

Comparison of resting energy equations and total energy expenditure in  
haemodialysis patients and body composition measured by multi-frequency  
bioimpedance

Ben Oliveira MRCP<sup>1</sup>, Sivakumar Sridharan PhD<sup>2</sup>, Ken Farrington FRCP<sup>2,3</sup>, Andrew  
Davenport FRCP<sup>1</sup>

<sup>1</sup> UCL Centre for Nephrology, Royal Free Hospital, University College London  
Medical School, London, UK

<sup>2</sup> Renal Unit, Lister Hospital, Stevenage, UK

<sup>3</sup> University of Hertfordshire, Hatfield, UK

Ben Oliveira	benoliveira@nhs.net
Sivakumar Sridharan	sivakumar.sridharan@nhs.net
Ken Farrington	ken.farrington@nhs.net
Andrew Davenport	andrewdavenport@nhs.uk

Address for correspondence

Andrew Davenport                      andrewdavenport@nhs.net

contact              andrewdavenport@nhs.net

UCL Centre for Nephrology, Royal Free Hospital, University College London,  
Rowland Hill Street, London NW3 2PF

tel    44-2074726457    fax    44-2073178591

short title    resting and total energy expenditure in haemodialysis patients

key words    haemodialysis    resting energy expenditure              total energy  
expenditure              total body water              body surface area              Kt/Vurea

word count	abstract	250
	body	2557
	figures	2
	tables	3
	references	40

Funding              grant -British Renal Society,  
No author has any conflict of interest

## Abstract

### Background

Waste products of metabolism are retained in haemodialysis (HD) patients. Patients with greater energy expenditure generate more waste products and may require more dialysis. To determine the amount of dialysis required, equations estimating resting (REE) and total energy expenditure (TEE) are required.

### Methods

We compared estimates of REE in HD patients using established equations with a novel equation recently validated in HD patients (HD equation). TEE was derived from REE (HD equation) and estimates of physical activity obtained by questionnaire. REE and TEE relationships with bioimpedance measured body composition were then determined.

### Results

We studied 317 HD patients; 195 males (61.5%), 123 diabetic (38.9%), mean age  $65.0 \pm 15.3$  and weight  $73.1 \pm 16.8$  kg. REE from HD Equation was  $1509 \pm 241$  kcal/day, which was greater than for Mifflin St Joer  $1384 \pm 259$ , Harris-Benedict  $1437 \pm 244$ , Katch-McArdle  $1345 \pm 232$  (all  $p < 0.05$  vs HD Equation), but less than Cunningham  $1557 \pm 236$  kcal/day. Bland Altman mean bias ranged from -263 to 55 kcal/day. TEE was 1727 (1558-1976) kcal/day, and on multi-variate analysis was positively associated with skeletal muscle mass ( $\beta$  23.3,  $p < 0.001$ ), employment ( $\beta$  406,  $p < 0.001$ ), low co-morbidity ( $\beta$  105,  $p = 0.006$ ),

and protein nitrogen appearance ( $\beta$  2.7,  $p=0.015$ ), and negatively with age ( $\beta$  -7.9,  $p<0.001$ ), and dialysis vintage ( $\beta$  -121,  $p=0.002$ ).

### Conclusions

Most standard equations underestimate REE in HD patients compared to the HD Equation. TEE was greater in those with higher skeletal muscle mass and protein nitrogen appearance, lower co-morbidity, age, and dialysis vintage, and the employed. Such Patients are more metabolically active and may require greater dialytic clearances.

## Introduction

Although haemodialysis is an established treatment for patients with chronic kidney disease (CKD), with around 3 million patients currently treated worldwide, 5-year mortality remains higher than that for some of the more common solid organ malignancies [1]. Dialysis treatments are currently designed to achieve an adequacy target in terms of solute clearance, using the dimensionless parameter  $Kt/V_{urea}$ , where  $K$  is dialyser urea clearance,  $t$  the dialysis session time and  $V$  the urea distribution volume (or Watson Volume [2]) equating to total body water. Yet, when tested by a randomised prospective multicentre trial increasing dialyzer  $Kt/V_{urea}$  clearance failed to demonstrate greater patient survival [3], although, post-hoc analysis suggested that higher haemodialysis doses were associated with a survival advantage for women [4]. There are a number of possible explanations for this association, one of which may be the scaling of haemodialysis dose based on total body water [5].

In CKD, the products of cellular metabolism accumulate and as such an alternative suggestion has been that the amount of dialysis a patient requires would depend upon their metabolic activity [6]. Metabolic activity comprises both resting metabolic rate and that secondary to physical activity. Resting energy expenditure (REE) is relatively greater in smaller animals compared to larger animals, and rescaling the dialysis dose by body surface area (BSA) has been reported to demonstrate an association between increasing  $Kt_{urea}/BSA$  and patient survival [7]. However, this approach fails to take in to account active energy expenditure. To be able to adjust the amount haemodialysis for an

individual patient then we need to develop simple methods of estimating total energy expenditure which are valid in patients with advanced CKD.

Several equations have been developed for estimating REE [8-12], but these did not include patients with CKD. As such we have recently developed an equation to estimate REE in dialysis patients and, based on this, a method to estimate total energy expenditure (TEE), which has been validated in doubly labelled water studies [13,14].

We wished to compare the HD Equation in haemodialysis patients with other equations commonly used to estimate REE, which were developed from other patient populations. In addition, we wished to determine whether there was an association between REE and TEE and body composition as measured by bioelectrical impedance.

### Patients and methods

We recruited a total of 317 adult patients under the care of a university hospital attending for outpatient thrice weekly haemodialysis. Patient demographics were obtained from computerised hospital records and comorbidity determined using a self-administered co-morbidity grading, based on medical conditions and complications, including diabetes mellitus (as defined by WHO criteria), cardiac disease, respiratory disease, liver disease, arthritis, depression and malignancy [15].

We compared estimates of REE using the HD Equation [13,14], with those calculated using the modified Harris-Benedict equation [8,9], the Mifflin St.

Joer [10], Katch McArdle [11] and Cunningham equations [12]. Physical activity data was obtained through the validated Recent Physical Activity Questionnaire (RPAQ) [16]. The RPAQ collects information about activities performed at home, work and leisure time and also the time spent on each activity in the preceding 4 weeks [13]. Physical activity data was determined by each reported activity being assigned a Metabolic Equivalent of Task (MET) value according to the Compendium of Physical Activities [16]. This was then combined with REE estimated using the HD equation to provide an estimate of TEE (see appendix)

Measurements of body composition were made using multi-frequency bioelectrical impedance assessments (MFBIA) (InBody 720, InBody, Seoul, South Korea). Bioimpedance measurements are routinely collected as part of determining HD patient target weight. Patients with pacemakers, and other implantable cardiac devices, and those unable to stand to measure bioimpedance were excluded from study. Measurements were performed in a standardised manner, post the mid-week haemodialysis session, after allowing for post-dialysis recovery [17,18]. Previous studies have validated this device against dual electron X ray absorptiometry [19]. Lean body mass index (LBMI) and fat mass index (FMI) were calculated by lean body mass (LBM) and fat mass (FM) divided by height squared, respectively. Skeletal muscle mass (SMM) was derived from measurement of limb muscle mass (appendicular muscle mass). Body surface area was calculated using the Gehan and George equation as recommended by the European Best Clinical Practice guidelines [20].

The Cunningham and Katch McArdle equations use an estimate of lean body mass [11,12], with lean body mass estimated by subtracting percentage body fat from patient weight. We calculated REE using both percentage body fat and also lean body mass measured by MFBI.

Patients dialysed using Fresenius 4008H (Fresenius Bad Homburg, Germany) or Dialogue R+ (BBraun, Melsungen, Germany) with high flux polysulfone dialyzers (Elisio, Nipro Corporation, Osaka, Japan) [21] and anticoagulated with single bolus low molecular weight heparin (Tinzaparin, Leo Laboratories, Hurley, Berkshire, UK) [22]. Haemoglobin and serum urea, creatinine and electrolytes were measured by standard laboratory analyzers (Sysmex XE5000, Sysmex Corporation, Kobe, Japan and Roche Cobra, Roche Instruments Ltd, Basingstoke, UK), and serum  $\beta$ 2 microglobulin was measured by rate nephelometry (www.Dako.com, Image 800 analyser, Beckman Coulter, High Wycombe, UK) [23].

Dialysis machines were regularly serviced and dialysate conductivity checked [24,25]. Haemodialysis adequacy was calculated as an equilibrated  $Kt/V_{urea}$ , and protein nitrogen appearance from pre- and post-dialysis measurements [26] and the inter-dialytic interval and bioimpedance total body water. Interdialytic urine collections were not available.

Ethical approval for determining energy expenditure was granted by the UK National Research Ethics Committee - North Wales and the study was registered in UK Clinical Research Network (CRN) Portfolio number 12023. All

patients provided written informed consent in keeping with the declaration of Helsinki.

### Statistical analysis

Statistical analysis was by t test, Man Whitney U test, paired t test and Wilcoxon rank sum pair test, ANOVA or Kruskal-Wallis analysis, with appropriate post hoc correction for multiple testing, Pearson or Spearman's correlation (GraphPad Prism version 6.0, San Diego, USA), and Bland Altman comparison (Analyse-It version 3.0, Leeds, UK). Variables associated with REE and TEE,  $p < 0.1$  and those thought to be clinically relevant were entered into a multivariable analysis and then eliminated in a step back manner if variables were not significant, unless they improved model fit (SPSS 22.0, SPSS University Chicago, USA). Multivariable models were checked for collinearity. Data are presented as mean  $\pm$  standard deviation, median (inter quartile range), or mean and 95% limits of agreement (CI), or as a percentage.

### Results

We studied 317 adult haemodialysis patients; 195 males (61.5%), 123 diabetic (38.9%), mean age  $65.0 \pm 15.3$  years, with a median dialysis vintage 3.3 (1.4-6.2) years. 138 (43.5%) were Caucasoid, 101 (31.9%) African/Afro-Caribbean, 65 (20.5%), South Asian, 9 (2.8%) East Asian, and the remainder of indeterminate ethnicity. The mean weight was  $73.1 \pm 16.8$  kg with a body mass index of  $26.2 \pm 5.8$  kg/m<sup>2</sup>, with a median co-morbidity grade of 2 (0-4). 41



patients (13%) were in employment. The mean equilibrated dialysis sessional  $Kt/V_{urea}$  was  $1.40 \pm 0.27$ , with a mean dialysis session time of  $236 \pm 26$  minutes, median ultrafiltration volume 1.8 (1.0-2.2) L, and daily protein nitrogen appearance rate based solely on change in serum urea during the inter-dialytic interval, 42.1 (30.8-53.5) g/day. Pre-dialysis haemoglobin was  $110.5 \pm 11.9$  g/L, serum albumin  $40.3 \pm 4.2$  g/L, cholesterol  $3.9 \pm 1.1$  mmol/L, C reactive protein (CRP) 4.0 (2-9) mg/L, urea  $18.0 \pm 5.2$  mmol/L, serum creatinine 710 (572-863)  $\mu$ mol/L, cholesterol  $4.0 \pm 1.0$  and glucose  $7.1 \pm 2.6$  mmol/L, serum  $\beta 2$  microglobulin  $28.6 \pm 9.4$  mg/L and post-dialysis serum urea  $4.6 \pm 1.8$  mmol/L. The median weekly erythropoietin dosage was 5000 (2000-8000) Iu/week.

The mean REE using the HD Equation was  $1532 \pm 237$  kcal/day, with a TEE of 1727 (1558 - 1976) kcal/day. The REE determined by the HD Equation was significantly greater than that for the modified Harris-Benedict, Mifflin St. Joer equations, and the Katch McArdle equation using lean body mass (Figure 1). REE was also calculated by estimating lean body mass from percentage body fat using the Katch McArdle and Cunningham equations, which over estimated REE compared to other equations (table 1).

Resting and total energy expenditure was less for female patients, who had less muscle mass, but greater body fat (table 1). Bland Altman plots showed that the majority of REE equations under estimated REE compared to the HD Equation, however using percentage body fat to estimate lean body mass, led to an over estimation of REE (Figure 2).

A number of demographic and dialysis associated variables and body composition measurements were associated with both REE and TEE (table 2). REE was greater in African-Afro-Caribbean patients compared to white or south Asians ( $1563\pm 245$  vs  $1492\pm 246$  and  $1434\pm 210$  kcal/day respectively),  $p<0.05$ , but TEE did not differ between ethnic groups. Patients in employment had greater REE ( $1613\pm 247$  vs  $1493\pm 237$  kcal/day,  $p<0.01$ ) and TEE ( $2268\pm 453$  vs  $1731\pm 307$  kcal/day,  $p<0.001$ ). There was no difference in REE or TEE between those with low and high co-morbidity (REE  $1507\pm 233$  vs  $1515\pm 262$  and TEE  $1813\pm 383$  vs  $1769\pm 352$  kcal/day).

Multivariable models showed that REE was independently associated with skeletal muscle mass, and negatively with age and duration of treatment with haemodialysis. TEE was also associated with skeletal muscle mass, and negatively with age and duration of treatment with haemodialysis, but was also associated with employment status, low co-morbidity and inter-dialytic protein nitrogen appearance rate determined by the increase in serum urea (table 3).

## Discussion

The kidney plays a key role in the excretion of the waste products of cellular metabolism. As serum urea has the highest serum concentration of any of these retention products of cell metabolism, then dialyzer urea clearance has been used to assess dialysis adequacy. However prospective clinical studies designed to investigate the effects of increasing dialyzer urea clearance targets failed to demonstrate any survival advantage [3]. Re-analysis of this

data, and other reports have suggested that the delivered amount of dialysis was affected by body size and gender [4,5,27]. Body size and gender are key determinants of energy expenditure [8], and it has been suggested that the amount of dialysis clearance required by patients should be adjusted for metabolic rate [6].

A number of equations estimating REE have been proposed over the last hundred years or so, which have been based on studies from various populations, generally including healthy subjects of varying body mass index and ages [8-12]. However body composition can be affected by CKD, particularly in terms of muscle wasting [28,29], as well as the potential effects of co-morbidities such as diabetes [30]. More recently an REE equation based on studies of UK patients on haemodialysis has been developed [13,14,31]. To determine how this CKD REE equation compared with standard equations estimating REE we studied a cohort of HD outpatients. We used multi-frequency bioelectrical impedance to measure body composition [32]. Although this is an accepted technique, bioimpedance measurements are affected by volume status, so we used bioimpedance measurements taken post-dialysis when patients were closest to their target weight, to minimise the effect of over hydration [33].

We found that the mean bias for both the modified Harris-Benedict  $\text{kg}^2/\text{m}^2$  [8,9] and Mifflin St. Joer [10] equations under estimated REE compared to the HD Equation, for both male and female HD patients. Both the Katch McArdle [11] and Cunningham [12] equations can be calculated either by using directly estimated lean body mass or lean body mass obtained by

subtracting percentage body fat from body weight. We used both methods entering lean body mass and percentage body fat measured by bioimpedance. Using lean body mass, mean bias for the Katch-McArdle equation under estimated REE, whilst the Cunningham equation over estimated REE. In contrast using percentage body fat both over estimated REE compared to the HD Equation.

Although the mean bias between the HD and the Harris-Benedict equation was modest at 73 kcal/day, the 95% limits of agreement of this and the other equations were very large for both genders. REE depends upon the metabolic activity of high energy internal organs; including the brain, liver, kidneys, and heart [34]. Increased REE in HD patients compared to healthy subjects would be supported by previous reports of impaired mitochondrial energy transfer and increased muscle breakdown in patients with kidney failure [28,29], and the effect of the dialysis treatment itself.

Using percentage body fat, REE calculated from the Katch-McArdle and Cunningham equations was significantly greater compared to that using lean body mass. Changes in body composition, in particular changes in muscle mass [27,28], alter the relationship between percentage body fat and muscle mass in CKD. Hence assumptions made based on body composition in healthy subjects may not hold for CKD patients.

All REE equations use anthropomorphic measurements. We noted that in addition to patient age and gender, REE was associated with anthropomorphic measurements, but also with ethnicity which has been reported to alter body

composition [35], dialysis session time, dialyzer surface area, pre-dialysis serum urea, creatinine, albumin and haemoglobin, and the inter-dialytic interval protein generation based on the increase in serum urea, along with body composition, and employment status. REE was inversely associated with haemodialysis vintage and dialysis dose (equilibrated Kt/V) on univariate analysis. Longer dialysis vintage could be associated with loss of residual renal function, although there was no association with  $\beta 2$  microglobulin concentrations. Previous studies have reported that the determination of dialysis dosing using Kt/V overestimates delivered dose in small patients and those with a lower pre-dialysis serum urea [4,5].

A multivariable model noted that REE derived by the HD Equation was independently associated with skeletal muscle mass, and negatively with both age and years of haemodialysis treatment. Both the Katch McArdle and Cunningham equations estimate REE based on lean body mass [11,12]. Muscle mass can influence energy and protein metabolism throughout the body, as muscle plays a key role in glucose uptake and storage, and is also a large potential reservoir of amino acids stored as protein, which can be released when supplies are needed elsewhere in the body [36]. Muscle mass declines with age [37], and previous reports have commented on reduced muscle glycogen stores in muscle biopsies from haemodialysis patients [38].

We also calculated TEE, by including energy expenditure due to physical activity [16]. Compared to REE, on univariate analysis TEE was positively associated with haemoglobin, and negatively with erythropoietin dose, and erythropoietin resistance. Higher haemoglobins may improve performance in

endurance athletes, such as cyclists, whereas the negative association with erythropoietin dose could be due to a number of confounders including erythropoietin resistance associated with inflammation and muscle wasting [39]. On multivariable analysis, we found that TEE was also associated with protein nitrogen appearance assessed by the inter-dialysis increase in serum urea. This is in keeping with reports of energy intake being associated with skeletal muscle mass [40], and also with the relationship of TEE and urea generation rate [31]. In addition, TEE was associated with employment status and low co-morbidity. It would be expected that patients with greater co-morbidity would be less physically active as would those who were not in employment.

If the amount of dialysis a patient requires is related to energy expenditure, then equations which are relatively simple to apply in routine clinical practice are required. Our study demonstrates that in this setting, estimates of REE obtained using an equation derived in HD patients are higher than those obtained using standard equations. Both REE and TEE were independently associated with skeletal muscle mass, and negatively with age and duration of treatment with haemodialysis. Understanding the relationship between body composition and energy expenditure is important for patients with kidney failure treated by dialysis, as patients with greater TEE generate more waste products of cellular metabolism, and may potentially require greater dialytic clearance.

The authors have no conflict of interest

None of the data contained in this report has been previously published in whole or part form

Funding grant British Renal Society and British Kidney Patient Association

## References

1. Steenkamp R, Rao A, Roderick P. UK Renal Registry 17th Annual Report: Chapter 5. Survival and Cause of Death in UK Adult Patients on Renal Replacement Therapy in 2013: National and Centre-specific Analyses. *Nephron*. 2015;129 Suppl 1:99-129
2. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *Am J Clin Nutr*. 1980; 33: 27-39
3. Eknoyan G, Beck GJ, Cheung AK, Daugirdas JT, Greene T, Kusek JW, Allon M, Bailey J, Delmez JA, Depner TA, Dwyer JT, Levey AS, Levin NW, Milford E, Ornt DB, Rocco MV, Schulman G, Schwab SJ, Teehan BP, Toto R: Haemodialysis (HEMO) Study Group. Effect of dialysis dose and membrane flux in maintenance haemodialysis. *N Engl J Med*. 2002; 347(25):2010-9
4. Depner T, Daugirdas J, Greene T, Allon M, Beck G, Chumlea C, Delmez J, Gotch F, Kusek J, Levin N, Macon E, Milford E, Owen W, Star R, Toto R, Eknoyan G: Dialysis dose and the effect of gender and body size on outcome in the HEMO Study. *Kidney Int*. 2004; 65: 1386-1394
5. Spalding EM, Chandna SM, Davenport A, Farrington K: Kt/V underestimates the haemodialysis dose in women and small men. *Kidney Int*, 2008; 74: 348-355
6. Daugirdas JT, Levin NW, Kotanko P, Depner TA, Kuhlmann MK, Chertow GM, Rocco MV: Comparison of proposed alternative methods for rescaling dialysis dose: resting energy expenditure, high metabolic rate organ mass, liver size, and body surface area. *Semin Dial* 2008; 21: 377-384
7. Daugirdas JT, Greene T, Chertow GM, Depner TA: Can rescaling dose of dialysis to body surface area in the HEMO study explain the different responses to dose in women versus men? *Clin J Am Soc Nephrol*, 2010;5: 1628-1636
8. Harris JA, Benedict FG: A biometric study of human basal metabolism. *Proc Natl Acad Sci U S A* 1918; 4: 370-373.
9. Roza AM; Shizgal HM. The Harris Benedict equation re-evaluated: resting energy requirements and the body cell mass. *Am J Clin Nutr* 1984; 40: 168-182

10. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO: A new predictive equation for resting energy expenditure in healthy individuals. *Am J Clin Nutr* 1990; 51:241-247.
11. McArdle W (2006). *Essentials of Exercise Physiology*. Lippincott Williams & Wilkins. p. 266 ISBN 9780495014836.
12. Dunford M (2007). *Nutrition for Sport and Exercise*. Brooks/Cole. p. 57. ISBN 9780781749916
13. Sridharan S, Wong J, Vilar E, Farrington K. Comparison of energy estimates in chronic kidney disease using doubly-labelled water. *J Hum Nutr Diet*. 2016;29(1):59-66
14. Vilar E, Machado A, Garrett A, Kozarski R, Wellsted D, Farrington K: Disease-Specific Predictive Formulas for Energy Expenditure in the Dialysis Population. *J Ren Nutr*. 2014; 24: 243-251
15. Sridharan S, Berdeprado J, Vilar E, Roberts J, Farrington K: A self-report comorbidity questionnaire for haemodialysis patients. *BMC Nephrol*, 2014;15: 134
16. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett DR, Jr., Tudor-Locke C, Greer JL, Vezina J, Whitt-Glover MC, Leon AS: 2011 Compendium of Physical Activities: A Second Update of Codes and MET Values. *Med Sci Sports Exerc*. 2011; 43: 1575-1581
17. Booth J, Pinney J, Davenport A. N-terminal proBNP--marker of cardiac dysfunction, fluid overload, or malnutrition in haemodialysis patients? *Clin J Am Soc Nephrol*. 2010; 5(6):1036-40
18. Nongnuch A, Campbell N, Stern E, El-Kateb S, Fuentes L, Davenport A. Increased post-dialysis systolic blood pressure is associated with extracellular over-hydration in haemodialysis outpatients. *Kidney Int*. 2015;87(2):452-7
19. Fürstenberg A, Davenport A. Comparison of multi-frequency bioelectrical impedance analysis and dual-energy X-ray absorptiometry assessments in outpatient haemodialysis patients. *Am J Kidney Dis*. 2011;57(1):123-9
20. Gehan EA, George SL. Estimation of human body surface area from height and weight. *Cancer Chemother Rep*. 1970;54(4):225-35
21. Vernon K, Peasegood J, Riddell A, Davenport A. Dialyzers designed to increase internal filtration do not result in significantly increased platelet activation and thrombin generation. *Nephron Clin Pract*. 2011;117(4):c403-8
22. Davenport A. Low-molecular-weight heparin as an alternative anticoagulant to unfractionated heparin for routine outpatient haemodialysis treatments. *Nephrology (Carlton)*. 2009;14(5):455-61
23. Oates T, Pinney JH, Davenport A. Haemodiafiltration versus high-flux haemodialysis: Effects on phosphate control and erythropoietin response. *Am J Nephrol*. 2011;33(1):70-5
24. Booth J, Pinney J, Davenport A. Changes in red blood cell size and red cell fragmentation during haemodialysis. *Int J Artif Organs*. 2010;33(12):900-5



25. Sandhu E, Crawford C, Davenport A. Weight gains and increased blood pressure in outpatient haemodialysis patients due to change in acid dialysate concentrate supplier. *Int J Artif Organs*. 2012;35(9):642-7
26. Daugirdas JT. Scaling haemodialysis dose. Kt over what ? *Am J Kid Dis* 2017; 69 (3): 331-333
27. Davenport A. Differences in prescribed Kt/V and delivered haemodialysis dose--why obesity makes a difference to survival for haemodialysis patients when using a 'one size fits all' Kt/V target. *Nephrol Dial Transplant*. 2013;28 Suppl 4:iv219-23
28. Fahal IH. Uraemic sarcopenia: aetiology and implications. *Nephrol Dial Transplant*. 2014;29(9):1655-65
29. Wang XH, Mitch WE. Mechanisms of muscle wasting in chronic kidney disease. *Nat Rev Nephrol*. 2014;10(9):504-16
30. Davenport A, Willicombe MK. Does diabetes mellitus predispose to increased fluid overload in peritoneal dialysis patients? *Nephron Clin Pract*. 2010;114(1):c60-6
31. Sridharan S, Vilar E, Berdeprado J, Farrington K. Energy metabolism, body composition, and urea generation rate in haemodialysis patients. *Hemodial Int*. 2013;17(4):502-9
32. Davies SJ, Davenport A. The role of bioimpedance and biomarkers in helping to aid clinical decision-making of volume assessments in dialysis patients. *Kidney Int*. 2014;86(3):489-96
33. Panorchan K, Nongnuch A, El-Kateb S, Goodlad C, Davenport A. Changes in muscle and fat mass with haemodialysis detected by multi-frequency bioelectrical impedance analysis. *Eur J Clin Nutr*. 2015;69(10):1109-12
34. Javed F, He Q, Davidson LE, Thornton JC, Albu J, Boxt L, Krasnow N, Elia M, Kang P, Heshka S, Gallagher D. Brain and high metabolic rate organ mass: contributions to resting energy expenditure beyond fat-free mass. *Am J Clin Nutr*. 2010; 91(4): 907-912
35. Davenport A, Hussain Sayed R, Fan S. The effect of racial origin on total body water volume in peritoneal dialysis patients. *Clin J Am Soc Nephrol*. 2011;6(10):2492-8
36. Argilés JM, Campos N, Lopez-Pedrosa JM, Rueda R, Rodriguez-Mañas L. Skeletal Muscle Regulates Metabolism via Interorgan Crosstalk: Roles in Health and Disease. *J Am Med Dir Assoc*. 2016 pii: S1525-8610(16)30113-X. doi: 10.1016/j.jamda.2016.04.019
37. Delmonico MJ, Harris TB, Visser M, Park SW, Conroy MB, Velasquez-Mieyer P, Boudreau R, Manini TM, Nevitt M, Newman AB, Goodpaster BH; Health, Aging, and Body: Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr*. 2009; 90: 1579-1585
38. Davenport A, King RF, Ironside JW, Will EJ, Davison AM The effect of treatment with recombinant human erythropoietin on the histological appearance and glycogen content of skeletal muscle in patients with chronic renal failure treated by regular hospital haemodialysis. *Nephron*. 1993;64(1):89-94

39. Abe M, Okada K, Maruyama T, Maruyama N, Matsumoto K, Soma M. Relationship between erythropoietin responsiveness, insulin resistance, and malnutrition-inflammation-atherosclerosis (MIA) syndrome in haemodialysis patients with diabetes. *Int J Artif Organs*. 2011;34(1):16-25.
40. Cameron JD, Sigal RJ, Kenny GP, Alberga AS, Prud'homme D, Phillips P, Doucette S, Goldfield G. Body composition and energy intake - skeletal muscle mass is the strongest predictor of food intake in obese adolescents: The HEARTY trial. *Appl Physiol Nutr Metab*. 2016;41(6):611-7

Figure 1: Resting energy expenditure (REE) measured using the HD Equation [7,8], with the modified Harris-Benedict equation [11,12], the Mifflin St. Joer [13], Katch McArdle [14] and Cunningham equations [15].

Figure 2a: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with the modified Harris-Benedict equation (mean bias women -96 (95% limits of agreement -244 to 52), men -263 (-855 to -329)).

Figure 2b: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with the Mifflin St. Joer equation (mean bias women -191 (-330 to -52), men -86 (-205 to 34)).

Figure 2c: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with the the Katch McArdle using lean body mass (mean bias women -214 (-550 to 121) mean bias men -160 (-560 to 239))

Figure 2d: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with the Cunningham equation using lean body mass; women mean bias -4.4 (-340 to 331), men 53 (-350 to 457)

Figure 2e: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with Katch McArdle equation calculated from % body fat with a mean bias for women 357 (-124 to 840) mean bias men 299 (-270 to 869)

Figure 2f: Bland Altman plots of resting energy expenditure (REE) kcal/day measured using the HD Equation compared with Cunningham equation calculated from % body fat with a mean bias for women mean bias 577 (83 to 1072), men 521 (-58 to 1101) respectively. .

Appendix

Resting Energy Expenditure (REE) was estimated from a newer novel predictive equation which was derived and validated in a cohort of HD patients [4].

$$\text{REE} = -2.497 * \text{Age}(\text{years}) * \text{Factor}_{\text{age}} + 0.011 * \text{Height}^{2.023}(\text{cm}) + 83.573 * \text{Weight}^{0.6291}(\text{kg}) + 68.171 * \text{Factor}_{\text{sex}}$$

where Factor age is 0 if age <65 and 1 if ≥65 and Factor sex is 0 if female and 1 if male

Physical activity data - Each reported activity was assigned a Metabolic Equivalent of Task (MET) value as per the Compendium of Physical Activities [16]. Sleep time per day was assumed to be 8 hours and any unreported time during the day was assumed as the time performing light activities at home. A Mean daily MET value was calculated.

Total Energy Expenditure (TEE) was estimated from the following equation.

$$\text{TEE} = \text{REE} * \text{Mean Daily MET}$$

Table 1: Table comparing male and female patients, in terms of body composition and resting energy expenditure (REE) estimated by five different equations, using either lean body mass or weight minus % body fat for the Katch McArdle and Cunningham equations. Data expressed as number, mean ± standard deviation, or percentage † p<0.05 vs REE HD equation \* p<0.05, \*\* p<0.01, p<0.001 vs male patients.

	Patients	Male	Female
number	317	195	122
Age years	65.0±15.9	66.9 ±15.2	63.4 ±15.5
Body mass index kg/m <sup>2</sup>	26.2±5.8	25.8 ±4.6	27.0 ±7.3
Pre dialysis serum urea mmol/L	18.0±5.2	18.3 ±5.1	17.6 ± 5.3
Equilibrated dialysis session Kt/Vurea	1.40±0.27	1.36 ±0.26	1.46 ±0.28**
% Body fat	31.6±11.8	29.0 ± 0.3	35.7 ±12.9***
Lean body mass kg	26.2±6.6	28.3 ±6.4	22.8 ±5.4***
Appendicular muscle mass kg	19.1±6.3	20.7 ±6.3	16.1 ±4.6***
Fat mass index kg/m <sup>2</sup>	23.4±12.3	21.9 ±10.4	26.4 ±14.8*
Fat free mass index kg/m <sup>2</sup>	17.4±2.7	17.9 ±2.6	16.4 ±2.6***
REE HD Equation kcal/day	1509±241	1572 ±215	1408 ±248***
REE Harris-Benedict kcal/day	1437±244†	1515 ±233	1311 ±206***
REE Mifflin StJoer kcal/day	1384±259†	1417 ±229	1218 ±240***
REE Katch McArdle kcal/day	1345±232†	1571 ±227	1206 ±188***
REE Cunningham kcal/day	1557±236	1631 ±224	1416 ±192***
REE Katch McArdle (%body fat)	1834±239	1873 ±387	1770 ±417**

kcal/day			
REE Cunningham (%body fat) kcal/day	2055±391	2095 ±364	1990 ±425**
Total energy expenditure kcal/day	1801±374	1890 ±369	1657 ±338***

Table 2:

Statistically significant univariate associations between resting energy expenditure (REE) and total energy expenditure (TEE) and patient demographics, dialysis factors and body composition. (r values) as Pearson or Spearman.

variable	REE		TEE	
	r	p	r	p
<b>demographics</b>				
Age yr	-0.455	<0.001	-0.521	<0.001
months of haemodialysis	-0.236	<0.001	-0.201	0.003
<b>Dialysis associated factors</b>				
session time hour	0.498	<0.001	0.318	<0.001
dialyzer surface area m <sup>2</sup>	0.469	<0.001	0.409	<0.001
Protein nitrogen appearance generation g/day	0.428	<0.001	0.405	<0.001
equilibrated Kt/V	-0.419	<0.001	-0.456	<0.001
<b>Pre dialysis blood results</b>				
creatinine umol/L	0.375	<0.001	0.395	<0.001
urea mmol/L	0.212	<0.001	0.249	<0.001
haemoglobin g/L	0.099	0.079	0.149	0.008
albumin g/L	0.146	0.011	0.221	0.001
weekly erythropoietin dose IU	-0.077	0.168	-0.120	0.031
erythropoietin resistance IU/week.kg.gHb	-0.258	<0.001	-0.268	<0.001
<b>Body size and composition</b>				
Weight kg	0.886	<0.001	0.743	<0.001

extracellular water L	0.719	<0.001	0.561	<0.001
intracellular water L	0.681	<0.001	0.643	<0.001
skeletal muscle mass kg	0.717	<0.001	0.640	<0.001
skeletal muscle mass index kg/m <sup>2</sup>	0.665	<0.001	0.643	<0.001
fat free mass kg	0.658	<0.001	0.279	<0.001
height m	0.619	<0.001	0.578	<0.001
body mass index kg/m <sup>2</sup>	0.521	<0.001	0.378	<0.001
fat free mass index kg/m <sup>2</sup>	0.481	<0.001	0.477	<0.001
body fat mass kg	0.461	<0.001	0.290	<0.001
fat mass index kg/m <sup>2</sup>	0.419	<0.001	0.272	<0.001
% body fat	0.125	0.029	0.036	0.534

Table 3:

Multivariable association with resting energy expenditure (REE) and total energy expenditure (kcal/day). Age years, Skeletal muscle mass (SMM) kg, log dialysis vintage (vintage) years, co-morbidity score Low vs High (Comorbidity), employment vs no employment (employment), protein nitrogen appearance (PNA) g/day. Standard error  $\beta$  (StE  $\beta$ ), standardised  $\beta$  (St  $\beta$ ), 95% confidence interval (95% CI). (REE model:  $r^2$  0.79, adjusted  $r^2$  0.62, TEE model:  $r^2$  =0.81, adjusted  $r^2$  0.64).

	$\beta$	StE $\beta$	St $\beta$	t	95% CI	p
<b>REE</b>						
age	-5.3	-0.69	-0.32	-7.6	-6.7 to -3.9	<0.001
SMM	14.9	1.02	0.62	14.7	13.0 to 16.9	<0.001
vintage	-96.7	22.9	-0.17	-4.2	-141.9 to -51.5	<0.001
<b>TEE</b>						
age	-7.9	1.25	-0.29	-6.3	-10.4 to -5.5	<0.001
SMM	23.3	2.87	0.40	8.1	17.5 to 28.9	<0.001
employment	406.5	49.7	0.37	8.2	308 to 505	<0.001
vintage	-121.2	38.1	-0.14	-3.2	-196 to -46	0.002
Co-morbidity	105.1	3.82	0.12	-2.8	30.5 to 181	0.006
PNA	2.7	1.09	0.12	2.5	0.5 to 4.8	0.015