Comparison of Dual-Energy X-Ray Absorptiometry to Four Other Methods to Determine Body Composition in Underweight Patients With Chronic Gastrointestinal Disease

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Assessment of body composition may provide important information about the nutritional status. The applicability of two safe and convenient methods for body composition analysis, bioelectrical impedance analysis (BIA) and dual-energy x-ray absorptiometry (DXA), in underweight patients with chronic gastrointestinal disease has been sparsely elucidated. Our objective was to compare measurements by DXA with four other methods. Furthermore, we compared total body water (TBW) by BIA using three different BIA equations with measurement of TBW by tritium dilution (TBW-^3H_2O). Nineteen clinically stable underweight patients with chronic gastrointestinal disease were included in the study (body mass index [BMI], 19.3 ± 1.2 kg/m^2). Body composition was assessed using total body potassium (TBK), isotope dilution of tritium (^3H_2O), anthropometry (skinfold thickness [SF]), BIA, and DXA. Fat-free mass (FFM) by DXA was in reasonable agreement with body composition measurements by TBK (mean difference$_{TBK-DXA}$ = −1.61 kg, r = .88, standard error of the estimate [SEE] = 4.66 kg) and ^3H_2O (mean difference$_{3H2O-DXA}$ = 0.98 kg, r = .93, SEE = 3.34 kg). Although mean values for FFM by DXA differed significantly versus BIA and SF, we found highly significant correlations between the measurements (r = .97 and r = .97, respectively). The mean TBW by BIA was overestimated by 1.9 and 3.1 L compared with TBW-^3H_2O when prediction equations for normal-weight subjects were used. We conclude that the DXA method is a valuable addition to the list of methods available for body composition studies in clinically stable underweight patients. Our data show that BIA equations for normal-weight subjects overestimated TBW in the patients studied.

MALNUTRITION frequently occurs in patients with chronic gastrointestinal disease, and is associated with increased morbidity and mortality.[1,2] Screening procedures to identify patients who are nutritionally at risk are usually based on changes in body weight and biochemical markers. However, weight as a single parameter does not reflect changes in body composition induced by the disease process, and biochemical markers such as serum albumin and transferrin may be confounded by concomitant liver disease, chronic inflammation, or iron-deficiency anemia. Therefore, estimations of body composition, including measurement of body stores of fat and protein, may provide valuable information for the clinician in the assessment of the nutritional status of underweight patients.

Techniques for accurate assessment of body composition are now available.[3,4] However, some require access to advanced technical equipment and others are unpleasant for the patient and therefore unsuitable for general use. Bioelectrical impedance analysis (BIA)[5] and dual-energy x-ray absorptiometry (DXA)[6,7] have gained wide acceptance for body composition analysis due to their safety and convenience. In previous studies in lean subjects, measurements by DXA were in reasonably good agreement with other methods to determine body composition.[8-11] Still, few studies have examined the limitations of BIA and DXA in underweight patients with chronic gastrointestinal disease.

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The aim of the present study was to compare measurements of fat mass (FM) and fat-free mass (FFM) by DXA with the methods of isotope dilution of tritium (^3H_2O) and total body potassium counting (TBK), as well as skinfold measurements (SF) and BIA. We studied a group of clinically stable underweight patients with chronic gastrointestinal disease. This study also investigated whether some of the presently used equations for calculation of total body water (TBW) by BIA produce reliable estimates in such patients.

SUBJECTS AND METHODS

Patients

Nineteen patients (11 women and 8 men) with low body weight and chronic gastrointestinal disease were included in the study. The patients were recruited from the outpatient clinic. At the time of inclusion, all patients had a body mass index (BMI) less than 20 kg/m^2, calculated as the weight in kilograms divided by the height in meters squared. However, on the day of investigation, two patients had gained weight and their BMI was increased slightly to 21.5 and 21.8 kg/m^2, respectively. The diagnoses were Crohn's disease (n = 12), ulcerative colitis (n = 4), and other (n = 3). Their age was 47.6 ± 15.3 years (mean ± SD) and BMI 19.3 ± 1.2 kg/m^2. All patients were considered to be in stable clinical condition, and no subjects had clinical signs of edema or dehydration. None of the patients were treated with diuretics, and only one patient received prednisolone therapy (5 mg daily for a period of 13 years). The study was performed in accordance with the Declaration of Helsinki II and with approval from the Ethics Committee of Copenhagen. Written informed consent was obtained from each patient before inclusion.

Study Protocol

Following an overnight fast, patients were weighed (after voiding) on a calibrated digital scale accurate within 0.1 kg (with the subjects wearing light clothes). Height was measured by a wall-mounted stadiometer to the nearest 0.1 cm. Measurements were performed twice and the average was used for calculations. Each subject then underwent an estimation of body composition by 5 different methods, ^3H_2O, TBK, BIA, SF, and DXA, in random order. Each patient had all measurements

performed consecutively on the same day. The patients were not allowed any intake of food or drinks during the study period.

Isotope Dilution of Tritium

TBW-^3H_2O was measured by isotope dilution of tritiated water (^3H_2O).[12] Initially, a baseline sample of serum was obtained for background correction. Subjects then received 100 μCi (3.7 MBq) of ^3H_2O intravenously. After an equilibration period of 2 to 3 hours, a second plasma sample (10 mL) was taken from a cubital vein. The radioactivity of 0.5 mL plasma water obtained by vacuum sublimation[12] was counted in a liquid scintillation counter (Packard Tri-Carb 4530; Packard, Downers Grove, IL) using 10 mL Ultima Gold (Packard) as the scintillation fluid. TBW-^3H_2O was calculated as 95% of the tritium dilution space, thereby correcting for nonaqueous exchangeable hydrogen. The total precision of a TBW determination is ±1.03 L. For calculation of body composition, the hydration of the FFM was assumed to be 73.2%, and thus FFM by ^3H_2O was determined as FFM = TBW/0.732. FM by ^3H_2O was calculated by subtracting FFM from body weight.

TBK

TBK was determined in a whole-body counter containing two plastic scintillators by counting the 1.46-MeV gamma rays emitted by the naturally occurring isotope ^{40}K, which comprises a constant fraction (0.012%) of all natural potassium. Before entering the steel room, all patients showered and dressed in hospital underwear to minimize environmental contamination. TBK was calculated by comparison to the activity in a phantom filled with potassium solution (5.00 g K/kg), the phantom being of equal weight to the person measured. Details regarding the use and validation of this instrument have been previously reported.[13] The determination of TBK has precision and accuracy errors of 2% and 3%.[14] Body composition estimates of FFM from TBK were derived from the following equations: FFM (kilograms) = TBK (millimoles)/62 for women and FFM (kilograms) = TBK (millimoles)/64.7 for men. These gender-specific factors were reported by Sjöström et al[15] and Kvist et al,[16] who compared ^{40}K-counting with tissue volumes by multiscan computed tomography. FM by TBK was calculated by subtracting FFM from body weight.

BIA

The principles for measurement of body composition by BIA have been previously described by Lukaski et al.[5] BIA was measured with the patient in the supine position using the standard tetrapolar technique with electrode placement at the wrist and ankle. The BIA 100 instrument (RJL Systems, Detroit, MI; 800 μA, single frequency, 50 kHz) was used according to the manufacturer's instructions. Body composition was calculated using both the equation supplied by the manufacturer (BIA-RJL) and the equation derived from a Danish cross-sectional population study (BIA-Heitmann).[13] In addition, we included an equation by Royall et al[10] developed with special reference to estimation of TBW in malnourished patients (BIA-Royall). The coefficient of variation (CV) for repeated measurements of impedance (ohm) over 4 hours with this instrument was 1.5% in our hands.

DXA

Measurements of body composition were performed with the Norland XR-36 DXA densitometer (Norland, Fort Atkinson, WI) with the subject supine. The host software was revision 2.5.2. and the scanner software revision 2.0.0. The theory and methodology for body composition by DXA have been previously described.[7] Briefly, the lightly dressed patient laid on a scan table for about 7 minutes while transverse scans approximately 1 cm apart were performed from top to heel. The instrument uses x-rays of two distinct energy levels that are attenuated by fat, bone, and lean mass to a different extent. By computerization of these data inputs, the DXA estimates of body composition are based on a 3-compartment model measuring total body bone mass content (BMC), FM, and nonskeletal lean tissue mass (LTM). FFM by DXA is calculated as LTM + BMC. Using a Lunar DXA device (DPX; Lunar Radiation, Madison, WI), Svendsen et al[6] compared measurements by DXA against postmortem chemical analysis of 7 pigs (weight, 35 to 95 kg). In this study, the accuracy (standard error of the estimate [SEE]) of in vivo measurements by DXA was 2.9%, 1.9 kg, and 2.7 kg for the percent fat, fat tissue mass, and lean body mass, respectively.[6] Recently, by adding known amounts of beef and lard on top of healthy subjects, Gotfredsen et al[17] estimated that the accuracy errors in vivo for changes in FM and FFM by the Norland XR-36 system are about 1 kg. To reduce beam-hardening effects, the Norland XR-36 uses dynamically changing samarium filtration. This is achieved by rapidly switching between 8 different combinations of samarium filter sheets during the scan, depending on the thickness and composition of the tissue. The filtration can be changed very rapidly (milliseconds <11).[17] The purpose of the dynamic filter change is to equalize the intensity of the x-ray beam to any absorber thickness, thereby reducing the influence of beam-hardening. Precision errors of body composition measurements by the Norland XR-36 densitometer have recently been reported by Hendel et al.[18] They were 2.2% for BMC, 2.7% for LTM, and 2.6% for FM%. In our hands, the between-measurement coefficient of variation for BMC, LTM, and FM was 1.5%, 1.6%, and 3.9%, respectively.

SF

Left-side skinfolds at 4 different sites (biceps, triceps, subscapular, and iliac crest) were taken in triplicate by a single observer with a Harpenden caliper (Holtain, Wales, England). The mean of three readings was used, and the percent body fat was calculated according to the age- and sex-specific equation from Durnin and Womersley.[19] The precision of this method has been reported to be ±3.5% in women and ±5% in men for the percent body fat.[20] FFM was calculated by subtracting FM from body weight.

Statistical Methods

Descriptive statistics were performed for all primary outcome measures. Results are expressed as the mean ± SD. Student's *t* test for paired observations was used to compare changes between repeated measurements of paired variables. A *P* value less than .05 was considered statistically significant. Differences between measurements by DXA and other methods were also compared by the Bland-Altman method[21] with calculation of the 95% limits of agreement. The strength of the relationship between variables was tested using simple linear regression analysis. A stepwise multiple linear regression analysis was performed to calculate the best-fitting equation to predict TBW by BIA. The Microsoft EXCEL statistical program version 5.0 (Microsoft, Redmond, WA) was used for all analyses.

RESULTS

DEXA weight, ie, the sum of FM, LTM, and BMC, was 55.8 ± 8.0 kg (mean ± 1 SD), significantly lower than the weight determined by an electronic scale (56.6 ± 8.3 kg, $P < .001$). However, the mean difference between the weight by DXA and weight by scale was only 1.4%. The mean values for FM, FFM, and TBW measured and computed by the various methods are listed in Table 1.

The results of paired comparisons of FM and FFM measurements by the various methods compared with DXA are shown in Table 2. For each model, the mean difference, *P* value as assessed by paired *t* test, correlation (Pearson's *r*), and SSE are presented. The mean value for FM by DXA differed slightly but significantly from all other methods except ^3H_2O. Compared

Table 1. Measurement of FM, FFM, and TBW by Different Methods in 19 Clinically Stable Underweight Patients With Chronic Gastrointestinal Disease

Method	FM (kg)	FFM (kg)	TBW (L)
DXA	15.1 ± 4.1	40.7 ± 9.9	
BIA-RJL	12.0 ± 2.4	44.5 ± 8.5	33.6 ± 6.2
BIA-Heitmann	10.7 ± 3.3	45.9 ± 9.3	32.4 ± 6.4
BIA-Royall			32.0 ± 4.8
^3H_2O	14.9 ± 4.1	41.7 ± 8.7	30.5 ± 6.3
SF	13.4 ± 4.0	43.2 ± 9.7	
TBK	17.5 ± 4.5	39.1 ± 9.4	

NOTE. Data are the mean ± 1 SD.

with DXA, BIA-RJL, BIA-Heitmann, and SF underestimated the mean FM by −2.96, −4.33, and −1.66 kg, respectively, whereas TBK overestimated the mean FM by 2.44 kg. The correlation coefficients between FM by DXA and BIA-RJL, BIA-Heitmann, and SF were high, in the range of .72 to .88. Lower correlation coefficients were found for the comparison between FM by DXA and ^3H_2O and TBK, namely .56 and .40, respectively. Bland-Altman plots[22] with calculation of the 95% confidence interval for the mean difference between FM by DXA and the other methods are shown in Fig 1. The limits of agreement for comparisons of FM estimates from BIA methods were narrower compared with TBK and ^3H_2O. However, the scatter of differences for FM by BIA-RJL compared with DXA decreased significantly with an increasing mean value of the two measurements ($r = -.60$, $P = .007$). The differences calculated for FM by BIA-Heitmann, ^3H_2O, SF, and TBK compared with DXA showed no significant correlations with the corresponding mean values. The analysis of TBK data demonstrated two subjects with particularly large deviations.

The mean value for FFM by DXA was not significantly different versus FFM by ^3H_2O and TBK, but FFM by DXA differed significantly versus FFM by BIA and SF (Table 2). However, the regression coefficients were high for all comparisons with DXA, from .88 for TBK to .98 for BIA-Heitmann. SEE values were 1.88 kg for BIA-Heitmann to 4.66 kg for TBK.

Table 2. Comparison of FM and FFM Estimates by Different Methods Versus DXA in 19 Clinically Stable Underweight Patients With Chronic Gastrointestinal Disease

Method	Mean Difference (kg)	P	r	SEE (kg)
FM				
BIA-RJL	−2.96	<.001	.72	2.62
BIA-Heitmann	−4.33	<.001	.88	1.59
^3H_2O	−0.15	.87	.56	3.48
SF	−1.66	.005	.85	2.21
TBK	2.44	.04	.40	4.21
FFM				
BIA-RJL	3.80	<.001	.97	2.62
BIA-Heitmann	5.17	<.001	.98	1.88
^3H_2O	0.98	.27	.93	3.34
SF	2.50	<.001	.97	2.29
TBK	−1.61	.16	.88	4.66

NOTE. Values are the mean difference with corresponding *P* value (Student's paired *t* test). Pearson's *r* and SEE (linear regression) are also shown.

The limits of agreement between FFM by DXA and the other methods are shown in Fig 2. The scatter of differences for FFM by BIA-RJL compared with DXA decreased significantly with an increasing mean value ($r = -.51$, $P = .025$). The differences calculated for FFM by BIA-Heitmann, ^3H_2O, SF, and TBK compared with DXA showed no significant correlation with the corresponding mean values. Also, mirroring the analysis of the FM data comparison between FFM by TBK and DXA, two subjects showed large deviations.

ANOVA on ranks on repeated measures was performed to test the agreement of measurements by BIA and SF compared with ^3H_2O and TBK. BIA and SF differed significantly from both TBK and ^3H_2O ($P < .05$), except for the comparison of FFM by ^3H_2O with SF. Table 3 shows that the mean TBW-^3H_2O (30.5 ± 6.3 L) was significantly lower than the mean estimates by the three different BIA equations, ie, BIA-Heitmann, BIA-RJL, and BIA-Royall. However, low SEEs and highly significant correlations with TBW-^3H_2O ($r > .90$) were found for all three prediction equations. The equation proposed by Royall et al,[10] developed specifically for malnourished underweight patients, yielded the lowest mean difference of 1.49 L in our patients, with a regression coefficient of .90 and a SEE of 2.17 L. This compares with the SEEs obtained by the other two equations. The relationship between TBW by BIA-Royall and TBW-^3H_2O is graphically depicted in Fig 3.

By a stepwise multiple regression analysis entering height^2/resistance, age, weight, and gender as independent variables (x) and TBW-^3H_2O as the dependent variable (y), the best-fitting prediction equation for estimation of TBW by BIA in our patients was TBW (liters) = $0.528H^2/\Omega - 0.146age + 12.224$. The best single predictor for TBW was height^2/resistance, followed by age. Introducing the variables of weight and gender did not significantly change the equation.

DISCUSSION

In principle, all methods used in this study except DXA are based on the 2-compartment model of human body composition dividing the body into FM and FFM. Each technique relies on specific assumptions. Thus, although isotopes of water offer a highly accurate and reproducible measure of TBW, the extrapolation to estimates of FM and FFM rests on the assumption of a constant 73.2% water content of the FFM. Likewise, calculation of FFM from TBK assumes a constant composition of FFM with respect to potassium. BIA requires a lack of alteration in fluid distribution, and the SF method operates on the assumption that a constant fraction of adipose tissue is located subcutaneously. Theoretically, DXA measurements may be influenced by a variation in soft tissue hydration, although it has been shown that a change in the hydration state has much less consequence for measurements by DXA than by other methods, for example, isotope dilution techniques.[23] Some of the assumptions underlying the various techniques may not hold with very sick or old patients. Thus, in malnourished patients, protein catabolism, fluid and electrolyte derangement, and bone loss may exist which may render several classic techniques inaccurate. However, from a clinical point of view, the patients investigated presented with chronic gastrointestinal disease and a somewhat reduced BMI, but all were clinically stable with no

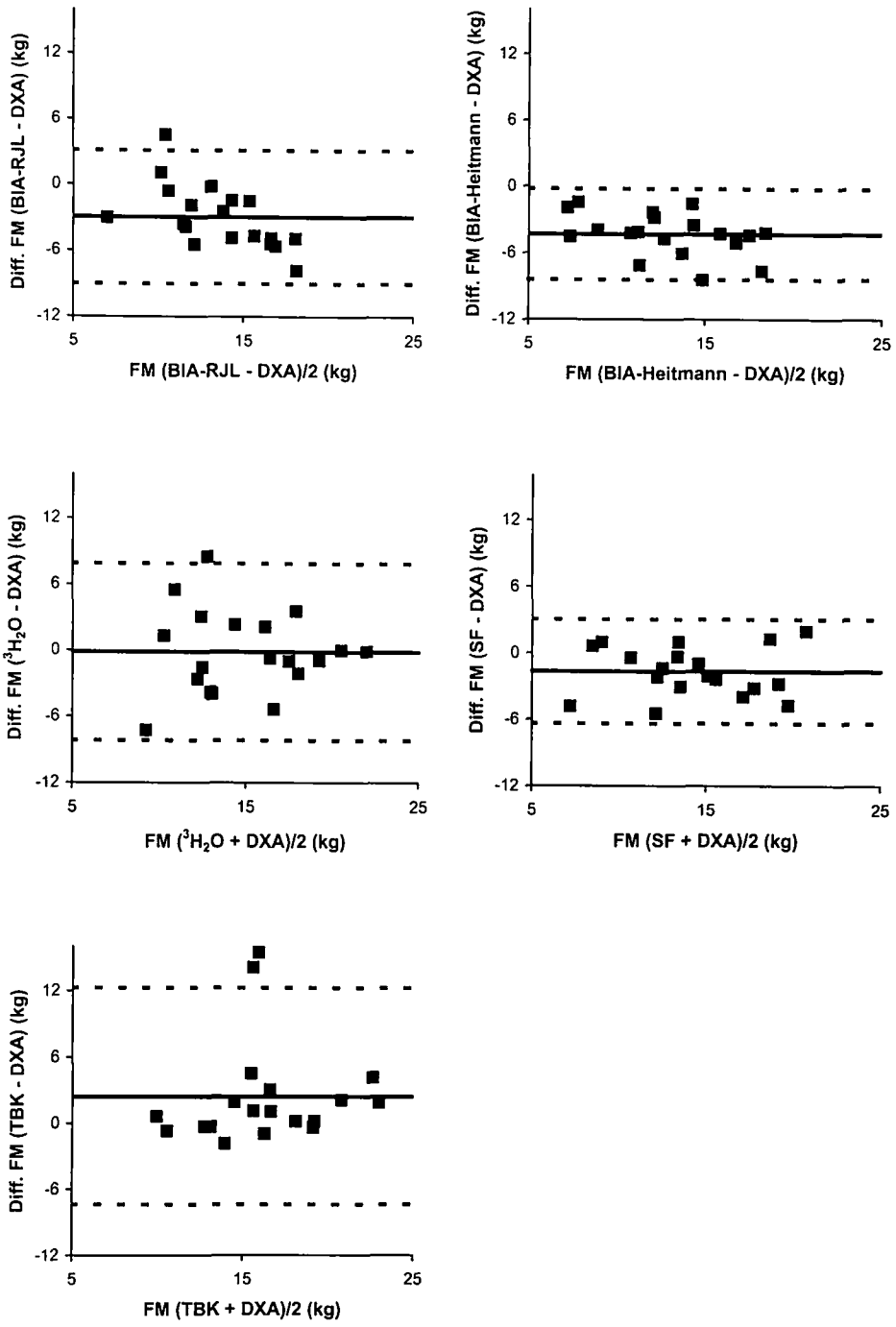

Fig 1. Difference between FM by 5 different methods versus DXA plotted against the mean value of the 2 measurements in 19 clinically stable underweight patients. (___) Mean difference; (---) 95% limits of agreement.

signs of edema or dehydration. Based on these considerations, we find that the 2-compartment model can be applied.

We found a reasonable agreement between DXA and ^3H_2O, with a mean difference of less than 1 kg for estimates of both FM and FFM. The favorable agreement between DXA and ^3H_2O in lean subjects has been previously reported.[10,24] Although the limits of agreement were not very narrow, there was no obvious bias when comparing the two methods.

Measurements of FFM by DXA were not significantly different versus FFM by TBK, and FM by DXA differed only slightly from FM by TBK. The agreement between measurements by the two methods was remarkably good in 17 of 19 patients as shown by the Bland-Altman plots. The two patients with large deviations were the two oldest in the group, 75 and 72 years of age, respectively. We applied gender-specific prediction equations,[15,16] but a possible relationship between age and the ratio of TBK to FFM is not accounted for. Therefore, we may have induced an error, as there is some evidence to suggest that the ratio of TBK to FFM declines with age.[25] This could explain the diverging results in these two

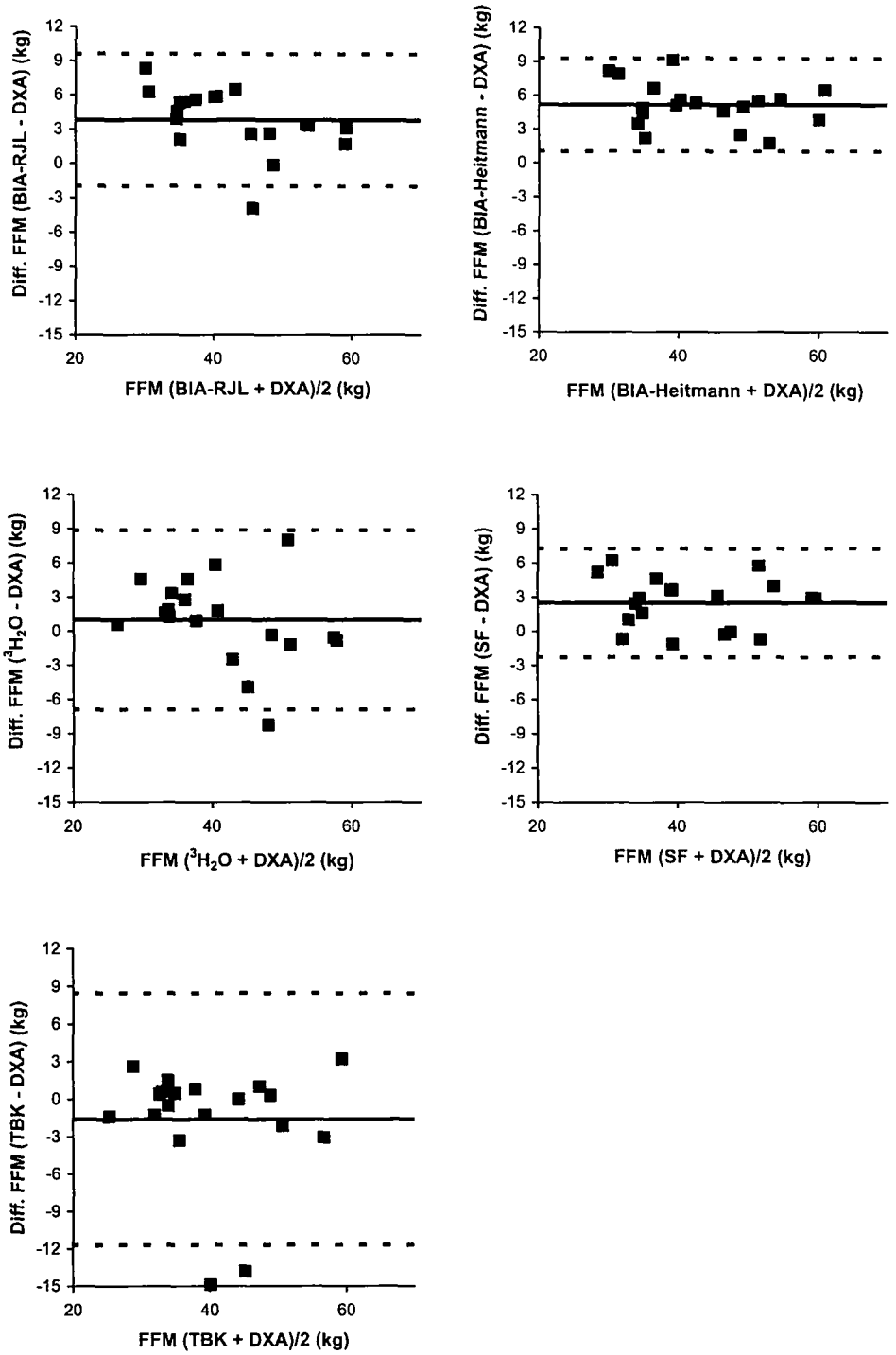

Fig 2. Difference between FFM by 5 different methods versus DXA plotted against the mean value of the 2 measurements in 19 clinically stable underweight patients with chronic gastrointestinal disease. (___) Mean difference; (---) 95% limits of agreement.

patients, as there is no reason to speculate that DXA technically should perform less well in older patients.[26-28]

In the present study, we found highly significant correlations between FM and FFM by SF and DXA measurements. Moreover, the SEEs were low, reflected by the narrow limits of agreement in the Bland-Altman plots. However, the mean values for measurements by SF differed slightly but significantly from DXA. The SF method may have limitations in underweight patients with chronic gastrointestinal disease. Thus, steroid therapy, often used in patients with inflammatory bowel disease, may alter the distribution of subcutaneous fat.

Although measurements of FM and FFM by BIA yielded significantly different absolute values compared with DXA, the correlations between the two methods were strong. The limits of agreement were narrow regardless of the equations used, but the equation supplied by the manufacturer (BIA-RJL) showed a systematic bias with a negative correlation between the difference between measurements and the absolute value of FM and

Table 3. Measurement of TBW by BIA Using Four Different Equations Compared With TBW-^3H_2O in 19 Clinically Stable Underweight Patients With Chronic Gastrointestinal Disease

TBW Method	Mean Difference (L)	*P*	*r*	SEE (L)
BIA-RJL	3.09	<.001	.90	2.81
BIA-Heitmann	1.89	<.01	.94	2.34
BIA-Royall	1.49	.04	.90	2.17

NOTE. Values are the mean difference with corresponding *P* value (Student's paired *t* test). Pearson's *r* and SEE (linear regression) are also shown.

FFM. The equations used for both BIA-Heitmann and BIA-RJL have been validated in normal-weight subjects by comparison to reference methods for body composition. The finding that FM and FFM by BIA in our study also differed significantly from measurements by TBK and ^3H_2O suggests that prediction equations developed in normal-weight subjects do not apply to underweight patients.

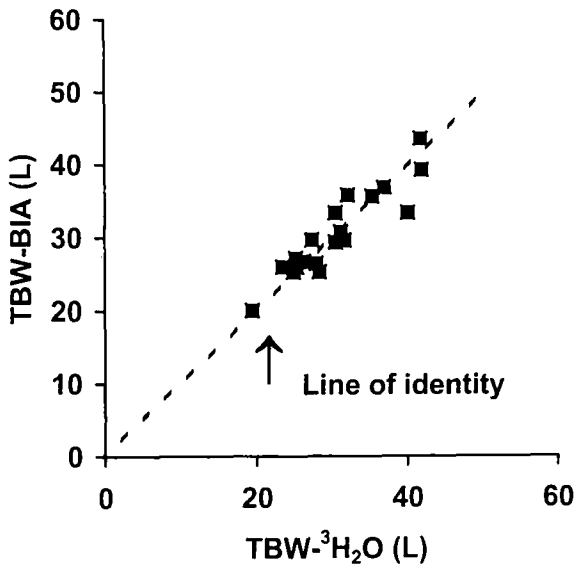

Fig 3. Relationship between TBW-^3H_2O versus TBW by the BIA equation of Royall et al in 19 clinically stable underweight patients.

The present study reports highly significant correlations between TBW-^3H_2O and TBW as analyzed by three different BIA equations. However, the mean values for TBW by the two BIA equations developed in normal-weight subjects were considerably higher than the mean TBW-^3H_2O. The overestimation of TBW by BIA compared with isotope dilution in underweight patients is consistent with data reported by others.[10,29] Thus, Simons et al[29] reported a systematic overestimation of TBW by BIA when applying 10 of the most widely used prediction equations to underweight cancer patients. Recently, Royall et al[10] published a prediction equation specifically developed for the calculation of TBW in underweight and malnourished patients with active Crohn's disease. This equation in fact yielded slightly better results in our patients compared with the two equations developed in normal-weight subjects. In our cases, we calculated the best-fitting prediction equation for TBW by BIA using stepwise multiple linear regression analysis. This equation differed from that of Royall et al in that adding body weight into the formula did not change the results significantly. Whether the revised BIA equation presented herein is applicable in other lean subjects remains to be tested and cross-validated in an independent sample against criterion standard isotopic methods.

In summary, we compared DXA with four other body composition techniques in underweight clinically stable patients with chronic gastrointestinal disease. We found that measurements by DXA agreed reasonably well with two widely used but technically demanding methods of body composition, ie, TBK counting and tritium isotope dilution. Although the mean values differed significantly between measurements by BIA, SF, and DXA, we found highly significant correlations and low SEEs. Considering that the mean values for FM by both BIA and SF differed significantly from TBK and ^3H_2O as well, we conclude that the prediction equations used with these methods cannot be applied in underweight patients without specific changes to the equations. In addition, our data indicate that measurements of TBW by BIA using equations developed in normal-weight subjects overestimate TBW in these patients.

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