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Authors
Noori, Nazanin
Kovesdy, Csaba P
Bross, Rachelle
et al.

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Novel Equations to Estimate Lean Body Mass in Maintenance Hemodialysis Patients

Nazanin Noori, MD, PhD[1], **Csaba P Kovesdy, MD**[5], **Rachelle Bross, RD, PhD**[1,2,3], **Martin Lee, PhD**[8], **Antigone Oreopoulos, MPH, PhD**[6], **Deborah Benner, RD**[9], **Rajnish Mehrotra, MD**[4,7], **Joel D Kopple, MD**[3,7,8], and **Kamyar Kalantar-Zadeh, MD, MPH, PhD**[1,4,7,8]

[1] Harold Simmons Center for Kidney Disease Research and Epidemiology, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA

[2] Division of Bionutrition, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA

[3] General Clinical Research Center, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA

[4] Department of Pediatric, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA

[5] Salem Veteran Affairs Medical Center, Salem, VA

[6] University of Alberta, Edmonton, Canada

[7] David Geffen School of Medicine at UCLA, Los Angeles, CA

[8] UCLA School of Public Health, Los Angeles, CA

[9] DaVita Nutrition, Irvine, CA

Abstract

Background—Lean body mass (LBM) is an important nutritional measure representing muscle mass and somatic protein in hemodialysis patients, in whom we developed and tested equations to estimate LBM.

Study Design—A study of diagnostic test accuracy.

Setting and Participants—The development cohort included 118 hemodialysis patients, with LBM measured using dual-energy -X-ray absorptiometry (DEXA) and near-infrared (NIR) interactance. The validation cohort included 612 additional hemodialysis patients with LBM measured using portable NIR interactance technique during hemodialysis.

Index Tests—3-month averaged serum concentrations of creatinine, albumin and prealbumin, normalized protein-nitrogen-appearance, mid-arm muscle circumference (MAMC), handgrip strength, and subjective global assessment of nutrition.

Correspondence: Kamyar Kalantar-Zadeh, MD, MPH, PhD, Harold Simmons Center for Chronic Disease Research and Epidemiology, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, and UCLA David Geffen School of Medicine and UCLA School of Public Health, 1124 West Carson Street, C1-Annex, Torrance, CA 90502, USA, Phone: 310-222-3891, Fax: 310-782-1837, kamkal@ucla.edu.

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Reference Test—LBM measured via DEXA in the development cohort and via NIR interactance in validation cohorts.

Results—In the development cohort, DEXA and NIR interactance were strongly correlated (r=0.94, p<0.001). DEXA-measured LBM correlated with serum creatinine, MAMC, handgrip strength but not with other nutritional markers. Three regression equations to estimate DEXA-measured LBM were developed based on each of these three surrogates and gender, height, weight, and age (and urea reduction ratio for the serum creatinine regression). In the validation cohort, the validity of the equations were tested against the NIR interactance measured LBM. The equation estimates correlated well with NIR interactance measured LBM ($R_2$21 ≥0.88), although in higher LBM ranges they tended to underestimate it. Median differences between equation estimates and NIR interactance-measured LBM were 3.4 (25th–75th percentile, −3.2 to 12.0) and 3.0 (25th–75th percentile, 1.1–5.1) kg for serum creatinine and 4.0 (25th–75th percentile, −2.6 to 13.6) and 3.7 (25th–75th percentile, 1.3–6.0) kg for MAMC.

Limitations—DEXA measurements were performed on a non-dialysis day whereas NIR interactance was obtained during the hemodialysis treatment, with likelihood of confounding by volume status variations.

Conclusions—Comparing to reference measures of LBM, equations using serum creatinine, MAMC, or handgrip strength and demographic variables can accurately estimate LBM in long-term hemodialysis patients.

Keywords

Hemodialysis; protein-energy wasting; lean body mass (LBM); serum creatinine; mid-arm muscle circumference (MAMC); handgrip strength; near-infrared (NIR); bioelectrical impedance analysis (BIA); nutritional status

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Accurate assessment of nutritional status and body composition individuals with chronic kidney disease, including in long-term hemodialysis patients, is crucial because malnutrition and wasting syndromes are among the strongest risk factors for morbidity and mortality.(1–3) The *International Society for Renal Nutrition and Metabolism* (ISRNM) Expert Panel, which has recently proposed the term “protein–energy wasting” in lieu of other terms for uremic malnutrition in chronic kidney disease, defines protein–energy wasting as “loss of body protein mass and fuel reserves”.(4) Reduced lean body mass (LBM) and muscle mass is one of the main components of protein–energy wasting.(5) Hence, accurate assessment of body composition including LBM is the key to reliable evaluation of the nutritional status in chronic kidney disease patients. Nevertheless, the optimal method for determining LBM in these patients remains debatable. Even though dual energy X-ray absorptiometry (DEXA) is considered a reference method for assessing body composition,(6–8) very few dialysis clinics have direct access to DEXA machines. Therefore, developing and testing equations that can estimate LBM based on routinely available clinical and nutritional measures that correlate with LBM is of paramount clinical relevance.(9)

Several previous studies, especially in peritoneal dialysis patients, have examined the association of LBM with other nutritional measures including several anthropometic and biochemical values, the subjective global assessment and normalized protein nitrogen appearance (nPNA), also known as normalized protein catabolic rate (nPCR).(10–11) Keshaviah *et al*.(12) found that LBM correlated with serum albumin, serum creatinine (SCr), and nPNA levels in peritoneal dialysis patients, whereas Szeto *et al*.(13) and Heimburger *et al*.(14) did not find good correlations of LBM with nutritional indices including serum albumin. To our knowledge, no studies have been conducted to examine the

validity of anthropometric or other nutritional measurements in predicting LBM in hemodialysis patients.(15–16)

In the present study we examined the correlation of DEXA measured LBM with a number of nutritional markers including serum concentrations of creatinine, albumin and prealbumin, anthropometric measurements including mid-arm muscle circumference (MAMC), handgrip strength, nPNA and subjective global assessment in 118 randomly selected hemodialysis patients. In this so-called "development cohort" we developed equations to estimate LBM based on these measures and compared their consistency with DEXA-measured LBM as the reference standard. Subsequently we tested the validity of created regression equations in a "validation cohort" of 612 additional hemodialysis patients in whom LBM was estimated using the portable near-infrared (NIR) interactance technique.

Methods

Patient Population

We studied hemodialysis patients who participated in the Nutritional and Inflammatory Evaluation in Dialysis (NIED) Study.(17) The original patient cohort was derived over 5 years from a pool of over 3,000 hemodialysis outpatients in eight *DaVita* chronic dialysis facilities in the South Bay Los Angeles area (see the NIED Study website at www.NIEDStudy.org for more details).(3,5,18–23) Included were outpatients who had been undergoing hemodialysis treatment for at least 8 weeks, who were 18 years or older and who signed the *Institutional Review Board* approved consent form. Participants with acute infections or an anticipated life expectancy of less than six months (e.g. due to a metastatic malignancy or advanced HIV/AIDS disease) were excluded.

From October 1, 2001, through December 31, 2006, 893 randomly invited hemodialysis patients from eight DaVita dialysis clinics in the Los Angeles South Bay area signed the informed consent form. Patients whose upper arm did not appear appropriate for mid-arm muscle measurements were excluded. In 730 remaining subjects the body composition was assessed using the portable NIR interactance technique and the triceps skinfold thickness and MAMC were measured in the dialysis clinic. One out of every five of these patients was also invited randomly to come to Harbor-UCLA General Clinical Research Center during a non-hemodialysis day to undergo additional tests including DEXA and other body composition measures, and 118 patients agreed and did so. This group was called the *development cohort*. Those remaining patients who did not attend the additional testing at the General Clinical Research Center and thus who underwent NIR interactance- but not DEXA-measured LBM (n=612) were called the *validation cohort* (see Figure 1). All participants refrained from eating and drinking for at least 4 hours before the tests, and did not consume alcohol or exercise for 24 hours before the testing.

Anthropometric Measures

Participants were weighed wearing a hospital gown, with no footwear. Body weight was measured to the nearest 0.1 kg on a GSE digital platform scale, model 350 (GSE Scale Systems, www.gse-inc.com). Height was measured to the nearest 0.1 cm using a wall mounted stadiometer (Ayrton Corp, model S100) with participants standing erect and arms hanging freely at their sides. Lange calipers (Cambridge Scientific Instruments, www.cambridgescientific.com) were used to measure triceps skinfold thickness.(24) Triplicate measurements were taken from the non dialysis-vascular-access arm. triceps skinfold thickness was used as an index test to estimate body fat.(25–26) MAMC was calculated by a previously described equation(27), by which the triceps skinfold thickness

multiplied by 3.142 was subtracted from the mid-arm circumference; all measurements were in centimeters.

After determining the subject's hand dominance, the dominant handgrip strength was measured in development cohort while seated with shoulder adducted and neutrally rotated, elbow flexed at 90 degrees, forearm in neutral position, the handle of the dynamometer adjusted at the second handle position and then asking the subjects to hold the handle and squeeze as hard as they can.

Dual Energy X-Ray Absorptiometry

The reference test for assessment of body composition was DEXA performed with a Hologic Series Delphi-A Fan Beam X-ray Bone Densitometer with software version 12.4 (Hologic Inc., www.hologic.com).(28) Measurements were performed as previously described (6–8) with participants wearing a hospital gown, with no metal snaps, and all artifacts removed. Scans were analyzed to determine lean mass, fat mass, bone mineral content and total body fluid percentage. Precision of body composition analysis was determined by weekly quality control assessments using a whole body phantom and tissue calibration step phantom composed of soft tissue- and lean tissue- equivalent materials.(6–8)

Near Infrared Interactance

In both the development and validation cohort of 118 and 612 subjects, respectively, portable NIR interactance technology was utilized in the 8 participating dialysis clinics to estimate LBM. A commercial NIR interactance sensor with a coefficient of variation of 0.5% for total body fat measurements (portable Futrex 6100, www.futrex.com) was used. NIR interactance measurements were performed by placing a Futrex sensor on the non-vascular access upper arm for several seconds, and entering the required data (date of birth, gender, weight and height) from each patient. NIR interactance measurements of fat mass have been shown to correlate significantly with DEXA measured fat mass in hemodialysis patients.(29)

Laboratory Tests

Pre-dialysis blood samples and post-dialysis serum urea nitrogen were obtained on a mid-week day which coincided chronologically with the drawing of quarterly blood tests in the DaVita facilities. The urea reduction ratio and single-pool Kt/V were used to represent the administered dialysis treatment dose.(30) All routine laboratory measurements were performed by DaVita® Laboratories (www.davita.com) using automated methods. In order to reduce intra-individual variation, the 3-month averaged values of the laboratory measures and urea reduction ratio during the study calendar quarter were calculated and used in this study.

Statistical Methods

Stepwise procedures were performed to select potential variables for the regression equations. The Pearson's correlation coefficients between DEXA-measured LBM (the reference test) and other relevant measures were first examined in the development cohort including after adjusting for case-mix. Case-mix variables included age, gender, race/ethnicity, diabetes, dialysis vintage, insurance (Medicare vs. others), marital status, modified Charlson comorbidity score, dialysis dose and residual kidney function. We created three equations to calculate LBM in the development cohort. To examine differences between LBM estimated by our equations and NIR interactance-measured LBM in the validation cohort, we employed both Difference Plots with Pearson correlation tests, which is a graphical-statistical approach based on Bland-Altman analysis for comparison of a field

method with a reference standard,(31) and the conventional Bland-Altman plots with Pitman test for trend.(32) Unless otherwise stated, results are summarized as mean±SD (standard deviation). Statistical analyses were carried out with Stata statistical software version 10.0 (Stata Corporation, www.stata.com).

Results

Table 1 shows the general characteristics of the study population in both the development cohort (n=118) and the validation cohort (n=612). Patients in the validation cohort were slightly older and included fewer men and African-Americans but more Hispanics compared to the development cohort. The mean vintage time and the triglyceride level were higher in the development and validation cohorts, respectively.

Table 2 shows both regression coefficients and correlation coefficients of DEXA measured LBM with relevant nutritional measures in the substudy of 118 patients of the development cohort using linear regression equations with LBM as the outcome. Model 1 is based on unadjusted (Pearson) correlations of each measure separately, Model 2 includes all the 7 surrogates in the model at the same time, and Model 3 also includes case-mix variables.

We used multiple linear regression analyses with least squares methods to develop the most parsimonious equations to predict LBM. Stepwise procedures led to the selection of 3 demographic variables (weight, height and gender), MAMC, SCr and handgrip strength. Hence we created three equations (Box 1) using each of these three variables separately in combination with the selected demographic variables of gender, height, and and weight. For the SCr-based equation we also included urea reduction ratio since SCr may be affected by the dose of hemodialysis treatment.

Figure 2 shows the distribution of LBM values via 4 different methods, i.e., measured directly via DEXA and estimated by each of the above 3 regression equations in 118 hemodialysis patients of the development cohort. As shown in Figure 2, the SCr-, MAMC-, and handgrip strength-based estimates of LBM exhibited similar means and variations compared to each other and also compared to the direct assessment of LBM using DEXA. NIR interactance-measured LBM correlated closely with DEXA-measured LBM in the development cohort ($r=0.94$, $p<0.001$). Hence, the NIR interactance-measured LBM was used in the validation cohort as the reference standard.

Tables 3 and 4 show comparisons of the performance of our equations against the NIR interactance-measured LBM in the development and validation cohorts, respectively. The analyses were repeated within the two mutually exclusive strata of above and below the median LBM to compare the performance of the equations within different ranges of LBM. All three equations tended to underestimate LBM especially in the higher ranges of LBM above its median. Table 5 and Figure 3 illustrate Difference Plot-based analyses and provide the correlation test results between the NIR interactance-measured LBM in the validation sample of 612 subjects and the LBM estimates derived from SCr and MAMC regression equations in the development cohort of 118 subjects. Compared to the NIR interactance-based LBM, both equations appeared accurate in predicting the LBM, although consistent measurement bias in form of underestimating the LBM was observed. In women, both equations had smaller mean differences in estimated LBM (mean difference with NIR interactance of 2.1 and 2.3 for SCr and MAMC respectively).Both equations tended to underestimate LBM among participants with higher LBM. Difference Plot analyses confirmed these findings (Figure 3). Note that handgrip strength was only assessed in the development cohort and not in the validation cohort; hence, its regression equation could not be further examined in the validation cohort.

In order to further verify the validity of the developed regression equations, we compared the NIR interactance-measured LBM with the MAMC and SCr regression equations in the validation cohort of 612 hemodialysis patients. Table 6 and Figure 4 show correlation coefficients and scatter plots, respectively, between the NIR interactance-measured LBM and the LBM estimates from each of the two regression equations. The correlation coefficients were similarly high in the validation cohort when compared to the development cohort of 118 subjects.

In the development cohort interaction terms with gender showed p-values>0.20 for MAMC and SCr and 0.14 for handgrip strength and were considered not meaningful. The calculated root mean square errors (RMSE) were the smallest in the equations based on SCr (3.43), handgrip strength (3.46) and MAMC (3.50, all p-values <0.001). Inclusion of all 3 predictors in the same regression equation did not improve RMSE (3.45). We also examined inclusion of quadratic terms, which did not improve the gain in regression equation.

Discussion

In the development cohort of 118 long-term hemodialysis patients, we examined the correlations between several nutritional measures and LBM measured by DEXA and found that SCr, MAMC, and handgrip strength had the highest correlations with LBM. We then developed three regression equations based on SCr, MAMC, and handgrip strength to estimate LBM. When validated against NIR interactance-measured LBM, the SCr and MAMC equations yielded accurate estimates of the LBM with reasonable concordance on the basis of both Difference Plots and Bland Altman analyses in the validation cohort of 612 hemodialysis patients. Compared to NIR interactance both equations appeared accurate in predicting the LBM; however, they tended to underestimate LBM in participants with higher LBM.

Assessment of body composition, which is classically divided into fat and fat-free mass, is an important task for providing required nutritional care to chronic kidney disease patients. Compared to body fat stores, which stores energy in form of adipose tissue, the fat-free mass includes muscle and visceral proteins and consists predominantly of water, protein and minerals. Conventionally referred to as LBM, this body compartment is heterogeneous and its measure is affected by abnormalities in fluid and electrolyte distribution commonly observed in kidney patient populations.(8)

The body mass index, which is an attempt to adjust the body weight for height, is the most commonly used surrogate of fat or LBM as well as nutritional status. The major limitation of the body mass index is its inadequacy to discriminate among the variations of the different constituents of body composition, i.e., fat mass vs. LBM. Therefore, an accurate evaluation of nutritional status needs a precise quantitative assessment of at least the two aforementioned components of body mass. Currently DEXA is considered a reliable reference method for body composition analysis and assessment of LBM in adult chronic kidney disease patients. Not withstanding its inability to differentiate between edema related vs. muscle associated water,(8,33–35) DEXA measurements are based on a three-compartmental models, i.e., total body minerals, fat-free soft mass or LBM, and fat tissue mass.(1–3) The equipment is not inexpensive, and requires trained personnel to operate. The DEXA machine is not a practical tool for routine use in chronic kidney disease patients due to its technical complexity, its space occupying scanner (it requires participants to be in supine position), exposure to radiation, relatively high cost, and need for trained and licensed personnel.(6)

To our knowledge no prior study has developed or validated different regression methods to estimate LBM in long-term hemodialysis patients, although several studies have done so in peritoneal dialysis patients.(7,13,36) In the current study we used DEXA as the reference method for assessing LBM and compared different measures of nutritional status in estimating LBM in hemodialysis patients. We found that serum albumin and prealbumin did not correlate well with DEXA-measured LBM. Although serum albumin is routinely measured in most dialysis patients, it is an insensitive indicator of nutritional status, esp. since it may take several months of sustained visceral protein depletion for hypoalbuminemia to develop.(37) Serum albumin may also be a marker of systemic inflammation.(38–39) Other visceral proteins have been used, including prealbumin,(14) which has a shorter half-life than albumin and a close correlation with nutritional status and which is a good predictor of clinical outcomes.(40)

However, prealbumin, too, did not correlate well with LBM in our study. During recent years, the subjective global assessment (41) has been used increasingly to assess nutritional status in dialysis patients (10,41–44). Subjective global assessment correlates well with many nutritional markers in these patients (10,14,42–43) and has a high predictive value for mortality.(44) However, in our study subjective global assessment did not correlate with DEXA measured LBM either. Although subjective global assessment reflects overall nutritional status, LBM may be more representative of the somatic protein pool.

We found that the SCr was among the 3 better correlates of LBM and that its regression equation that was combined with demographics and urea reduction ratio was adequately accurate to estimate LBM in hemodialysis patients. SCr is affected by muscle mass, kidney function or dialysis adequacy and dietary protein (meat) intake.(45) The dietary variation can be mitigated if averaged values over a long period of time are used, as we did in our study by using 3 month-averaged SCr. We also included 3 month-averaged urea reduction ratio in the regression equation so that variations in SCr based on changes in dialysis dose and adequacy can be compensated for. Since SCr is measured at least monthly in all dialysis patients in the USA and most other countries, we believe that our equations can conveniently be used to estimate LBM in these patients.

We also found that MAMC yielded a reliable estimate of LBM. Although the use of anthropometric methods is an indirect and rather insensitive means of evaluation, with several inherent errors including the influence of hydration status, the findings in our study pertaining to MAMC is consistent with some other prior studies that used DEXA as the reference standard.(14) MAMC has traditionally been used as a convenient and non-invasive method for estimating LBM despite its limited reproducibility and precision due to high intra- and inter-observer measurement variability.(8,46–47) In our study we found a good correlation between MAMC and LBM especially in men. We also found that handgrip strength, which is a convenient assessment method for upper extremity muscle strength, correlated well with DEXA-measured LBM. The handgrip strength is a simple test for assessment of muscle strength in dialysis outpatients,(42,48) but its utility to estimate LBM has only studied in non chronic kidney disease patients.(14) In our study the handgrip strength had a strong correlation with LBM especially in women. Evidence suggests that handgrip strength may be a good measure of nutritional status and a predictor of mortality and complications in surgical patients.(49–50) Second, handgrip strength has also been reported to correlate closely with other nutritional parameters, e.g. protein index (assessed by neutron activation) in surgical patients (51) and fat-free mass (assessed by anthropometry) in patients with chronic heart failure.(52) Third, handgrip strength has been reported to improve with nutritional supplementation (53–54) indicating that its variation is a function of nutritional interventions, finally, some studies found that handgrip strength is lower among malnourished dialysis patients.(42,48)

Our study should be qualified for its relatively large proportions of African American and Hispanics and for potential selection bias due to exclusion of patients whose upper arm deemed inappropriate for NIR interactance or anthropometric measurement. Furthermore, all three equations tended to underestimate LBM especially in the higher ranges of LBM above its median (see Tables 3 and 4). Another potential limitation is that we DEXA in the development cohort but not in the validation cohort, where instead the NIR interactance was used. However NIR interactance measurements of lean and fat mass correlate closely with DEXA.(29) Differences in the characteristics of the people in the development vs. validation cohort could also affect the results. We should note that variation in fluid status may affect DEXA measurements, whereas NIR interactance and anthropometric measurements are less prone to this confounder. Our NIR interactance based validation studies show that the DEXA-based regression equations were adequately valid, augmenting the robustness of our developed equations. We did not compare DEXA or field methods to underwater weighing or air displacement techniques; however, these elaborate and cumbersome techniques are rarely used in dialysis patient studies.

In conclusion, in long-term hemodialysis patients our novel equations to estimate LBM based on SCr, MAMC or handgrip strength appear valid and yield accurate estimates of DEXA or NIR interactance-measured LBM, even though in higher LBM ranges they may underestimate it. SCr, MAMC and handgrip strength are practical and inexpensive assessments that can be used for routine assessment of nutritional status or in clinical or epidemiologic studies, bearing their limitations in mind. Given emerging studies that indicate the association of greater muscle mass with better survival in hemodialysis patients, (55–56) additional studies using these or other reference standards and equations are needed to verify the accuracy and reliability of our developed regression equations.

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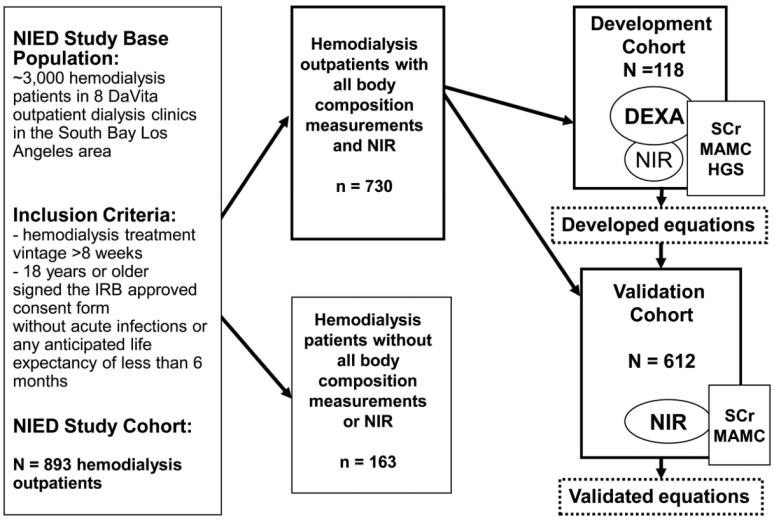

Figure 1.

Flow diagram of the development and the validation cohort

LBM, lean body mass; DEXA, Dual energy X-ray absorptiometry; SCr; serum creatinine; MAMC, mid arm muscle circumference; HGS, handgrip strength, NIR: near infra-red

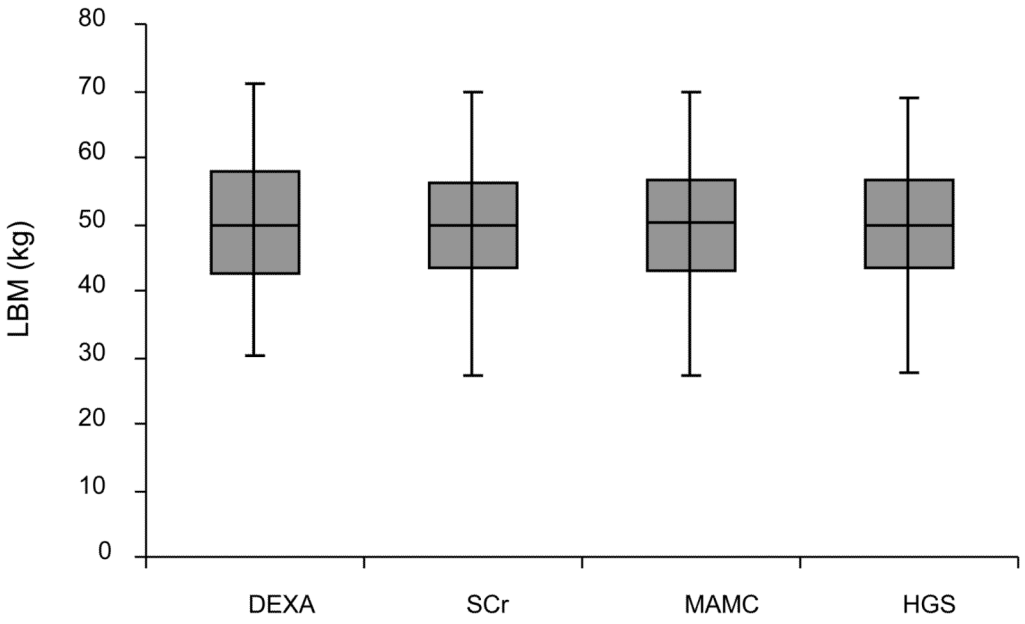

Figure 2.

Box plots of LBM measured directly be DEXA and estimated indirectly by SCr, MAMC, and handgrip strength using different 3 regression equations (see text) in the development cohort of 118 hemodialysis patients. The lower and upper box boundaries are the 25th and 75th percentiles, the line within the box is the median, and the whiskers extend to min and max.

LBM, lean body mass; DEXA, Dual energy X-ray absorptiometry; SCr; serum creatinine; MAMC, mid arm muscle circumference; HGS, handgrip strength

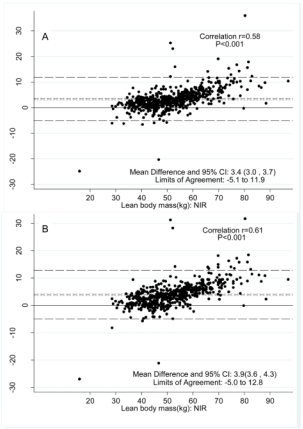

Figure 3.

Difference plots between LBM using NIR interactance as reference standard and the 2 equations based on SCr and MAMC in the validation cohort of 612 hemodialysis patients. Medium dashed line is the difference, long dashed lines are limits of agreement (mean ±2SD) and short dashed lines are 95% confidence intervals for the difference.

LBM, lean body mass; DEXA, Dual energy X-ray absorptiometry; NIR, near-infrared; SCr; serum creatinine; MAMC, mid arm muscle circumference.

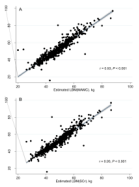

Figure 4.

Scatter plots, regression line and 95% confidence intervals, reflecting the correlations between the NIR interactance-measured LBM and the LBM estimated by MAMC (Panel A) and SCr (Panel B) in the validation cohort of 612 hemodialysis patients. Shaded areas reflect the 95% confidence intervals.

LBM, lean body mass; NIR, near-infrared; SCr; serum creatinine; MAMC, mid arm muscle circumference.

Table 1

Demographic and clinical characteristics of hemodialysis patients in the development and validation cohorts upon body composition measurement

	Development cohort (n= 118)	Validation cohort (n= 612)
Age (y)	49±11	54±15
Men(%)	57	53
Diabetes (%)	52	53
Race/ethnicity (%)		
African-American	40	30
Hispanic	38	53
Weight (kg)	74.5±18.4	72.3±19.0
Height (inch)	65.3.9±4.1	65.1±4.3
Body mass index (kg/m^2)	27.0±6.0	26.6±6.2
Lean body mass (kg)		
By DEXA	49.8±9.9	n/a
By NIR interactance	55.3±10.5	52.2±11.6
Dialysis vintage (months)	41.1±32.9	30.7±33.7
Dialysis dose (kt/V)	1.7±0.3	1.6±0.3
nPNA or nPCR (gr/kg per day)	1.11±0.22	1.06±0.24
Laboratory measurements		
Blood hemoglobin (gr/dl)	12.2±0.7	12.0±1.0
Serum albumin (gr/dl)	4.0±0.3	3.9±0.4
Serum creatinine (mg/dl)	10.8±3.0	10.1±3.3
prealbumin (transthyretin) (mg/dl)	30.6±9.6	28.1±9.6
total iron binding capacity (mg/dl)	210.9±35.3	206.6±40.0
total cholesterol (mg/dl)	147.2±41.1	150.1±42.3
LDL cholesterol (mg/dl)	80.9±28.9	82.6±34.5
HDL cholesterol (mg/dl)	36.1±13.4	35.2±13.6
triglycerides (mg/dl)	148.2±122.6	163.2±105.7
serum urea nitrogen (mg/dl)	63.0±16.2	63.3±15.1

Values are presented as mean ± standard deviation or percentage. Abbreviations: DEXA, dual-energy X-ray absorptiometry; NIR, near-infrared; LDL, low-density lipoprotein; HDL, high-density lipoprotein; nPCR normalized protein catabolic rate nPNA normalized protein nitrogen appearance

conversion factors for units: hemoglobin and albumin in g/dL to g/L, ×10; serum creatinine in mg/dL to micromole/L, ×88.4; total, LDL, and HDL cholesterol in mg/dL to mmol/L, ×0.02586; triglycerides in mg/dL to mmol/L, ×0.01129; serum urea nitrogen in mg/dL to mmol/L, ×0.357.

Table 2

Regression and Pearson correlation coefficients of DEXA-measured LBM with measures of nutritional status

	Model 1 (unadjusted)	Model 2 (all 7 measures included together)	Model 3 (all 7 measures and case-mix variables included)
Regression coefficients:			
MAMC	1.73 (1.39 to 2.07)[a]	1.19 (1.15 to 1.83) [a]	1.05 (0.59 to 1.51) [a]
handgrip strength	0.39 (0.22 to 0.56) [a]	0.32 (0.19 to 0.45) [a]	0.33 (0.16 to 0.44) [a]
SCr	1.14 (0.53 to 1.75) [a]	0.64 (0.18 to 1.09) [a]	1.54 (0.64 to 2.43) [a]
Serum albumin	−1.81 (−8.14 to 4.86)	−3.90 (−8.60 to 0.71)	−2.15 (−8.19 to 3.89)
Serum prealbumin	0.01 (−0.20 to 0.21)	−0.16 (−0.31 to −0.01) [a]	−0.11 (−0.31 to 0.00)
SGA	−0.79 (−1.80 to 0.22)	−0.42 (−1.07 to 0.22)	−0.44 (−1.26 to 0.38)
nPNA	−9.59 (−17.46 to −1.72) [a]	−0.48 (−6.32 to 5.36)	−3.55 (−12.36 to 5.26)
Correlation coefficients:			
MAMC	0.69***	0.68***	0.57**
handgrip strength	0.40***	0.46***	0.52*
SCr	0.33***	0.28**	0.46*
Serum albumin	−0.05	−0.17	−0.10
Serum prealbumin	0.00	−0.22*	−0.16
SGA	−0.15	−0.13	−0.16
nPNA	−0.22*	−0.01	−0.12

Note: Analysis is performed with 7 selected measures of the nutritional status in the development cohort of 118 hemodialysis patients. Values in parentheses are 95% confidence intervals. Model 1 includes each surrogate separately without adjustment; Model 2 includes all the 7 surrogates in the model; Model 3 includes all 7 surrogates plus case-mix variables. Statistical correlations were observed among the DEXA-measured LBM values and BMI, MAMC, handgrip strength and SCr but not with other nutritional markers.

* p value 0.05 to 0.01;

** p value 0.01 to 0.001;

*** p value <0.001

[a] summary estimate is statistically significant (p<0.05).

Abbreviations: DEXA, Dual energy X-ray absorptiometry; MAMC, mid arm muscle circumference; SCr, serum creatinine; SGA, subjective global assessment, nPNA, normalized protein nitrogen appearance; LBM, lean body mass.

Table 3

Performance of SCr-, handgrip strength-, and MAMC-based equations relative to NIR interactance-measured LBM

	All Patients (n=118)	Patients with estimated LBM		
		<50 kg (n=59)	>=50 kg (n=59)	
Median difference , kg*				
SCr equation	4.2 (3.5 to 4.7)	2.3 (1.4 to 3.1)	5.5 (4.3 to	6.4)
MAMC equation	3.7 (3.4 to 5.1)	2.2 (1.3 to 3.0)	5.8 (3.9 to	6.7)
handgrip strength equation	4.1 (3.5 to 5.2)	2.5 (2.0 to 2.9)	5.6 (4.8 to	7.0)
IQR for differences, kg**				
SCr equation	3.9 (−0.8 to 10.4)	2.2 (−0.9 to 5.1)	4.0 (−2.5 to	11.3)
MAMC equation	4.3 (−1.3 to 10.8)	2.4 (−1.5 to 7.0)	3.9 (−1.4 to	11.1)
handgrip strength equation	4.3 (−0.4 to 10.0)	1.7 (−2.5 to 5.7)	3.8 (0.2 to	10.4)
RMSE				
SCr equation	2.9	1.7	3.0	
MAMC equation	2.6	2.0	2.7	
handgrip strength equation	2.7	1.9	2.8	

Analysis performed in the development cohort of 118 hemodialysis patients. The values are calculated for all subjects and across the mutually exclusive strata of above and below the median LBM, which was 50 kg. The 95% confidence intervals are given in parentheses for median difference and interquartile ranges.

* Median difference refers to NIR interactance-measured LBM minus estimated LBM.

** Interquartile range refers to the distance between the 25th and 75th percentiles.

LBM; lean body mass; SCr: serum creatinine.; MAMC, mid arm muscle circumference; IQR, interquartile range; NIR, near-infrared; RMSE, root mean square error

Table 4

Performance of SCr- and MAMC-based equations relative to NIR interactance-measured LBM

	All Patients (n=612)	Patients with estimated LBM	
		<51 kg (n=306)	>=51 kg (n=306)
Median difference, kg*			
SCr equation	3.4 (−3.2 to 12.0)	1.4 (−5.5 to 7.2)	5.4 (−0.7 to 15.9)
MAMC equation	4.0 (−2.6 to 13.6)	1.7 (−4.3 to 7.6)	6.3 (−0.2 to 16.2)
IQR for differences, kg**			
SCr equation	3.0 (1.1 to 5.1)	1.7 (0.2 to 3.1)	4.8 (3.0 to 7.1)
MAMC equation	3.7 (1.3 to 6.0)	2.0 (0.2 to 3.4)	5.7 (4.1 to 8.0)
RMSE			
SCr equation	4.10	2.98	4.26
MAMC equation	4.27	3.17	4.23

Analysis performed in the validation cohort of 612 hemodialysis patients. The values are calculated for all subjects and across the mutually exclusive strata of above and below the median LBM, which was 51 kg. The 95% confidence intervals are given in parentheses for median difference and interquartile ranges. Note that in the Validation Cohort, handgrip strength was not performed.

* Median difference refers to NIR interactance-measured LBM minus estimated LBM.

** Interquartile range refers to the distance between the 25th and 75th percentiles.

LBM; lean body mass; SCr: serum creatinine.; MAMC, mid arm muscle circumference; IQR, interquartile range; NIR, near-infrared; RMSE, root mean square error

Table 5

Difference Plot analyses comparing NIR interactance-measured LBM with SCr- and MAMC-based estimates of LBM

	Limits of agreement	Mean difference (95% CI)	Correlation* (r)	Correlation P-value
Women (n= 298)				
SCr-estimated LBM	−5.7 to 9.9	2.1 (1.6 to 2.6)	0.45	<0.001
MAMC-estimated LBM	−5.8 to 10.4	2.3 (1.8 to 2.8)	0.47	<0.001
Men (n= 314)				
SCr-estimated LBM	−3.8 to 12.9	4.6 (4.1 to 5.0)	0.62	<0.001
MAMC-estimated LBM	−3.0 to 14.0	5.5 (5.0 to 6.0)	0.59	<0.001
All (n=612)				
SCr-estimated LBM	−5.1 to 11.9	3.4 (3.0 to 3.7)	0.58	<0.001
MAMC-estimated LBM	−5.0 to 12.8	3.9 (3.6 to 4.3)	0.61	<0.001

Difference Plot analyses are based on a modified Bland-Altman test and was performed in the validation cohort of 612 hemodialysis patients.

* Pearson correlation between difference and NIR interactance values.

SCr: serum creatinine. LBM, lean body mass; MAMC, mid arm muscle circumference; CI, confidence interval. NIR, near-infrared

Table 6

Mean values of LBM and correlation coefficients between the NIR interactance-measured LBM and estimated LBM

	Total n= 612	Women n= 298	Men n= 314
LBM, kg			
NIR interactance-measured LBM	52.2±11.6	44.6±8.5	59.1±9.6
SCr-estimated LBM	48.7±9.8	42.5±7.3	54.6±7.9
MAMC-estimated LBM	48.3±9.6	42.3±7.3	54.0±8.0
Correlations (r) [*], [a]			
SCr-estimated LBM	0.93	0.88	0.91
MAMC-estimated LBM	0.93	0.87	0.90

Values shown are mean +/− SD for LBM measurements or estimates. Analyses based on all 612 hemodialysis patients in the validation cohort.

[*] All *P*-values <0.001

[a] Pearson's correlation coefficients (r) between the NIR interactance-measured LBM and each of the 2 estimates of LBM using the SCr- and MAMC-based LBM estimating equations in 612 long-term hemodialysis patients of the validation cohort.

SCr: serum creatinine. LBM, lean body mass; MAMC, mid arm muscle circumference; NIR, near-infrared

Box 1

LBM Estimation Equations

$$LBM_{SCr} = 0.34^{*}SCr\,(mg/dL) + 5.58^{*}\{1 \text{ if female; } 0 \text{ if male}\} + 0.30^{*}\text{weight (in kg)} + 0.67^{*}\text{height (in inches)} - 0.23^{*}URR - 5.75$$

$$LBM_{HGS} = 9.09^{*}HGS\,(\text{unit}) + 5.15^{*}\{1 \text{ if female; } 0 \text{ if male}\} + 0.33^{*}\text{weight (in kg)} + 0.74^{*}\text{height (in inches)} - 29.06$$

$$LBM_{MAMC} = 0.28^{*}MAMC\,(\text{cm}) + 5.52^{*}\{1 \text{ if female; } 0 \text{ if male}\} + 0.28^{*}\text{weight (in kg)} + 0.82^{*}\text{height (in inches)} - 35.30$$

Abbreviations: LBM, lean body mass; SCr, serum creatinine; MAMC, mid-arm muscle circumference; HGS, handgrip strength; URR, urea reduction ratio.