ORIGINAL ARTICLE

Equations for estimating resting energy expenditure in patients on peritoneal dialysis

Xiao Xu[1,2], Nanzha Abi[1], Zhikai Yang[1], Tiantian Ma[1], Nan Zhang[1], Yingdong Zheng[3] and Jie Dong[1]

[1]Renal Division, Department of Medicine, Peking University First Hospital; Institute of Nephrology, Peking University; Key Laboratory of Renal Disease, Ministry of Health; Key Laboratory of Renal Disease, Ministry of Education; Research Units of Diagnosis and Treatment of Immune-mediated Kidney Diseases, Chinese Academy of Medical Sciences; Beijing, China, [2]Department of Ultrasonography, Peking University First Hospital, Beijing, China and [3]Department of Epidemiology & Biostatistics, School of Public Health, Peking University, Beijing, China

Correspondence to: Jie Dong; E-mail: jie.dong@bjmu.edu.cn

ABSTRACT

Background. In peritoneal dialysis (PD) patients, determining energy expenditure is essential for recommending energy intake in nutrition management.
Objective. We aimed to develop and validate a resting energy expenditure (REE) equation for patients with PD and compare it to previously available REE equations in dialysis patients.
Design. This cross-sectional study enrolled 200 patients with PD from two hospitals in Beijing, China. Stepwise linear regression analysis was used to derive a new REE equation (eREE-PD) based on actual REE (aREE) measured using indirect calorimetry (IC) in the development dataset. The eREE-PD value was then validated with aREE in the validation dataset and compared with values from existing equations obtained in general populations and those developed for chronic kidney disease and dialysis patients, in terms of bias, precision, and accuracy.
Results. The bias, precision, and accuracy of the eREE-PD equation were significantly better than those of the Harris–Benedict, WHO, and Schofield equations ($P < .005$) and comparable to the Mifflin equation ($P = .541$ for bias, .988 for precision, and .359 for accuracy), with IC as the reference method. Either bias, precision or accuracy of the eREE-PD were significantly better than eREE-V, eREE-B$_{scr}$, and eREE-C$_{FFM}$ equations significantly ($P < .005$) and similar to eREE-CKD, eREE-B$_{crp}$, and eREE-C$_{weighht}$ equations ($P > .05$ for bias, precision, and accuracy). The bias, precision, and accuracy of the eREE-PD equation were consistent across subgroups categorized by hs-CRP levels.
Conclusion. The eREE-PD equation, based on age, sex, and weight data, may serve as a reliable and practical tool for estimating REE in patients with PD, aiding in individualized nutritional management. However, external validation in other populations is required to confirm its generalizability beyond the studied cohort.

Keywords: chronic kidney disease, indirect calorimetry, peritoneal dialysis, resting energy expenditure

---

KEY LEARNING POINTS

What was known:
- For patients with CKD, the precondition for recommending energy intake in nutrition management is the determination of energy expenditure.
- However, indirect calorimetry, which is the gold-standard measurement for resting energy expenditure (REE), is known to be both expensive and time-consuming.

This study adds:
- Our study is the first study to develop an REE equation only for PD patients using IC as the reference method.
- This new equation only requires the collection of readily available clinical data, suggesting its feasibility in clinical practice.

Potential impact:
- Based on readily available clinical information concerning patients with peritoneal dialysis, our new equation provided reliable and accurate estimates of REE as a practical tool to be applied prior to nutritional counseling in clinical practice.

INTRODUCTION

It is well known that metabolic disturbances are common in patients with chronic kidney disease (CKD) and gradually worsen with declining kidney function. In end-stage kidney disease, the prevalence of protein-energy wasting (PEW) has been reported to reach as high as 28%–80% in hemodialysis and peritoneal dialysis (PD) [1–3]. PEW is also closely associated with substantially increased morbidity, mortality, and reduced quality of life in dialysis patients [4–7]. Accordingly, numerous interventions aimed at improving PEW have been broadly studied, but the results remain inconclusive [8–11]. These highlight the importance of maintaining nitrogen balance and energy homeostasis in dialysis patients.

The 2020 KDOQI Clinical Practice Guideline for Nutrition in CKD recommends a dietary energy intake of 25–35 kcal/kg/day for patients with CKD. Meanwhile, energy intake requirements should be individualized, taking all elements relevant to energy demands such as age, physical activity, comorbidities, body composition, and nutrition status into account [12–15]. Resting energy expenditure (REE) accounts for 60%–75% of the total energy expenditure in most sedentary individuals and is considered the most stable component [16]. Indirect calorimetry (IC) is considered the gold-standard method for measuring REE but requires specific equipment, qualified staff, and appropriate environmental conditions [16]. It is necessary to explore alternative methods for estimating REE in this population.

Several equations have been developed to estimate REE for general population [17–20], non-dialyzed CKD patients [21, 22], or hemodialysis [23–25]. Cassiana *et al.* [26] and Mariana *et al.* [27] found hemodialysis and PD patients had similar REE levels when unadjusted with age, weight, or other factors influencing REE. However, as previously demonstrated, hemodialysis patients had increased REE during the dialysis session. Unlike hemodialysis, PD therapy is persistent, absorbing energy from the dialysate. Given the varying catabolic effects of different dialysis modalities, REE equations developed for hemodialysis patients may not be applicable to PD patients. Therefore, we aimed to develop and validate a novel equation for estimating REE using a PD patient dataset and to compare its precision and accuracy with existing equations used for the general population, non-dialyzed CKD, and hemodialysis patients.

MATERIALS AND METHODS

Study design and patients

We recruited outpatients undergoing PD according to inclusion and exclusion criteria from two hospitals in Beijing, China. The inclusion criteria comprised patients: (i) aged ≥18 years; (ii) undergoing PD for >3 months; and (iii) who consented to participate in all aspects of the study. We excluded patients: (i) with acute complications to hospitalization 1 month prior to the study; (ii) with acute or chronic infections, cancer in the past year; (iii) with thyroid dysfunction; (iv) with acute onset of podagra; (v) with respiratory diseases (asthma, pleural effusion, pneumothorax, COPD); (vi) with a history of hormonal drug use; (vii) during pregnancy or lactation; and (viii) who could not maintain posture and complete the REE test. Recruited patients were scheduled for the relevant examinations. The study protocol was approved by the Ethics Committee of Peking University First Hospital, and the study was conducted in accordance with the Declaration of Helsinki. Each patient gave written informed consent to participate in the study. This trial was registered at clinicaltrials.gov as NCT04947839.

Demographic and biochemical measurements

Demographic and clinical data including age, sex, height, weight, primary renal disease, cardiovascular disease (CVD), and diabetes mellitus were collected. Standing height was measured without shoes using a fixed stadiometer to the nearest 1 cm. Weight was measured using a calibrated digital scale. CVD was recorded if any of the following conditions were present: angina, congestive heart failure (classes III and IV) as defined by the New York Heart Association, transient ischemic attack, history of myocardial infarction or cerebrovascular accident, or peripheral arterial disease [28].

Blood samples were collected following an overnight fast. Biochemistry data in relation to hemoglobin, serum albumin, triglyceride, total cholesterol, high-density lipoprotein and low-density lipoprotein, glucose, uric acid, urea, creatinine, calcium, and phosphate were obtained using an automatic chemistry analyzer (Hitachi Chemicals, Tokyo, Japan). Serum levels of high-sensitivity C-reactive protein (hs-CRP) were measured using immune rate nephelometry and normal values were <3 mg/l.

Serum intact parathyroid hormone (iPTH) was measured using a chemiluminescence assay (reference range 15–65 pg/ml).

Small-molecule solute clearance, including urea and creatinine, was measured by collecting 24-hour urine and dialysate. Small solute clearance was defined as total, peritoneal, and renal urea clearance (K_t/V) and creatinine clearance (Ccr).

REE

Actual REE (aREE) was measured using IC, with a VMax 29 n metabolic cart (CareFusion, Yorba Linda, CA, USA). Patients fasted overnight (over 12 hours). After 30 minutes resting, they completed the measurements between 8 a.m. and 11 a.m. in a quiet, dimly lit room maintained at a constant humidity (room temperature, 20–25°C). During the test, patients were instructed to lie supine for 15 minutes, breathe calmly, and avoid hyperventilation, fidgeting, or falling asleep. Oxygen consumption and carbon dioxide production were measured at 30-second intervals. Data were recorded only when the patients were in steady-state conditions, and the average O_2 and CO_2 volumes were used to calculate REE using a Weir equation [29]. REE was also estimated using the equations obtained in general populations, namely the Harris–Benedict equation (eREE-HB) [17], Mifflin equation (eREE-Mifflin) [18], WHO equation (eREE-WHO) [19], and Schofield equation (eREE-Schofield) [20] and equations obtained in CKD and hemodialysis patients, including our newly derived equation in CKD patients (eREE-CKD equation) [22], the equation from Vilar *et al*. (the eREE-V equation) [25], the equations from Byham-Gray *et al*. (the eREE-B_{crp} equation and the eREE-B_{scr} equation) [23], and the equations from Cuppari *et al*. (the eREE-C_{weight} equation and the eREE-C_{FFM} equation) [24]. These REE equations are all listed in Supplementary Table 1.

Lean body mass (LBM)

LBM was first calculated using our previously published formula (LBM-HGS, lean body mass estimated from hand grip strength equation) [30], which demonstrated minimal bias when compared to the gold-standard dual-energy X-ray absorptiometry. Then, LBM was also measured using multiple-frequency bioimpedance analysis (LBM-BIA) (Fresenius Medical Care). This procedure has been described in detail elsewhere [31]. Briefly, a patient was positioned supine for a minimum of 10 min, then standard tetrapolar electrodes were placed on the dorsal surface of their left wrist and on the anterior aspect of their left ankle.

Statistical analysis

Normally distributed data are presented as mean ± standard deviation (SD). Non-normal data are presented as median values using an interquartile range (IQR). Categorical variables are expressed as percentages or ratios. All participants were randomly stratified into the development dataset (50% of patients) and the validation data set (50% of patients) according to age (18–45 years, 45–60 years, and >60 years) and sex. Student's t, nonparametric, or chi-squared tests were used to compare the differences in variables between cohorts, as appropriate.

After applying univariate Spearman's correlation analyses to ascertain the relationship between variables (all demographic and biochemical measurements) and aREE, a stepwise linear regression analysis was performed to select potential predictors for incorporation into eREE-PD in the development dataset. Considering that the LBM was highly correlated with weight, we added LBM-HGS, LBM-BIA, or weight to the model to choose the best-fit regression model.

To validate the performance of the new equation, the eREE-PD value was compared with aREE in the validation dataset, expressed by the bias, precision, and accuracy, and used independent t-test in the subgroups. Bias was assessed as the median difference between the estimated and measured REE values, precision was assessed as the SD of the absolute value of difference, and accuracy was defined as the percentage of estimates differing by >10% from the measured REE (1-P10) [32]. Patients were categorized into subgroups according to hs-CRP levels (<3 vs. ≥3 mg/l) to examine the performance of the newly derived equation.

To compare the performance between the eREE-PD equation and several existing equations, bias, precision, and accuracy of eREE-HB, eREE-Mifflin, eREE-WHO, eREE-Schofield, eREE-CKD, eREE-V, eREE-B_{crp}, eREE-B_{scr}, eREE-C_{weight}, and eREE-C_{FFM} in reference to aREE were also calculated. The values from these nine equations were compared with aREE in the validation dataset using block analysis of variance (Dunnett t-test). The performance of eREE-PD was further compared with existing equations using block analysis of variance (Dunnett t-test) for bias and precision, the McNemar Test for accuracy, and Bland–Altman analysis for assessing agreement between eREE-PD and actual REE, identifying any systematic bias and limits of agreement.

All probabilities were two-tailed, and the level of significance was set at 0.05. Statistical analysis was undertaken using SPSS for Windows software version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Participant characteristics

A total of 200 PD patients completed the examinations and measurements required for this study. The entire dataset was randomly divided into a development dataset ($n = 100$) and a validation dataset ($n = 100$) (Fig. 1). The basic demographic and clinical characteristics of the development and validation cohorts are shown in Table 1. There were no significant differences in demographic data, comorbidities, and biochemical data between the two datasets ($P > .05$).

Development of new equations for estimating REE

We constructed an eREE-PD equation using the development dataset. Spearman's correlation analyses showed that aREE was significantly correlated with age ($r = -0.25, P = .013$), sex ($r = 0.58, P < .001$), height ($r = 0.61, P < .001$), weight ($r = 0.72, P < .001$), LBM-HGS ($r = 0.72, P < .001$), LBM-BIA ($r = 0.64, P < .001$), serum creatinine ($r = 0.39, P < .001$), hemoglobin ($r = -0.16, P = .043$), total Ccr ($r = 0.23, P = .021$), and absorbed glucose from dialysate ($r = 0.30, P = .002$). No significant associations were found between aREE and albumin, hs-CRP, glycosylated hemoglobin (HbA1c), iPTH, or other biochemical markers. Regarding the stepwise procedure, multiple regression analysis was performed to select potential variables for the regression equation from all variables associated with REE in the Spearman's correlation analyses. Table 2 lists the regression coefficients for aREE using the variables of age, sex, weight, and constant, which was the best-fit regression model. The R-squared value for the eREE-PD equation was 0.724. When LBM-BIA or LBM-HGS was used instead of weight, the R-square values for the equation decreased to 0.560 and 0.658, respectively.
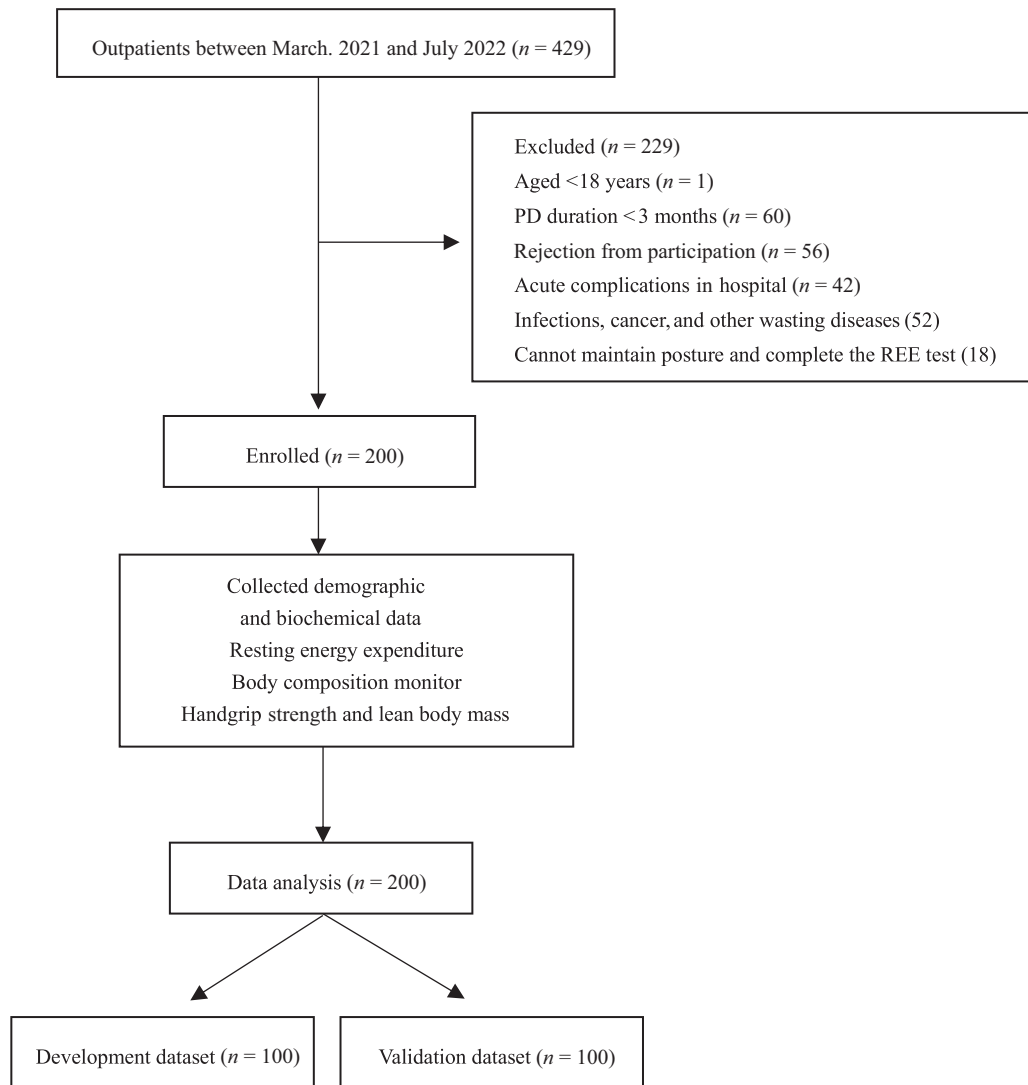
Figure 1: Flow chart of the study.

Validation of new equations and comparisons with existing equations

The mean aREE measured using IC in the validation dataset was 1445.6 kcal/day in males and 1156.2 kcal/day in females. The estimated REE using the eREE-PD equation was not significantly different from aREE. By contrast, REE values estimated using the existing equations obtained in the general population, such as REE-HB, REE-WHO, and REE-Schofield, all highly overestimated REE in both males and females, and the Mifflin equation highly overestimated REE in male (P < .001 or .01 for all) (Fig. 2). As for REE values estimated using equations obtained in hemodialysis patients, eREE-V overestimate REE, and eREE-C$_{FFM}$ underestimate REE in both male and female. There were no significant differences between eREE-B$_{scr}$, eREE-B$_{crp}$, eREE-C$_{weight}$, and aREE (Fig. 3).

The eREE-PD value was further compared with aREE measured using IC expressed by the bias, precision, and accuracy (Table 3). The bias between eREE-PD and aREE was small, with a mean of 11.1 kcal (range −106.5, 78.2). The SD of the absolute value of the difference in the eREE-PD equation was 96.5(80.3,

113.6) kcal, indicating good precision. A 1-P10 value of 35% for eREE-PD indicated high accuracy, as a lower 1-P10 suggests fewer estimates deviating >10% from the measured REE. To examine the performance of the equations in subgroups with varying degrees of inflammation, the analyses were repeated in mutually exclusive strata, i.e. a hs-CRP level higher or lower than 3 mg/l. Comparisons in terms of bias, precision, and accuracy of the eREE-PD equation in the subgroups showed no differences (P > .05).

Regarding the performance of the eREE-PD equation compared with several existing equations obtained from the general population (Table 3, Supplementary Figure), the bias of the eREE-PD value (11.1 kcal) was smaller than eREE-HB, eREE-WHO, and eREE-Schofield (P < .001 for all) values using aREE as the reference and similar with eREE-Mifflin (P = .541). The SD for the absolute value of the difference in the eREE-PD value (96.5 kcal) was smaller than eREE-WHO and eREE-Schofield (P < .005 for all) values and similar to eREE-HB (P = .384), and eREE-Mifflin (P = .988). In terms of percentage accuracy, the 1-P10 for the eREE-PD value (35.0%) was significantly lower than eREE-Schofield (53%, P = .006) and eREE-WHO (58%, P < .001). No differences in terms

Table 1: Demographic and clinical characteristics of PD patients in the development and validation datasets.

	Cross-sectional datasets			
Variates	Total ($n = 200$)	Development cohort ($n = 100$)	Validation cohort ($n = 100$)	P
Age, years	52.4 ± 13.1	52.2 ± 13.0	52.6 ± 13.3	.817
Male, n (%)	112 (56.0)	56 (56.0)	56 (56.0)	1.000
DM, n (%)	79 (39.5)	41 (41.0)	38 (38.0)	.664
CVD, n (%)	45 (22.5)	24 (24.0)	21 (21.0)	.611
PD duration, month	22.5 (8.0, 51.5)	25.5 (9.0, 57.8)	20.0 (8.0, 40.0)	.147
Primary kidney disease, n (%)				.905
Hypertension nephrosclerosis	29 (14.5)	16 (16.0)	13 (13.0)	
Diabetic nephropathy	47 (23.5)	21 (21.0)	26 (26.0)	
Glomerular disease	81 (40.5)	43 (43.0)	38 (38.0)	
Others	43 (21.5)	20 (20.0)	23 (23.0)	
Height (cm)	165.7 ± 8.6	166.0 ± 8.5	165.4 ± 8.8	.622
Weight (kg)	67.2 ± 14.5	68.5 ± 15.3	65.9 ± 13.6	.210
BMI (kg/m^2)	24.3 ± 4.0	24.6 ± 4.1	23.9 ± 3.8	.214
Handgrip strength (kg)	268.9 ± 102.9	265.7 ± 104.9	272.2 ± 101.3	.659
Charlson score	3 (2,5)	3 (2,5)	3 (2,5)	.387
aREE (kcal/day)	1338.7 ± 271.1	1359.1 ± 276.1	1318.3 ± 265.7	.288
Laboratory data				
Serum albumin (g/l)	36.8 ± 3.6	36.7 ± 3.7	36.9 ± 4.5	.731
Hemoglobin (g/l)	112.4 ± 13.0	111.9 ± 13.4	112.9 ± 12.6	.591
Hs-CRP (mg/l)	1.8 (0.8, 5.7)	2.0 (0.8, 5.9)	1.6 (0.6, 4.6)	.201
Blood glucose (mmol/l)	5.7 ± 2.0	5.7 ± 1.8	5.7 ± 2.2	.797
HbA1c (%)	6.0 ± 1.4	5.9 ± 1.0	6.1 ± 1.7	.508
Urea nitrogen (mmol/l)	24.3 ± 5.6	24.2 ± 5.6	24.4 ± 5.7	.723
Serum creatinine μmol/l	964.2 ± 252.9	989.0 ± 253.5	939.5 ± 251.1	.167
Serum calcium (mmol/l)	2.3 ± 0.2	2.3 ± 0.2	2.3 ± 0.2	.323
Serum phosphorus (mmol/l)	1.7 ± 0.4	1.7 ± 0.4	1.8 ± 0.4	.714
Serum sodium (mmol/l)	138.6 ± 2.5	138.5 ± 2.5	138.7 ± 2.6	.561
Serum potassium (mmol/l)	4.4 ± 0.6	4.4 ± 0.6	4.3 ± 0.7	.523
Total cholesterol (mmol/l)	3.9 ± 1.0	4.0 ± 1.1	3.9 ± 0.9	.365
Triglycerides (mmol/l)	1.5 (1.0, 2.2)	1.5 (1.1, 2.3)	1.5 (1.0, 2.2)	.431
iPTH (pg/ml)	251.4 (157.3, 344.4)	264.3 (170.8, 355.1)	214.4 (148.3, 344.4)	.160
Total (Kt/v)	1.9 ± 0.4	1.9 ± 0.3	1.9 ± 0.4	.945
Renal (Kt/v)	0.4 (0, 0.7)	0.3 (0, 0.7)	0.4 (0, 0.7)	.495
Peritoneal (Kt/v)	1.5 ± 0.5	1.5 ± 0.5	1.4 ± 0.5	.116
Total Ccr (ml/min/1.73 m^2)	47.2 ± 8.9	47.3 ± 8.8	47.1 ± 9.0	.919
Renal Ccr (ml/min/1.73 m^2)	5.7 (0, 12.5)	4.9 (0, 12.2)	6.3 (0, 13.5)	.240
Peritoneal Ccr (ml/min/1.73 m^2)	39.7 ± 11.6	40.3 ± 11.3	39.0 ± 11.8	.433
Absorbed glucose (g)	50.7 ± 18.1	49.3 ± 18.0	52.2 ± 18.0	.259

Abbreviation: DM, diabetes mellitus.
*Significant difference between the groups.

Table 2: Regression coefficients between aREE and variables selected by multiple linear regression analysis based on the development dataset and the new-derived equation (eREE-PD).

	aREE			
Variables	Coefficients	T	P value	R^2
Age	−5.7	−4.9	<.001	0.724
Sex	111.6	2.9	.004	
Weight	11.6	9.3	<.001	
Constant	795.7	7.8	<.001	

Equation: eREE-PD (kcal) = (1 if male; 0 if female) × 111.6–5.7 × age (years) + 11.6 * weight (kg) + 795.7

Statistical test: stepwise linear regression analysis

of bias, precision, or accuracy were found between subgroups with hs-CRP <3 or hs-CRP ≥3 mg/L, regardless of the equation used for estimating REE.

Concerning the performance of the eREE-PD equation and several existing equations obtained from CKD and dialysis patients (Table 4, Supplementary Figure), the bias of the eREE-PD value (11.1 kcal) was smaller than eREE-V and eREE-C$_{FFM}$ ($P < 0.001$ for both) values using aREE as the reference and similar with eREE-cKD, eREE-B$_{crp}$, eREE-B$_{scr}$, and eREE-C$_{weight}$ ($P > .05$). The SD for the absolute value of the difference in the eREE-PD value (96.5 kcal) was smaller than eREE-V, and eREE-C$_{FFM}$ ($P < .001$ for all) values and similar to eREE-B$_{crp}$ ($P = .751$), eREE-B$_{scr}$ ($P = .631$), and eREE-C$_{weight}$ ($P = .770$). In terms of percentage accuracy, the 1-P10 for the eREE-PD value (35.0%) was significantly lower than eREE-V (70.0%, $P < .001$) and eREE-C$_{FFM}$ (70.0%, $P < .001$) and similar with eREE-CKD, eREE-B$_{crp}$, eREE-B$_{scr}$, and eREE-B$_{weight}$ ($P > .05$). No differences in terms of bias, precision, or accuracy in subgroups with hs-CRP <3 or hs-CRP ≥3 mg/l were found, no matter what equations were used for estimating REE in eREE-CKD, eREE-V, eREE-B$_{scr}$, eREE-B$_{crp}$, and eREE-Cweight.
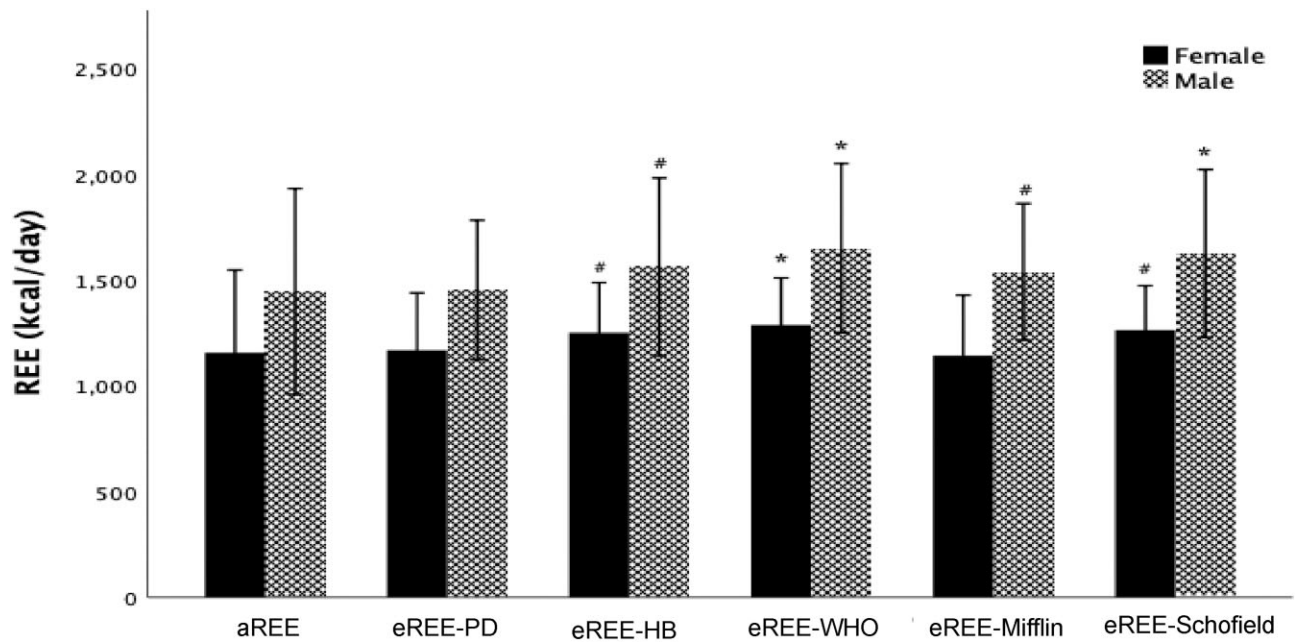
Figure 2: REE estimated by the newly derived equation and the equations obtained in general populations compared with REE measured by IC (aREE) in the validation dataset (*n* = 100). *P < .001 REE measured by equations compared to aREE in male or female; #P < .01 REE measured by equations compared to aREE in males or females. Statistical test: block analysis of variance.
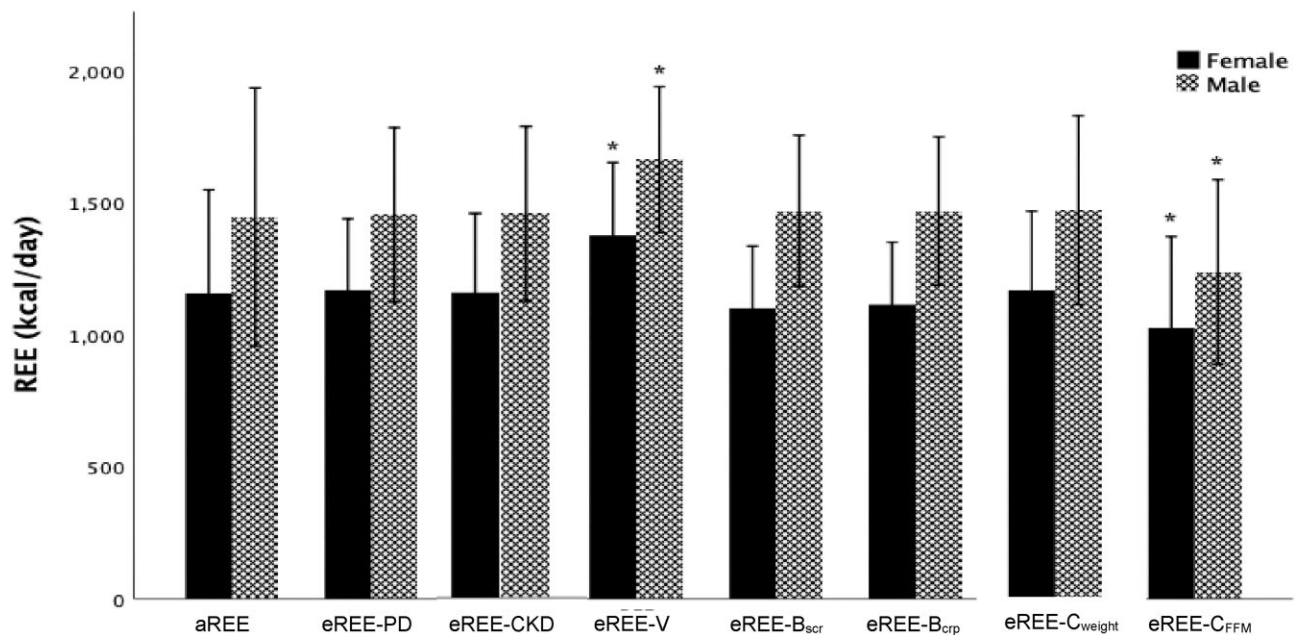

Figure 3: REE estimated by the newly derived equation and the equations obtained in CKD and hemodialysis patients compared with REE measured by IC (aREE) in the validation dataset (*n* = 100). *P < .001 REE measured by equations compared to aREE in males or females; #P < .01 REE measured by equations compared to aREE in males or females. Statistical test: block analysis of variance.

DISCUSSION

We developed a novel equation to estimate REE in dialysis patients. Our results showed that REE estimated using demographic data, such as age, sex, and weight, was strongly predictive of REE measured using IC. The performance of the newly derived eREE-PD equation remained consistent across patient subgroups categorized by hs-CRP levels. Compared with the performance of traditional equations broadly derived from the general population [24, 25, 33–37] and several new REE equations for dialysis patients [23–25], the eREE-PD equation was more reliable, considering its lower bias, improved precision, and higher accuracy compared to the eREE-HB equation, eREE-WHO equation, eREE-Schofield equation, eREE-V equation, and

Table 3: Performance of eREE-PD and equations obtained in general populations based on the difference between eREE and aREE.

	Validation dataset (n = 100)		P	Hs-CRP ≥ 3 mg/l (n = 32)	Hs-CRP < 3 mg/l (n = 68)	p
Bias-median difference						
eREE-PD	11.1 (−106.5, 78.2)	Ref.	Ref.	7.1 (−186.5, 83.0)	11.1 (−89.4, 78.2)	.790
eREE-HB	−86.1 (−205.9, −4.2)	−97.9 (−162.6, −33.2)	<.001	−73.4 (−289.6, −7.0)	−94.6 (−188.2, −1.0)	.636
eREE-WHO	−167.4 (−272.4, −46.1)	−163.1 (−227.8, −98.4)	<.001	−100.5 (−343.2, −30.3)	−178.3 (−247.6, −57.3)	.463
eREE-Mifflin	−32.0 (−138.4, 64.3)	−37.0 (−101.7, 27.7)	.541	−18.2 (−193.0, 88.8)	−34.6 (−133.8, 60.5)	.517
eREE-Schofield	−143.9 (−249.3, −24.9)	−139.1 (−203.8, −74.4)	<.001	−85.0 (−329.2, 17.2)	−152.6 (−230.9, −29.5)	.393
Precision SD of the difference						
eREE-PD	96.5 (80.3, 113.6)	Ref.	Ref.	107.9 (47.1, 221.2)	80.6 (43.4, 162.1)	.117
eREE-HB	124.1 (103.9, 141.8)	31.3 (−16.5, 79.1)	.384	107.6 (59.6, 289.6)	124.9 (47.6, 188.2)	.812
eREE-WHO	145.8 (125.3, 162.8)	78.7 (30.9 126.5)	<.001	165.2 (79.2, 343.2)	178.3 (71.2, 247.6)	.760
eREE-Mifflin	114.0 (92.5, 132.9)	12.6 (−35.2, 60.4)	.988	98.9 (49.6, 255.8)	103.3 (40.1, 151.6)	.683
eREE-Schofield	139.5 (120.4, 157.4)	64.2 (16.4, 112.0)	.003	157.1 (49.6, 329.2)	154.9 (64.2, 230.9)	.803
Accuracy, within ±10% of aREE, n (%)						
eREE-PD	65 (65.0)		Ref.	18 (56.3)	47 (69.1)	.208
eREE-HB	59 (59.0)		.362	20 (62.5)	39 (57.4)	.625
eREE-WHO	42 (42.0)		.001	16 (50.0)	26 (38.2)	.266
eREE-Mifflin	60 (60.0)		.359	16 (50.0)	47 (64.7)	.161
eREE-Schofield	47 (47.0)		.006	16(50.0)	31(45.6)	.680

Abbreviation: REE, resting energy expenditure; aREE, REE measured by indirect calorimetry; eREE, REE measured by equation; eREE-CKD, REE measured by the new equation. eREE-HB, REE measured by Harris Benedict equation; eREE-WHO, REE measured by WHO equation; eREE-Mifflin, REE measured by Mifflin equation; eREE-Schofield, REE measured by Schofield equation; Hs-CRP, high-sensitive C-reactive protein; SD, standard deviation. Statistical test: total validation dataset (*P*): block analysis of variance (Dunnett *t*-test) for bias and precision with the data present as the difference between the value of existing equations and eREE-CKD; McNemar Test for accuracy; subgroup analysis (*p*): independent *t*-test with the data present as quartiles.

eREE-C$_{FFM}$ equation. At the same time, the eREE-PD equation performed similarly to the eREE-Mifflin, eREE-B$_{crp}$, eREE-B$_{scr}$, and eREE-C$_{weight}$ equations.

Similar to our study performed in non-dialyzed CKD patients [22], the total body weight seems better than LBM at reflecting REE levels. Cuppari *et al.* also found weight performed much better in REE equations than FFM in 189 hemodialysis and PD patients [24]. In our research, weight also performed better than FFM, with $R^2 = 0.724$ vs 0.560 and 0.658. Considering the importance of constructing an easily-applied eREE in clinical practice, estimation of REE based on body weight may have better clinical utility [23, 24]. The Mifflin equation was developed from 498 healthy adults and almost half of them were obese. Given the similar proportion of obesity in the population, our newly derived equation showed a performance comparable to the Mifflin equation. The absence of the gold standard in determining LTM may have implications for the accuracy of the results, necessitating further verification.

Most REE equations developed for dialysis patients are based predominantly on data from hemodialysis (HD) patients. In 2014, Vilar *et al.* enrolled 200 HD patients and predicted REE levels using age, height, weight, and gender data (eREE-V). They defined age as a categorical variable with a cut-off value of 65 years old. Owing to the loss of age information, the eREE-V equation did not perform well in a US dataset [38] or our dataset, with a low accuracy (P10) of 30%–46%. In 2018, Byham-Gray *et al.* combined key disease-specific determinants of REE, such as CRP (eREE-B$_{crp}$), Scr (eREE-B$_{scr}$), or HbA1c in 116 HD patients to develop REE equations with age, gender, and weight [23]. In 2019, Cuppari *et al.* used age, gender, weight, or FFM variable data from 58 PD patients and 131 HD patients to develop REE equations [24]. Our newly derived equation enrolled similar variables used in those studies and thus its performance was similar to the eREE-B$_{crp}$, eREE-B$_{scr}$, and eREE-C$_{weight}$ equations, which had also shown a good performance in HD patients. However, compared

with the eREE-B$_{crp}$ and eREE-B$_{scr}$ equations, the variables in the eREE-PD and eREE-C$_{weight}$ equations were fewer and more easily accessible, making them more feasible for use in dialysis patients.

Our data did not support the notion that dialysis modalities influence the association between key variables and REE. Cassiana *et al.* [26] and Mariana *et al.* [27] found that REE of PD patients was not different from hemodialysis patients. Our previous research performed in 1:3 age, gender, weight, and diabetes-matched 40 hemodialysis and PD patients [39] also observed similar REE levels, i.e. 1432.6 ± 339.4 kcal in hemodialysis patients and 1334.6 ± 271.8 kcal in PD patients. PD patients seemed have a higher respiratory quotient (RQ) due to the ratio of glucose and fat metabolism being higher caused by glucose absorption from dialysate fluid [40]. On the other hand, hemodialysis patients had higher oxygen consumption due to the intradialytic process of catabolic metabolism [24, 41]. Both the product of RQ and oxygen consumption contribute to the basal metabolic rate of the body, which may explain why there was no difference in REE between hemodialysis and PD patients. The difference in RQ and oxygen consumption between hemodialysis and PD patients may be offset, which can explain why there was no difference in REE between hemodialysis and PD patients.

The association between inflammation, parathyroid hormone (PTH) level, and REE has been investigated in several studies [23, 42–44]. Our data did not find these associations, which is supported by previous findings that the difference in REE was not apparent among patients in a mild inflammatory state or low PTH levels [13, 24, 44, 45]. Of note, previous studies reported that the LBM, which had the closest relationship with REE in healthy people, measured using gold-standard dual-energy X-ray absorptiometry and anthropometry method, contributed to only 35% and 43% of the variance, respectively, in REE among patients on hemodialysis [24, 46]. In this study, body weight and LBM obtained from bioimpedance contributed 64% and 46%

Table 4: Performance of eREE-PD and equations obtained in CKD and hemodialysis patients based on the difference between eREE and aREE.

	Validation dataset (n = 100)		P	Hs-CRP ≥ 3 mg/l (n = 32)	Hs-CRP < 3 mg/l (n = 68)	p
Bias-median difference						
eREE-PD	11.1 (−106.5, 78.2)	Ref.	Ref.	7.1 (−186.5, 83.0)	11.1 (−89.4, 78.2)	.790
eREE-CKD	−22.8 (−120, 85.9)	−12.4 (−44.8, 19.9)	.451	−28.9 (−204.7, 87.0)	−9.7 (−104.3, 85.9)	.308
eREE-V	−212.2 (−314.8, −113.7)	−208.2 (−272.9, −143.5)	<.001	−240.8 (−398.4, −120.7)	−201.9 (−310.5, −106.1)	.354
eREE-B$_{scr}$	11.2 (−89.7, 128.1)	20.9 (−43.8, 85.7)	.259	43.4 (−134.5, 132.9)	0.5 (−79.7, 128.1)	.909
eREE-B$_{crp}$	15.2 (−79.4, 109.1)	15.6 (−49.1, 80.3)	.421	26.1 (−164.7, 90.2)	7.8 (−71.2, 111.5)	.358
eREE-C$_{weight}$	−14.0 (−126.3, 78.1)	−9.87 (−74.6, 54.8)	.622	13.3 (−142.6, 94.2)	−15.6 (−123.5, 68.4)	.496
eREE-C$_{FFM}$	169.2 (58.2, 307.4)	184.1 (118.8, 249.3)	<.001	265.7 (71.5, 377.2)	147.1 (53.2, 227.3)	.011
Precision SD of the difference						
eREE-PD	96.5 (80.3, 113.6)	Ref.	Ref.	107.9 (47.1, 221.2)	80.6 (43.4, 162.1)	.117
eREE-CKD	98.1 (82.6, 114.2)	6.6 (−26.8, 39.9)	.699	113.3 (46.9, 256.7)	87.3 (51.0, 148.0)	.067
eREE-V	144.6 (126.9, 165.4)	115.4 (67.6 163.2)	<.001	241.2 (152.7, 398.4)	201.9 (106.1, 310.5)	.045
eREE-B$_{scr}$	98.7 (80.5, 117.2)	8.4 (−39.4,56.2)	.631	130.6 (65.8, 237.6)	95.5 (45.5, 167.5)	.058
eREE-B$_{crp}$	101.4 (81.8, 123.2)	5.6 (-42.2, 52.9)	.751	127.4 (44.0, 216.2)	86.9 (50.0, 165.6)	.382
eREE-C$_{weight}$	102.4 (85.4, 119.7)	5.1 (−42.7, 52.9)	.770	96.0 (45.5, 220.5)	102.5 (34.5, 160.0)	.103
eREE-C$_{FFM}$	168.2 (129.0, 209.6)	105.2 (57.0, 153.4)	<.001	265.7 (102.9, 377.2)	170.6 (98.0, 239.1)	.042
Accuracy, within ±10% of aREE, n (%)						
eREE-PD	65 (65.0)		Ref.	18 (56.3)	47 (69.1)	.208
eREE-CKD	66 (66.0)		.882	19 (59.4)	47 (69.9)	.117
eREE-V	30 (30.0)		<.001	7 (21.9)	23 (33.8)	.224
eREE-B$_{scr}$	59 (59.0)		.238	15 (46.9)	44 (64.7)	.091
eREE-B$_{crp}$	60 (60.0)		.332	15 (46.9)	45 (66.2)	.066
eREE-C$_{weight}$	64 (64.0)		.999	19 (59.4)	45 (66.2)	.509
eREE-C$_{FFM}$	30 (30.0)		<.001	7 (21.9)	23 (33.8)	.224

Statistical test: total validation dataset (P): block analysis of variance (Dunnett *t*-test) for bias and precision with the data present as the difference between the value of existing equations and eREE-CKD; McNemar Test for accuracy; subgroup analysis (*p*): independent *t*-test with the data present as quartiles.

of the variance respectively in REE. Similarly, in our previous research on CKD patients, body weight and LBM obtained from bioimpedance contributed 67% and 52% of the variance in REE, respectively. Therefore, it is still necessary to explore whether other factors related to the progression of kidney failure influence REE to further improve the performance of REE equations.

This study had several strengths. To our knowledge, our study is the first to develop an REE equation only for PD patients using IC as the reference method. This new equation only requires the collection of readily available clinical data, suggesting its feasibility in clinical practice. Patients were evenly distributed in the development and validation datasets, which provided a unique opportunity to validate the eREE-PD equation across varied degrees of inflammation. Several equations broadly applied in the general population and dialysis patients were compared with our new equation to validate its good performances in terms of bias, precision, and accuracy. Our equation provides a reliable equation for the goal of specific nutritional counseling for PD patients.

Our study had some limitations. First, we included only clinically stable patients, as acute comorbidities can rapidly affect metabolic status and body composition. Our new equation cannot be applied to patients who did not meet our inclusion criteria. Second, we cannot exclude the possibility that other potential factors that were not measured may be associated with REE. Further research should consider more factors involved in the progress of kidney failure to improve the precision and accuracy of REE equations. Third, we only used the Carefusion equipment for IC measurements, potentially necessitating the inclusion of additional equipment for IC measurements to validate the performance of our equations. Finally, to confirm its generalizability that extends beyond the studied cohort, external validation in alternative populations is demanded.

In conclusion, this study performed in clinically stable patients undergoing PD constructed a newly derived REE equation only consisting of age, gender, and weight, which showed good performance in predicting the REE with small bias, good precision, and accuracy. Therefore, it should be considered as a practical tool to evaluate energy expenditure prior to nutritional counseling in clinical practice. Further studies are needed to validate this equation in larger, more diverse patient population.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

ACKNOWLEDGEMENTS

FUNDING

DATA AVAILABILITY STATEMENT

Data described in the paper, code book, and analytic code will not be made available because the Management of China's Human Genetic Resources does not allow sharing of information.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

This trial was registered at clinicaltrials.gov as NCT04947839. URL: https://clinicaltrials.gov/ct2/show/NCT04947839?term=NCT04947839&draw=2&rank=1

REFERENCES

1. Koppe L, Fouque D, Kalantar-Zadeh K. Kidney cachexia or protein-energy wasting in chronic kidney disease: facts and numbers. *J Cachexia Sarcopenia Muscle* 2019;**10**:479–84. https://doi.org/10.1002/jcsm.12421

2. Kovesdy CP, Kopple JD, Kalantar-Zadeh K. Management of protein-energy wasting in non-dialysis-dependent chronic kidney disease: reconciling low protein intake with nutritional therapy. *Am J Clin Nutr* 2013;**97**:1163–77. https://doi.org/10.3945/ajcn.112.036418

3. Carrero JJ, Thomas F, Nagy K *et al*. Global prevalence of protein-energy wasting in kidney disease: a meta-analysis of contemporary observational studies from the International Society of Renal Nutrition and Metabolism. *J Ren Nutr* 2018;**28**:380–92. https://doi.org/10.1053/j.jrn.2018.08.006

4. Kittiskulnam P, Chuengsaman P, Kanjanabuch T *et al*. Protein-energy wasting and mortality risk prediction among peritoneal dialysis patients. *J Ren Nutr* 2021;**31**:679–86. https://doi.org/10.1053/j.jrn.2020.11.007

5. Lodebo BT, Shah A, Kopple JD. Is it important to prevent and treat protein-energy wasting in chronic kidney disease and chronic dialysis patients? *J Ren Nutr* 2018;**28**:369–79. https://doi.org/10.1053/j.jrn.2018.04.002

6. Gregg LP, Bossola M, Ostrosky-Frid M *et al*. Fatigue in CKD: epidemiology, pathophysiology, and treatment. *CJASN* 2021;**16**:1445–55. https://doi.org/10.2215/CJN.19891220

7. von Haehling S, Anker MS, Anker SD. Prevalence and clinical impact of cachexia in chronic illness in Europe, USA, and Japan: facts and numbers update 2016. *J Cachexia Sarcopenia Muscle* 2016;**7**:507–9. https://doi.org/10.1002/jcsm.12167

8. Hernández Morante JJ, Sánchez-Villazala A, Cutillas RC *et al*. Effectiveness of a nutrition education program for the prevention and treatment of malnutrition in end-stage renal disease. *J Ren Nutr* 2014;**24**:42–49. https://doi.org/10.1053/j.jrn.2013.07.004

9. Karavetian M, Ghaddar S. Nutritional education for the management of osteodystrophy (nemo) in patients on haemodialysis: a randomised controlled trial. *J Renal Care* 2013;**39**:19–30. https://doi.org/10.1111/j.1755-6686.2012.00327.x

10. Martin-Alemañy G, Valdez-Ortiz R, Olvera-Soto G *et al*. The effects of resistance exercise and oral nutritional supplementation during hemodialysis on indicators of nutritional status and quality of life. *Nephrol Dial Transplant* 2016;**31**:1712–20. https://doi.org/10.1093/ndt/gfw297

11. Rhee CM, You AS, Koontz Parsons T *et al*. Effect of high-protein meals during hemodialysis combined with lanthanum carbonate in hypoalbuminemic dialysis patients: findings from the FrEDI randomized controlled trial. *Nephrol Dial Transplant* 2017;**32**:1233–43.

12. Ikizler TA, Burrowes JD, Byham-Gray LD *et al*. KDOQI Clinical Practice Guideline for nutrition in CKD: 2020 update. *Am J Kidney Dis* 2020;**76**:S1–S107. https://doi.org/10.1053/j.ajkd.2020.05.006

13. Kamimura MA, Draibe SA, Avesani CM *et al*. Resting energy expenditure and its determinants in hemodialysis patients. *Eur J Clin Nutr* 2007;**61**:362–7. https://doi.org/10.1038/sj.ejcn.1602516

14. Avesani CM, Kamimura MA, Cuppari L. Energy expenditure in chronic kidney disease patients. *J Ren Nutr* 2011;**21**:27–30. https://doi.org/10.1053/j.jrn.2010.10.013

15. Ramos-Acevedo S, Rodríguez-Gómez L, López-Cisneros S *et al*. Nutritional status and other clinical variables are associated to the resting energy expenditure in patients with chronic kidney disease: a validity study. *Front Nutr* 2022;**9**:881719. https://doi.org/10.3389/fnut.2022.881719

16. Trumbo P, Schlicker S, Yates AA *et al*. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein and amino acids. *J Am Diet Assoc* 2002;**102**:1621–30. https://doi.org/10.1016/S0002-8223(02)90346-9

17. Harris JA, Benedict FG. A biometric study of basal metabolism in man. Washington, DC, USA: Carnegie Institution of Washington, 1919, Publication No. 279.

18. Mifflin MD, St Jeor ST, Hill LA *et al*. A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990;**51**:241–7. https://doi.org/10.1093/ajcn/51.2.241

19. Energy and protein requirements. Report of a joint FAO/WHO/UNU expert consultation. *World Health Organ Tech Rep Ser* 1985;**724**:1–206.

20. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985;**39**:5–41.

21. de Oliveira Fernandes T, Avesani CM, Aoike DT *et al*. New predictive equations to estimate resting energy expenditure of non-dialysis dependent chronic kidney disease patients. *J Nephrol* 2021;**34**:1235–42. https://doi.org/10.1007/s40620-020-00899-7

22. Xu X, Yang Z, Ma T *et al*. Novel equation for estimating resting energy expenditure in patients with chronic kidney disease. *Am J Clin Nutr* 2021;**113**:1647–56. https://doi.org/10.1093/ajcn/nqaa431

23. Byham-Gray LD, Parrott JS, Peters EN *et al*. Modeling a predictive energy equation specific for maintenance hemodialysis. *J Parenter Enteral Nutr* 2018;**42**:587–96. https://doi.org/10.1177/0148607117696942

24. Fernandes TO, Avesani CM, Kamimura MA *et al*. Estimating resting energy expenditure of patients on dialysis: de-

velopment and validation of a predictive equation. *Nutrition* 2019;**67-68**:110527. https://doi.org/10.1016/j.nut.2019.06.008

25. Vilar E, Machado A, Garrett A *et al*. Disease-specific predictive formulas for energy expenditure in the dialysis population. *J Ren Nutr* 2014;**24**:243–51. https://doi.org/10.1053/j.jrn.2014.03.001

26. Góes CR, Vogt BP, Sanches ACS *et al*. Influence of different dialysis modalities in the measurement of resting energy expenditure in patients with acute kidney injury in ICU. *Clin Nutr* 2017;**36**:1170–4. https://doi.org/10.1016/j.clnu.2016.08.008

27. Oliveira MC, Bufarah MNB, Ponce D *et al*. Longitudinal changes in nutritional parameters and resting energy expenditure in end-stage renal disease. *Braz J Nephrol* 2020;**42**:24–30. https://doi.org/10.1590/2175-8239-jbn-2018-0169

28. Smith SC, Jr., Jackson R, Pearson TA *et al*. Principles for national and regional guidelines on cardiovascular disease prevention: a scientific statement from the World Heart and Stroke Forum. *Circulation* 2004;**109**:3112–21. https://doi.org/10.1161/01.CIR.0000133427.35111.67

29. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. *J Physiol* 1949;**109**:1–9. https://doi.org/10.1113/jphysiol.1949.sp004363

30. Dong J, Li YJ, Xu R *et al*. Novel equations for estimating lean body mass in peritoneal dialysis patients. *Perit Dial Int* 2015;**35**:743–52. https://doi.org/10.3747/pdi.2013.00246

31. Cheng LT, Tang W, Wang T. Strong association between volume status and nutritional status in peritoneal dialysis patients. *Am J Kidney Dis* 2005;**45**:891–902. https://doi.org/10.1053/j.ajkd.2005.01.037

32. Inker LA, Schmid CH, Tighiouart H *et al*. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012;**367**:20–29. https://doi.org/10.1056/NEJMoa1114248

33. El-Kateb S, Sridharan S, Farrington K *et al*. Comparison of resting and total energy expenditure in peritoneal dialysis patients and body composition measured by dual-energy X-ray absorptiometry. *Eur J Clin Nutr* 2016;**70**:1337–9. https://doi.org/10.1038/ejcn.2016.120

34. Kamimura MA, Avesani CM, Bazanelli AP *et al*. Are prediction equations reliable for estimating resting energy expenditure in chronic kidney disease patients? *Nephrol Dial Transplant* 2011;**26**:544–50. https://doi.org/10.1093/ndt/gfq452

35. Oliveira B, Sridharan S, Farrington K *et al*. Comparison of resting energy equations and total energy expenditure in haemodialysis patients and body composition measured by multi-frequency bioimpedance. *Nephrology* 2018;**23**:748–54. https://doi.org/10.1111/nep.13112

36. Hung R, Sridharan S, Farrington K *et al*. Comparison of estimates of resting energy expenditure equations in haemodialysis patients. *Int J Artif Organs* 2017;**40**:96–101. https://doi.org/10.5301/ijao.5000575

37. El-Kateb S, Sridharan S, Farrington K *et al*. Comparison of equations of resting and total energy expenditure in peritoneal dialysis patients using body composition measurements determined by multi-frequency bioimpedance. *Clin Nutr* 2018;**37**:646–50. https://doi.org/10.1016/j.clnu.2017.02.007

38. Bailey A, Brody R, Sackey J *et al*. Current methods for developing predictive energy equations in maintenance dialysis are imprecise. *Ann Med* 2022;**54**:909–20. https://doi.org/10.1080/07853890.2022.2057581

39. Fu G, Xu X, Guo SS *et al*. Comparison of the resting energy expenditure in peritoneal dialysis and hemodialysis patients. *Chin Blood Purif* 2022;**21**:749–53. https://doi.org/10.3969/j.issn.1671-4091.2022.10.010

40. Khan SF, Ronco C, Rosner MH. Counteracting the metabolic effects of glucose load in peritoneal dialysis patients; an exercise-based approach. *Blood Purif* 2019;**48**:25–31. https://doi.org/10.1159/000499406

41. Ikizler TA, Wingard RL, Sun M *et al*. Increased energy expenditure in hemodialysis patients. *J Am Soc Nephrol* 1996;**7**:2646–53. https://doi.org/10.1681/ASN.V7122646

42. Avesani CM, Draibe SA, Kamimura MA *et al*. Resting energy expenditure of chronic kidney disease patients: influence of renal function and subclinical inflammation. *Am J Kidney Dis* 2004;**44**:1008–16. https://doi.org/10.1053/j.ajkd.2004.08.023

43. Utaka S, Avesani CM, Draibe SA *et al*. Inflammation is associated with increased energy expenditure in patients with chronic kidney disease. *Am J Clin Nutr* 2005;**82**:801–5. https://doi.org/10.1093/ajcn/82.4.801

44. Cuppari L, de Carvalho AB, Avesani CM *et al*. Increased resting energy expenditure in hemodialysis patients with severe hyperparathyroidism. *J Am Soc Nephrol* 2004;**15**:2933–9. https://doi.org/10.1097/01.ASN.0000141961.49723.BC

45. Bazanelli AP, Kamimura MA, da Silva CB *et al*. Resting energy expenditure in peritoneal dialysis patients. *Perit Dial Int* 2006;**26**:697–704. https://doi.org/10.1177/089686080602600615

46. Byham-Gray L, Parrott JS, Ho WY *et al*. Development of a predictive energy equation for maintenance hemodialysis patients: a pilot study. *J Ren Nutr* 2014;**24**:32–41. https://doi.org/10.1053/j.jrn.2013.10.005