Estimation of lean body mass by creatinine kinetics increases the prevalence of muscle wasting in peritoneal dialysis patients compared to bioimpedance

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Abstract

Dialysis patients are at increased risk for muscle wasting, and time efficient screening tests are required for to allow for early detection. Creatinine kinetics have been advocated to estimate lean body mass (LBM) in peritoneal dialysis (PD) patients, and can be readily calculated in clinical practice from peritoneal dialysate effluent and urine collections. Bioimpedance is increasingly available, and we compared methods in 434 PD patients (55% men, 33.3% diabetics), mean age 55.2±16.2 years. LBM was lower by creatinine kinetics (47.8±16.6 kg men, 37.8±11.2 kg women) vs bioimpedance (53.2±11.5 kg men, 39.2±7.2 kg women), $p<0.01$. The prevalence of muscle wasting was much greater using creatinine kinetics (72.4% men, 52.4% women) vs bioimpedance (55.2% men, 37.3%), $p<0.05$. Estimates of LBM were much lower using creatinine kinetics compared to bioimpedance. Studies reporting the prevalence of muscle loss in PD patients will differ depending upon the method used to estimate muscle mass.

Introduction

Dialysis patients are at increased risk of muscle wasting, and muscle wasting is associated with increased risk for mortality. Peritoneal dialysis (PD) patients have additional protein losses in the spent dialysate. For routine clinical practice simple screening tests are required to detect muscle wasting (sarcopenia) at an early stage to allow for intervention. Several methods have been advocated for assessing lean body mass in dialysis patients and creatinine kinetics is one method supported by the Kidney Disease Outcome Quality

Initiative (KDOQI) clinical guidelines committee [1]. Creatinine kinetics have been used to estimate lean body mass in PD patients [2]. Bioimpedance devices are being increasingly used in clinical practice, and can be used to assess body composition [3], and studies have reported that bioimpedance provides equivalent results to dual-energy x-ray absorptiometry (DXA) in PD patients [4]. As the prevalence of muscle wasting varies considerably between studies in PD patients, we wished to compare the estimations of lean body mass using creatinine kinetics and bioimpedance to determine whether the method used changed the reported prevalence of muscle wasting.

Materials and Methods

Creatinine kinetics were calculated from corresponding 24-hour spent peritoneal dialysate effluents, 24-hour urine collections and serum samples, using standard equations [5], when patients attended for routine testing of peritoneal membrane function. Enzymatic methods were used to measured creatinine to exclude interference from glucose [6]. Multifrequency segmental bioimpedance was performed in a standardised manner after patients had voided and peritoneal dialysate drained out (InBody700, Seoul, Korea) [7]. The bioimpedance machine was regularly serviced and calibrated. Muscle wasting was defined by age and gender matched reference data obtained from the National Health and Nutritional Survey (NHANES) [8].

This retrospective audit complied with the UK National Health Service (NHS) guidelines for clinical audit and service development.

Statistical analysis

Data is presented as mean ± standard deviation, median (interquartile range), or as percentage. Standard statistical tests were used to analyse data. using Prism 7.0 (Graph Pad, San Diego, USA) and SPSS 24 (SPSS, University of Chicago, Chicago, USA) and Analyse It 4.0 (Analyse-It, Leeds, UK). Statistical significance was taken as $p<0.05$.

Results

We compared lean body mass estimated by creatinine kinetics and bioimpedance in 434 PD patients (table 1). Lean body mass estimated by creatinine kinetics was lower for both men (47.8±16.6 kg) and women (37.8±11.2 kg) vs bioimpedance (53.2±11.5 kg men, 39.2±7.2 kg women), $p<0.01$. The mean bias on Bland Altman analysis showed creatinine kinetics under-estimating lean body mass compared to bioimpedance by 3.8 kg (Figure 1), with mean bias less for women 1.6 kg (95% limits of agreement -18.5 to 21.8 kg), and 5.5 kg (-22.5 to 33.5 kg). Using NHANES reference data, the prevalence of muscle wasting was 72.4% for men and 52.4% for women by creatinine kinetics vs 55.2% for men and 37.3% for women using bioimpedance, $p<0.05$. Dividing patients according to ethnicity lean body mass was not statistically different (European: females 19.7 (14.0-27.9), males 21.3 (14.7-33.4); Asian: females 19.1 (17.0-29.8), males 21.4 (14.4-31.2); African Afro-Caribbean: females 19.8 (14.0-33.4), males 17.9 (12.9-30.9) kg, respectively.

Discussion

Studies in dialysis patients have repeatedly reported that loss of muscle mass is strongly associated with an increased risk in mortality. Once established protein energy wasting is difficult to reverse, and as such simple screening tests are required for every day clinical practice. The routine samples obtained when PD patients attend for assessment of peritoneal membrane function allow estimation of lean body mass by calculating the creatinine index [5], and this method has been supported by the KDOQI committee [1]. A validation study of creatinine index reported similar estimates of lean body mass to those obtained with DXA in PD patients, although the number of patients studied was very small [2]. Bioimpedance devices are now more readily available in clinical practice, with estimates of body composition in both haemodialysis and PD patients reported to correlate strongly with DXA measurements [4,9].

Studies reporting on the prevalence of loss of muscle mass (sarcopenia) in dialysis patients have varied in results, and as such we wished to determine whether some of this variance could be due to the method used to estimate muscle mass. We found that creatinine kinetics under-estimated lean body mass compared to that measured with bioimpedance, and the mean bias was greater for men compared to women, as male dialysis patients typically have greater muscle mass and are more physically active [10]. We had too few anuric patients to determine whether potential differences in non-renal creatinine excretion and metabolism resulted in in greater bias, compared to those with residual

renal function. We did not find differences between ethnic groups, but this may have been due to analysis of small numbers and differences in patient demographics. Similarly we did not observe a difference with peritoneal transport status.

When we then compared estimates of muscle mass with recognized age and gender matched reference data [7], we found that the prevalence of muscle loss (sarcopenia) was significantly greater when using creatinine kinetics. When calculating creatinine kinetics, although urinary and peritoneal creatinine can be measured by routine laboratory methods, the higher glucose concentration in the spent peritoneal dialysate effluent may interfere with standard Jaffe creatinine assays. To overcome this potential error, we used enzymatic methods. In the steady state, estimation of lean body mass and creatinine kinetics are closely correlated in healthy subjects, however in dialysis patients greater amounts of creatinine are secreted into the intestine, some of which is then reabsorbed, and then a variable proportion is converted back to creatine [5]. As such creatinine kinetics, potentially under-estimates lean body mass in patients with chronic kidney disease, and we found that the creatinine kinetics under-estimated lean body mass compared to bioimpedance, with the mean bias being greater for male compared to female PD patients, leading to reporting a much higher prevalence of muscle wasting using creatinine kinetics compared to bioimpedance. Our study using bioimpedance supports previous studies which compared lean body mass estimated by creatinine kinetics with that using isotopic potassium [5]. We noted that there were wide limits of agreement

between methods for individual patients, which may relate to variation in dietary intakes and body composition.

Our study would suggest that creatinine kinetics is a less reliable method of assessing lean body mass in PD patients and leads to an over estimation of the prevalence of muscle wasting.

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The authors have no conflict of interest

The data presented in this paper has not been previously published in part or full form

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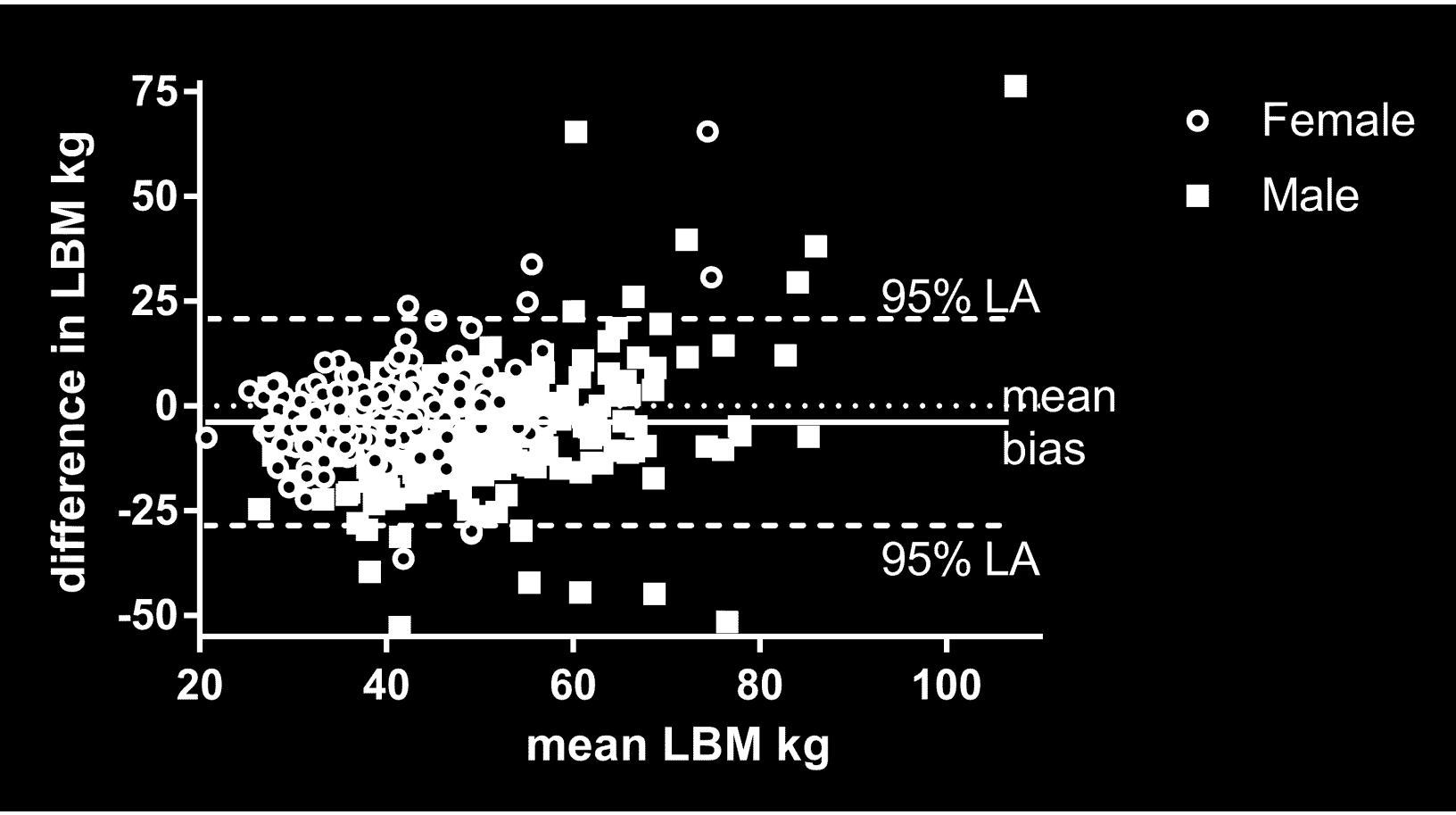
Figure 1: Bland Altman plot comparing lean body mass measured by bioimpedance and creatinine kinetics showing mean bias and 95% limits of agreement.

Table 1. Demographics of peritoneal dialysis patients used for estimation of lean body mass by Creatinine kinetics and Bioimpedance. Peritoneal dialysis modality, peritoneal membrane transport status, and urea dialysis clearance (weekly Kt/Vurea), laboratory tests and multifrequency bioimpedance body composition. Results shown as median (25th, 75th percentile) or number (percentage).


75
50
25
0
-25
-50
difference in LBM kg
20
40
60
80
100
mean LBM kg
95% LA
mean
bias
95% LA
Female
Male