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Lean mass modulates glomerular filtration rate in males of normal and extreme body composition

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Abstract

Background: Understanding determinants of glomerular filtration rate (GFR) is important in aiding prediction and interpretation of kidney function. Body composition is known to affect GFR but is not included in current screening of kidney disease. We investigated the association between GFR and body composition in healthy young men with differing body mass but without known diabetes or kidney injury.

Methods: Three groups were recruited: normal BMI (n = 22) with a body mass index (BMI) <25 kg/m^2, muscular (n = 23) with BMI ≥30 kg/m^2 and bioelectrical impedance body fat ≤20% and obese (n = 22) with BMI ≥30 kg/m^2 and bioelectrical impedance body fat ≥30%. Dietary analyses, GFR clearance by ^{99m} Tc-DTPA, urine protein and body composition by dual-energy X-ray absorptiometry were measured in all participants. Linear and nonlinear associations of constituents of body composition with GFR were assessed.

Results: Muscular men had a higher GFR (mean 186.4 mL/min; 95% CI 171.7–201.1) than normal BMI and obese groups (P = 0.0007). Urine protein and albumin excretion were not elevated in any participants. On multiple regression analysis (r^2 = 0.60), the variables with strong associations with GFR were age (P = 0.0009) and lean mass (P = 0.0001). Fat mass, protein intake and smoking status were not associated. Skeletal muscle mass correlated significantly with GFR in all subgroups.

Conclusion: Age and lean mass were strong determinants of GFR. Estimates of GFR should therefore be indexed to an estimate of lean mass.

Introduction

Insight into the factors affecting glomerular filtration rate (GFR) in subjects without kidney disease may assist with separating normal from abnormal kidney function and this may help provide strategies for prevention.

Although not entirely understood, in subjects with obesity, renal structure and function have been shown to be progressively altered. Several studies showed an association between obesity and glomerular hyperfiltration,[1] chronic kidney disease (CKD)[2] and end-stage renal failure.[3] Glomerular hyperfiltration, signified by increases in GFR, often predicts development of nephropathy in patients with type 1 diabetes.[4] Different mechanisms of hyperfiltration are postulated.[5–7] In diabetes, the chain of events includes incremented glomerular intracapillary pressure and glomerulosclerosis with subsequent loss of GFR.

Hyperfiltration in obese individuals diminishes after a reduction in bodyweight,[8,9] suggesting body composition may be involved in the regulation of GFR. However, it is not certain whether a reduction in lean or fat mass reduces hyperfiltration to normal levels. Current guidelines do not address how hyperfiltration should be incorporated into CKD screening.

Two important concepts regarding the effect of body composition on kidney function warrant investigations. First, although not widely documented, several studies have shown that lean mass is correlated with GFR.[10–13] Second, there is growing evidence that normalising GFR to body surface area (BSA) may not be entirely appropriate as humans have a fixed number of nephrons that must increase filtration in order to meet the demands of body size.[7] Therefore accuracy of prediction equations in estimating GFR is questionable especially for those with

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extremes of body size. This is crucial in clinical practice for purposes such as drug dosing, which is often guided by an estimate of GFR.

We therefore aimed to investigate the differences in GFR in subjects with different body compositions and to evaluate independent variables associated with GFR measured by ^{99m} Technetium-diethylene triaminepentaacetic acid (DTPA). As the relative effects of fat versus lean mass on GFR are unknown, we also examined the hypothesis that body composition modulates GFR in healthy people.

Methods

Subjects

The study was given ethical approval by the Upper South B Ethics Committee (reference number: URB/09/051). We recruited age-matched males with 'normal body composition', and males with extremes of body composition, particularly those with an increased muscle mass, and those with a high body fat.

Participants were screened for body mass index (BMI) and body fat percentages by bioelectrical impedance (BIA) using a TANITA fat analyser scale. BMI was calculated using the formula, weight divided by height squared (kg/m^2), and characterised using the World Health Organization's definition of BMI reference range as: 'normal' BMI (BMI = 18.5–25 kg/m^2) (n = 22); 'muscular' (BMI ≥30 kg/m^2, with a BIA body fat of <20 %) (n = 23); and 'obese' groups (BMI ≥30 kg/m^2, with a BIA body fat of >30%) (n = 22). Participants with known diabetes or thyroid dysfunction or unsuitable BMI or body fat percentages were excluded.

Tc-DTPA GFR, a 4-hour urine collection, dietary intake and body composition by dual-energy X-ray absorptiometry (DEXA) analysis were subsequently undertaken for all eligible participants. Values of GFR were reported as raw measured values (mL/min) and adjusted for body surface area (BSA) (mL/min/1.73 m^2) by the Du Bois–Du Bois method.[14] Samples were analysed for plasma and urine creatinine, cystatin C, high-sensitivity C-reactive protein, urine protein and urine albumin, and the results for the plasma samples were described elsewhere.[15]

Urine measurements

Urine protein and albumin concentrations were measured by immunoturbidimetric assays (Roche Diagnostics, Indianapolis, IN, USA). These were undertaken to confirm that participants were free from kidney dysfunction according to current guidelines.[16]

Dietary analysis

All eligible participants were asked to complete a 4-day diet record prior to the second study visit. Participants were asked not to change their habitual diet consumption, to estimate the quantities eaten using a combination of photographs and household measures,[17] and to supply information on the intake of dietary supplements. Nutrient analyses for each participant were undertaken using Foodworks Professional 2009, Version 6.0.2562 (Xyris Software Ltd, Brisbane, Qld, Australia) to access New Zealand FOODfiles 2004 (Crop and Food and Research, Palmerston North, and Ministry of Health, Wellington, New Zealand).

Measurement of lean mass and estimation of skeletal muscle mass

Body composition was determined by DEXA in participants using a GE Lunar Prodigy Scanner (GE Medical Systems, Madison, WI, USA). DEXA determines mass and composition by using dual-energy X-rays and photoelectric absorption, and therefore differentiates between lean mass, fat mass, bone mineral content and regional distribution. Although BIA was used initially to screen participants, DEXA was used for end-point body composition analyses. Regional distributions are shown in Appendix I. The android region was defined as the region around the mid-section of the body, gynoid as the region around the hips and thighs, and appendicular as the combination of arms and legs. Skeletal muscle mass was calculated using the equation of Kim *et al*., based on appendicular lean tissue mass free of intermuscular fat.[18]

Statistical analysis

Statistical analyses were undertaken with MedCalc® Version 11.2.1.0 (Mariakerke, Belgium), SPSS (IBM SPSS Statistics for Windows, Version 20.0.0.2, Chicago, IL, USA) and NCSS statistical software (version 07.01.04). GFR distributions were normal using the Kolmogorov–Smirnov test (P = 0.50) and therefore logarithmic data transformation was not done. Multivariate analysis and Bonferroni adjustment for post hoc analysis were performed to determine the significance of differences between variables of interest within the three groups of participants. Linear and nonlinear regressions were determined for each variable plotted against raw GFR. To assess for nonlinearity, scatter diagrams between individual variables of interest versus GFR on the horizontal axis were viewed individually to determine whether a

Table 1 Participant characteristics; mean (ranges). *P*-values show the between-subject effects

	Normal BMI	Muscular	Obese	Significance of between-subject effects (*P*-value)
Age (years)	32.2 (19.1–51.4)	32.1 (19.0–52.0)	33.4 (20.0–50.8)	0.885
Weight (kg)	74.0 (62.0–88.8)†,‡	101.8 (76.8–114.8)†,§	106.6 (87.6–124.4)‡	<0.0001
BMI (kg/m^2)	23.6 (19.8–25.2)†,‡	32.1 (30.0–34.4)†,§	34.2 (30.0–42.0)‡,§	<0.0001
GFR (mL/min)	135.9 (104.6–195.6)†	186.4 (121.1–237.1)†,§	159.2 (112.4–211.9)§	<0.0001
GFR (mL/min/1.73 m^2)	122.8 (93.1–172.8)†	146.4 (103.4–178.5)†,§	123.4 (89.0–159.5)§	<0.0001
BIA body fat (%)	16.8 (9.0–22.0)‡	19.0 (15.0–28.0)§	35.5 (30.0–54.0)‡,§	<0.0001
DEXA body fat (%)	17.0 (6.8–29.7)†,‡	22.2 (13.7–27.9)†,§	37.0 (30.0–52.8)‡,§	<0.0001
Total body fat (kg)	12.0 (4.9–20.1)†,‡	21.6 (10.3–27.7)†,§	37.8 (29.1–62.8)‡,§	<0.0001
Total lean mass (kg)	58.7 (43.0–72.8)†,‡	75.5 (62.4–88.9)†	64.1 (49.7–79.3)‡	<0.0001
Skeletal muscle mass (kg)	32.2 (23.7–39.7)†	42.2 (35.6–50.9)†,§	35.3 (28.0–47.5)§	<0.0001
Appendicular lean mass (kg)	27.1 (20.0–33.4)†	35.5 (30.0–42.8)†,§	29.7 (23.6–39.9)§	<0.0001
Urine creatinine	16.6 (12.1–33.4)†	26.9 (16.0–59.9)†,§	18.2 (12.9–23.9)§	<0.0001
Excretion (mmol/24 h/L)				
Urine protein/creatinine ratio (g/mol)	11.7 (0.1–25.0)†	7.5 (2.8–14.3)†	8.6 (4.2–15.6)	0.009
Urine albumin/creatinine ratio (g/mol)	0.51 (0.15–1.08)	0.42 (0.10–1.26)	0.56 (0.04–4.28)	0.121
Total dietary protein intake (g)	129 (7–398)	154 (44–256)§	92 (45–216)§	0.003
Total fat intake (g)	85.2 (42.0–167.3)	89.2 (30.0–149.5)	77.3 (27.2–142.1)	<0.0001
Water intake (L)	2.9 (1.1–8.4)	3.0 (0.9–5.3)	2.2 (1.1–4.2)	0.153
Sodium intake (g)	3.1 (1.3–7.6)	3.7 (1.1–8.1)	2.9 (1.2–7.3)	0.479

†Differences between normal BMI group and muscular group significantly different ($P < 0.05$). ‡Differences between normal BMI group and obese group significantly different ($P < 0.05$). §Differences between the muscular group and obese group significantly different ($P < 0.05$). BMI, body mass index.

nonlinear relationship with GFR existed. The SPSS curve fitting menu allowed quick evaluations of linear, quadratic, cubic, inverse, logarithmic and power functions. We assessed r^2 values and significance of curve based on the F test, *P*-values and whether the 95% confidence intervals (CI) for the parameter estimates included zero. For variables with a significant *P*-value, and assessed together with estimates differing from zero, we further explored inverse, quadratic and cubic functions.

The association of body composition with GFR was examined using raw GFR results which were uncorrected for BSA. Using the 'all possible regression' selection in NCSS, multiple regression analyses were performed to determine variables which had the most significant associations with GFR. This allowed assessment of models which were similar to those performed using forward stepwise regression. After the selection of 'best fit' variables, the variables were explored in the model using multiple linear regression analysis. *P*-values < 0.05 were deemed as statistically significant.

Results

Participant characteristics

The study group consisted of 67 males between 18 and 52 years. The normal BMI group included moderately, often physically active (≤3 h of exercise per week) subjects. The muscular group were physically active (at least 4 h of cardiovascular exercise per week), and comprised mainly of bodybuilders, rugby players and other sportsmen. Subjects in the obese group were not actively participating in physical exercise (<3 h/week). In the whole group, only seven participants were current smokers, with only four smoking more than five cigarettes a day. Thirteen subjects reported the use of medication (no antihypertensive drugs). Table 1 summarises characteristics of the three groups.

Body composition results

Table 1 shows the differences in body composition for the three groups of participants. The muscular group had higher total lean mass: 75.5 kg (95% CI, 72.3–78.61) than the normal BMI: 58.7 kg (95% CI, 55.5–61.9); however, these were not different from those of the obese group: 64.1 kg (95% CI, 60.9–67.3). The obese group had the most body fat: 37.8 kg (95% CI, 35.2–40.3) ($P < 0.0001$). Appendix I further shows the distribution of lean and fat mass for the three groups of participants, and their correlations with GFR. There was no significant association between total lean mass and total fat mass ($r = 0.074$, $P = 0.55$) for the 67 subjects as a whole. Skeletal muscle mass was significantly associated with GFR in all subgroups ($P = 0.04$).

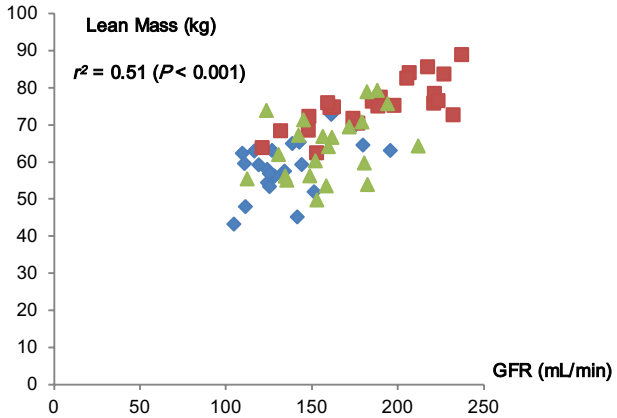

Figure 1 Graph of ^{99m} Technetium-diethylene triaminepentaacetic acid glomerular filtration rate (GFR; mL/min) plotted against total lean mass (kg). (◆), Normal body mass index (BMI); (■), muscular; (▲), obese.

GFR results

Interpretation of GFR is based on CKD staging by the National Kidney Foundation (NKF).[16] A GFR > 90 mL/min was considered normal. When GFR was adjusted for BSA (GFR/BSA), the obese and normal BMI groups had similar GFR/BSA results (P = 0.91), which were within the expected range (Table 1). The muscular group had a significantly higher GFR/BSA values (P = 0.0007) than the other two groups (Table 1). Without adjusting for BSA, the muscular group had the highest GFR, followed by the obese and normal BMI groups (P < 0.0001) (Table 1, Fig. 1).

Urine protein and microalbumin results

None of the participants had overt proteinuria (urine protein/creatinine ratio >22.9 g/mol), high urine albumin or impaired kidney function (GFR <60 mL/min/1.73 m^2) by current criteria.[16]

Nutrient analyses

Fifteen subjects reported taking protein supplements (normal BMI – 4, muscular – 10, and obese – 1). For the three groups of participants, percentage energy from protein differed only between the muscular and obese groups (P = 0.0072, Table 1). Total fat intake, sodium consumption and water intake were not different amongst the groups (Table 1).

Determinants of GFR

GFR correlated with age (r = –0.33, P = 0.005), weight (r = 0.57, P < 0.0001), BMI (0.49, P < 0.0001), skeletal muscle mass (r = 0.69, P < 0.0001), lean mass (r = 0.72, P < 0.0001), urine creatinine excretion (r = 0.32, P = 0.009) and total protein intake (r = 0.29, P = 0.02) on univariate analyses of the whole cohort (Figs 1,2). Neither total fat nor percentage fat was associated with GFR in the whole cohort or in subgroup analyses (Fig. 3, Appendix I). There

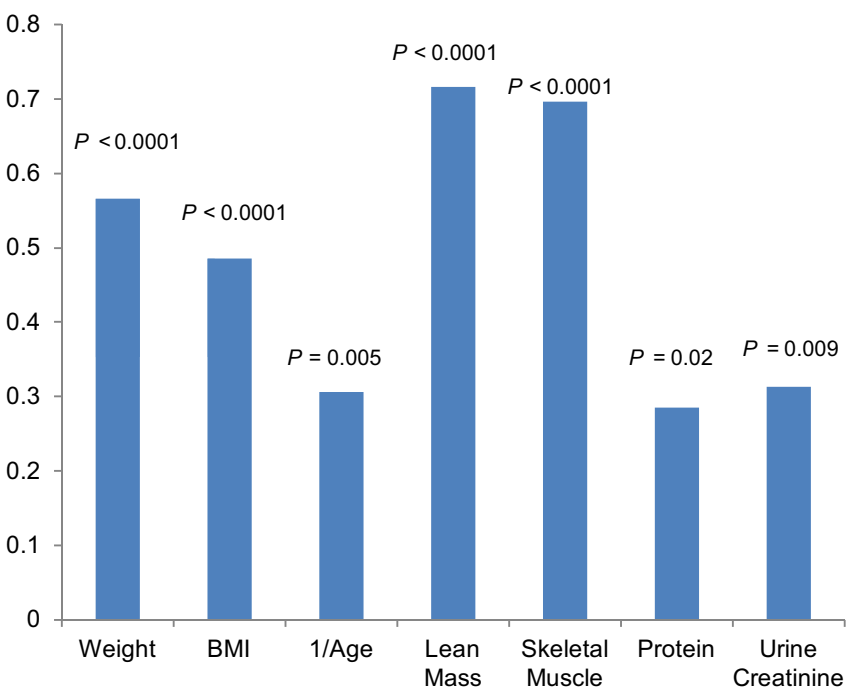

Figure 2 Univariate significant correlations (P < 0.05) with glomerular filtration rate (GFR) (mL/min). Variables not found to be significantly correlated with GFR include total fat (P = 0.18), percentage skeletal muscle (P = 0.64), percentage fat (P = 0.98), percentage protein intake (P = 0.09) and protein intake per bodyweight (P = 0.64).

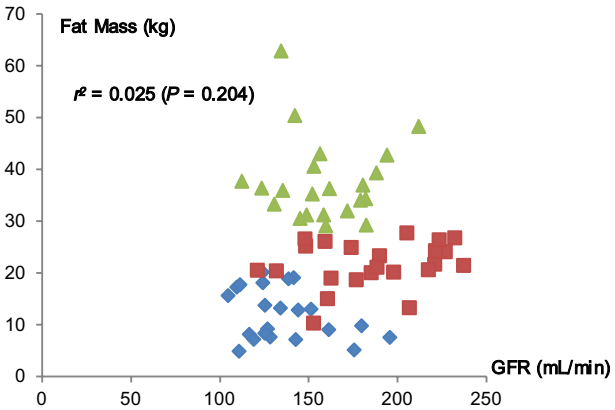

Figure 3 Graph of ^{99m} Technetium-diethylene triaminepentaacetic acid glomerular filtration rate (GFR; mL/min) plotted against total body fat (kg). (◆), Normal body mass index (BMI); (■), muscular; (▲), obese.

was no evidence of nonlinearity between variables of interest and GFR in this study cohort, therefore all subsequent multiple regression analyses utilised linear regressions.

Several models were further compared using multiple regression analysis to determine co-variables related to GFR (Table 2). Using the 'all possible regression' selection function identified age, total lean mass, truncal fat and gynoid lean mass as the four-variable model with the highest r^2 with a value of 0.64 with GFR. Forcing these same variables into a multiple linear regression model with GFR demonstrated that truncal fat (P = 0.09) was non-significant. Subsequent remodelling with the remaining three variables, that is, age (P = 0.003), lean mass (P < 0.0001) and gynoid lean (P = 0.03), were well correlated, r^2 = 0.62. As gynoid lean and total lean mass are not independent, we excluded gynoid lean as the less significant variable. Subsequent regression analysis yielded a good correlation (r^2 of 0.60) between GFR and the model which only included age and lean mass. The final derived multiple regression equation (Eqn 1) was:

$$\text{GFR} = 38.3 - 0.997\,(\text{Age}) + 2.34\,(\text{Total Lean Mass}) \quad (1)$$

We then evaluated the effect of bone mineral content as the 'other' body constituent in the above model, together with smoking and taking dietary supplements as categorical variables to predict GFR. Individually and in combination, the observed correlations did not provide a significant enhancement in r^2 values. Similarly, neither protein, water nor salt intake added significance to the age and lean mass model.

Table 2 Models of multiple regression analysis of GFR predictors for our study participants

Independent variables	All subjects (n = 67) P-value	r^2 value for model
Model 1		0.64
Age (years)	0.0002	
Total lean mass	<0.0001	
Gynoid lean	0.03	
Truncal fat	0.08	
Model 2		0.62
Age (years)	0.0003	
Total lean mass	<0.0001	
Gynoid lean	0.03	
Model 3		0.60
Age (years)	0.0009	
Total lean mass	<0.0001	

Discussion

The purpose of this study was to investigate whether body constituents and, secondarily, the effect of protein intake, could affect GFR in a population with varying body composition. We purposely chose subjects with normal body composition, together with subjects with extreme muscularity and extreme body fat, to determine the relative effects of lean versus fat mass on GFR. The unique inclusion of controls, muscular and obese subjects in similar proportions demonstrated little overall correlation between lean mass and fat mass (r = 0.074). Crucially this allowed clear discrimination between the effects of each 'independent' variable in the regression analyses in the whole cohort.

The study revealed that lean mass and age were the most important determinants of raw measured GFR and that this GFR was independent of protein intake and smoking status in a group of healthy young men. The increased measured Tc-DTPA GFR was observed in all study groups, and particularly the increased GFR levels in the obese group decreased to normal levels after normalisation to BSA (Table 1). This observation is clinically important and suggests that the historical practice of indexation of GFR to a BSA of 1.73 m^2 is inappropriate in those with extremes of body composition.

A model of age and lean mass only explained for 60% of GFR variance, suggesting other unaccounted-for factors. These may include blood pressure, which may account for the association of increased GFR levels in obese and muscular participants. However, the association of GFR with lean mass in the normal BMI group (Appendix I), considered to be healthy controls and theoretically likely to have normal blood pressure, suggests that lean mass may modulate GFR independently of blood pressure, and the presence of diabetes. The absence of proteinuria or microalbuminuria in the cohort suggests

that the association of lean mass with GFR was also independent of kidney injury.

Although our subjects presented with increased GFR levels which might be considered high, the study was not designed to investigate mechanisms of hyperfiltration. Documented mechanisms of hyperfiltration in other studies include: acute protein intake,[19] chronic excessive habitual protein intake[20] and androgen usage.[21,22] Brenner and colleagues proposed that maladaptive glomerular haemodynamic changes occur in hyperfiltering subjects in response to a reduction in functional nephron number.[23] In most cases, renal structural abnormality is often present,[5,21,22,24–28] which may perpetuate disease progression towards kidney dysfunction.

The effect of body composition on renal function has not been extensively investigated. Most studies of obesity have reported crude BMIs, but this parameter does not adequately differentiate body composition. One Japanese study, which included lean thigh volume measured using CT, suggested that lean rather than fat body mass could explain the association between BMI and increased creatinine clearance.[11] Urine creatinine excretion declined with Cr-EDTA GFR in obese hyperfiltering subjects after intestinal bypass surgery for weight loss in the study of Brøchner-Mortensen *et al*.,[8] suggesting improvement in GFR was a function of loss of muscle mass. Janmahasatian *et al*. reported that 'over'-compensation of GFR (to a lower GFR) was evident in obese individuals after GFR normalised for bodyweight.[29] After normalising GFR data against lean mass, no apparent difference in GFR between obese and control individuals was present, leading the authors to conclude that renal function is more closely related to lean body mass than fat mass.[29] Similarly, correcting GFR to BSA in our obese participants inherently underestimated high levels of measured GFR to normal levels. Delanaye *et al*. have criticised the practice of indexing GFR to BSA,[30] and explained that 'the higher the weight, the higher the BSA and the indexed GFR will decrease'. This calls for other types of correction to GFR, particularly an index that could consider the kidney's role in regulating body fluid.

A recent report suggests that GFR is related to body fat distribution, and that central adiposity is associated with lower GFR.[31] However, that study used waist-to-hip measurements as surrogates of central adiposity rather than direct measurements. Our study does not support the suggestion that central adiposity, defined by android and gynoid fat mass, is associated with GFR, nor did the ratio of android to gynoid fat mass (results not shown). Our data suggest that lean mass exerted a greater influence on GFR than any other variable as shown in the multiple regression analyses. We hypothesise that there is an important link between lean mass and GFR. First, a relationship between skeletal muscle mass and GFR in normal healthy people may exist through fluid balance. In compartmental models of body composition analysis, fat free mass compartments are divided into three basic physiological compartments: body cell mass, extracellular volume and extracellular solids.[32] The association between skeletal muscle mass and extracellular volume in our study participants was $r^2 = 0.47$ ($P < 0.001$). This association supports the idea that lean mass, which includes skeletal muscle together with the contained significant blood volume, can modulate GFR through renal fluid regulation. Teleologically, this could be explained by the need to excrete a toxic waste, creatinine, the major by-product of skeletal muscle mass and hence the need to regulate excretion through renal clearance.[33]

Strengths of this study include the use of a gold standard GFR measurement and having three clearly defined and distinct groups separated by body composition. Assessment of dietary intake also allowed analysis of the effects of protein, salt (sodium), water intake and other micronutrients on renal function. Limitations of the study include the absence of blood pressure recordings and the applicability of results to only males and to subjects with normal to high GFR. Results from another study showed lean mass to be associated with creatinine clearance in subjects without hypertension, suggesting the association we observed here is independent of blood pressure.[11] Finally, individuals with higher GFR levels in our study may be in a 'pre-pathological' state which should ideally be identified by screening and longitudinal follow-up.

Conclusion

Our study results suggest age and lean mass to be strong determinants of GFR. Based on our multiple regression modelling, we estimate that GFR decreases by 1 mL/min/year of age together with an increase of 2.3 mL/min/kg of lean mass in healthy men. This too warrants further investigation. The strong association of GFR with lean mass in our data supports the case for indexation of GFR to lean body mass. Renal impairment may then be assessed against a better estimate of expected physiological function.

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Appendix I

Correlation of uncorrected glomerular filtration rate with regional lean and fat mass for subgroups.

Body composition parameter	Mean results for regional body composition (kg) (95% CI) [Correlation of individual variables (*r*) with GFR (mL/min) (*P*-values)]		
	Normal BMI	Muscular	Obese
Lean mass (kg)			
Total lean mass	**58.7 (55.5–61.9) [0.49 (0.02)]***	**75.5 (72.3–78.6) [0.76 (<0.0001)]*,*****	64.1 (60.9–67.3) [(0.36 (0.09)]***
Total truncal lean	**27.6 (25.9–29.2) [0.47 (0.03)]***	**35.4 (33.7–37.0) [0.58 (0.003)]*,*****	30.3 (28.7–31.9) [0.24 (0.29)]***
Total android lean	**3.7 (3.5–4.0) [0.37 (0.09)]*,****	**4.9 (4.6–5.1) [0.70 (0.0002)]***	4.5 (4.3–4.7) [0.18 (0.41)]**
Total gynoid lean	**8.7 (8.1–9.3) [0.40 (0.06)]***	**11.1 (10.5–11.7) [0.60 (0.003)]*,*****	9.6 (8.9–10.2) [0.30 (0.17)]***
Total appendicular lean	**27.1 (25.4–28.8) [0.48 (0.02)]***	**4.9 (4.6–5.1) [0.62 (0.002)]*,*****	**29.7 (28.0–31.3) [0.43 (0.04)]*****
Total arm lean	**7.6 (6.9–8.2) [0.48 (0.02)]***	11.0 (10.4–11.7) [0.23 (0.28)]*,***	**8.0 (7.4–8.6) [0.45 (0.03)]*****
Total leg lean	**19.5 (18.3–20.7) [0.44 (0.04)]*,****	**24.5 (23.3–25.7) [0.66 (0.0006)]*,*****	21.7 (20.5–22.9) [0.39 (0.07)]**,***
Total skeletal muscle mass	**32.2 (30.3–34.2) [0.49 (0.02)]***	**42.3 (40.3–44.3) [0.62 (0.002)]*,*****	**35.3 (33.3–37.3) [0.43 (0.04)]*****
Fat mass (kg)			
Total fat mass	12.0 (9.4–14.5) [–0.03 (0.89)]*,**	21.6 (19.1–24.1) [0.24 (0.27)]*,***	37.8 (35.2–40.3) [–0.03 (0.90)]**,***
Total truncal fat	6.9 (5.3–8.5) [–0.12 (0.60)]*,**	13.0 (11.4–14.6) [0.22 (0.32)]*,***	22.4 (20.8–24.0) [–0.13 (0.58)]**,***
Total android fat	1.2 (0.86–1.5) [–0.37 (0.08)]*,**	2.2 (1.8–2.5) [0.20 (0.35)]*,***	4.1 (3.8–4.4) [–0.17 (0.44)]**,***
Total gynoid fat	2.3 (1.9–2.8) [–0.32 (0.14)]*,**	3.9 (3.5–4.3) [0.12 (0.59)]*,**	6.4 (6.0–6.8) [0.03 (0.91)]**,***
Total appendicular fat	4.6 (3.3–5.9) [–0.25 (0.25)]*	7.9 (6.6–9.2) [0.22 (0.30)]*,***	15.4 (14.1–16.7) [0.01 (0.95)]***
Total arm fat	1.0 (0.6–1.4) [–0.21 (0.34)]*,**	1.9 (1.6–2.3) [0.08 (0.73)]*,***	3.6 (3.2–4.0) [–0.06 (0.79)]**,***
Total leg fat	3.6 (2.6–4.6) [–0.26 (0.25)]*,**	6.1 (5.0–7.1) [0.25 (0.26)]*,***	11.8 (10.8–12. 9) [0.04 (0.87)]**,***

Significant results are highlighted in bold. *Differences between normal BMI group and muscular group significantly different ($P < 0.05$). **Differences between normal BMI group and obese group significantly different ($P < 0.05$). ***Differences between the muscular group and obese group significantly different ($P < 0.05$). BMI, body mass index; CI, confidence interval; GFR, glomerular filtration rate.