Clinical Nutrition ESPEN 29 (2019) 142–148

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Body composition in patients with primary neuromuscular disease assessed by dual energy X-ray absorptiometry (DXA) and three different bioimpedance devices

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ARTICLE INFO

Article history:
Received 24 October 2018
Accepted 2 November 2018

Keywords:
Body composition
Neuromuscular disease
Bioimpedance
Phase angle
BIS
MFBIA
Dual energy x-ray absorptiometry (DXA)

SUMMARY

Background: Patients with primary neuromuscular disease have reduced muscle mass, and use of body mass index to assess nutritional status and body composition can therefore be questioned. Dual emission X-ray absorptiometry (DXA) can estimate muscle mass, but is not always readily available. Bioimpedance is a simple, portable and "easy to use" method for the assessment of body composition.

Objectives: To assess muscle mass by DXA in 143 patients with primary neuromuscular disease and validate three bioimpedance devices; Impedimed SFB7, ($BIS_{IMPEDIMED}$), Xitron4200 (BIS_{XITRON}) and Tanita MC180MA ($MFBIA_{TANITA}$).

Methods: Body composition was assessed by DXA in 143, by $BIS_{IMPEDIMED}$ in 116, by $MFBIA_{TANITA}$ in 104 and by BIS_{XITRON} in 35 patients.

Results: Muscle mass assessed by DXA, and phase angle (PhA) were below reference values in all female and 96% of male patients. $BIS_{IMPEDIMED}$ underestimated muscle mass by 6.5 ± 14.2 kg ($p < 0.001$), but this could be corrected after exclusion of resistance (Ri) values > 3500 Ohm ($p = 0.84$). $MFBIA_{TANITA}$ overestimated muscle mass by 30.8 ± 9.1 kg ($p < 0.001$) with systematic bias, whereas BIS_{XITRON} was in agreement with DXA, and without systematic bias. Muscle mass was strongly correlated to PhA ($r_{PEARSON} = 0.75$, $p < 0.01$).

Conclusion: Patients with primary neuromuscular disease have proportionally more fat and less muscle mass than the population in general, despite normal BMI. Muscle mass can be assessed by bioimpedance in these patients, but performance and bias depends on device. Phase angle by bioimpedance correlates to muscle mass, and could therefore potentially be used a surrogate measure of muscle mass during follow up.

1. Introduction

Patients with primary neuromuscular disease, and especially muscular dystrophies, often have reduced muscle mass and higher proportion of fat mass compared to healthy subjects [1]. Assessment of body composition or nutritional status by body mass index (BMI) might therefore be misleading. Thus, alternative methods to assess body composition have been used such as magnetic resonance imaging (MRI) [2,3], dual energy X-ray absorptiometry (DXA) [4] and different bioimpedance analysis (BIA) devices [4–6].

Body composition can be assessed by a variety of methods, with DXA being frequently considered and used as a reference or "gold-standard" due to its ability to precisely assess both fat mass (FM) and fat free mass (FFM), with insignificant radiation exposure [7]. However, DXA equipment is expensive and accessible only in body composition laboratories or for bone density measurements. Bioimpedance is a simple, portable and "easy to use" method for the assessment of body composition which has been favorably validated for use in many populations with normal hydration but less favorably in subjects with altered hydration states [8,9]. Instead,

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https://doi.org/10.1016/j.clnesp.2018.11.004
2405-4577/

List of abbreviations

ADP	Air Displacement Pletysmography
BIA	BioImpedance Analysis
BIS	Bioimpedance Spectroscopy
$BIS_{IMPEDIMED}$	BIS by Impedimed SF7
BIS_{XITRON}	BIS by Xitron 4200
BMD	Becker muscular dystrophy
BMI	Body Mass Index
DM1	Myotonic dystrophy type 1
DMD	Duchenne muscular dystrophy
DXA	Dual energy X-ray Absorptiometry
ECV	Extracellular volume
Fc_{BIS}	Critical/Characteristic Frequency (at maximum reactance)
FFM	Fat Free Mass
FFMI	Fat Free Mass Index
FM	Fat Mass
FMI	Fat Mass Index
FSHD	FascioFacioscapulo-humeral muscular dystrophy
ICV	Intracellular volume
LGMD	Limbgirdle muscular dystrophy
Mc_{BIS}	Cell membrane capacitance in the Cole equivalent circuit
$MFBIA_{TANITA}$	Multifrequency bioimpedance by Tanita MC180 MA III
MRI	Magnetic Resonance Imaging
PhA	Phase Angle
Re_{BIS}	Resistance of the extracellular compartment in the Cole equivalent circuit
Ri_{BIS}	Resistance of the intracellular compartment in the Cole equivalent circuit
SMA	Spinal muscular atrophy
SMM	Skeletal Muscle Mass
SMI	Skeletal Muscle Mass Index
SPhA	Standardized Phase Angle
TBW	Total Body Water

other different bioimpedance approaches have been proposed, such as multifrequency-BIA (MFBIA) and bioelectrical impedance spectroscopy (BIS).

We have previously found BIS derived by Xitron 4200 to correctly estimate FM and FFM compared to DXA in elderly Swedes [10] but to underestimate FFM compared to DXA in patients with cancer [11]. Skeletal muscle mass (SMM) can also be estimated by BIS using predictive equations based on DXA in elderly people [10]. We have also found 8-electrode MFBIA by TANITA MC-180 MA III to underestimate FM and thus overestimate FFM, and to be both biased and imprecise compared to air displacement pletysmography (ADP) [12] and DXA in obese Swedish women [13].

This study was conducted primarily to assess the body composition and muscle mass in patients with primary neuromuscular diseases with dual energy X-ray absorptiometry (DXA) as the reference method, and secondly to compare the performance of three different bioimpedance devices for bedside assessment of body composition. This study is a part of the overall aim to describe renal function in relation to muscle mass in patients with primary neuromuscular disease.

2. Patients and methods

2.1. Patients

In total 143 patients (77 women and 66 men) with a mean age of 46 (range 18–79) years underwent DXA scans. Impedance measurements where performed in 116 patients by Impedimed, in 104 by Tanita and in 35 by Xitron, the different numbers were due to technical and logistical reasons.

The majority of patients (n = 93, 51 women/42 men) had Myotonic dystrophy type 1 (DM1), 19 patients (12/7) had Facioscapulo-humeral muscular dystrophy (FSHD), 19 patients (11/8) had Limbgirdle muscular dystrophy (LGMD), 7 patients (3/4) had Spinal muscular atrophy (SMA), 3 men had Becker muscular dystrophy (BMD) and 2 had Duchenne muscular dystrophy (DMD) as diagnosis of their primary neuromuscular disease.

Inclusion criteria were primary neuromuscular disease, and reduction in muscle function ranged from a near normal muscular strength to severe weakness, wheelchair users and the need of assisted ventilation with Bilevel Positive Airway Pressure (BiPAP). Patients were assessed for illness stage according to three levels: Slight (minimal weakness that does not affect walking or daily activities), Moderate (obvious weakness with difficulties in walking, some distal muscles or small motoric regions may be severely weak), Severe weakness (great difficulties in walking or wheel chair users). The included patients had no previously known history of renal disease or reduced renal function. Patients with ongoing medication with corticosteroids were not excluded. Exclusion criteria were congenital DM1, an estimated survival less than 1 year, known ischemic heart disease, malignancy or an inadequately treated endocrine disease.

In addition, patients assessed by $BIS_{IMPEDIMED}$ with Ri > 3500 Ohm were excluded, only in an attempt to improve the performance of SMM, leaving 75 measurements to further analysis.

This cross-sectional observational study was carried out between 1 October 2010 and 31 January 2014. The study was approved by the regional ethics committee of Gothenburg, Sweden, registration number 492-10. Written informed consent was obtained from all participants. Study procedures were performed according to the principles of the Declaration of Helsinki.

2.2. Methods

All measurements of body composition were carried out at the body composition laboratory, Clinical Nutrition Unit at Sahlgrenska University Hospital, Sweden. Anthropometric measurements included body weight to the nearest 0.1 kg in light underclothing on an electronic scale (MC-180 MA III, Tanita, Tokyo, Japan) and body height by a wall mounted stadiometer. The same body height was used for all body composition analyses.

2.2.1. Dual energy X-ray absorptiometry (DXA)

Fat mass and FFM were measured by DXA (Lunar Prodigy, GE Lunar Corp, Madison, WI), with an in-house precision in duplicate measurements of 2.2% for FM and 0.8% for FFM. Skeletal muscle mass (SMM) was derived from appendicular lean soft mass from DXA as described by Kim [14].

2.2.2. Multifrequency bioimpedance (MFBIA)

In addition to measuring body weight, Tanita MC-180 MA III is an 8-electrode multifrequency bioimpedance (MFBIA) device that measures body composition by proprietary equations (not presented in the manual), with a manufacturer reported accuracy of 2%

Table 1
Body composition in patients with primary neuromuscular disease, by anthropometry assessed by dual energy X-ray absorptiometry (DXA) (n = 143) and bioimpedance (Impedimed SFB7) (n = 109) (TBW, ECV, ICV and PhA).

	Women (W) N = 77	Men (M) N = 66	All patients N = 143	W vs M By *t*-test[a]
Age (yrs)	45.7 ± 13[b]	46.3 ± 15	46 ± 14	0.71
Height (cm)	165 ± 6.2	178.2 ± 8.2	171 ± 10	<0.001
Weight (kg)	72.5 ± 20.6	81.3 ± 15.2	76.6 ± 18.6	0.005
Body mass index (kg/m^2[b])	26.5 ± 6.8	25.6 ± 4.2	26.1 ± 5.8	0.38
Fat Mass Index (kg/m^2[b])	12.3 ± 4.8	9.7 ± 3.8	11.1 ± 4.6	<0.001
Fat Free Mass Index (kg/m^2[b])	14.1 ± 2.9	16.0 ± 2.9	15.0 ± 3.0	<0.001
Fat mass$_{DXA}$ (%)	45.2 ± 8.3	37.0 ± 11.1	41.4 ± 10.4	<0.001
Muscle mass$_{DXA}$ (%)	21.7 ± 4.0	27.8 ± 7.2	24.7 ± 6.5	<0.001
Fat mass$_{DXA}$ (kg)	33.7 ± 13.8	30.6 ± 11.6	32.3 ± 12.9	0.14
Fat Free mass$_{DXA}$ (kg)	38.6 ± 8.7	50.8 ± 10.8	44.2 ± 11.4	<0.001
Muscle mass$_{DXA}$ (kg)	15.7 ± 4.4	22.7 ± 7.0	18.9 ± 6.7	<0.001
Muscle mass index$_{DXA}$ (kg)	6.3 ± 1.7	7.6 ± 2.0	6.4 ± 1.9	<0.001
TBW$_{IMPEDIMED}$[b]	30.2 ± 8.6	36.5 ± 9.6	33.1 ± 9.5	<0.001
ECV$_{IMPEDIMED}$[b]	13.9 ± 3.4	17.9 ± 3.6	15.8 ± 4.0	<0.001
ICV$_{IMPEDIMED}$[b]	16.3 ± 5.2	18.6 ± 6.6	17.4 ± 6.1	0.06
Phase angle (PhA) 50 kHz (°)	3.6 ± 1.2	4.2 ± 1.2	3.9 ± 1.5	0.047

Numbers are means ± SD.
DXA = dual X-ray absorptiometry; Muscle Mass = Skeletal Muscle Mass, TBW = Total Body Water, ECW = extracellular volume; ICW = intracellular volume.
[a] *p*-value, independent sample *t*-test.
[b] n = 59 women and n = 50 men.

[15]. This was done in 104 patients. Fat mass and FFM, as well as the Cole-Cole parameters Re$_{BIS}$, Ri$_{BIS}$ cell membrane capacitance (Mc$_{BIS}$) and critical frequency (Fc$_{BIS}$) were at the same occasions measured by the bioimpedance spectroscopy device Impedimed SFB7 (BIS$_{IMPEDIMED}$) in 116 patients.

In addition, 35 patients were assessed by the BIS device (BIS$_{XITRON}$) (Xitron Hydra 4200, Xitron Technologies, San Diego, USA), with an in-house precision expressed as coefficient of variation of 0.4% for FFM.

2.2.3. Phase angle (PhA) and muscle mass by BIS

Phase angle (PhA$_{BIS}$) or Φ in degrees at 50 kHz was derived from BIS$_{IMPEDIMED}$ by default and from BIS$_{XITRON}$ as $\Phi = 57.297 \times \text{atan}(Xc/R)$ where Xc is the reactance and R the resistance [16]. Skeletal muscle mass (SMM) was derived from BIS$_{XITRON}$ and BIS$_{IMPEDIMED}$ as described by Tengvall [10].

3. Statistical analyses

Results are presented as mean ± SD. Normal distribution was tested by one sample Kolmogorov's tests. Age distribution between different diagnoses was assessed by Kruskal–Wallis test, and gender distribution by Chi-square test.

Differences in body composition between patients with different neuromuscular disease were assessed by ANOVA with *post hoc* Bonferoni adjustment. Differences between patients with different neuromuscular disease and body composition data from reference populations were assessed by one sample *t*-test. Differences between DXA and bioimpedance methods were assessed using paired *t*-tests. The performance of MFBIA and BIS in relation to the reference method DXA, including systematic bias, was evaluated with Bland–Altman plots. All analyses were performed using SPSS version 21.0 (IBM, Somers, NY, USA).

4. Results

Body composition in 143 patients with primary neuromuscular diseases is presented in Table 1. Gender differences were evident with greater body height, weight, muscle mass and percent muscle mass in men, whereas women had a larger proportion of body fat. No gender differences were found for FM or BMI.

There were no significant differences in age or gender between patients with DM1, FSH or LGM (data not shown).

Compared to a contemporary Swedish reference population with the same average age and age-range [17], both female and male patients with primary neuromuscular disease had on average similar body height, weight, BMI, FFM and FFMI. Patients with primary neuromuscular disease had higher FM (+10.3 kg in females/+10.5 kg in males), FMI and percent FM (+12/13% units) and lower SMM (−6.5/−9.6 kg), SMI (−2.1/2.9 kg/m^2) and percent muscle mass (−11/−12% units), $p < 0.001$ for all.

Fat free mass, muscle mass (and hence SMI), differed between patients with different types of neuromuscular diseases, as shown in Figs. 1 and 2 (statistics in footnotes). Muscle mass and SMI were similar in patients with FSHD and DM1, while both were higher than in patients with LGMD. Muscle mass in patients with FSHD

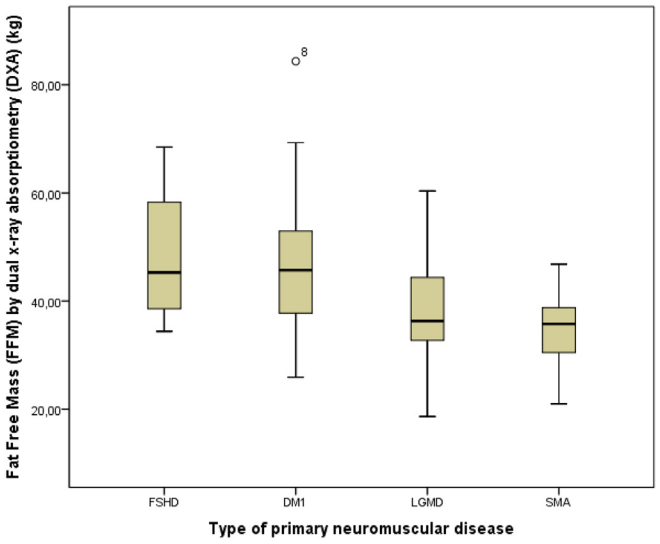


Fig. 1. Fat free mass (FFM) by dual energy X-ray absorptiometry (DXA) in patients with different primary neuromuscular diseases (n = 138). FSHD = Facioscapulohumeral muscular dystrophy (n = 19) differs from LGMD and SMA ($p < 0.05$ by ANOVA with post hoc Bonferoni). DM1 = Myotonic dystrophy type 1 (n = 93), differs from LGMD, ($p < 0.05$). LGMD = Limb-girdle muscular dystrophy (n = 19), differs from DM1 and FSHD ($p < 0.05$). SMA= Spinal muscular atrophy (n = 7), differs from FSHD ($p < 0.05$).

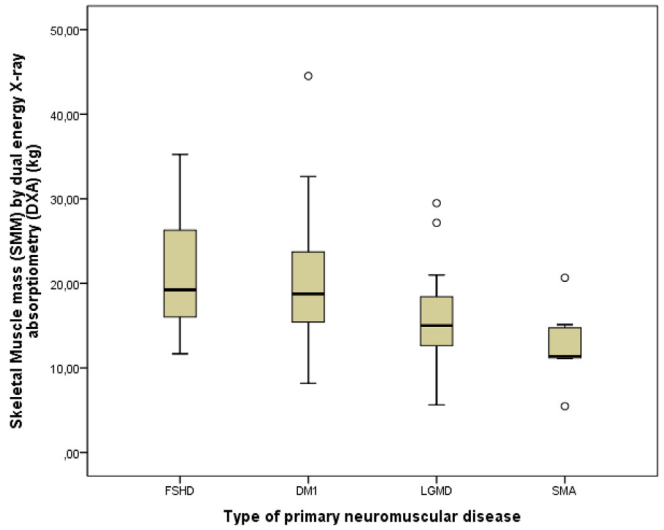


Fig. 2. Skeletal muscle mass (SMM) by dual energy X-ray absorptiometry (DXA) in patients with different primary neuromuscular diseases (n = 138). FSHD = Facioscapulohumeral dystrophy, n = 19, differs from LGMD, n = 19 and SMA, n = 7 ($p < 0.05$ by ANOVA with post hoc Bonferoni). DM1 = Myotonic dystrophy type 1, n = 90, differs from LGMD, and SMA ($p < 0.05$). LGMD = Limb-girdle muscular dystrophy, differs from DM1 and FSHD ($p < 0.05$). SMA = Spinal muscular atrophy, differs from FSHD, and DM1 ($p < 0.05$).

was higher than in patients with SMA ($p < 0.05$ for all). SMI in three men with Becker muscular dystrophy varied between 6.57 and 12.25, and two men with Duchenne muscular dystrophy both had a SMI of 4.08.

Muscle mass by DXA was strongly correlated to PhA ($r_{PEARSON} = 0.75$, $p < 0.01$). PhA also differed between different types of neuromuscular disease; as shown in Fig. 3 (statistics in footnotes). In addition, using Spearman's correlation, PhA was negatively correlated to the clinical staging in neuromuscular disorders regardless of diagnosis; −0.58, $p < 0.01$ (n = 100), and even more so in DM1: −0.63, $p < 0.01$ and LGM: −0.64, p = 0,05, but not in FSH -0.44, (NS). PhA differed significantly between different stages, as shown in Fig. 4.

When PhA was adjusted for body composition by SMMI and FMI with ANOVA, PhA at stage slight was still significantly higher than in stages moderate and severe, whereas gender and age did not affect the results.

Differences in the estimation of FM and SMM by DXA and the three bioimpedance devices are presented in Table 2, and graphically by Bland Altman plots in as shown in Fig. 5.

FM was correctly and without systematic bias estimated on a group level by $BIS_{IMPEDIMED}$, although with broad limits of agreement (LoA). $MFBIA_{TANITA}$ underestimated FM while BIS_{XITRON} overestimated FM, both with broad LoA but neither showed any systematic bias according to Bland–Altman plots (not shown).

Muscle mass was correctly estimated by BIS_{XITRON} using a predictive equation developed for elderly [10], and with no systematic bias related to the average SMM, according to Bland Altman plots (not shown). $BIS_{IMPEDIMED}$ without any exclusion, underestimated SMM with both strong systematic bias and very broad LoA. Muscle mass expressed from proprietary equations by $MFBIA_{TANITA}$ was heavily overestimated by 31 ± 6.5 kg compared to DXA, again with strong systematic bias and extremely broad LoA.

Compared to a large German population [18] average PhA was lower in patients with primary neuromuscular diseases; 3.6° vs 5.99° in female and 4.2° vs 6.57° in male patients, $p < 0.0001$ for both. None of the female patients and only two of the male patients had a normal PhA value. In addition, a small gender difference was detected with PhA = 3.6° in female vs 4.2° in male patients, p = 0.047. One patient with Becker muscular dystrophy had PhA = 1.6°, one patient with Duchenne muscular dystrophy had PhA = 2.6° and four patients with Spinal muscular atrophy had on average PhA = 2.9° (not shown).

In 31 patient assessed by both $BIS_{IMPEDIMED}$ and BIS_{XITRON} R_i values and variation differed by 1292 Ohm between devices, with $BIS_{IMPEDIMED}$ Ri = 3472 ± 2722 (range 1287–13,934) Ohm *v s* BIS_{XITRON} R_i = 2178 ± 637 (range 942–3479) Ohm (p = 0.007). We therefore excluded $BIS_{IMPEDIMED}$ measurements with Ri > 3500 Ohm, leaving 75 measurements to further analysis, of which 20 also had a BIS_{XITRON} reading. $BIS_{IMPEDIMED}$ and BIS_{XITRON} R_i values still differed by 279 Ohm (p = 0.017), whereas $BIS_{IMPEDIMED}$ now

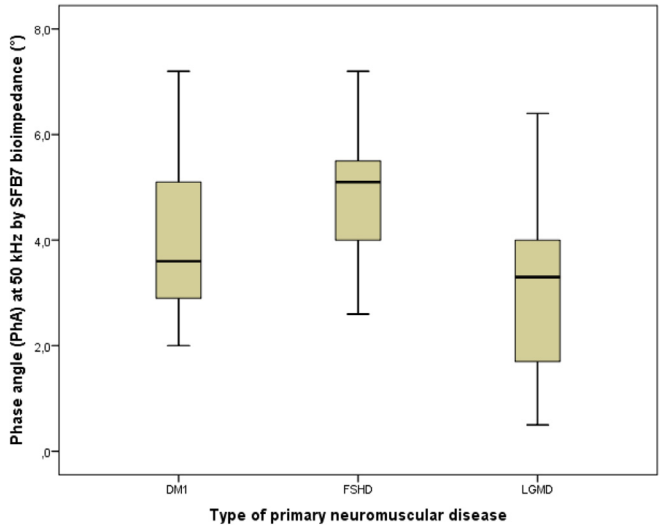


Fig. 3. Phase angle (PhA) at 50 kHz by Impedimed SFB7 bioimpedance in different primary neuromuscular diseases. DM1 = Myotonic dystrophy type 1, n = 68, differs from LGMD = Limbgirdle muscular dystrophy, n = 17 and FSHD, n = 17 $p < 0.05$ for all by ANOVA with post hoc Bonferoni.

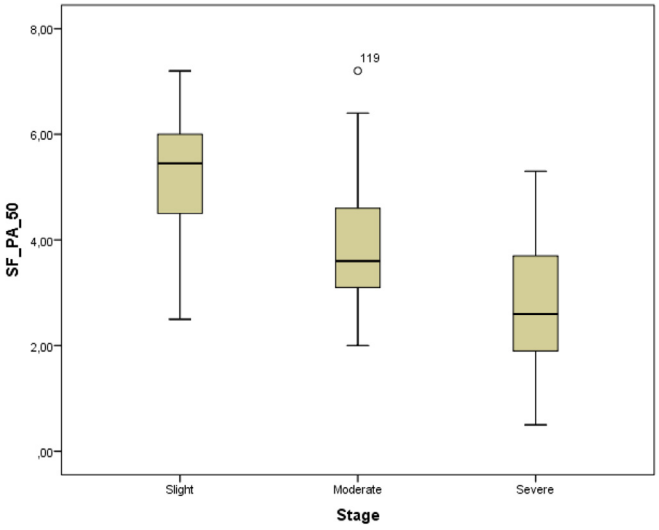


Fig. 4. Phase angle (PhA) at 50 kHz by Impedimed SFB7 bioimpedance according to clinical staging in primary neuromuscular diseases. Slight = minimal weakness, (n = 26), Moderate = obvious weakness (n = 49), Severe = severe weakness/wheel chair users. Differences between stages $p < 0.05$ for all by ANOVA with post hoc Bonferoni.

Table 2
Differences in the assessment of fat mass (FM) and skeletal muscle mass (SMM) between dual X-ray absorptiometry (DXA) and three different bioimpedance devices in patients with primary neuromuscular disease (n = 143).

	n	kg	p^1	LoA	rP	BA rP	BA p^2
FM DXA − XITRON	35	−4.0 ± 5.8	<0.001	−15.6–7.6	0.90	0.15	0.38
FM DXA − IMPEDIMED	116	1.2 ± 6.3	0.035	−11.4–13.8	0.88	0.06	0.56
FM DXA − IMPEDIMEDexcl.	75	4.0 ± 5.3	<0.001	−6.6–14.6	0.92	0.02	0.87
FM DXA − TANITA	103	8.0 ± 7.7	<0.001	−7.4–23.4	0.78	0.16	0.11
SMM DXA − XITRON	35	−0.2 ± 2.7	0.57	−5.6-5.2	0.89	0.33	0.06
SMM DXA − IMPEDIMED	116	6.5 ± 14.2	<0.001	−21.9–34.9	0.61	0.82	<0.001
SMM DXA − IMPEDIMEDexcl	75	0.1 ± 3.1	0.84	−6.1–6.3	0.86	0.35	0.002
SMM DXA − TANITA	103	−30.8 ± 9.1	<0.001	−12.6–50.8	0.60	0.56	<0.001

Data presented as mean differences in kg ± SD, and with ±2 SD limits of agreement (LoA).
XITRON = bioimpedance by Xitron 4200, IMPEDIMED = bioimpedance by Impedimed SFB7, TANITA = bioimpedance by Tanita MC 180 MA III, excl = $BIS_{IMPEDIMED}$ with R_i > 3500 Ohm cases excluded, rP = Pearson's correlation.
p^1 = by paired *t*-test.
p^2 = by linear regression.
BA = Bland–Altman regression for systematic bias expressed as $r_{Pearson}$ with p-values for the linear regression differences between reference method and secondary methods *versus* the mean of both methods.

underestimated FM by 4.0 ± 5.3 kg compared to DXA ($p < 0.001$) but correctly estimated SMM at 0.1 ± 3.1 kg compared to DXA ($p = 0.84$), although with systematic bias as seen in Fig. 6. PhA by $BIS_{IMPEDIMED}$ was significantly lower in patients with Ri > 3500 Ohm 2.6 vs 4.5°, compared to those >3500 Ohm, $p < 0.0001$. PhA by Xitron in the 31 patients assessed was on average 0.23° higher than by SFB7 ($p = 0.006$).

5. Discussion

In this cross-sectional study we confirm that patients with neuromuscular disease have proportionally more fat and less muscle mass than the general population, despite normal BMI, as estimated by DXA. We also found that bioimpedance spectroscopy (BIS) by Impedimed correctly estimated FM, whereas MFBIA by Tanita underestimated FM (and hence overestimated FFM) compared to DXA in patients with primary neuromuscular disease. BIS by Xitron slightly overestimated FM but correctly estimated muscle mass, compared to DXA (despite estimated by an equation derived in elderly) without systematic bias. In contrast, $BIS_{IMPEDIMED}$ underestimated SMM, and $MFBIA_{TANITA}$ heavily overestimated SMM compared to DXA, both with strong systematic bias.

When very high resistance (Ri) measurements were excluded, leaving 75 assessments, $BIS_{IMPEDIMED}$ underestimated FM, but then correctly estimated SMM compared to DXA.

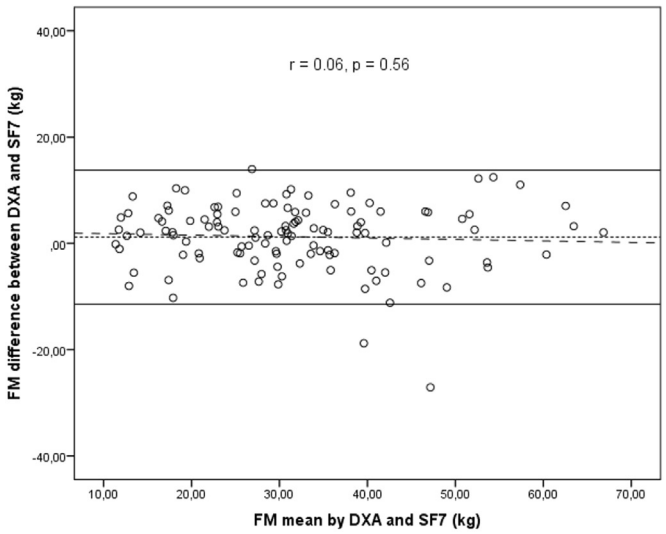
Using a similar but not identical bioimpedance device in 15 boys with Duchenne's muscular dystrophy, MacDonald et al. found Xitron 4000 to overestimate FM compared to DXA by Hologic [19], thus in line with our findings. Mok et al. found single-frequency bioimpedance to correctly assess *changes* in FM in 26 patients with Duchenne's muscular dystrophy, but to underestimate FM compared to DXA, underpinning the fact that bioimpedance devices often have better precision than accuracy [4]. This could potentially be due to different softwares. Using a multi-frequency bioimpedance device in 10 boys with Duchenne's muscular dystrophy, Elliott et al. found Bodystat 1500MD to underestimate FM compared to a 3-component model, using isotopic dilution and air-displacement pletysmography as the reference methods [6]. This difference was however reduced when using external predictive equations, applied to the "raw" bioimpedance values.

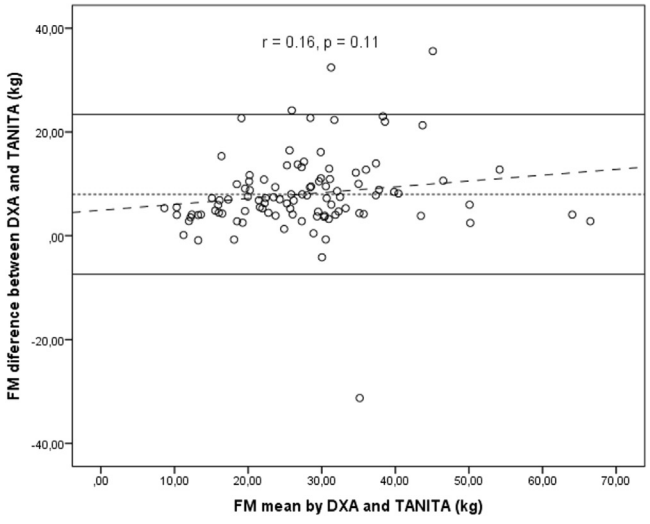
Neuromuscular disease might alter the proportion between fat and muscle mass compared to healthy subjects, rendering the interpretation of BMI difficult [1]. Indirect methods such as bioimpedance (BIA) might have limited capacity to estimate body composition in this group of patients. Still, the ease and advantage of a bedside assessment and the possibility to access further information than body composition data, make it worthwhile to assess and test the performance of different bioimpedance methods. Previous studies indicate that BIA has sufficient precision to detect changes in body composition [4]. This also makes BIA a clinically relevant tool and beneficial for patients with primary neuromuscular diseases.

In addition to body composition, there might also be additional information to be gained directly from the electrical properties revealed during the measurements. Phase angle (PhA) is considered a compound measure of not only body cell mass, which has close relation to muscle mass, but also of the neurophysiological function and properties of the cell membrane [20]. Overall PhA was found to be lower in patients with neuromuscular disease as compared to a large German population [18]. This could be due to moderate numbers of patients, but could also mirror the specific body composition with less muscle mass and more FM in both gender. In addition, PhA differed between subtypes of neuromuscular diseases. In patients with primary neuromuscular disease, we found a significant 0.56° average gender difference in PhA. This difference could probably be explained by different types of primary neuromuscular diseases in women and men.

We also found PhA by bioimpedance to correlate well with muscle mass as determined by DXA, and to be significantly lower in patients where $BIS_{IMPEDIMED}$ detected very high Ri values, possibly reflecting low muscle mass and/or deranged cell membrane function. Since PhA by bioimpedance correlates to muscle mass it could potentially be used a surrogate measure of muscle mass during follow up of patients, more so as PhA also correlate well to clinical staging of primary neuromuscular disease.

As expected, DXA revealed a very high occurrence of sarcopenia defined as low muscle mass, where every woman and almost every man had subnormal muscle mass as compared to a normal population. Nevertheless, body mass index, height and weight in our patient group did not differ from a healthy reference population, thus underpinning the need to assess body composition in more detail in patients with primary neuromuscular disease. With normal BMI our patients had on average 10 kg or 12% units more fat in both sexes, but 6.5 kg lower muscle mass in women and almost 10 kg lower in men. Thus, in patients with primary neuromuscular disease relative obesity might easily be overlooked if only BMI is measured and recorded.





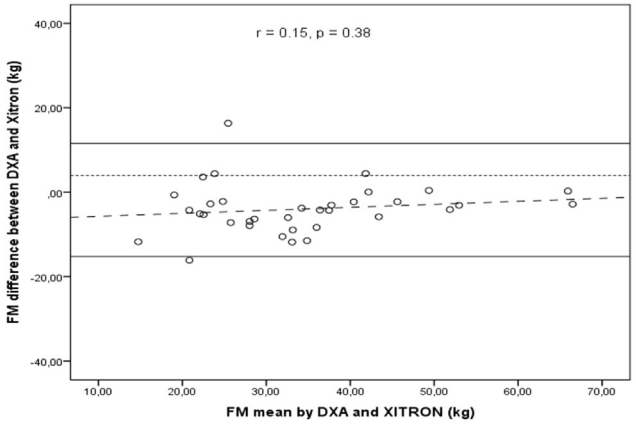
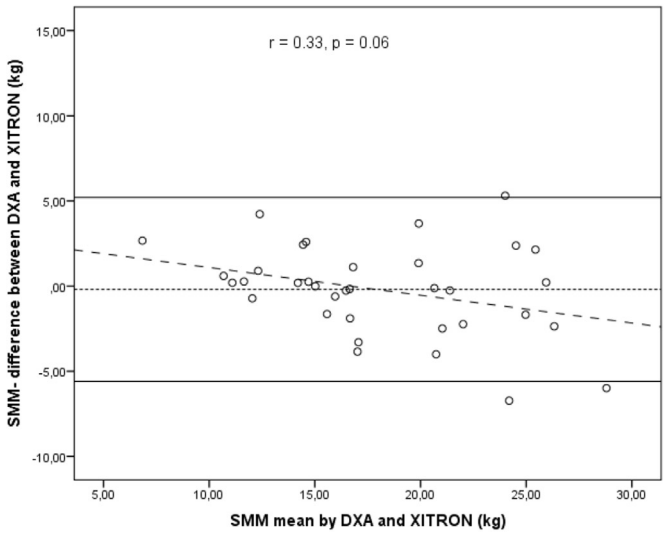


Fig. 5. Estimation of fat mass by three bioimpedance devices, Xitron and SFB7 compared to DXA by Bland–Altman plots in neuromuscular disease.

6. Strengths and limitations

The strengths include that the study population, although moderate, is larger than in previous corresponding studies [1–4,6] and that we used DXA as reference method in all patients since DXA is considered to be the "gold-standard" when measuring body composition. In addition, we used and compared three different



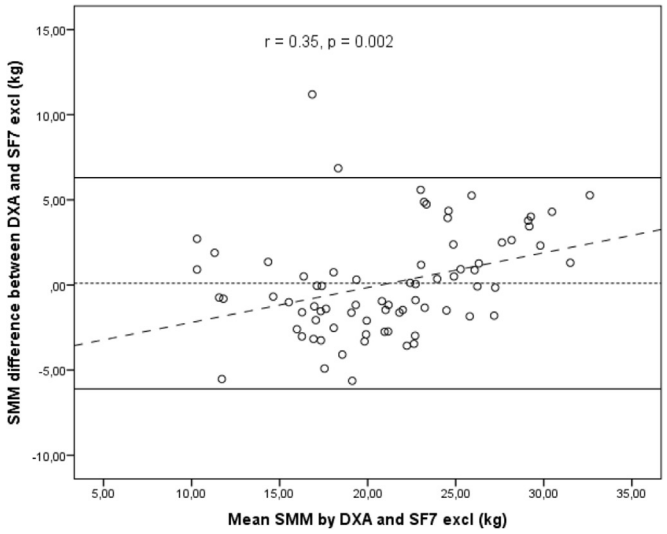


Fig. 6. Estimation of muscle mass by two bioimpedance devices, Xitron and SFB7 compared to DXA, by Bland–Altman plots in neuromuscular disease with Ri > 3500 Ohm excluded.

bioimpedance devices but a slight limitation is that none of these were used in all patients. This was unplanned but due to technical and logistic reasons such as shifting devices during the long inclusion period. The generalizability to other patients with reduced muscle mass due to other diseases should thus be further evaluated.

7. Conclusions

Patients with primary neuromuscular diseases have an altered body composition with more fat and less muscle mass compared to the general population, despite normal BMI when assessed with DXA. Using body mass index to assess nutritional status and body composition in patients with primary neuromuscular disease is therefore questionable and relative obesity might easily be overlooked.

Muscle mass can be assessed by bioimpedance also in primary neuromuscular disease, but performance and bias depends heavily on device, and these must thus be validated.

Bioimpedance assessment of phase angle correlates to both muscle mass and to clinical staging, and is suggested as an easily obtained objective surrogate measure of muscle mass for longitudinal follow up.

Conflict of interest

The authors declare no conflict of interest. MKS is currently employed by Amgen AB.

Funding

This study received support from the Muscular Foundation, the Wennerström Foundation and Gothenburg Medical Society.

Author statements

LE: responsible for the DXA and bioimpedance assessments, analyzed and interpreted data, drafted the manuscript, revised it, and approved the final version. AA: designed the study, interpreted data, and approved the final version. MKS: designed the study, interpreted data, and approved the final version. CL: designed the study, interpreted data, and approved the final version.

Acknowledgements

We thank research nurses Karin Håkansson and Blanka Andersson for help in reviewing medical records and for skilful assistance in finding and including patients in our study, and research nurse Inger Olander at the Department of Nephrology for all help with daily practicalities. We acknowledge the skilful DXA and bioimpedance assessments by BMA Vibeke Malmros and nurse Annika Alklind at the body composition laboratory.

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