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Original Paper

Estimation of Urinary Creatinine Excretion and Prediction of Renal Function in Morbidly Obese Patients: New Tools from Body Composition Analysis

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Key Words
Urinary creatinine excretion • Creatinine clearance • Prediction of renal function • eGFR • Electrical body impedance analysis • Body cell mass

Abstract
Background/Aims: In obese subjects the accuracy of prediction of renal function is quite low. The aim of this study was to obtain a more accurate estimate of urinary creatinine excretion (UCr), creatinine clearance (CCr), and GFR from body cell mass (BCM). ***Methods:*** Seventy-three adult morbidly obese patients (BMI 35.2-64.5 kg/m^2) were examined. BCM was calculated from body impedance analysis. CCr was measured (mCCr) and was predicted from BCM and antropometric data ($_{MR\text{-}BCM}$CCr), with Cockcroft and Gault ($_{C\&G}$CCr) and Salazar and Corcoran ($_{S\&C}$CCr) formulas. GFR was predicted from BCM (BCM GFR) and with MDRD and CKD-EPI formulas. ***Results:*** Multiple regression (MR) indicated a strict linear correlation between UCr, BCM and anthropometric data. UCr predicted from MR equation ($_{MR\text{-}BCM}$UCr) was very similar to measured UCr. $_{MR\text{-}BCM}$CCr (168±46 mL/min) and mCCr (167±51 mL/min) were also similar, while significant differences were found between mCCr, $_{C\&G}$CCr and $_{S\&C}$CCr. The correlation and the agreement between $_{MR\text{-}BCM}$CCr and mCCr were closer and prediction error was lower than the other formulas. BCM GFR (125±32 mL/min) had close correlations and agreements with MDRD GFR and CKD EPI formulas. ***Conclusions:*** In morbidly obese patients the measurement of BCM meliorates the prediction of UCr and CCr, and allows the prediction of GFR.

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Introduction

An accurate evalutation of renal function is relevant to obese subjects, since obesity may concurr to cause kidney disease. The "gold standard" method to assess renal function is the direct measurement of glomerular filtration rate (GFR) from the clearance of inulin, or of other glomerular tracers (^{51}Cr-EDTA, ^{99m}Tc-DTPA)[1, 2]. Since the measurement of inulin clearance is cumbersome and radioisotopic methods are not universally available, renal function is commonly evaluated by measuring plasma creatinine (PCr) or creatinine clearance (CCr). The poor sensitivity of PCr does not allow to ascertain a reduction in renal function of a minor degree. Furthermore, PCr levels are influenced by the amount of muscle mass. On the other hand, the usefulness of CCr in the evaluation of renal function is greatly reduced by the high variability of this measurement, mainly due to the difficulty in obtaining an accurate collection of 24-hour urine [3, 4]. Aiming to simplify the procedure and to avoid the need for urine collection, different methods have been proposed to estimate CCr from PCr [5, 6]. Unfortunately, in obese patients the accuracy of prediction of renal function by means of formulas based on PCr and anthropometric data is quite low. In particular, Cockcroft & Gault formula ($_{C\&G}$CCr) overestimates CCr in obese patients. The inaccuracy in the estimate of UCr is probably the major cause of error of prediction formulas in obese patients.

Total body electrical impedance analysis (BIA) is commonly used to evaluate fat mass (FM), fat-free mass (FFM) and body cell mass (BCM) in renal patients [7-10]. The values of FFM obtained with BIA were not significantly different from those of DXA [11]. It is well known that 24-hour UCr is strictly correlated to the amount of muscle mass [12, 13]. Our previous data in chronic kidney disease (CKD) patients demonstrated that the value of BCM, which is the body compartment consisting mainly from muscle mass, is strictly correlated with 24 UCr and that it is possible to predict renal function from the values of BCM combined with PCr concentrations [14-16].

The aim of this study was to evaluate if the measure of BCM allows a more accurate estimate of UCr and CCr and the prediction of GFR in obese patients.

Patients and Methods

Patients

Inclusion criteria. Adult obese patients randomly selected from those scheduled for first bariatric surgery. Body mass index (BMI) >35 kg/m^2.

Exclusion criteria. History and/or laboratory data suggestive of CKD.

Examined patients. Eighty patients were randomized to enter the study. One patient was excluded for prehexisting CKD. Six patients had not the measure of the reference test (CCr). The flow diagram of the examined patients is reported (Fig. 1). The clinical and demographic data of the remaining 73 patients are reported in Table 1. All patients gave their informed consent to participate to the study, which was conducted in accordance with the ethical guidelines proposed by the Declarations of Helsinki. The study "Prediction of GFR from body composition analysis" was approved by the Istitutional Review Board of AOUP.

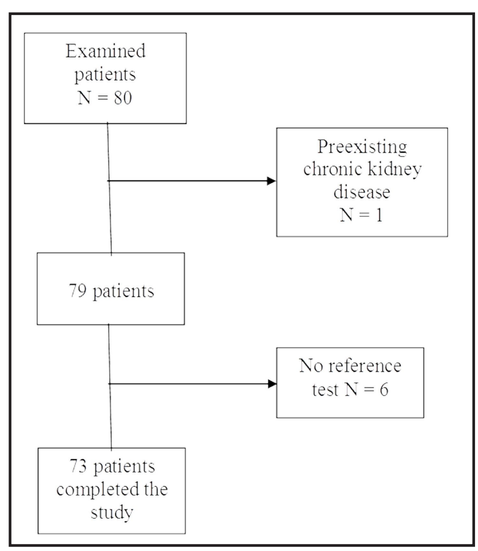

Fig. 1. Flow diagram of the examined patients.

Anthropometric measurements

Height, waist and hip circumferences were measured at the nearest cm. Body weight (BW) was measured with an electronic scale at the nearest 100 g.

Table 1. Main clinical and anthropometric data of the 73 patients (53 females). Median values and interquartile ranges (IQR 25-75) are reported

	Range	Median	IQR 25-75
Age, years	19-66	46.0	39.0-55.3
Height, cm	147-198	166.0	158.8-170.3
Body weight, kg	82.5-210.0	117.0	108.0-140.4
Body surface, m^2	1.80-3.19	2.22	2.02-2.33
Body mass index, kg/m^2	35.2-64.5	44.1	40.4-48.6
Waist circunmference, cm	98-174	126	117-140
Hip circumference, cm	118-174	141	131-150
Sistolic blood pressure, mmHg	110-200	144	131-152
Diastolic blood pressure, mmHg	66-125	90	80-96
Serum creatinine, mg/dL	0.57-1.06	0.76	0.65-0.85
Serum cystatin C, mg/L	0.50-1.51	0.89	0.77-0.97
Urinary proteins, mg/24h	0-1944	169	111-267
Urinary albumin, mg/24 h	0-1874	7.4	0-33

Table 2. Body composition and urinary creatinine excretion: body weigth (BW), body surface area (BSA), body mass index (BMI), body cell mass (BCM), fat mass (FM), 24-hour urinary creatinine excretion (UCr, mg), ratios UCr/BCM (mg/kg), and UCr/BW (mg/kg). Median values and interquartile ranges (IQR 25-75) are reported. The statistical significance of the differences between women and men is reported

Number	Women 53		Men 20		
	Median	IQR 25-75	Median	IQR 25-75	P
BW, kg	113.0	104.0-121.4	144.8	138.3-168.5	<0.0001
BSA, m^2	2.15	2.05-2.23	2.50	2.42-2.74	<0.0001
BMI, kg/m^2	43.1	39.7-46.1	48.4	44.9-52.6	0.0004
Waist circumference, cm	120.5	114-129	149	143-163	<0.0001
Hip circumference, cm	140	131-146	148	133-156	0.1666
Waist/Hip ratio	0.88	0.84-0.91	1.04	0.99-1.08	<0.0001
Waist/Heigth ratio	0.74	0.70-0.79	0.86	0.82-0.91	<0.0001
FM, kg	56.2	49.2-65.3	61.6	53.9-76.7	0.0833
FM, % BW	50.0	46.4-53.8	41.9	37.9-46.0	<0.0001
BCM, kg	31.5	28.8-33.8	50.0	42.2-53.5	<0.0001
BCM, % BW	27.4	25.6-30.1	33.2	29.6-34.7	0.0001
UCr, mg	1428	1321-1769	2433	2085-2932	<0.0001
UCr/BCM, mg/kg	48.2	42.7-54.2	50.2	41.8-57.2	0.4283
UCr/BW, mg/kg	13.2	12.0-15.2	15.4	14.0-17.5	0.0010

Body composition analysis: measurement of body cell mass

The values of resistance and reactance were measured with a single frequency (0.4 mA, 50 KHertz) electrical impedance plethysmograph (EFG - Akern, Firenze, Italy) in patients lying supine, while fasting. Two electrodes were placed on the dorsal surface of the right hand, and two on the dorsal surface of the right foot [8]. BCM and FM were calculated, according to manufacturer's equation, from the values of resistance and reactance combined with body height and weight (Table 2).

Measurement and prediction of renal function: 24h urinary creatinine excretion, creatinine clearance, glomerular filtration rate

The patients were hydrated with 150 mL of tap water per os every 30 min, from time -30 min to time 90 min, and were instructed to collect 2-hour urine. The emptying of bladder was checked at the beginning of the clearance and immediately after the end of the clearance period, measuring three bladder diameters by means of a bidimensional ultrasound scanner (MyLab 25, Esaote Biomedica, Firenze, Italy). Urine volume was measured in our laboratory. A urine sample from the urine collection and a blood sample were drawn and immediately analyzed. Serum and urinary concentrations of creatinine were measured with a rate-blanked creatinine/Jaffé method traceable to IDMS reference method (CREA Roche/Hitachi automated analysis for Hitachi 917, Roche Diagnostics, Mannheim, Germany; reference intervals for serum concentration are

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0.50–0.90 mg/dL in women and 0.70-1.20 mg/dL in men). Serum cystatin C was measured with a particle enhanced immune-nephelometric method (N Latex Cystatin C, Siemens Healthcare, Erlangen, Germany; reference intervals 0.53-0.95 mg/L). Two hours urinary creatinine excretion (mg) was calculated as UCr (mg/dL) x urinary output in 2 h (dL). The measured 2-hours urinary creatinine (UCr) was reported to 24-hours UCr, and expressed as mg/24 hours. The linear correlation between 24-hours UCr and BCM, and for comparison with BW were tested. UCr (mg/24 hour) was estimated from the relationship between UCr and BCM [14]. Then the anthropometric and biochemical determinants of UCr excretion were determined by means of a stepwise multiple regression analysis to produce a more accurate prediction of UCr (see below).

Creatinine clearance (mCCr) was measured with the standard formula UCr (mg/dL) x UVol (mL/min) / PCr (mg/dL). CCr was also predicted from the estimate of UCr from BCM and anthropometric data ($_{MR\text{-}BCM}$CCr, see below) and, for comparison, by means of Cockcroft & Gault formula ($_{C\&G}$CCr) [5] and Salazar & Corcoran formula ($_{S\&C}$CCr) [6].

$$_{C\&G}\text{CCr (mL/min)} = \frac{(140 - \text{Age years}) \times \text{Body weigth kg}}{\text{PCr mg/dL} \times 72} \quad (\times 0.85 \text{ if female})$$

$$_{S\&C}\text{CCr (mL/min)} = \frac{(137 - \text{Age years}) \times (0.285 \times \text{Body weigth kg}) + (12.1 \times \text{Heigth m}^2)}{\text{PCr mg/dL} \times 51} \quad \text{(male)}$$

$$_{S\&C}\text{CCr (mL/min)} = \frac{(146 - \text{Age years}) \times (0.287 \times \text{Body weigth kg}) + (9.74 \times \text{Heigth m}^2)}{\text{PCr mg/dL} \times 60} \quad \text{(female)}$$

Finally, GFR was predicted from the value of BCM and PCr according to our previously published formula [17], as

$$\text{BCM GFR (mL/min)} = \frac{\text{BCM} \times 2.554}{\text{PCr mg/dL}} - 0.8 \text{ in women}$$

$$\text{BCM GFR (mL/min)} = \frac{\text{BCM} \times 2.700}{\text{PCr mg/dL}} - 2.9 \text{ in men}$$

GFR was also predicted from MRDR 4 variables IDMS traceable creatinine formula (MDRD GFR) and with CKD-EPI formulas (CKD-EPI GFR) [18].

Measured and predicted values of CCr and GFR are expressed as mL/min [19].

Statistical analysis

The normality of distribution of data was checked using D'Agostino-Pearson test. Data are reported as means ± standard deviation, or as median and interquartile range 25-75 (IQR 25-75) as appropriate. The significance of the differences between two independent samples was tested using the non-parametric Mann–Whitney tests or by means of Student t test, as appropriate. The concordance correlation coefficient between predicted and measured values of UCr and CCr, and between the different predictions of GFR was tested [20]. The agreements between predicted and measured values were tested with Band and Altman plots [21] The significance of the differences among correlation coefficients was tested [22]. Stepwise multiple regression analysis was used to establish the determinants of UCr excretion [23]. Mean prediction errors of predicted versus measured values was calculated [24]. Statistical analysis was performed mainly using MedCalc Statistical Software version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). A p value <0.05 was considered statistically significant.

Results

The main antropometric data of the 73 examined patients are reported in Table 1. The BMI ranged between 35 and 40 kg/m^2 in 16 patients; 40-45 kg/m^2 in 26; 45-50 kg/m^2 in 13, and was >50 kg/m^2 in 18; 20 patients were diabetics (type 2); 35 pts were hypertensive; serum creatinine was normal in all patients. BW, BSA, BMI, waist circumference, waist/hip ratio, BCM, BCM%BW, and UCr were significantly higher in men, while FM%BW was significantly higher in women (Table 2). UCr, BCM and the ratio UCr/BW were significantly

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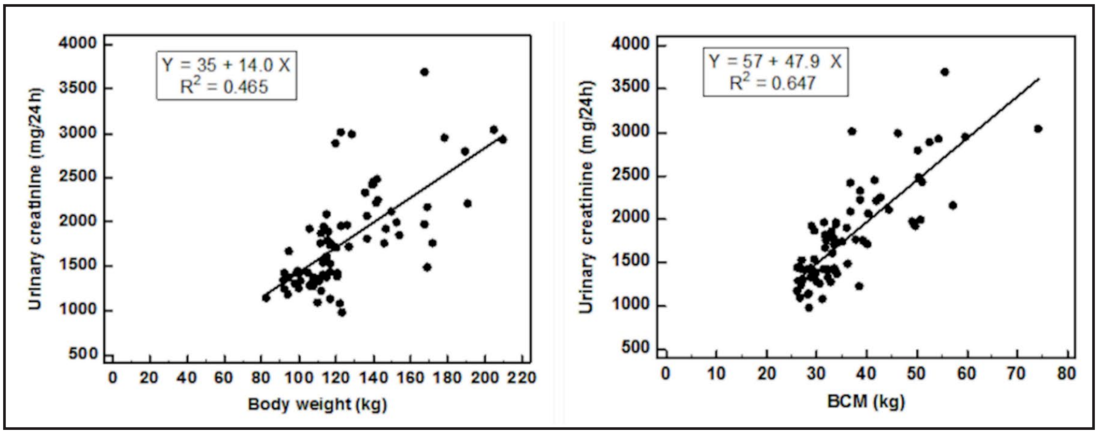

Fig. 2. Correlation of 24-hour urinary creatinine excretion (24h Ucr) with body weight and body cell mass (BCM). Parameters of linear correlation and correlation coefficients r^2 are reported.

higher in men than in women: UCr = 2509±504 vs 1544±320 mg/24h ($p<0.0001$); BCM = 49.2±8.8 vs 31.8±3.8 kg ($p=0.001$); UCr/BW = 16.6±3.9 vs 13.4±2.4 mg/kg , $p=0.001$. No significant difference ($p=0.4283$) was found between men and women in the ratio UCr/BCM: 51.8±11.3 and 48.6±7.6 mg/kg, respectively. These ratios represent the milligrams of creatinine excreted in the 24-hour urine per kilogram of BCM. They are quite similar to those previously found in a group of 30 non-obese CKD patients: 50.8 mg/kg in men and 47.9 mg/kg in women [14]. A close linear correlation was found between UCr and BCM ($r=0.804$, $p<0.0001$), which was slightly higher ($p=0.1121$) than that with body weight ($r = 0.682$, $p<0.0001$). However, as indicated by the r^2 value of 0.647, the amount of BCM justified only in part the UCr (Fig. 2). The determination coefficient (r^2) of multiple regression (MR) analysis between measured UCr (dependent variable) and BCM, gender, age, height, body weight, BMI, and PCr, as independent variables was 0.725 (Table 3). In particular, UCr was positively correlated with BCM and heigth an negatively with age; body weight, body mass index and PCr were not included in the model. The multiple correlation coefficient was 0.8517, slightly higher than that between UCr and BCM, and significantly higher ($p=0.011$) than the correlation coefficient between UCr and BW.

24 hour UCr was estimated from MR equation as:
$_{MR\text{-}BCM}UCr$ (mg/24 hours) = BCM (kg) x 30.2 + height (cm) x 19.95 – age (years) x 8.35 -2222. Then, $_{MR\text{-}BCM}CCr$ was calculated from $_{MR}UCr$, as:
$_{MR\text{-}BCM}CCr$ (mL/min) = $_{MR\text{-}BCM}UCr$ (mg)/ PCr (mg/mL) x 1440 min.

Examples of prediction of UCr and CCr
Patient # 17, male, age 43 years, height 175 cm, BCM 42.8 kg; PCr 0.83 mg/dL; measured UCr 2246 mg/24h; measured CCr 188 mL/min;
$_{MR\text{-}BCM}UCr = (42.8*30.2) +(175*19.95) – (43*8.35) – 2222 = 2203$ mg/24h
$$_{MR\text{-}BCM}CCr = \frac{2203 \text{ mg/24h}}{0.0083 \text{ mg/mL x 1440 min}} = 184 \text{ mL/min}$$
Patient # 3, female, age 65 years, height 155 cm, BCM 26.3 kg, PCr 0.82 mg/dL; measured UCr 1283 mg/24h; measured CCr 109mL/min;
$_{MR\text{-}BCM}UCr = (26.3*30.2) +(155*19.95) – (65*8.35) – 2222 = 1121$ mg/24h
$$_{MR\text{-}BCM}CCr = \frac{1121 \text{ mg/24h}}{0.0082 \text{ mg/mL x 1440 min}} = 95 \text{ mL/min}$$

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Table 3. Multiple linear regression modeling (stepwise) for creatinine excretion (mg/24 h) based on body cell mass (BCM), height, age. Multiple correlation coefficient = 0.8517. Variables not included in the model: body weight, body mass index, and plasma creatinine

Independent	Coefficient	Standard	t	P
Constant	-2222			
BCM, kg	30.2	5.87	5.140	<0.0001
Age, years	-8.35	3.18	-2.628	0.011
Heigth, cm	19.95	5.83	3.420	0.001

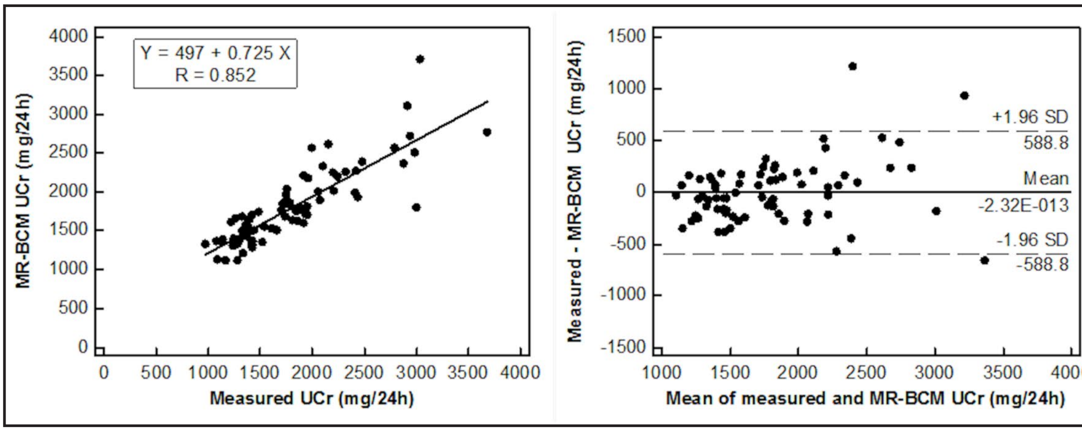

Fig. 3. Correlation and agreement plots between measured urinary creatinine (UCr) and urinary creatinine predicted from body cell mass and multiple regression analysis equation ($_{MR-BCM}$UCr).

Table 4. Prediction of creatinine clearance (CCr): Comparison of measured CCr with the different predictions. Prediction from multiple regression and body cell mass ($_{MR-BCM}$CCr); Cockcroft & Gault ($_{C\&G}$CCr); Salazar & Corcoran ($_{S\&C}$CCr). All values are expressed as mL/min (median values and interquartile ranges 25-75 are reported). The significances of the differences with measured CCr are reported

	Women 53		Men 20	
	Median	IQR 25-75	Median	IQR 25-75
Measured CCr, mL/min	151.0	124.5-172.0	188.4	163.0-246.1
$_{MR-BCM}$CCr, mL/min	154.5 p=0.8720	127.3-170.1	199.9.0 p=0.9138	176.9-225.5
Mean prediction error, mL/min	18.6		34.5	
$_{C\&G}$CCr, mL/min	173.6 p=0.0068	137.8-214.6	216.7 p=0.2134	184.5-274.9
Mean prediction error, mL/min	48.5		77.9	
$_{S\&C}$CCr, mL/min	135.1 p=0.0785	108.5-170.5	166.0 p=0.0045	137.4-190.4
Mean prediction error, mL/min	25.6		49.9	

The correlation between measured UCr and $_{MR-BCM}$UCr was quite high (r= 0.852, p<0.0001). The mean prediction error was 300 mg. The mean difference between predicted and measured UCr was 4.4 mg and the range of agreement between the measures was satisfactory: between – 589 and + 589 mg in 95% of patients (Fig. 3).

$_{MR-BCM}$CCr was quite similar to mCCr (Table 4, Fig. 4) with a higher correlation, a closer agreement and a lower prediction error than $_{C\&G}$CCr. The accuracy of $_{MR-BCM}$CCr was always

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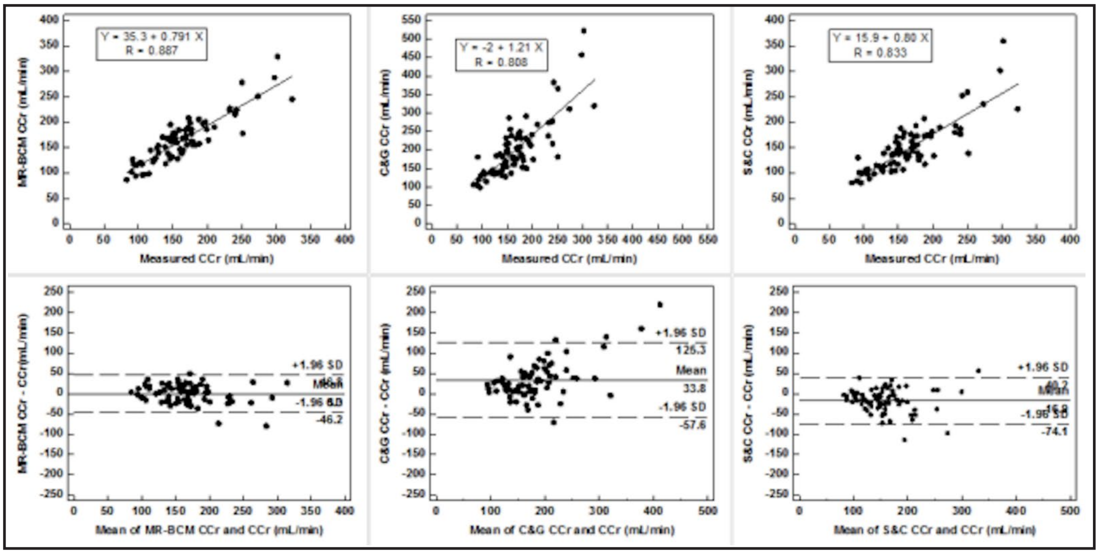

Fig. 4. Correlation and agreement plots between predicted clearances and measured creatinine clearance (CCr). ${}_{\text{MR-BCM}}$CCr=creatinine clearance predicted from body cell mass and multiple regression correlation equation; ${}_{\text{C\&G}}$CCr=creatinine clearance predicted according to Cockcroft and Gault; ${}_{\text{S\&C}}$CCr = creatinine clearance predicted according to Salazar and Corcoran.

better than that of ${}_{\text{C\&G}}$CCr and ${}_{\text{S\&C}}$CCr, as indicated by the higher percentage of values having a difference versus measured CCr ≤ 10, 15, 20, and 30% (Table 5). The mean difference between ${}_{\text{MR-BCM}}$CCr and mCCr was 0.3 mL/min (p=0.732), while that of ${}_{\text{C\&G}}$CCr was 33.8 mL/min (p=0.004) and that of ${}_{\text{S\&C}}$CCr was -16.9 mL/min (p=0.017). Furthermore, the differences with mCCr were normally and symmetrically distributed around the zero value, while those of ${}_{\text{C\&G}}$CCr were skewed to the right and

Table 5. Accuracy of the different estimates of creatinine clearance (CCr). Percentage of predicted values of having a difference versus measured CCr ≤ 10, 15, 20, 30%. CCr predicted from multiple regression and body cell mass (${}_{\text{MR-BCM}}$CCr); Cockcroft & Gault (${}_{\text{C\&G}}$CCr); Salazar & Corcoran (${}_{\text{S\&C}}$CCr)

Difference vs measured CCr	${}_{\text{MR-BCM}}$CCr	${}_{\text{C\&G}}$CCr	${}_{\text{S\&C}}$CCr
≤30%	97.3	72.6	90.4
≤20%	89.0	53.4	75.3
≤15%	69.9	41.1	58.9
≤10%	49.3	26.0	42.5

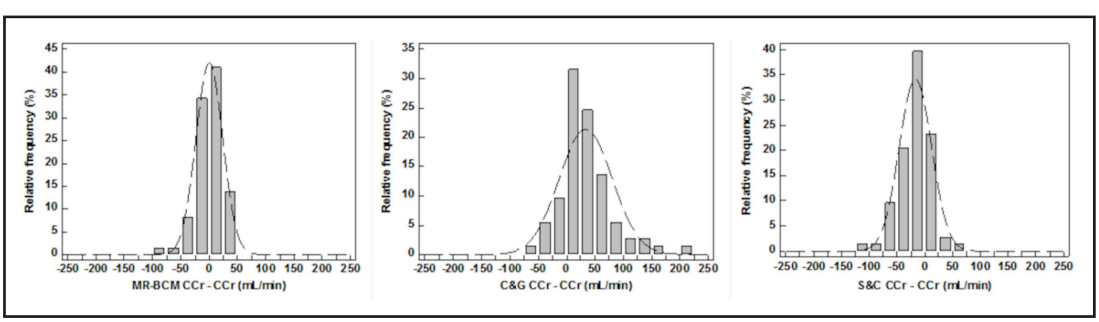

Fig. 5. Differences between predicted and measured creatinine clearances: histograms of frequency distributions. ${}_{\text{MR-BCM}}$CCr=creatinine clearance predicted from body cell mass and multiple regression correlation equation; ${}_{\text{C\&G}}$CCr=creatinine clearance predicted according to Cockcroft and Gault; ${}_{\text{S\&C}}$CCr = creatinine clearance predicted according to Salazar and Corcoran.

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Table 6. Prediction of glomerular filtration rate (GFR): BCM GFR (predicted from body cell mass) versus MDRD idms GFR, CKD-EPI cr GFR, and CKD EPI cr-cys. All values are expressed as mL/min (median values and interquartile ranges 25-75 are reported). The significances of the differences between the different estimates are reported

	Women 53		Men 20	
	Median	IQR 25-75	Median	IQR 25-75
BCM GFR, mL/min	117.5 p=0.941 vs MDRD GFR p=0.107 vs CKD EPI p=0.142 vs CKD EPI cr-cys	100.5-128.1	142.7 p=0.607 vs MDRD GFR p=0.589 vs CKD EPI cr p=0.884 vs CKD EPI cr-cys	129.7-183.5
MDRD GFR, mL/min	110.1 p=0.089 vs CKD EPI cr p=0.107 vs CKD EPI cr-cys	89.7-132.1	139.9 p=0.317 vs CKD EPI cr p=0.726 vs CKD EPI cr-cys	121.2-165.9
CKD EPI cr GFR, mL/min	119.8 p=0.559 vs CKD EPI cr-cys	100.6-142.8	153.4 p=0.995 vs CKD EPI cr-cys	135.0-167.4
CKD EPI cr-cys GFR, mL/min	119.6	99.0-144.7	142.9	126.7-177.5

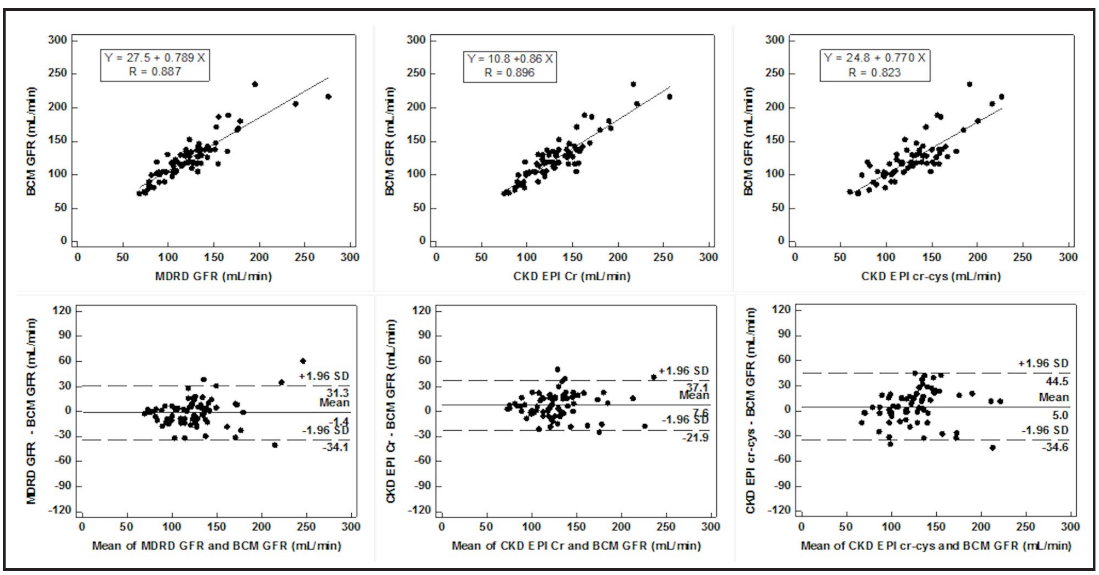

Fig. 6. Correlation and agreement plots between different prediction of glomerular filtration rate (GFR). BCM GFR = GFR predicted from body cell mass (BCM); MDRD GFR = GFR predicted from MDRD formula; CKD EPI cr = GFR predicted from CKD EPI creatinine formula; CKD EPI cr-cys = GFR predicted from CKD EPI creatinine and cystatin C formula.

those of $_{S\&C}$CCr were skewed to the left confirming, respectively the overestimation and underestimation of mCCr by C&G and by S&C formulas (Fig. 5).

Finally, close correlations and good agreements were found between BCM GFR and MDRD GFR and CKD-EPI formulas (Fig. 6, Table 6). The slight differences (+1.4 mL/min versus MDRD GFR, -7.6 mL/min versus CKD EPI cr, and -5.0 mL/min versus CKD EPI cr-cys) were statistically not significant The correlations of BCM GFR with MDRD GFR, CKD EPI cr, and CKD EPI cr-cys were not significantly different in the 42 patients with BMI≤45 kg/m^2 versus the 31 patients with BMI>45 kg/m^2. No relevant differences were found in the agreements of BCM GFR with the other predictions of GFR in patients with BMI lower or higher than 45 kg/m^2.

Discussion

Obesity is considered an important risk factor for the development and progression of CKD. Different hemodynamic, metabolic and endocrine mechanisms have been hypothesized to produce an impairment in renal morphology and function in obese subjects [25-27]. Recent data indicate that even the so called metabolically healthy obesity is associated with a higher incidence of CKD [28-30]. The early recognition of renal functional impairment may be useful to stop the development and progression of CKD. For this purpose, there is a need for precise, accurate, reproducible and simple methods, suitable for repeated measurements, to assess renal function. Unfortunately, none of the methods currently used to evaluate GFR rate fulfills these requirements. Radioisothopic methods measure the clearance of radioactive tracers to assess GFR [1, 2]. They are precise and accurate but are expensive, somewhat complicated and not available everywhere. Plasma creatinine concentration has a low sensitivity as a marker of early impairment of renal function, and allows only a gross estimate of GFR. Furthermore, plasma creatinine concentrations depends also on the rate of creatinine production by the muscle mass. The usefulness of CCr is greatly reduced by its low precision and accuracy, due to incorrect collection of 24-hour urine and to the variability of urinary creatinine excretion [4]. Different methods have been proposed to predict CCr from PCr and some anthropometric data, avoiding urine collection. The Cockcroft and Gault formula, which predicts urinary creatinine production, and hence excretion, from gender, age and body weight of subjects, is widely employed in CKD patients [5]. However, in obese patients the C&G formula necessarily overestimate the measured clearances, due to the increase in body weight determined by a disproportionate amount of fat mass as a percentage of body weight. Different modifications have been proposed to C&G formula considering different estimates of "lean" or "ideal" body weigth instead of the actual body weigth [31-33]. To meliorate the prediction of CCr in obese patients Salazar and Corcoran developed a formula which employes an estimate of fat-free body mass [6]. Also S&C formula seems unadequate in severe obesity [31]. Other formulas, proposed to predict GFR from PCr and other anthropometric data in CKD patients, have not fully validated in severely obese subjects [34, 35]. It is also debated if formulas based on serum cystatin C are more adequate or, to the contrary, may produce a misclassification of CKD stages due to the production of cystatin C by fat cells [36-38]. The inaccuracy in the prediction of UCr from actual body weigth and also from estimated lean body weigth is probably the major cause of error of creatinine based prediction formulas. BIA is a simple and validated method to evaluate body composition and BCM [7, 9, 14]. The present study was addressed to evaluate the possibility to obtain a more accurate prediction of UCr, hence of CCr, and even GFR from the measure of BCM obtained with BIA in a group of morbidly obese patients scheduled for bariatric surgery. Limitations of this study are its monocentric nature and the need for further external validation of the proposed prediction formulas. Recently, other authors confirmed the accuracy of the prediction of UCr and CCr from BCM and suggested that this method may become particularly helpful for the evaluation of patients with abnormal body composition [39]. The results of our study indicate that an accurate prediction of UCr is possible when the measurement of BCM is added in the prediction formula. This result is in agreement with the fact that muscle mass, which is the compartment where creatinine is produced, represents the major constituent of BCM. We already demonstrated that the value of BCM is strictly correlated with creatinine excretion in CKD patients and with creatinine generation in maintenance haemodialysis patient [10, 14, 15]. The present study confirms that in severely obese subjects CCr can be predicted accurately from BCM and anthropometric data, similarly to non-obese CKD patients [14, 15]. Furthermore, the relationship between UCr and BCM was similar in men and in women, allowing to use the same formula to estimate UCr and CCr, differently from C&G and S&C formulas. The prediction errors of the BCM based formula resulted definitely lower than those of C&G formula and also of S&C formula. The high accuracy in the predictions of UCr from BCM, which is the body compartement mainly composed by muscle mass, determines the better performance of BCM based prediction of CCr versus C&G and S&C estimates. This hypothesis is in agreement with the report of better results for estimating CCr measuring muscle mass than those based on demographics [40]. Finally, our results indicate that in severely obese patients, without impairment in renal function, it is possible to predict GFR from the value of BCM and PCr, with a precision similar to MDRD and CKD-EPI formulas. We already found, in CKD patients with either normal body weight, overweigth [16] or moderately obese , that the measured GFR has a closer agreement with BCMGFR than with MDRDGFR [16, 17]. Due to its simplicity and low cost, the prediction of UCr, CCr and GFR obtained from the measure of BCM is feasible to repeated measurements of renal function. In the mean time, the impedance analysis allows also to estimate the nutritional status and the balance between fat mass and muscle mass, that may change in relation with dietary and/or surgical interventions for the treatrment of obesity. Since in the setting of weight fluctuation, the estimated GFR differs significantly from measured GFR, it has been suggested that clinical trials should carefully assess anthropometrics, and measure directly GFR or examine alternative filtration markers not affected by muscle mass [41]. Indeed the method that we propose corrects the relationship between PCr and GFR for the production rate of creatinine by muscle mass, estimated by the value of BCM, thus reducing the prediction error of creatinine based formulas. This method should be more adequate to evaluate renal function after bariatric surgery, when the amount of muscle mass may be differently affected by the decrease in body weight.

Conclusion

It is possible to estimate urinary creatinine excretion and renal function from BIA and plasma creatinine concentration, avoiding urine collection. In particular, the BCM based formulas predict more accurately creatinine clearance than C&G and S&C formulas and the estimate of GFR from BCM is in good agreement with other eGFR predictions.

Disclosure Statement

None to declare.

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