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Original article

Underweight patients with anorexia nervosa: Comparison of bioelectrical impedance analysis using five equations to dual X-ray absorptiometry

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SUMMARY

Background & aims: Body weight changes do not reflect the respective changes of body compartments, namely fat-free mass (FFM) and fat mass (FM). Both bioelectrical Impedance Analysis (BIA) and the Dual X-ray absorptiometry (DXA) measure FFM and FM.
This study in underweight patients with anorexia nervosa (AN) aims to compare measurements of FM and FFM done by DXA and BIA using 5 different BIA equations already validated in healthy population and to identify the most suitable BIA equation for AN patients.
Methods: Fifty female patients with AN (BMI = 14.3 ± 1.49, age = 19.98 ± 5.68 yrs) were included in the study. Body composition was measured by DXA (Delphi W, Hologic, Bedford, MA) and by 50 kHz BIA (FORANA, Helios) using 5 different BIA equations validated in healthy population (Sun, Geneva, Kushner, Deurenberg and Roubenoff equations). Comparison between the DXA and the 5 BIA equations was done using the sum of the squares of differences and Bland–Altman plots.
Results: The Deurenberg equation gave the best estimates of FFM when compared to the measurements by DXA (FFM_{dxa} = 35.80 kg versus $FFM_{deurenberg}$ = 36.36 kg) and very close estimates of FM (FM_{dxa} = 9.16 kg and $FM_{deurenberg}$ = 9.57 kg) The Kushner equation showed slightly better estimates for FM ($FM_{kushner}$ = 9.0 kg) when compared to the DXA, but not for FFM. Sun equation gave the broadest differences for FM and FFM when compared with DXA.
Conclusion: The best available BIA equation to calculate the FFM and the FM in patients with AN is the Deurenberg equation. It takes into account the weight, height and age and is applicable in adults and adolescents AN patients with BMI of 12.8–21.0, and for ages between 13.4 and up to 36.9 years.

1. Introduction

Malnutrition in Anorexia Nervosa (AN) is a serious somatic aspect that deeply affects the psychiatric condition[1,2] and impacts the body composition of the patient.[3] The fat mass (FM), fat-free mass (FFM) and total body water (TBW) are not always affected to the same extent due to the variable impact of factors such as physical exercise, vomiting, laxative abuse and diet. For instance, patients with AN who achieve an extreme weight loss by semi-starvation can have a different body composition profile from patients who achieve the weight loss primarily through prolonged

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intensive exercise.[4] Body weight and body mass index (BMI, kg/m^2) have been widely used in previous research on AN as the sole nutritional assessment tools. However, in cases of severe malnutrition, body weight alone is not a sensitive tool to determine nutritional status.[5,6] The loss of body cell mass can be compensated by extracellular fluid accumulation and thus cannot be accurately sensed by body weight measurement.[5,7] Complementary to body weight measurements, assessing the body's muscle and fat stores may provide valuable information to the clinician for the diagnosis and treatment of malnutrition in AN as well as for assessing the dynamic patient's response to nutritional and other therapies.

In AN patients, clinically available bedside methods for measuring body composition are Bioelectrical Impedance Analysis (BIA) and Dual X-ray absorptiometry (DXA). They are safe and convenient methods for measuring body composition.[8,9] In some situations, the cost of the equipment, the need of a trained operator and the lack of portability limit the use of DXA. Consequently, BIA, a non-invasive, simple and inexpensive method could be of great use for clinician dealing with AN patients. However, BIA has not been yet validated against a reference 4-compartment-model in AN patients. Still, few studies have examined the limitations of BIA in underweight patients with AN.[9]

Some previous studies have compared BIA in AN or underweight patients to DXA and to other methods of body composition measurements, but they have always used one specific equation[10–15] (usually the equation provided by BIA manufacturer) and none of them compared different equations of BIA.

This study in underweight patients with AN aims to compare measurements of FM and FFM done by DXA or by BIA using 5 different equations already validated in healthy population and to identify the most suitable available BIA equation for AN patients.

2. Methods

2.1. Subjects

Fifty female AN patients were included in the study. AN diagnosis was according to the DSM-IV criteria based on the CIDI 2.1[16] with the following BMI criteria: BMI < 10th percentile up to 17 years of age, and BMI < 17.5 for 17 years of age and above. The patients were recruited consecutively from the inpatient treatment facilities of 4 centers in Paris, France: Institut Mutualiste Montsouris, Maison des adolescents (Cochin), Sainte Anne hospital and Paul Brousse hospital. Patients had to be in stable clinical condition, had no clinical signs of edema or dehydration at the time of inclusion, did not receive diuretics and should not be suffering from chronic diseases such as diabetes, Crohn's disease and other metabolic disorders. This study was part of a larger one called EVHAN (evaluation of hospitalization for AN (Eudract number: 2007-A01110-53, registered in Clinicaltrials)). This study protocol was approved by the Ile-de-France III Ethics Committee and the CNIL (Commission nationale de l'informatique et des libertés). Written informed consent was obtained from each patient before inclusion.

2.2. Anthropometry

Body weight was measured with a standard balance beam scale (SECA, Germany) to the nearest 0.1 kg in underwear. The subject in light clothes, shoes off, was standing still in the middle of the scale's platform. Height was measured with a stadiometer (SECA, Germany) to the nearest 0.1 cm. The subject was standing with heels together, arms to the side, legs straight, shoulder relaxed and head in the horizontal plane ("look straight ahead"). BMI was calculated as the body weight in kilograms divided by the height in meters squared.

2.3. Bioelectrical impedance analysis

The principles for measurement of body composition by BIA have been previously described by Kyle et al.[7] Briefly, BIA was measured using the Bioelectrical Analyzer (FORANA, Helios, Frankfurt, Germany) using used an alternating electric current at 50 kHz and 800 mA and 4 skin electrodes (BIANOSTIC, DataInput, Darmstadt, Germany) positioned on the right wrist and ankle. Practically, the patient was laying in the supine position on a bed for the analysis and the skin was cleaned with 70% alcohol for better conductance. Resistance (R) and Reactance (Xc) in Ohm were determined. The BIA measures were done in the morning between 10 and 12 a.m. before the DXA measurements.

2.3.1. Selection of BIA equations

From the previously validated equations (Table 1), 5 equations were selected to calculate FFM and FM, according to the following criteria: -equations validated in healthy Caucasian subjects; -age range compatible with our AN patients, -characteristics of our BIA analyzers. We added 1 further equation to the set that has been validated in elderly population: as we are working with AN subjects, we made the hypothesis that AN patients might be clinically close to elderly population (i.e., low muscle mass, low total bone mass, etc.).

2.4. DXA

Measurements of body composition were performed with DXA scan (Delphi W (S/N 70446), Hologic, *Inc*, *Bedford*, *Massachusetts-USA, software version 12.6*) giving the regional distribution of FFM, FM and bone mineral content (BMC). The Array mode was used. The principle of DXA has been previously described.[17] Briefly, the lightly dressed patient lay on the scanner table and the whole body was scanned. The DXA scanner has an X-ray source, X-ray detectors that record absorption data at two energy levels (a high energy and a low energy), and an interface with a computer system for

Table 1
Studies and BIA equations for determining fat free mass showing the criterion of measure and the BIA machine used.

Study	Population	*N*	Criterion measure	Equations	BIA
Deurenberg *et al.*[20]	Healthy subjects > 16 yr	661	Multi-compartment + densitometry	$FFM = -12.44 + 0.34 \times Ht^2/R_{50} + 0.1534 \times height + 0.273 \times weight - 0.127 \times age + 4.56 \times sex$ (men = 1, women = 0)	RJL-101
Kushner *et al.*[22]	Healthy subjects 17–66 yr	40	^2H_2O	TBW for women $= 8.315 + 0.382 \times Ht^2/R_{50} + 0.105 \times weight$ $FFM = TBW/0.732$	RJL-101
Kyle *et al.* (Geneva)[23]	Healthy subjects 19–94 yr	343	DXA	$FFM = -4.104\,1 + (0.518 \times Ht^2/R_{50}) + (0.231 \times weight) + (0.130 \times Xc) + (4.229 \times sex$; men = 1, women = 0)	Xitron
Roubenoff *et al.* [28]	Elderly	294	DXA	FFM for women $= 7.7435 + 0.4542 \times Ht^2/R_{50} + 0.1190 \times weight + 0.0455 \times Xc$	RJL-101
Sun *et al.*[24]	Healthy subjects 12–94 yr	1095	Multi-compartment	FFM for women $= -9.529 + 0.696 \times Ht^2/R_{50} + 0.168 \times weight + 0.016 \times R_{50}$	RJL-101

Sex specific equations (i.e. women) are presented unless the equation is for both sexes.
FFM: fat free mass; Ht: height; *R*: resistance; Xc: reactance.

processing and analyzing the absorption data. Body tissues absorb differently X-ray energy. Assumptions regarding the level of hydration, bone edge detection, and body thickness are used to convert absorption data into mass values for bone (BMC), fat (FM), and lean tissue mass components (LTM). FFM by DXA is calculated as LTM + BMC. DXA was measured on the same day right after BIA measurements.

2.5. Statistical methods

The SPSS 17.0 statistical program was used for all analyses. Descriptive statistics were performed for all primary outcome measures. Results are expressed as the mean ± SD. The strength of the relationship between the reference method and the different BIA equations was tested using Pearson's correlation and linear regression. Student's t test for paired observations (i.e. FM or FFM) was then used to compare measurements done by the DXA and by the BIA for the same subject. A Statistical significance was considered when $p < 0.05$. Further analysis for determining the best BIA equation compared to the DXA was to calculate the Sum of the squares of differences (Σ) between estimates of body compartments (FFM and FM) from the DXA and each of the equations: (e.g. for FFM: Σ (FFM DXA-sun FFM)^2). The smallest sum (Σ) is for the BIA equation that gives the closest results to the DXA.

Differences between measurements by DXA and different BIA equations were also compared by the Bland–Altman method[18] with calculation of the 95% limits of agreement.

3. Results

3.1. Patients' characteristics, body compartments estimates and their comparison

Table 2 summarizes the patients' characteristics. Twenty-five subjects had the restrictive type and the other twenty-five had the binge/purging type. Measurements of body weight by scale (45.93 ± 6.51 kg) and by DXA (44.97 ± 6.67 kg) are significantly correlated ($r = 0.98$ and $p < 0.05$).

Correlation coefficients and differences between FM and FFM obtained from DXA and each of the 5 BIA equations are presented in Table 3, as well as in Figs. 1 and 2.

Table 2
Characteristics, fat-free mass and fat mass as measured by Dual X-ray Absorptiometry or Biolelectrical Impedance Analysis of 50 women with anorexia nervosa.

Patient's characteristics	Mean	SD	Minimum	Maximum
Type of AN (%)	50 % ($n = 25$) AN-restrictive		50 % ($n = 25$) AN-binge/purge	
Age (years)	19.98	5.68	13.40	36.90
Weight (kg)	45.93	6.51	32.20	60.20
Height (cm)	163.53	6.27	147.00	173.00
BMI (kg/m^2)	17.1	1.93	12.8	21.0
Resistance: R50 (Ohm)	671.44	71.11	518.00	912.00
Reactance: Xc50 (Ohm)	57.98	8.70	40.00	74.00
Fat-free mass (kg)				
DXA	35.80	4.08	25.75	44.91
BIA				
Sun	39.53	3.56	31.43	47.35
Geneva	34.93	3.78	26.25	43.44
Kushner	36.93	4.22	27.72	46.21
Deurenberg	36.36	3.86	27.70	44.37
Roubenoff	34.17	2.90	28.11	40.43
Fat mass (kg)				
DXA	9.16	3.55	3.10	16.12
BIA				
Sun	6.40	3.80	−3.17	15.63
Geneva	11.00	3.39	4.01	19.91
Kushner	9.00	3.07	0.90	16.65
Deurenberg	9.57	3.37	0.84	17.93
Roubenoff	11.77	4.25	1.57	22.56

BMI: Body Mass Index; SD: standard deviation.

Table 3
Correlation coefficients and differences between the FM and FFM obtained from the Dual X-ray Absorptiometry (DXA) and each of the 5 bioelectrical impedance analysis equations.

	r	t
FFM_{DxA} (kg) with FFM_{BIA} calculated by:		
Sun	0.907[a]	−15.30[b]
Kushner	0.909[a]	−4.49[b]
Geneva	0.887[a]	3.25[b]
Deurenberg	0.887[a]	−2.07
Roubenoff	0.877[a]	5.59[b]
FM_{DxA} (kg) with FM_{BIA} calculated by:		
Sun	0.891[a]	11.29[b]
Kushner	0.878[a]	0.68
Geneva	0.891[a]	−7.98[b]
Deurenberg	0.873[a]	−1.65
Roubenoff	0.901[a]	−9.89[b]

DXA: Dual X-ray Absorptiometry; FFM: fat free mass; FM: fat mass; BIA: Bioelectrical Impedance Analysis; r: correlation coefficient; t: paired sample t-test.
[a] : Correlation coefficients are significant at a p level <0.01.
[b] : Differences are significant at a p level <0.01.

3.2. Agreement between the DXA and BIA measurements

Results about FFM show that Deurenberg equation has the smallest Σ (206.2) compared to the other equations (Sun: 854.5; Roubenoff: 356.2; Kushner: 218.8; and Geneva: 217.1). However, for the FM the Kushner equation has the smallest Σ (143.6), followed by the Deurenberg equation (178.9) (Geneva: 304.6), Roubenoff: 523.8; and (Sun: 538.0).

The agreement for FFM and FM between DXA and the 5 different equations of BIA is reported as the Bland–Altman plots (Figs. 3 and 4). For FFM, the plots show a strong agreement between Deurenberg equation and DXA with Deurenberg equation overestimating on average 0.5 kg. A good agreement is also seen with Geneva and Kushner equations. On the contrary Sun equation shows the lowest agreement with a mean difference of 3.8 kg.

For FM, the best agreement was found between Kushner equation and DXA with a mean difference of 0.2 kg, followed by

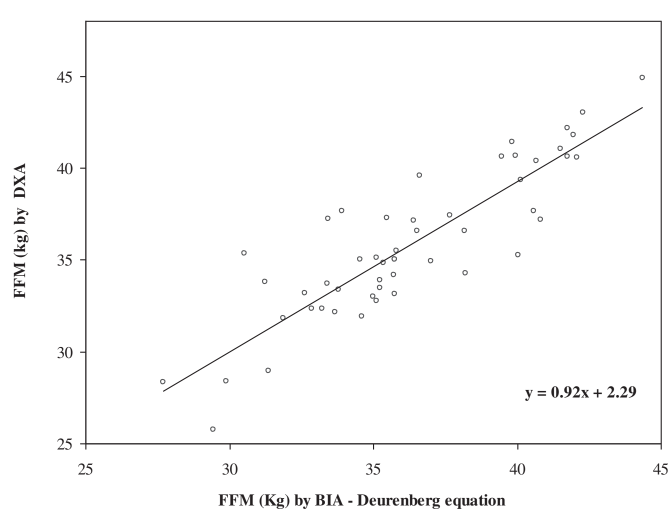

Fig. 1. Deurenberg equation estimate of fat-free mass (FFM) plotted against FFM from DXA with the corresponding regression equation in dots ($R^2 = 0.767$) and a reference line in solid.

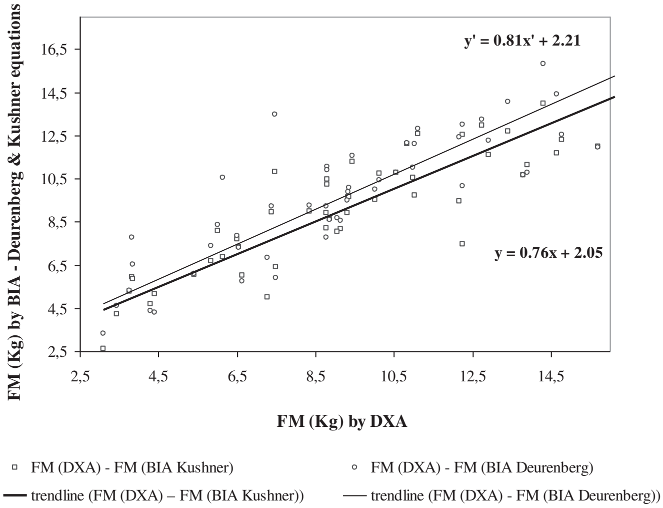

Fig. 2. Deurenberg and Kushner equations estimates of fat mass (FM) plotted against FM from DXA with the corresponding regression equations in dots ($R^2 = 0.741$ for Deurenberg) and in dashes ($R^2 = 0.773$ for Kushner) and a reference line in solid.

Deurenberg equation with an average overestimation of 0.4 kg. Sun equation had the weakest agreement with the DXA.

3.3. Effects of BMI and age on the measurements by DXA and BIA

We correlated BMI then age with the delta of FFM from DXA and from BIA in order to better understand if the difference in estimates of FFM is related to BMI or age. Table 4 shows the absence of correlation between BMI and age with the delta of measurements of FFM.

4. Discussion

This study in underweight patients with AN aims to compare measurements of FM and FFM done by DXA or by BIA using 5 different equations already validated in healthy population and to identify the most suitable available BIA equation for AN patients. The results show that Deurenberg equation gave the best estimates of FFM when compared to the measurements by DXA and very close estimates of FM too. Kushner equation showed slightly better estimates for FM when compared to the DXA, but not for FFM.

A successful treatment in AN is based on nutritional rehabilitation and weight restoration. Thus the starting point is to have a good nutritional assessment at diagnosis and during follow-up. The nutritional status deserves to be completely assessed, and not only limited to body weight or BMI because body weight alone does not reflect the evolution of the different body compartments during refeeding in AN.[9] In cases of severe malnutrition, body weight and/or BMI are not sensitive tools to determine the nutritional status.[5,6] Trocki et al.[19] showed that in adolescents with AN, changes in BMI do not correlate well with changes in body composition.[9] Loss of body cell mass can be compensated by extracellular fluid accumulation and thus cannot be accurately sensed by body weight or BMI measurement.[7]

Thus, it is valuable that the treating team assesses the nutritional status of AN patient with a simple, inexpensive and clinically available method such as the BIA.

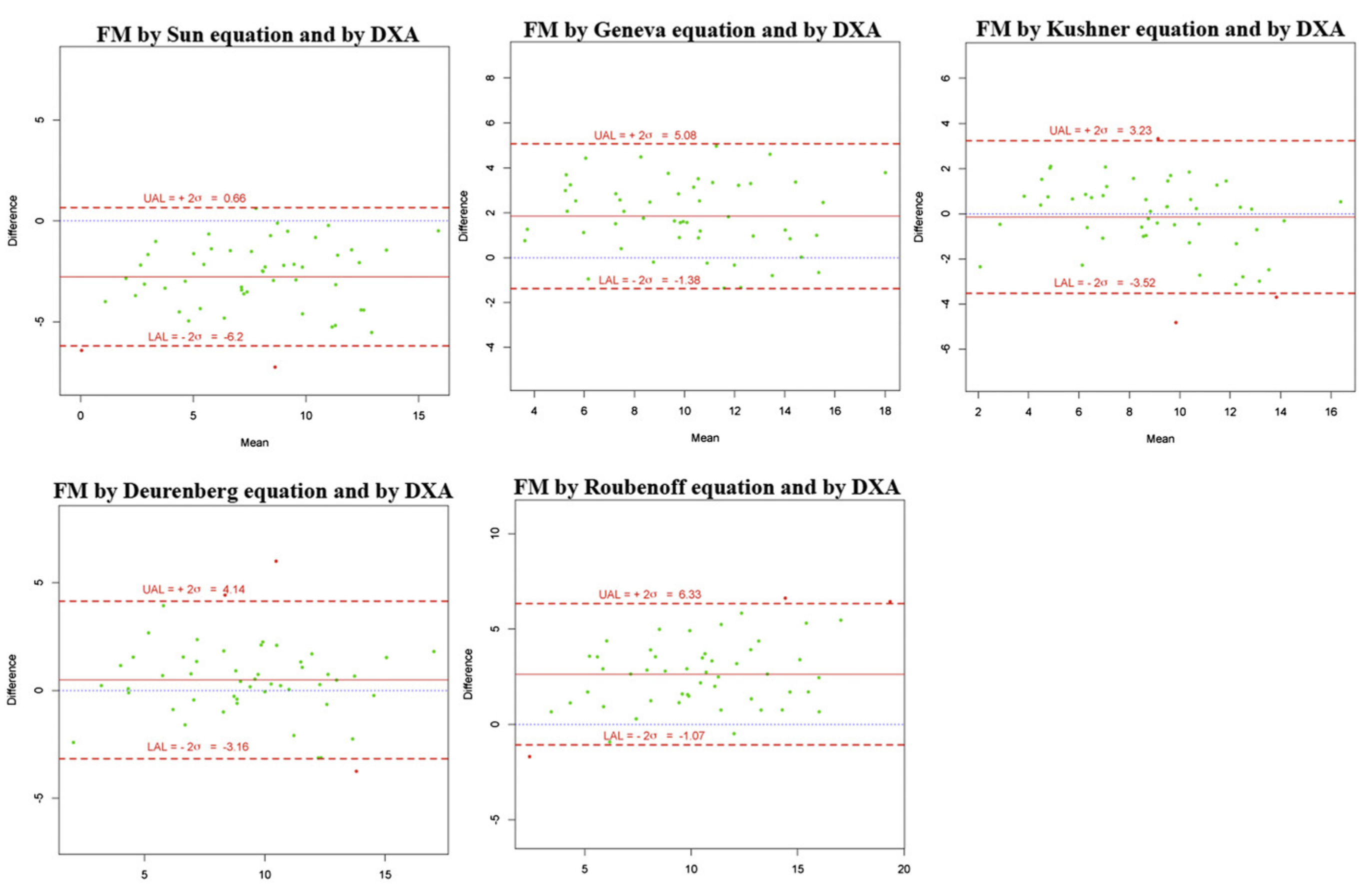

Fig. 3. Bland–Altman analysis for fat-free mass (FFM) between the DXA and the 5 different equations of BIA. The figures show the limits of agreement calculated as mean difference ±2SD. UAL: upper agreement limit; LAL: lower agreement limit.

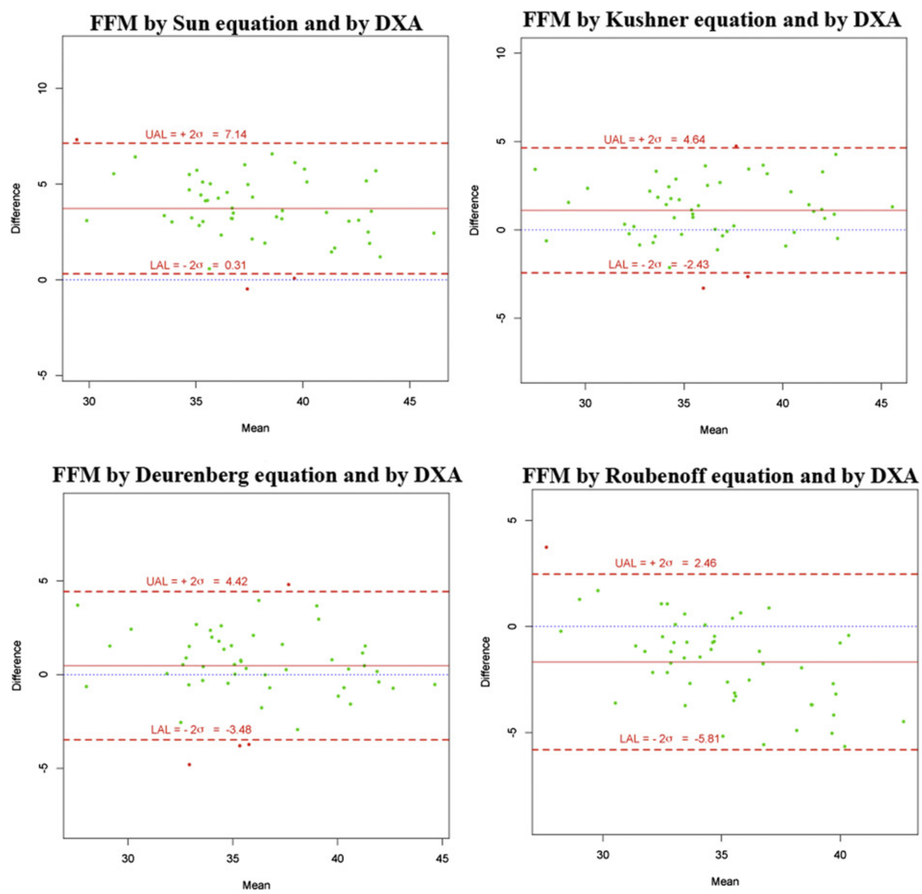

Fig. 4. Bland–Altman analysis for fat mass (FM) between the DXA and the 5 different equations of BIA. The figure shows the limits of agreement calculated as mean difference ±2SD. UAL: upper agreement limit; LAL: lower agreement limit.

4.1. Comparison between BIA equations

Among the 5 selected BIA equations, Deurenberg Equation[20] showed to be the most reliable in determining the body composition when compared to DXA. FFM determined by Deurenberg age and sex-specific equation was very close to FFM from DXA (no significant difference between the 2 measurements). Deurenberg et al.[21] have shown previously that in children and young adults between 7 and 25 years old the BIA equation is strongly dependent on age, and after 13 years it is also strongly dependent on sex. Our sample population, which is composed of 85% of females between 13 and 25 years old, might explain why the only equation that includes age, comes up as the best equation in predicting the FFM.

Kushner[22] and Deurenberg equations showed to be the most reliable in determining FM in AN. However, estimation of FM by Kushner equation is very indirect as they calculated FM from FFM that was calculated from TBW.

Regarding Geneva equation, reliable in healthy adult populations, the investigators did not include the age but included instead the reactance (Xc), while developing the equation, as they found that the reactance correlated the most with age.[23]

Furthermore, our results showed that Sun equation might be inappropriate to use in AN population although it was validated in subjects with extreme BMI (14 and 39 kg/m^2): the results when compared to DXA, showed wide ranges of differences for AN subjects. Actually, Sun equation was developed using both sexes, different ethnicity and all ages together.[24] Previous studies[11] have used the Sun equation in AN by choice and have found that BIA equations should not be used in anorexic patients with a BMI < 15 kg/m^2.

Roubenoff equation validated in elderly did not give close estimates of FFM and FM when applied to AN. AN subjects even when hospitalized can maintain high levels of physical activity[25] and thus can partially preserve their muscle mass which is not the case in elderly who lose particularly their muscle mass (sarcopenia) in spite of their negative energy balance. The ESPEN (European

Table 4
Correlation coefficients of BMI and age with the difference in FFM results obtained from the Dual X-ray Absorptiometry (DXA) and each of the 5 Bioelectrical Impedance Analysis (BIA) equations ($N = 50$).

		Delta FFM (DXA and SUN)	Delta FFM (DXA and Geneva)	Delta FFM (DXA and Kushner)	Delta FFM (DXA and Deurenberg)	Delta FFM (DXA and Roubenoff)
BMI	*r*	−0.154	−0.183	0.264	−0.114	−0.002
	p	0.286	0.203	0.064	0.431	0.987
Age	*r*	−0.159	0.055	0.135	0.034	0.131
	p	0.270	0.704	0.349	0.815	0.364

BMI: Body Mass Index; DXA: Dual X-ray Absorptiometry; BIA: Bioelectrical Impedance Analysis; FFM: fat free mass; *r*: correlation coefficient.

Society for Parenteral and Enteral Nutrition) recommendation to use population-specific equations or equations that adjust FFM and FM changes with age because BIA equations developed in young subjects can result in large bias in older subjects.[8]

4.2. Comparison between scale weight and weight measured by DXA

Our results show an underestimation of weight measured by DXA Hologic compared to scale weight. This difference is of almost 1 kg and is independent from the BMI. Previous work in obese population, showed that there was no difference between scale weight and different of DXA instruments (QDR 4500-A NPM, HPM and Prodigy) for BMI < 30 kg/m^2[26] Also Slosman et al.[27] have found that DXA is very precise in determining body weight. This difference might be due to the severe leanliness of the subjects.

5. Limitations

A limitation of our study is that we have chosen one specific kind of DXA machine as a reference method and different DXA machines can give slightly different estimates of body compartments. Future investigations should compare BIA equations with more then one kind of DXA machines.

Another limitation is that measurements were limited to one time. Several measurements and longitudinal assessment are needed especially in AN population as there is a marked shift in body fluids during refeeding and this can affect the estimates of body compartments by BIA.

Furthermore, absurd estimates were obtained for Sun equation e.g. negative values for FM, because of the severe leanness at the individual level of some subjects.

6. Conclusion

The best available BIA equation to calculate FFM and FM in patients with AN is the Deurenberg equation. It takes into account the weight, height and age of the patient and is applicable with BMIs of 12.8–21.0, and for ages between 13.4 and up to 36.9 years. It is an important matter that it is applicable in adolescents as AN patients are usually of young age.

The evaluation of body composition in AN improves the management and personalization of treatment. A practical approach would be to use at the start of the treatment BIA and DXA because DXA assesses also the bone mineral density and then at follow-up visits, BIA can be used for body composition assessment.

Future studies are needed in order to develop a new specific equation for AN and severely undernourished populations.

Statement of authorship

LM carried out the studies and data analyses and drafted the manuscript. NG conceived the study. SK and JM participated in the design of the study. BF advised on the statistical analysis. DR, CV, CN and CB participated in the coordination and helped to execute the study. CP supervised the work and actively corrected the draft of the manuscript.

Conflict of Interest

None of the authors has declared a conflict of interest.

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