity is a potentially important modifiable source of morbidity in SMA.

1. Introduction

Spinal muscular atrophy (SMA) is a progressive, recessively inherited, neuromuscular disease characterized by weakness and muscle atrophy due to loss of spinal cord motor neurons. Traditionally this disease, particularly in its most severe type I form (Werdnig–Hoffman), has been associated with considerable morbidity and mortality [1], although there have been advances in recent years with proactive medical care that have altered its natural course [1]. Despite progress at clinical, preclinical and molecular levels, and improved understanding of its molecular pathogenesis, optimal nutritional management and ideal growth parameters remain poorly described. While there is potential morbidity associated with being overweight as well as with malnutrition in this population, few articles presently in the literature specifically address body composition, growth expectations or anthropometric measures [2]. Recently Messina et al. reported a high frequency of swallowing dysfunction and subnormal weight in a cohort of patients with SMA type II [3]. While limited by available methodology (this study was based on parental estimation of weight obtained via telephone survey and did not incorporate other anthropometric measures or assessment of body composition), the authors speculated that the observed low body weight may reflect malnutrition or failure to thrive secondary to poor feeding specific to this population (SMA type II) [3].

Body mass index (BMI, weight in kg/height in m^2) has been widely utilized to screen for overweight in otherwise healthy children [4,5], with BMI greater than the 85th and 95th percentiles for healthy children [6] connoting "at risk for overweight" and "overweight", respectively. Studies have called into question, however, the applicability of BMI for a number of groups, including Asians [7], postmenopausal women [8] and persons with spinal cord injury [9–12]. Recent literature has eschewed relatively crude measures of excess body fat such as BMI and skin-fold based estimates of percentage body fat (%BF) in favor of direct descriptions of body composition such as the fat-free mass index (FFMI, kg of lean mass/height in m^2) and fat-mass index (FMI, kg of fat mass/height in m^2) [4,13,14], applying similar percentile cutoffs (above 85th percentile for "at risk of overweight", above 95th for "overweight" [6]) to FMI to define overweight status. Fat mass estimation using dual-energy X-ray absorptiometry (DXA) has emerged as a viable and reproducible technique for directly assessing relative body composition in the pediatric population [15–18]. Recently this technique has been utilized by the New York Pediatric Rosetta Body Project to describe body composition in a large sample of healthy children and define body composition parameters for normal children based on age, race and gender [4,13,14]. While it has

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not been widely studied in SMA for feasibility, reproducibility and correlation with other measures overtime, DXA may represent a useful technique for measuring body composition, and hence muscle atrophy and excess adiposity, in this population.

Utilizing DXA to assess absolute fat and fat-free mass and incorporating anthropometric data to determine BMI, FMI and FFMI values in a cohort of 25 children and adolescents with SMA (including types I–III) enrolled in a natural history study of the disease, we postulate that application of standard BMI percentiles obtained from cohorts of normal subjects underestimates total body fat in these patients, thus underestimating overweight in this population. Moreover, we hypothesize that children with SMA have reduced FFMI and increased FMI when compared to gender and age-matched reference data obtained from the National Health and Nutrition Examination Survey (NHANES III; 1988–1994) and the New York Pediatric Rosetta Body Project.

2. Patients and methods

2.1. Subjects

Twenty-five consecutive pediatric-aged (5–18 years) patients with SMA (11 girls, 14 boys, aged 5–17 years) for whom DXA was performed as part of an ongoing natural history study at Columbia-Presbyterian Medical center in New York City were selected for the study. This is a well described, genetically characterized cohort of patients for whom a battery of clinical, demographic and anthropometric data has been recorded on an ongoing basis as part of scheduled follow-up assessments and care. Demographic and descriptive measures of these patients are incorporated into Table 1. The Hammersmith Scale of motor function, expanded (HSMFE) is a 66 point scale designed and validated for assessment of motor function in SMA [19,20]. Forced vital capacity (FVC) has likewise been found reliable, valid and feasible in children above 5 years of age with SMA, using standard technique [21]. DXA was only performed on two children with SMA type I. Both children (aged 9.75 and 12.5 years) are fully BiPAP dependent (precluding pulmonary function testing) and score zero on the HSMFE. HMFSE and FVC values for these two patients were excluded from the cohort characteristics depicted in Table 1 (see footnotes).

2.2. Anthropometrics

For all subjects who were able to stand erect, height was measured while standing to the nearest centimeter with a stadiometer. For subjects unable to stand erect, stature was measured on a flat table in a supine position. Every effort was made to account for any contractures. Weight of the subject and the wheelchair was obtained to the nearest kilogram with a wheelchair balance scale (Pelstar, Bridgeview, IL) with the subject in the wheelchair. Then the wheelchair was weighed by itself and subtracted from the total weight. Subjects able to sit unsupported or to stand were weighed directly on a standard balance scale. BMI was calculated from measured weight and height.

2.3. DXA

Whole body DXA scans were performed using Lunar models DPX with pediatric software 3.8G and DPX-L with pediatric software 1.5G (GE Lunar Corporation, General Electric, Madison, WI) in accordance with the manufacturer's instructions [22]. Each scan provided estimates of subjects' fat mass and fat-free mass in kilograms and %BF. Technique, coefficient of variation, and quality control procedures (i.e. usage of phantoms to simulate bone, fat and fat-free tissues) has been described previously [4]. FMI and FFMI was then calculated for each patient by dividing estimated fat and lean mass (kg), respectively, by measured height in meters, squared (kg/m^2).

Age- and gender-specific BMI reference values developed by CDC [5] through the National Health and Nutrition Examination Survey (NHANES III; 1988–1994) were used to assign BMI percentiles based on this extensive cohort of 33,994 healthy volunteers, aged 2 months to 80 years, to study participants. Age, gender and race-controlled reference values for %BF [4], FFMI and FMI [13] were obtained from data published by the Pediatric Rosetta Study at St. Luke's-Roosevelt Hospital Center in New York (1995–2000), a cross-sectional study of pediatric body composition in 1208 healthy children and adolescents whose mean height, weight, and BMI were

Table 1
Demographic and body composition data for the study cohort.

	Total cohort	Summary characteristics by age (mean ± SD)		Summary characteristics by SMA type (mean ± SD)	
		Aged 5–11 years	Aged 12–18 years	SMA Types I and II	SMA Type III
N	25	16	9	15	10
Boys/girls	14/11	9/7	5/4	9/6	5/5
Age	9.1 ± 4.3	6.2 ± 1.9	14.2 ± 1.8	8.2 ± 3.4	10.4 ± 5.3
Hammersmith score of motor function[a]	28.1 ± 15.1	27.6 ± 14.8	28.7 ± 16.1	11.0 ± 7.3	44.7 ± 14.3
Forced vital capacity (% expected)[a]	78.9% ± 25.4%	77.0% ± 17.2%	80.7% ± 32.5%	60.6% ± 23.7%	94.1% ± 14.8%
Use of BiPAP or CPAP	5 (20%)	3 (19%)	2 (22%)	5 (33%)	0 (0%)
Use of gastrostomy tube	3 (12%)	1 (6%)	2 (22%)	3 (20%)	0 (0%)
Body mass index (BMI)	16.7 ± 5.4	16.5 ± 6.0	17.1 ± 4.5	16.2 ± 6.4	17.4 ± 3.7
Fat-free mass index (FFM in kg/m^2)	9.4 ± 2.0	9.4 ± 2.1	9.4 ± 2.1	8.9 ± 2.1	10.2 ± 1.6
Z-Score[b]	−4.6 ± 1.9**	−4.5 ± 2.0**	−4.7 ± 1.6**	−5.0 ± 2.1**	−3.9 ± 1.2**
Fat-mass index (FM in kg/m^2)	6.2 ± 3.0	7.1 ± 4.4	7.2 ± 2.5	7.4 ± 4.5	6.7 ± 2.5
Z-Score[b]	1.0 ± 1.3**	1.0 ± 1.5*	1.0 ± 1.0*	0.8 ± 1.5	0.6 ± 1.1
Percentage body fat (%BF)	39.7% ± 8.9%	39.2% ± 10.3%	40.6% ± 6.0%	41.4% ± 10.0%	37.2% ± 6.4%
Subjects with BMI > 25	1 (4.0%)	1 (6.3%)	0 (0.0%)	1 (6.7%)	0 (0.0%)
BMI above 50th percentile for age	11 (44.0%)	8 (50.0%)	3 (33.3%)	6 (40.0%)	5 (50.0%)
BMI above 85th percentile (>1 SD above mean) for age	5 (20.0%)	5 (31.3%)	0 (0.0%)	5 (33.3%)	0 (0.0%)
Above 50th percentile for FMI	19 (76.0%)	12 (75.0%)	7 (77.8%)	10 (66.7%)	9 (90.0%)
Above 85th percentile (>1 SD above mean) for FMI	10 (40.0%)	6 (37.5%)	4 (44.4%)	7 (46.7%)	3 (30.0%)
Above 95th percentile (>2 SD above mean) for FMI	5 (20.0%)	4 (25.0%)	1 (11.1%)	4 (26.7%)	1 (10.0%)

* $p < 0.05$; ** $p < 0.005$; SD, standard deviation.
[a] Values exclude two subjects with SMA type 1 (see text).
[b] *Z*-Score calculated from normative values for fat mass, fat-mass index, fat-free mass and fat-free mass index from New York Pediatric Rosetta Body Project by age, race and gender (see Table 2) [1].