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FULL PAPER

Measurement of total and visceral fat mass in young adult women: a comparison of MRI with anthropometric measurements with and without bioelectrical impedance analysis

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Objective: MRI is established for measurement of body fat mass (FM) and abdominal visceral adipose tissue (VAT). Anthropometric measurements and bioelectrical impedance analysis (BIA) have been proposed as surrogates to estimation by MRI. Aim of this work is to assess the predictive value of these methods for FM and VAT measured by MRI.

Methods: Patients were selected from cohort study PPS-Diab (prediction, prevention and subclassification of Type 2 diabetes). Total FM and VAT were quantified by MRI and BIA together with clinical variables like age, waist and hip circumference and height. Least-angle regressions were utilized to select anthropometric and BIA parameters for their use in multivariable linear regression models to predict total FM and VAT. Bland–Altman plots, Pearson correlation coefficients, Wilcoxon signed-rank tests and univariate linear regression models were applied.

Results: 116 females with 35 ± 3 years and a body mass index of 25.1 ± 5.3 kg/m^2 were included into the analysis. A multivariable model revealed weight (β = 0.516, p < 0.001), height (β = −0.223, p < 0.001) and hip circumference (β = 0.156, p = 0.003) as significantly associated with total FM measured by MRI. A additional multivariable model also showed a significant predictive value of FM_{BIA} (β = 0.583, p < 0.001) for FM. In addition, waist circumference (β = 0.054, p < 0.001), weight (β = 0.016, p = 0.031) in one model and FM_{BIA} (β = 0.026, p = 0.018) in another model were significantly associated with VAT quantified by MRI. However, deviations reached more than 5 kg for total FM and more than 1 kg for VAT.

Conclusion: Anthropometric measurements and BIA show significant association with total FM and VAT.

Advances in knowledge: As these measurements show significant deviations from the absolute measured values determined by MRI, MRI should be considered the gold-standard for quantification.

INTRODUCTION

Obesity, which is linked to poor diet and physical inactivity, is among the top three causes of death in the western world.[1] In particular, visceral fat plays a pivotal role in development of Type 2 diabetes and metabolic syndrome.[2]

Yet, the most commonly used definitions for overweight and obesity are based on a body mass index (BMI) of ≥25 and ≥30 kg/m^2[3] and have a very limited value for the estimation of body fat distribution (BFD). As a result, additional anthropometric measurements like waist-to-height ratio, and waist-to-hip ratio (WHR) were introduced for better clinical

estimation of visceral fat.[4] Furthermore, bioelectrical impedance analysis (BIA) combined with weight and height has been advocated as cost-effective method for estimation of BFD.[5] Yet, measurements in BIA can be significantly confounded by parameters like muscle mass and BMI.[6] In contrast, image-guided quantification of visceral fat using CT or MRI offers a non-invasive estimation of body composition at a high resolution which may be less susceptible to confounding parameters. While CT has some relevance in analysis of scans acquired in the clinical routine preventing additional radiation dose, MRI is a potential alternative: Due to its excellent contrast in depicting soft tissues such as fat without ionizing radiation it is regarded as gold-standard for a dedicated quantification of body fat.[7,8] However, effectiveness of MRI for estimation of adipose tissue in comparison to anthropometric measurements with and without BIA remains unclear.[9] Although MRI offers a quantitative image-based estimation of adipose tissue, it is significantly more complicated and costly than anthropometric and/or BIA measurements.

Therefore, the aim of this study was to compare the quantification of total and visceral fat mass based on clinical and BIA measurements to quantification in MRI.

METHODS AND MATERIALS

Patient population

Study subjects with a full set of anthropometric, BIA and MRI measurements available were included from the cohort study PPS-Diab (prediction, prevention and subclassification of Type2 diabetes). The study recruited females 3–16 months after an index pregnancy that was either normoglycemic (44 of 116 participants) or complicated by gestational diabetes (72 of 116 participants) defined according to the IADPSG criteria.[10] The PPS-Diab study has been described in detail before.[11] All study subjects provided written informed consent and the study was approved by the institution review board of University Hospital, LMU Munich.

Anthropometrics

Weight and fat mass were estimated using a BIA scale (Tanita BC-418, Tanita Corporation, Tokyo, Japan). 0.5 kg was subtracted for clothing. Height was assessed to the nearest of 0.5 cm. BMI was calculated as weight divided by the square of height (kg/m^2). Waist (WC) and hip circumferences (HC) were obtained by tape measurement and the WHR was calculated by division of WC by HC. Anthropometric and BMI measurements were performed at the baseline visit, whereas MRI was performed on a separate day.[11]

Magnetic resonance imaging

Magnetic resonance examinations were performed with a 3 Tesla system (Ingenia or Achieva, Philips Healthcare, Best, Netherlands). Whole body imaging was performed with an anterior body coil and a posterior coil integrated in the tabletop. Subjects were scanned in supine position with arms extended above the head. For the determination of adipose and lean tissue distribution, an axial mDixon sequence (repetition time 4.0 ms, first echo time 1.45 ms, second echo time 0.7 ms, flip angle 10°, slice thickness 10 mm, gap 10 mm, 208 × 161 matrix, 520×400×190 field of view) or an axial T_1 weighted (T_1W) sequence (repetition time 672 ms, echo time 7.6 ms, flip angle 90°, slice thickness 10 mm, gap 10 mm, 208 × 197 matrix, 520 × 400×190 field of view) were used. Out of the 116 subjects 99 females (85.3%) received the mDixon and 17 females (14.7%) the T_1W protocol given that the mDixon sequence was not available at the Department of Radiology, University Hospital, LMU Munich in the first 6 months of the study. 7–10 stacks were acquired depending on the patient's height. Scan time was approximately 20 min in both sequences. Semi-automatic segmentation of body fat compartments was performed using SliceOmatic 4.3 v. 11 (TomoVision). Visceral adipose tissue (VAT) was defined as fat between diaphragm, pelvic floor and abdominal musculature. Total subcutaneous adipose tissue (SAT) was determined from wrist to ankle excluding the mammae due to the large variety regarding the status of breastfeeding. Two threshold values were individually set for the separation of SAT and VAT. Manual adjustments were performed to account for signal inhomogeneities. Periumbilical visceral fat was measured on a single slice at the height of the umbilicus as published literature suggests, that it can offer a sufficient estimation of the visceral adipose tissue.[12] Preliminary segmentations were generated by a doctoral student and validated and—if applicable—corrected by one of two experienced MRI readers (MRI experience of 5 and 3 years respectively). The overall segmentation time per patient was 1.5 h. The reproducibility of body fat estimation in sectional imaging has been confirmed in previous studies.[13,14]

Pre-analytical study for the validation of a modified Dixon sequence compared to an axial T_1 weighted sequence

As mentioned above, a change in the imaging protocol during the study required a comparison of mDixon and T1 sequences. Therefore, in a pre-analytical study comparability of modified Dixon (mDixon) sequence and T_1W sequence and the interscan reliability were investigated. Therefore, 10 young healthy female volunteers with a mean age of 24.1 ± 2.6 years and a mean BMI of 22.3 ± 3.8 kg/m^2 were scanned twice with each MRI technique.

Bioelectrical impedance analysis

Single-frequency BC-418 MA 8-contact electrode BIA (Tanita Corporation, Tokyo, Japan was used for measurement of total fat mass (FM) and visceral fat level (VFATL).[15] Body weight was assessed to the nearest of 0.1 kg and for standardization 0.5 kg was subtracted from total weight due to clothing. GMON Pro Software was used to export the obtained data for further analyses (Medizin & Service GmbH, Chemnitz, Germany). Measurements were carried out in all females after an overnight fast of at least 12 h.

Statistical analyses

Statistical analyses were carried out using SAS statistical software package v. 9.2 (SAS Institute Inc.), SPSS Statistics v. 22 (International Business Machines Corporation, IBM) and GraphPad Prism (GraphPad Software Inc.). FM in kg was calculated as fat in liter (l) measured in MRI multiplied with the factor of density for fat (0.9 kg l^{-1}).[16] For the pre-analytical study, Wilcoxon signed-rank tests were used to test

for significant differences between different MRI techniques (mDixon sequence *vs* T_1W) and runs. All variables were normally distributed and baseline characteristics are given as mean ± standard deviation (SD) and minimum (min) and maximum (max). Least-angle regressions with the Schwarz Bayesian information criterion were used with all baseline variables for initial variable selection for the prediction of total FM and VAT.[17] Pearson correlation coefficients were calculated for the association of two measurement methods and linear regression models were applied for the quality assessment of BIA or anthropometric data to predict the analogue MRI values. In particular, models were designed in a stepwise approach: for FM a model assessing the association with BIA measurements and for VAT a model assessing the association with relevant anthropometric measurements was applied before adding other independent variables to the models. Differences between methods were plotted against the means of MRI-measured and clinical parameters-/clinical parameters + BIA-/BIA-predicted FM and VAT, respectively, by Bland–Altman plots.[18] A p-value below 0.05 was regarded as statistically significant.

RESULTS

Patient characteristics

A total of 116 of 214 females were included into the analysis. 62% of all females (n = 72) had had gestational diabetes. Anthropometric measurements were carried out 9 ± 3 months post-delivery. Females had a mean age of 35 ± 4 years and a mean BMI of 25.1 ± 5.3 kg/m^2. Total FM in kg measured by MRI was 22.7 ± 9.9 kg and by BIA 23.3 ± 10.9 kg. MRI was carried out 45 ± 42 days after the baseline visit. Further characteristics are summarized in Table 1. No significant differences were detected in body fat determination with T_1W and mDixon sequence (Supplementary Material 1).

Evaluation of important parameters for prediction models

Least-angle regression variable selection was applied to identify the most relevant clinical and BIA variables for the prediction of FM and VAT. A simple methodical equivalent (Figure 1, solid line) to the computed ideal models (asterisks, Figure 1) was selected:

Weight, height, HC and WC were the relevant clinical parameters for the prediction of total FM measured by MRI (Figure 1A). With BIA parameters included, FM_{BIA}, HC, weight and WC were identified as most pertinent clinical parameters for the prediction of total FM (Figure 1B).

For prediction of the abdominal VAT measured by MRI, WC and weight were the most important clinical predictors (Figure 1C). In a model which included BIA parameters, WC and FM_{BIA} were identified as best predictors.

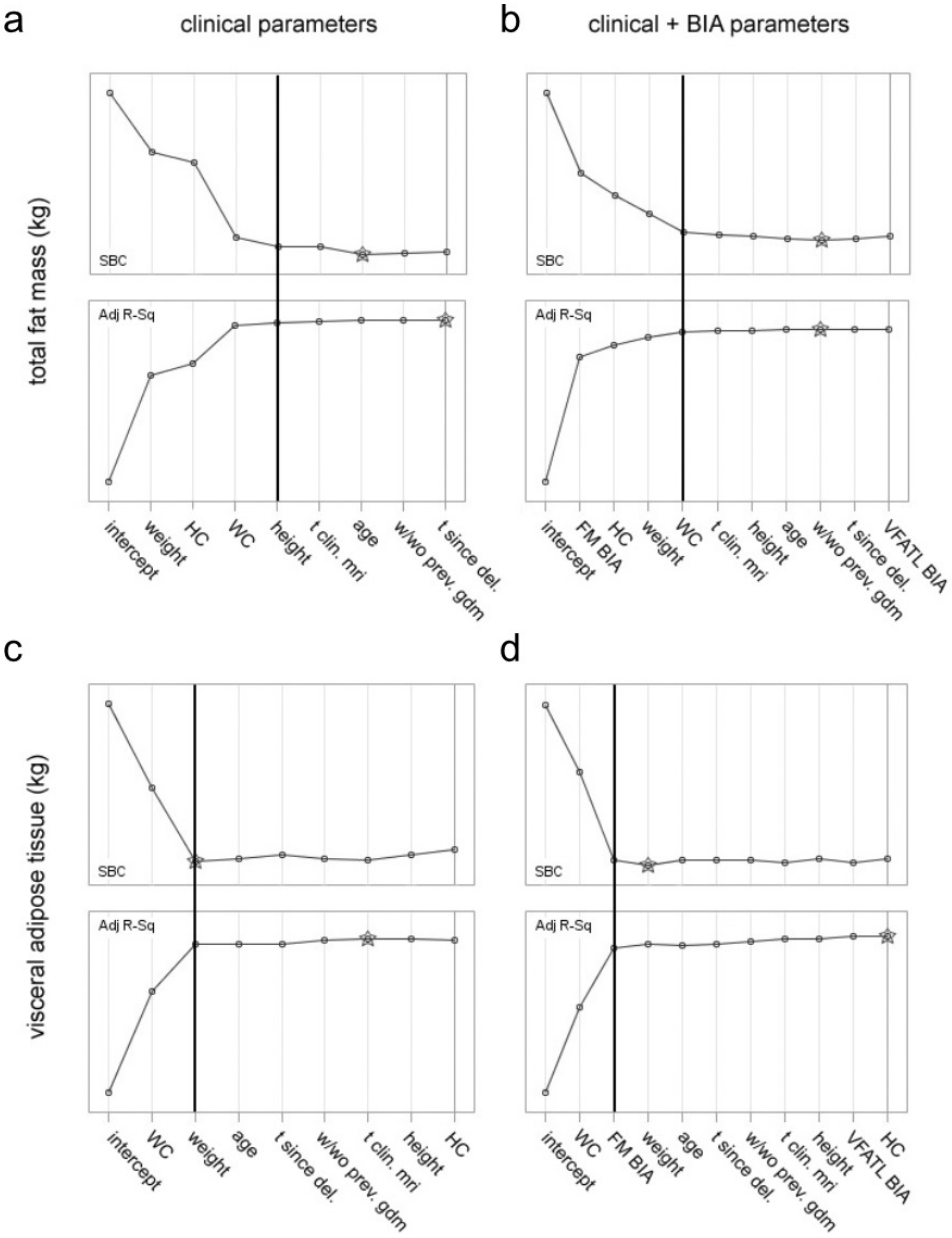
For all prediction models, time post-delivery, post-gestational diabetes mellitus status as well as time between the MRI and BIA measurements had only relevance for prediction of total/visceral FM. Scatterplots of anthropometric, MRI, BIA measures can be found in the Supplementary Material 1.

Table 1. Patient characteristics of 116 females

	n (%)	Mean ± SD	Min, max
Clinical characteristics			
Post-gestational diabetes mellitus	72 (62)		
Months post-delivery	116	9.4 ± 3.0	3.5, 16.2
Age (years)	116	35 ± 4	27, 46
Waist circumference (cm)	116	81 ± 11	63, 120
Hip circumference (cm)	116	100 ± 11	80, 134
WHR	116	0.81 ± 0.06	0.67, 0.95
Height (cm)	116	167 ± 6	150, 185
BMI (kg/m^2)	116	25.1 ± 5.3	17.5, 44.1
BIA parameters			
Weight (kg)	116	69.9 ± 14.8	46.3, 117.2
Total FM (kg)	116	23.3 ± 10.9	7.6, 62.7
$VFATL_{BIA}$	116	4.5 ± 2.9	1.0, 16.0
MRI parameters			
Total FM (kg)	116	22.7 ± 9.9	9.7, 56.2
VAT (kg)	116	1.8 ± 1.0	0.3, 4.4
Periumbilical visceral fat (cm^2)	116	0.12 ± 0.08	0.0, 0.42

WHR, waist-to-hip ratio; BMI, body mass index; Total FM, total fat mass; VFATL, visceral fat level; BIA, bioelectrical impedance analysis; VAT, visceral adipose tissue.

Figure 1. Least-angle regression analyses for the selection of parameters for clinical models. (a, b) Total fat mass (kg); (c, d) visceral adipose tissue (kg). Solid line, relevant parameters for prediction equations; asterisk, computed ideal model for prediction equations; BIA,bioelectrical impedance analysis; HC, hip circumference; FM, total fat mass; SBC, Schwarz Bayesian criterion; VFATL, visceral fat level; t since del., time sincedelivery; t clin. MRI, time between clinical parameters and MRI; WC, waistcircumference; w/wo prev. GDM, with/without previous GDM.



Prediction of total FM by clinical and BIA parameters

After the identification of relevant clinical and BIA parameters for the prediction of total FM (Figure 1A,B), respective multivariable linear regressions models for prediction were defined (Table 2, Model 1–3).

In a multivariable regression model utilizing clinical parameters (Table 2, Model 2), weight ($p < 0.001$), height ($p < 0.001$) and HC ($p = 0.003$) had significantly impact on FM, whereas WC did not reach significance ($p = 0.360$).

A regression model including clinical and BIA parameters (Table 2, Model 3), showed a significant impact of HC ($p = 0.001$) and FM_{BIA} ($p < 0.001$) on FM, whereas WC ($p = 0.209$) and weight ($p = 0.526$) were not significant. The use of FM_{BIA} in a univariate linear regression model (Table 2, Model 1) for total FM had less predictive value (adjusted $R^2 = 0.924$, SEE = 2.72 kg).

Bland–Altman plots were created to visualize the similarity of total FM between MRI and the calculated prediction equations. Mean between-method bias reached between 0.097 for total FM with clinical parameters (Figure 2A) and −0.014 for total FM

Table 2. Prediction of visceral adipose tissue (kg) and total fat mass (kg) by clinical parameters or by clinical parameters plus BIA or BIA alone

	Model 1		Model 2		Model 3		Model 4		Model 5	
	FM		FM		FM		VAT		VAT	
	β	*p*	β	*p*	β	*p*	β	*p*	β	*p*
Weight			0.516	**<0.001**	0.049	0.526	0.016	0.031		
Height			−0.223	**<0.001**						
HC			0.156	**0.003**	0.176	**0.001**				
WC			0.051	0.360	0.068	0.209	0.054	**<0.001**	0.051	**<0.001**
FM_{BIA}	0.872	**<0.001**			0.583	**<0.001**			0.026	**0.018**
Adj R^2	0.924		0.933		0.933		0.743		0.745	
SEE	2.72		2.56		2.56		0.5		0.5	

WC, waist circumference; HC, hip circumference; SEE, standard error of estimates, FM, total fat mass; BIA, bioelectrical impedance analysis. *N* = 116. Model1: Association of BIA with FM; Model 2: Association of anthropometricmeasurements with FM; Model 3: Association of anthropometric measurements and BIA with FM; Model 4: Association of relevant anthropometric measurements withVAT; Model 5: association of WC and BIA with VAT.

with clinical and BIA parameters (Figure 2B). Additionally, analyses of between-method differences and averages revealed no significant trend for higher total FM (both $r < 0.200$). In contrast, the Bland–Altman plot of total FM by MRI and BIA (Figure 2C) revealed significant overestimation by BIA with increasing total FM ($r = -0.340$, $p = 0.0002$).

Prediction of VAT by clinical and BIA parameters

After the identification of relevant clinical and BIA parameters for the prediction of VAT (Figure 1C,E), respective multivariable linear regressions models for prediction were defined (Table 2, Model 4–5).

In a multivariable regression model utilizing clinical parameters (Table 2, Model 4), and a model utilizing clinical and BIA parameters (Table 2, Model 5) each variable was significant (WC with $p < 0.001$, weight with $p = 0.031$ and FM_{BIA} with $p = 0.018$).

Bland–Altman analyses were plotted to visualize the similarity of VAT between MRI and the calculated prediction equations. Mean between-method bias reached from −0.0256 for VAT with clinical parameters (Figure 3A) to −0.0263 for VAT with clinical and BIA parameters (Figure 3B). Furthermore, analyses of between-method differences and averages revealed significant positive correlations ($r = 0.270$, $p = 0.003$ for clinical parameters and $r = 0.272$, $p = 0.003$ for clinical and BIA parameters, respectively).

Periumbilical visceral fat

The correlation of periumbilical visceral fat with VAT was overall good ($r = 0.722$, $p < 0.0001$), but only 51.7% of VAT variation could be explained by the use of this variable.

DISCUSSION

In this study, potential multivariable regression models for prediction of total FM and VAT quantified by MRI were investigated. Weight, height, HC and WC were identified predictors for FM. In particular, the adjusted R^2 of FM is explained by weight to a large extend. Hip also has some relevance in this context in the patient collective assessed. Yet, the relevance of weight in the context of FM is not surprising given the evident positive association of body fat mass and total weight. BIA did not yield additional value in this setting. Also, Bland–Altman plot of total FM by MRI and BIA revealed significant overestimation by BIA with increasing total FM. Variables with significant association with VAT included WC and weight, and WC and total FM_{BIA}, respectively. However, deviations of model predictions and MRI reached more than 5 kg for total FM and more than 1 kg for VAT in all models. Compared to the mean total FM of 22.7 kg and the mean VAT of 1.8 kg these changes have to be regarded as clinically significant, especially for the estimation of VAT. Also, the use of periumbilical visceral fat in MRI could not predict VAT precisely.

Previous studies have proposed use of BIA,[19] ultrasonography[20] or skinfold thickness measurements[21,22] for estimation of VAT. In our patient collective, the use of BIA did not yield additional value for prediction of FM to clinical parameters alone. Similar to the findings presented in this work, earlier studies revealed systematic errors in single- and multi frequency-BIA scales in comparison to dual-energy X-ray absorptiometry for normal-weight and overweight females concerning FM.[23,24] Other studies showed that BIA tended to overestimate FM with increasing BMI and thereby underestimated FM.[25–28] Therefore, according to these studies, especially in the setting of obese females MRI may be the method of choice. Also a previous study showed that total body fat estimated by BIA (Tanita BC-418) was not useful to represent abdominal fat and weakly correlated with obesity-risk factors.[29] In this work, the best and simplest prediction of VAT in kg included WC and weight or WC and total FM_{BIA}, respectively. Since these models showed a positive trend for increasing VAT, severe obese females may be overestimated in their VAT by these regression equations. However, as the study population consisted mainly of patients from the overweight group and consisted of a limited number of obese patients,

Figure 2. Bland-Altman plots for total FM. Difference between total fat mass measured by MRI and calculated formula *vs* average total fat mass measured by the two methods for the 116 subjects. Solid line, average difference between the two methods; dotted lines, mean ± 1.96 SD.FM, fat mass; SD, standarddeviation.

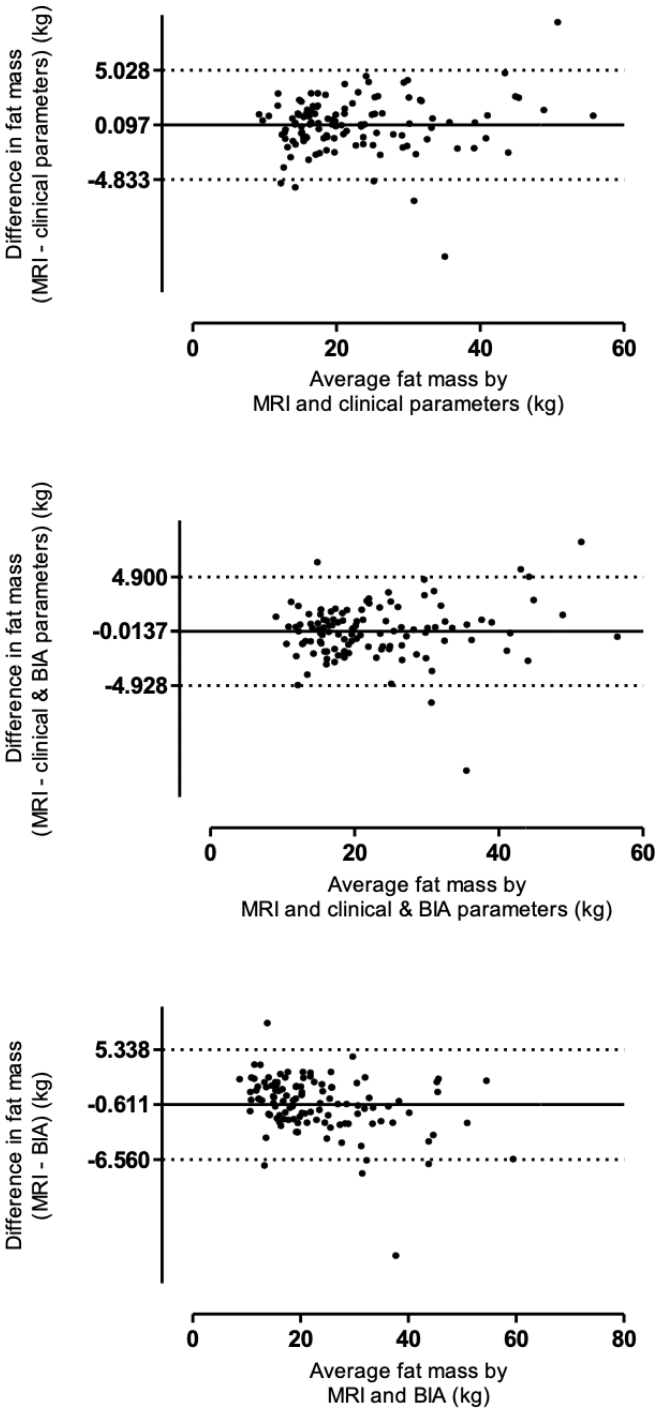
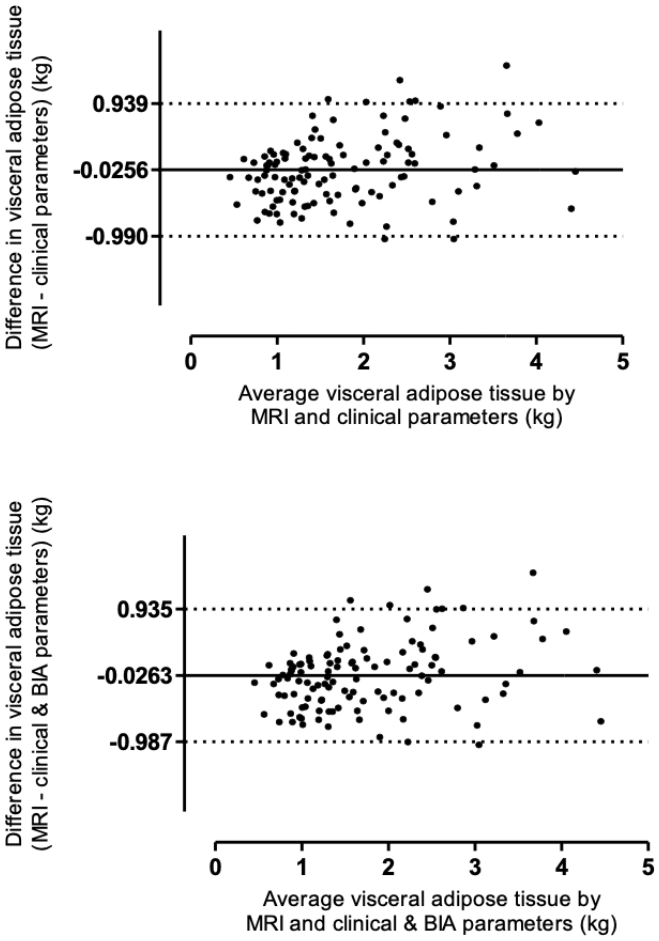


Figure 3. Bland–Altman plots for VAT. Difference between visceral adipose tissue measured by MRI and calculated formula *vs* average visceral adipose tissue measured by the two methods for the 116 subjects. Solid line, average difference between the two methods; dotted lines, mean ± 1.96 SD. VAT,visceral adipose tissue; SD, standard deviation.



these conclusions may need further validation in other patient collectives. Concerning WHR, our results are in line with previous studies that showed the failure of WHR to predict VAT precisely.[6,30] Besides, VFATL was strongly dependent on BMI (data not shown), which is conformable with previous results from Browning et al, where VAT measured by BIA correlated with total abdominal adipose tissue (abdominal SAT and VAT), but not with VAT measured by MRI.[31] This study and others[9,32] propose that VAT measurement by BIA is not a useful proxy method in comparison to MRI. As pointed out above, measurement of VAT was additionally performed at a single slice at the height of the umbilicus. This approach was suggested by Borkan et al[12] and is supported evidence from multiple analyses indicating that a singular slice can offer an appropriate estimation of VAT.[8,33,34] Yet, the localization of the umbilicus can vary depending on the positioning of a patient in the MRI scanner.[35]

The results presented in this study should be interpreted in the context of its design. Since data were acquired in a homogenous cohort of young females, results cannot be transferred easily to other collectives consisting of males or older patients. Although time distance of BIA and MRI measurements were not fully standardized and did not seem to have a significant statistical influence, they cannot be fully ruled out as

confounder. However, the most significant weight changes occur in the first 6 weeks of pregnancy,[36] whereas the baseline visit was performed on average 9 months post-partum. Also, there is evidence suggesting that pregnancy itself does not necessarily lead to long-term weight changes when compared to matched non-pregnant suspects.[37]

Due to a change of MRI hardware during the study period, MRI scans were acquired on two distinct 3 Tesla MRI systems offered by the same vendor. However, scanning and sequence protocols were set up on both scanners as described in the "Materials and Methods" section.

In conclusion, possible clinical and BIA surrogate parameters for approximate prediction of FM and VAT have been investigated. They may be suitable as an initial estimation of total FM and VAT and in settings were MRI screening is not feasible. However, especially for VAT, which is of high clinical relevance as a risk factor, MRI imaging remains the gold-standard, as it can offer higher diagnostic confidence.

KEY POINTS

Anthropometric measurements and bioelectrical impedance analysis are suitable for estimation of body fat.

However, these measurements show significant deviations to the absolute values measured by MRI.

Therefore, MRI remains gold-standard for accurate quantification.

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