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A single weekly Kt/Vurea target for peritoneal dialysis patients does not provide an equal dialysis dose for all

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Abstract

Dialysis adequacy is traditionally based on urea clearance, adjusted for total body volume (Kt/Vurea), and clinical guidelines recommend a Kt/Vurea target for peritoneal dialysis (PD). We wished to determine whether adjusting dialysis dose by resting (REE) and total energy expenditure (TEE), would alter the delivered dialysis dose.

We determined REE and TEE by equations based on doubly labelled isotopic water studies, and adjusted Kturea for REE and TEE.

We studied 148 PD patients, 97 male (65.5%), 54 diabetic (36.5%), mean age 60.6±17.6 years. The mean REE was 1534±241 kcal/day and TEE 1974±414 kcal/day. Adjusting Kt for REE showed a reduced delivered dialysis dose (ml /kcal/day) for women vs men (5.5±0.4 vs 6.2±0.6), age < 65 vs > 65 years (5.6±0.56 vs 6.4±0.5), weight < 65 kg vs >80 kg (5.8±0.6 vs 6.1±0.5), low co-morbidity vs high co-morbidity (6.2±0.6 vs 5.9±0.6), all $p<0.01$. Adjusting for TEE showed reduced dosing for those employed vs no employment (4.3±0.7 vs 4.8±0.8), low frailty vs high frailty score (4.5±08 vs 5.0±0.7), both $p<0.01$.

Adjusting the dialysis target dose for REE shows that for the same Kt urea, women, younger, smaller and less co-morbid patients would all receive less dialysis, and adjusting for TEE additionally shows that those employed and physically fitter would receive less dialysis. The current paradigm for a single target Kt/Vurea for all PD patients does not take into account energy expenditure and metabolic rate, and may lead to lowered dialysis delivery for the younger more active female patient.

Introduction

More than 2 million patients with end stage kidney disease are currently treated by dialysis worldwide, with around 300,000 treated by peritoneal dialysis. As with for haemodialysis, there are clinical guidelines recommending that patients receive a minimal amount of dialysis based on urea clearance [1]. These urea based clearance targets are derived from observational studies [2]. However prospective studies comparing different peritoneal dialysis regimes designed to achieve different urea clearance targets consistently failed to demonstrate any advantage for greater urea clearance, in terms of patient morbidity or mortality [3-5]. Indeed peritoneal dialysis technique and patient survival have been linked to preservation of residual renal function [6], rather than peritoneal dialysis urea clearance [7].

The amount of urea clearance, Kt/Vurea, for dialysis patients are currently based on volume of distribution of urea, total body water (TBW) derived from anthropomorphic measurements [8]. However total body water varies with body composition, as some tissues, such as muscle contain more water than fat [9], and also varies between racial groups [10], and patients with diabetes and other co-morbidities [11]. As such for the same Kt/Vurea, the delivered urea clearance has been suggested to differ between patients [12].

Rather than dosing the amount of dialysis required on urea clearance based on volume of distribution, an alternative approach based upon metabolic activity has been proposed [13]. Urea is generated as a by-product of

intracellular nitrogen metabolism. Total body metabolic activity is a composite of resting metabolic rate and that due to physical activity. Previous studies in peritoneal dialysis patients have concentrated on measuring resting energy expenditure (REE) [14,15], but this under estimates total energy expenditure (TEE), by excluding that due to activity energy expenditure (AEE),

We recently validated an assessment of TEE, and REE in dialysis patients using a patient self-reported questionnaire and double isotopic labelled water [16]. To establish whether there is a difference in the amount of dialysis delivered for a fixed Kt/Vurea target, we calculated urea clearance adjusted for energy expenditure, to determine whether some groups of patients would be disadvantaged under current clinical guideline recommendations.

Patients and methods

Adult patients with end stage kidney disease established on peritoneal dialysis were recruited from University College London partner hospitals when attending for outpatient assessments of peritoneal dialysis adequacy. Corresponding spent dialysate effluent, 24 hour urine collections and serum samples were analysed by standard methods, and weekly dialysis dose calculated as Kt/Vurea. Protein Nitrogen Appearance rate was estimated using the Bergström equation, and normalised for body weight (nPNA) g/kg/day [17]. Patient demographics were obtained from computerised hospital records and comorbidity determined using a self-administered co-morbidity grading [18], and a recognised frailty score [19].

Total body water was calculated using the Watson equation [20]. In addition we measured total body water by bioimpedance (InBody 720, InBody, Seoul, South Korea; Body Composition Monitor (BCM), Fresenius, Bad Homberg, Germany) which was performed in a standardised manner in 118 patients [21,22]. Bioimpedance measurements made by the BCM and InBody were standardised using previously derived equations [23].Body surface area was calculated using the Gehan and George equation as recommended by the European Best Clinical Practice guidelines [24]..

Physical activity data was obtained using the Recent Physical Activity Questionnaire (RPAQ) [16], which collects information about both activity and the time spent performing activities over the preceding four weeks; encompassing activities performed at home, work and during leisure time. The RPAQ has been validated against doubly labelled water technique in general population [16], and has been shown to be a reliable tool for estimation of energy expenditure in patients with chronic kidney disease [25]. 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 [26]. The equations for calculating REE and TTE are detailed in the Appendix.

UK clinical guidelines recommend a minimum weekly Kt/V of 1.7 [1]. Hence, in order to compare minimum dialysis targets using alternative scaling parameters, weekly Kt was calculated as $Kt = 1.7 * V$. Corresponding target values of Kt/BSA, Kt/REE and Kt/TEE were calculated by dividing daily Kt by the respective parameters.

Ethical approval was granted by the UK National Research Ethics Committee - Essex and the study was registered in UK Clinical Research Network (CRN) Portfolio number 14018. All patients provided written informed consent in keeping with the declaration of Helsinki.

Statistical analysis

Statistical analysis was by students' t test, or Mann Whitney U test, ANOVA and Kruskal Wallis , with appropriate post hoc correction, Pearson or Spearman's test for univariate correlation (GraphPad Prism version 6.0, San Diego, USA) and step backward linear regression, of variables on univariate analysis of $p<0.1$, with log transformation of variables which were not normally distributed, and removal of variables which were not statistically significant unless they improved model fit, and models were checked for collinearity (SPSS version 22, University of Chicago, Illinois, USA), and Bland Altman comparison (Analyse-It version 3.0, Leeds, UK). Data are presented as mean ± standard deviation, median (inter quartile range), or mean and 95% confidence limits (CL), or as a percentage.

Results

We studied 148 patients, 97 male (65.5%), 54 diabetic (36.5%), mean age 60.6±17.6 years, with a median duration of peritoneal dialysis 9.1 (3.5-25.2) months. The median co-morbidity score was 2 (0-3.8), and frailty score 4 (2-5). 43.2% of patients were Caucasian, 27.1% African-Afro-Caribbean, 24.3% South

159 Asian, and 5.4% Far Asian. A minority, 20.3% of patients had some form of
160 employment.

161 Mean haemoglobin was 109.9±14.8 g/l, with a serum albumin 36.5±5.5 g/l
162 and serum C reactive protein (CRP) 6 (2-16) mg/l. Mean weight of the cohort was
163 73.6±16.7 kg, BMI 26.0±4.9 kg/m2, and BSA 1.86±0.24 m^2. The majority of
164 patients were treated by automated peritoneal dialysis cyclers (APD) 85.8% vs
165 14.2% by continuous ambulatory peritoneal dialysis (CAPD). The median total
166 weekly Kt/Vurea was 2.15 (1.8-2.71), with a median 24 hour urine volume of 946
167 (450-1249) ml/day. The mean REE was 1534±241 kcal/day and TEE 1974±414
168 kcal/day. Mean PNA was 64.5±19.7 g/day and nPNA 0.89±0.26 g/kg/day.

169 Male patients were heavier than female (77.0±15.6 vs 72.6±16.6 kg), and
170 had greater REE and TEE (table 1). Patients who were employed, those with
171 greater weight, and greater PNA had higher TEE (Table1), whereas those with
172 greater frailty and co-morbidity, and those who were diabetic and Asian
173 patients tended to have lower TEE.

174 We then adjusted a weekly Kturea of 1.7 for all patients for both BSA
175 and TBW. Bland Altman analysis showed that for both men and women the
176 adjusted Kturea was greater for smaller patients with a relatively greater BSA
177 to TBW, and lower for larger patients with a relatively lower BSA compared to
178 TBW (Figure 1).

179 In a subset of 118 (79.7%) of the study group; 75 male (63.6%), 33
180 diabetic (28.5%), mean age 59.3±18.2 years, with a median duration of peritoneal
181 dialysis 9.4 (3.8-25.5) months, we also measured TBW by bioimpedance. The

mean weight of this cohort was 73.1±16.6 kg with a body mass index of 26.0±4.9 kg/m^2, with a median co-morbidity grade of 2 (0-4) and frailty score of 4 (2-5), and did not differ from the main study group. There was no significant difference in TBW: Watson equation 40.3±6.1 vs bioimpedance 40.6±3.4 L, mean difference on Bland Altman analysis 0.72 L (Figure 2). There were positive correlations between BSA and both REE and TEE ($r=0.92$, $p<0.001$ and $r=0.59$, $p<0.001$) and also between TBW and both REE and TEE ($r=0.85$, $p<0.001$ and $r=0.62$, $p<0.001$) respectively.

We then calculated Kt values for a prescribed Kt/V of 1.7 using for both Watson and bioimpedance estimates of TBW These values were then patients from adjusted by BSA, REE and TEE. The results are shown in Table 2 and Figure 3 for different patient groups For the same prescribed dialysis dose, women, younger patients, those employed and those weighing less (Figure 3) received less dialysis than men, older patients, those not employed and heavier patients (table 2). In addition generally patients with less co-morbidity and frailty and non-Asian races also tended to receive less dialysis than those who were more co-morbid, frail and of Asian ethnicity.

We used a step backward approach to develop multivariable models of adjusted Kt, including all variables with $p<0.1$ on univariate analysis, and then eliminating variables which were not significant or did not improve model fit to determine associations with adjusted dialysis dose. Sex was a significant predictor of Kt/BSA. Sex and age were significant predictors of Kt/REE. the predominant variables (table 3). For Kt/TEE, sex, age and employment were

common predictive factors whether Kt was derived using TBW derived by Watson and bioimpedance methods. Both high co-morbidity, and diabetes were additional predictive factors for TEE adjusted using the Watson formula for TBW (table 3).

Discussion

Traditionally the target dialysis for patients with end stage kidney failure has been based on urea clearance adjusted for total body water volume. However multiple prospective trials have failed to show an association between greater peritoneal dialysis urea clearance and survival [3,4,7]. Cellular metabolism, in particular protein turnover generates waste products which accumulate in patients with end stage kidney failure. As these azotaemic toxins are generated by cellular metabolism, it has been suggested that the amount of dialysis required for patients should be based on metabolic rate, rather than urea clearance [2]. Studies to-date have concentrated on measuring resting metabolic rate [3], but this ignores physical activity, and as such potentially under estimates energy expenditure. We used equations based on patient self-reported physical activity questionnaires, which have been validated using doubly labelled isotopic water [4], to estimate REE and TEE. As expected energy expenditure was associated with body weight, male sex and younger age group [27]. Patients with higher REE and TEE had greater PNA rate due to increased urinary and peritoneal urea losses However we also noted that although REE was

similar, TEE was lower with increasing frailty and co-morbidity, in particular diabetes, and those without employment compared to those patients with lower frailty and co-morbidity scores, who were not diabetic or those with employment. We also found that patients from an Asian background had lower TEE compared to Caucasoids and African-Afro-Caribbean patients. This is in keeping with previous observations of lower energy expenditure, particularly with South Asians, and this has been suggested to be due to differences in terms of body composition, related to brown fat tissue stores [28].

We then compared the delivered dialysis dose for the minimum weekly KtVurea target as recommended by clinical practice guidelines [1], using Kt calculated by both the Watson formula [20], and also total body water measured by bioimpedance [29]. We found no significant difference between total body water by either method, although previous reports from haemodialysis patients have reported differences [9]. However the major differences between total body water derived by the Watson formula and bioimpedance were with obese patients with a body mass index of > 35, and in our study group < 2% had a body mass index of this level. We adjusted the delivered dialysis dose by both BSA, which is relatively greater for patients with lower total body water, and relatively lower for those with greater total body water and also for both REE and TEE. Adjusting Kt for BSA, which has been advocated for haemodialysis patients, we found that this resulted in a lower dose being delivered to women and those with a high protein nitrogen appearance rate and lower body weight. Whereas adjusting for REE, then female patients, and those who were younger,

weighed less, and who had lower protein nitrogen appearance along with those with frailty and co-morbidity scores, and other ethnicities than Asian all received relatively less delivered dialysis. When Kt was adjusted for TEE, then women, younger patients and those weighing less, who were employed, and those with less frailty, in particular those with diabetes, all would receive less delivered dialysis dosing compared to men, heavier patients, those without employment and the more frail, co-morbid patient and those with diabetes.

Previous studies targeting a dialysis dose defined by a weekly KtVurea for peritoneal dialysis patients have not shown an advantage for one target compared to another [3,4]. Our study shows that achieving the same urea clearance does not equate to the same delivered dose of dialysis, and as such potentially adds explanation as to why prospective studies have failed to show a significant benefit for one KtVurea target for all patients. Although we accepted that using Kt/Vurea for dialysis dosing has some limitations [31], more recent observational studies have suggested an advantage for adjusting Kt for BSA [30]. However we found that although adjusting for BSA detected a difference between sexes and body weight, those who had higher nitrogen appearance rates. Whereas in particular adjusting for TEE showed that in addition, younger fitter patients received relatively less dialysis dose delivered compared to older, more frail, co-morbid and diabetic patients. As such we suggest that a single Kt/Vurea target dose us not applicable to all patients, and the dose of dialysis should be increased for those who are more physically active with greater TEE.

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References

1. Woodrow G, Davies SJ. Peritoneal Dialysis (PD) (Guidelines PD 3.1 – 3.3).http://www.renal.org/guidelines/modules/peritoneal-dialysis-in-ckd#sthash.Br67xjah.dpuf
2. Jansen MA, Termorshuizen F, Korevaar JC, Dekker FW, Boeschoten E, Krediet RT. Predictors of survival in anuric peritoneal dialysis patients. Kidney Int. 2005;68(3):1199-205
3. Paniagua R, Amato D, Vonesh E, Correa-Rotter R, Ramos A, Moran J, Mujais S; Mexican Nephrology Collaborative Study Group. Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis: ADEMEX, a Prospective, Randomized, Controlled Trial. J Am Soc Nephrol 2002;13(5):1307-20
4. Lo WK, Ho YW, Li CS, Wong KS, Chan TM, Yu AW, Ng FS, Cheng IK. Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. Kidney Int 2003;64(2):649-56
5. Paniagua R, Amato D, Vonesh E, Guo A, Mujais S; Mexican Nephrology Collaborative Study Group. Health-related quality of life predicts outcomes but is not affected by peritoneal clearance: The ADEMEX trial. Kidney Int. 2005;67(3):1093-104
6. Churchill DN, Taylor DW, Keshaviah PR. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcome. J Am Soc Nephrol 1996;7:198-207
7. Bargman JM, Thorpe KE, Churchill DN; CANUSA Peritoneal Dialysis Study Group. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol. 2001;12(10):2158-62
8. Watson PE, Watson ID, Batt RD. Total body water volume for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 1980;33:27-39
9. 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

10. 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

11. Davenport A, Willicombe MK. Does diabetes mellitus predispose to increased fluid overload in peritoneal dialysis patients? Nephron Clin Pract. 2010;114(1):c60-66

12. 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

13. 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

14. Bazanelli AP, Kamimura MA, da Silva CB, Avesani CM, Lopes MG, Manfredi SR, Draibe SA, Cuppari L. Resting energy expenditure in peritoneal dialysis patients. Perit Dial Int. 2006;26(6):697-704

15. Wang AY, Sea MM, Tang N, Sanderson JE, Lui SF, Li PK, Woo J. Resting energy expenditure and subsequent mortality risk in peritoneal dialysis patients. J Am Soc Nephrol. 2004;15(12):3134-43

16. Sridharan S, Wong J, Vilar E, Farrington K. Comparison of energy estimates in chronic kidney disease using doubly-labelled water. J Hum Nutr Diet. 2015 Jul 15 PMID: 26173618

17. Bergström J, Heimbürger O, Lindholm B. Calculation of the protein equivalent of total nitrogen appearance from urea appearance. Which formulas should be used? Perit Dial Int. 1998;18(5):467-73

18. Sridharan S, Berdeprado J, Vilar E, Roberts J, Farrington K: A self-report comorbidity questionnaire for haemodialysis patients. BMC Nephrol, 2014;15: 134

19. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489-95

20. Watson PE, Watson ID, Batt RD. Total body water volume for adult males and females estimated from simple anthropometric measurements. Am J Clin Nutr 1980;33:27-39

21. Davenport A. Effect of intra-abdominal dialysate on bioimpedance-derived fluid volume status and body composition measurements in peritoneal dialysis patients. Perit Dial Int. 2013;33(5):578-9

22. Fürstenberg A, Davenport A. Assessment of body composition in peritoneal dialysis patients using bioelectrical impedance and dual-energy x-ray absorptiometry. Am J Nephrol. 2011;33(2):150-6

23. McCafferty K, Fan S, Davenport A. Extracellular volume expansion, measured by multi-frequency bioimpedance, does not help preserve residual renal function in peritoneal dialysis patients. Kidney Int. 2013

24. Dombros N, Dratwa M, Feriani M, Gokal R, Heimbürger O, Krediet R, Plum J, Rodrigues A, Selgas R, Struijk D, Verger C; EBPG Expert Group on

Peritoneal Dialysis. European best practice guidelines for peritoneal dialysis. 7 Adequacy of peritoneal dialysis. Nephrol Dial Transplant. 2005;20 Suppl 9:ix21-ix23

25. 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

26. 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

27. Finkel T. The metabolic regulation of aging. Nat Med. 2015;21(12):1416-23

28. Boon MR, Bakker LE, van der Linden RA, van Ouwerkerk AF, de Goeje PL, Counotte J, Jazet IM, Rensen PC. High prevalence of cardiovascular disease in South Asians: Central role for brown adipose tissue? Crit Rev Clin Lab Sci. 2015;52(3):150-7

29. 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

30. Ramirez SP, Kapke A, Port FK, Wolfe RA, Saran R, Pearson J, Hirth RA, Messana JM, Daugirdas JT. Dialysis dose scaled to body surface area and size-adjusted, sex-specific patient mortality. Clin J Am Soc Nephrol. 2012;7(12):1977-87.

31. Daugirdas JT. Kt/V (and especially its modifications) remains a useful measure of haemodialysis dose. Kidney Int. 2015;88(3):466-73

Figure 1: Relationship between body surface area (BSA) and Watson total body water for man and women.

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Figure 2: Bland Altman analysis of total body water (TBW) measured by bioimpedance or calculated by Watson equation. Mean difference 0.72 L (95% limits of agreement -9.2 to +10.7 L).

Figure 3: Adjusted daily urea clearance according to body weight. Fixed weekly Kt of 1.7urea adjusted for body surface area (BSA) and resting energy (REE) and total energy (TEE) expenditure using Watson total body water (W) or bioimpedance measured total body water (BIA).* $p < 0.05$, and ** $p < 0.01$ vs weight < 64 kg after Bonferroni correction.

Table 1. Estimates of daily resting energy expenditure (REE) and total energy expenditure (TEE) in patients according to age, co-morbidity, frailty and ethnicity groupings. Daily protein nitrogen appearance (PNA) g/day. Results expressed as mean ±standard deviation, or median (interquartile range). *p<0.05, ** p<0.01 comparing groups, adjusted for multiple comparisons (Bonferroni method).

variable	REE kcal/day	TEE kcal/day
male	1597±217	2029±423
female	1412±240**	1868±377*
Age < 65 years	1646±209	2173±392
Age > 65 years	1408±211**	1750±314**
Non-diabetic	1522±233	2021±435
diabetic	1556±254	1893±366*
employed	1577±237	2305±511
not employed	1523±242	1890±340**
Low comorbidity	1532±245	2012±441
High comorbidity	1539±231	1862±300
Low frailty score	1533±227	2049±453
High frailty score	1535±256	1894±353*
Weight < 64 kg	1305±151	1706±306
Weight 64-80 kg	1514±142**	1973±414**
Weight > 80 kg	1775±159**	2233±339**
PNA < 60 g/day	1450±214	1826±317
PNA > 60 g/day	1622±229**	2133±438**
Non Asian	1561±225	2060±462
Asian	1522±243	1866±359*

Table 2. Comparison for a fixed total weekly Kt/V of 1.7 (urea clearance L/m^2/day, or ml urea clearance/kcal/day) adjusted for body surface area (BSA), resting energy expenditure (REE), total energy expenditure (TEE) for peritoneal dialysis patients comparing sexes, age (years), diabetic, employment status, and co-morbidity, weight and ethnicity. Diabetic (DM), High (H) and Low (L) frailty, co-morbidity (Comorb), protein nitrogen appearance (PNA) employed (employ +), not employed (employ -), ethnicity (Asian vs other races). *p<0.05 **p<0.01 after Bonferroni post hoc correction for multiple testing.

variable	Kt/BSA	Kt/REE_W	Kt/TEE_W	Kt/REE_{BIA}	Kt/TEE_{BIA}
Male	5.13±.0.36	6.15±9.61	4.96±0.71	6.23±0.62	4.93±0.70
Female	4.42±0.40**	5.50±0.41**	4.23±0.65**	5.64±0.64**	4.27±0.71**
Age < 65	4.83±0.46	5.58±0.55	4.29±0.53	5.93±0.73	4.52±0.81
Age > 65	4.95±0.42	6.38±0.49**	5.18±0.61**	6.12±0.62	4.93±0.65**
DM yes	4.96±0.45	6.03±0.58	5.00±0.69**	5.92±0.65	4.93±0.69*
DM no	4.84±0.46	5.90±0.66	4.53±0.82	6.06±0.71	4.57±0.78
H frailty	4.91±0.47	6.06±0.66	4.96±0.75	6.01±0.61	4.90±0.71
L frailty	4.86±0.43	5.85±0.60*	4.46±0.78**	6.01±0.75	4.54±0.78**
HComorb	4.99±0.43	6.19±0.63	5.14±0.66	5.91±0.63	4.90±0.63
LComorb	4.85±0.45	5.87±0.62**	4.55±0.80**	6.05±0.71	4.62±0.81
Employ -	4.89±0.43	5.99±0.61	4.87±0.72	5.96±0.73	4.81±0.75
Employ +	4.89±0.54	5.82±0.71	4.07±0.82**	6.19±0.51	4.31±0.72**
H PNA	4.79±0.40	5.91±0.62	4.75±0.78	5.77±0.70	4.56±0.70
L PNA	4.95±0.48*	5.98±0.68	4.62±0.87	6.23±0.59*	4.81±0.81
Asian	4.87±0.46	5.97±0.65	4.67±0.85	6.10±0.65	4.71±0.76
Other	4.87±0.42	5.90±0.60	4.79±0.69	5.79±0.76*	4.64±0.80

Table 3. Multivariable step backward models for weekly Kt adjusted for Body surface area (BSA), resting energy expenditure (REE), and total energy expenditure (TEE), using both total body water calculated by Watson equation (W) and measured by bioimpedance (BIA). Unstandardised β (β), standard error (StE), standardised β (Standard β), 95% Confidence limits (95% CL). Protein nitrogen accumulation rate (PNA).
Adjusted for BSA model $r^2$0.60, adjusted 0.59, model adjusted for REE_W $r^2$0.60, adjusted 0.59, model adjusted for REE_{BIA} $r^2$0.42, adjusted 0.37, model adjusted for TEE_W $r^2$0.42, adjusted 0.3, and adjusted for TEE_{BIA} $r^2$0.35, adjusted 0.33 . Sex (female vs male), age years, high co-morbidity (H).

	β	StE β	Standard β	t	95% CL	p
Kt_{urea}/BSA						
sex (M)	0.70	0.05	0.77	13.5	0.6-0.87	<0.001
Kt_{urea}/REE_W						
sex (M)	0.58	0.08	0.44	7.5	0.43-0.74	<0.001
age	0.02	0.01	0.54	9.3	0.2-0.25	<0.001
Kt_{urea}/REE_{BIA}						
PNA	0.01	0.01	0.37	4.4	0.01-0.02	<0.001
sex (M)	0.39	0.12	0.28	3.2	0.15-0.63	0.002
age	0.01	0.01	0.19	2.3	0.01-0.01	0.025
Kt_{urea}/TEE_W						
sex (M)	0.59	0.10	0.35	6.1	0.40-0.79	<0.001
age	0.02	0.01	0.44	7.5	0.02-0.013	<0.001
no employment	0.52	0.11	0.26	4.5	0.29-0.74	<0.001
comorbidity H	0.30	0.11	0.16	2.7	0.01-0.52	0.009
diabetic	0.21	0.10	0.12	2.0	0.01-0.41	0.045
Kt_{urea}/TEE_{BIA}						
sex (M)	0.51	0.13	0.33	3.8	0.25-0.77	<0.001
age	0.01	0.01	0.32	7.5	0.01-0.02	<0.001
no employment	0.44	0.15	0.24	3.0	0.15-0.74	0.004

Appendix

Resting Energy Expenditure (REE) was estimated from a newer novel predictive equation which was derived and validated in a cohort of HD patients [18].

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

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 [19]. 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.

$$TEE = REE * Mean\ Daily\ MET$$

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