Accuracy of the estimation of V and the implications this has when applying Kt/Vurea for measuring dialysis dose in peritoneal dialysis

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**Abstract**

**Background** Current guidelines for the prescription of peritoneal dialysis (PD) dose rely on a single cut-off ‘minimal’ value of Kt/V. To apply this in the clinic this requires an accurate estimation of V, the volume of urea distribution that equates to the total body water, (TBW). This analysis sought to determine the accuracy to which V can be estimated.

**Methods** A literature search was undertaken of studies comparing TBW estimation using two or three of the following methods: isotopic dilution (gold standard), anthropometric equations (e.g. Watson formula) and bioimpedance analysis. Studies of healthy and dialysis populations of all ages were included. Mean differences and 95% limits of agreement (LOA) were extracted and pooled.

**Results** In 42 studies (29 including dialysis subjects) the between method population means were typically within 1 to 1.5 L of each other, although larger bias was seen when applying anthropometric equations to different racial groups. However the 95% LOA for all comparisons were consistantly wide, typically ranging ±12-18% of the TBW. For a typical individual whose TBW is 35L with a measured Kt/V of 1.7 this translates into a range of Kt/V 1.4-2.05.

**Conclusions** There are limitations to the accuracy of estimation of V which call into question the validity of applying a single threshold Kt/V value as indicative of adequate dialysis. This should be taken into account in guideline development such that if a target Kt/V were deemed appropriate that this should expressed as a range; alternatively single targets should be avoided and dialysis dose should be determined according to patient need.

**Introduction**

In adopting a uniform method of measurement of the dialysis dose prescribed and delivered to peritoneal dialysis (PD) patients it was decided early on to borrow from haemodialysis (HD) the Kt/Vurea concept that was originally developed following the US National Dialysis Collaborative study.(1) Since then it has become apparent that there are many problems with this approach which are summarised in Table 1; in particular there is little evidence that the prescribed peritoneal Kt/Vurea is a good surrogate measure of what matters to patients, e.g. uremic symptom control or survival,(2,3) as well as a number of conceptual concerns, such as an over-emphasis on low molecular weight solute clearance, questionable assumptions of the urea kinetic model and problems with scaling.(4,5) For example it has been argued that V should be deremined from the ideal rather than the actual body weight as a means to avoiding overdialysis in the obese and underdialysis in the malnourished.

Despite these concerns – and the lack of evidence that targeting a higher Kt/Vurea necessarily translates into clinical benefit – there is a clear need to bench mark the amount of dialysis delivered and that the dialysis volume prescribed must – at least in part – be proportionate to the size and metabolic needs of the individual. Thus, some standard approach to normalising the dialysis dose needs to be agreed, while recognising the limitations of the accuracy of the measurement, the fact that more than one approach to dose normalisation can be made and that the actual dose may require stratifying to patient need.

This raises a further difficulty with Kt/Vurea – how accurately can it be measured? There are important differences in how this is derived for PD when compared to HD, reflecting the different kinetics of the modalities (intermittent versus steady state), and thus how V, the volume of distribution of urea, is determined. In PD, solute removal is easily measured by collecting dialysate effluent, whereas estimating V is more difficult. The volume of urea distribution in generally taken to be the total body water (TBW) given that urea is highly soluble both in water and cell membranes. Vurea is thus determined by the same tools used to estimate TBW, generally using three approaches: dilution of isotopes of water (most commonly stable isotopes 2H2O and H218O, but also radioactive 3H2O), bioelectrical impedance (BI) and a number of anthropometric equations, most commonly the Watson formula(6) in adults or an equation developed by the Paediatric PD Study Consortium, (PPDSC) (7,8) that has replaced the formula of Mellits and Cheek in children.(9) While the isotopic methods are considered the gold standard, these are not readily available or practical in the clinic, although point of care testing has been developed and used in the clinic setting.(10,11) There is, therefore, a built-in degree of error in the estimation of V which should be taken into account when interpreting the Kt/Vurea result. The main purpose of this short paper is to estimate the size of this error by undertaking an analysis of the published literature of comparative studies, deriving an evidence based estimate of measurement error (95% limits of agreement, LOA), and discussing the implications this has for the application of Kt/Vurea in the clinic.

**Methods**

A literature search was undertaken to identify studies in which comparisons for estimating TBW were made by two or more of the following three methods: Isotopic methods, bioimpedance methods (no restriction on device type of manufacturer) and/or the Watson (adult) or PPDSC (children) anthropometic methods, excepting the studies from which these equations were originally derived.(6) Given the very large number of published anthropmetric equations this restriction to two equations was necessary to avoid multiple comparisons, and focus on those advocated for use at the time these studies were published (subsequently newer equations have been advocated that are variably used and these will be dicussed later). Studies were included in the analysis (see tables 2-4, and graphical representations, Figures 1-3) if they reported accuracy (mean differences with standard errors) such that 95% limits of agreement could be determined. Studies of non-dialysis subjects across a range of body sizes were included (excluding studies of specific non-renal diseases, e.g. HIV) for comparison purposes as well as studies of HD and PD patients. Search terms included and their yields are shown in the supplemental Table 1.

Mean differences and 95% confidence intervals for limits of agreement between methods were determined using the methods described by Bland and Altman(12) and expressed graphically. Pooled limits of agreement were calculated from the un-weighted averages expressed as a percentage of the total body water for normal subjects and dialysis respectively. Weighting was not possible nor meaningful given the heterogeneity of the study subject (age, gender, race,) or methodologies used (BI devices, isotopes). These were used to demonstrate the effect that accuracy of measurement would have on the measurement of Kt/V, expressed as for a patient with a value of 1.7 and an average TBW (typically 35 L) as reported for that method.

**Results**

44 studies were identified, 31 that included dialysis patients. One large study was excluded from the pooled analysis as data on overall limits of agreement could not be extracted, but this important study was included separately in the results section and the overall conclusions and were very consistent.(13)

*Comparison of Bioimpedance methods with isotopic dilution*

9 studies in non-dialysis subjects including elderly patients, elderly inpatients, lean and obese subjects, children and elite athletes and 11 in dialysis patients (217 HD, 173 PD) are included in Table 2. The mean difference between the methods for non-dialysis subjects was 0.25L ±1.85, with low bias across a wide range of body sizes/compositions and 1.18 L ±3.2 for dialysis patients over a much smaller range, but including children. However, the 95% limits of agreement were substantial, being on average -11.6, +13.5% of TBW for non-dialysis subjects and -12.6, +18.6% for dialysis patients, see Table 2 and Figure 1. Translating this into what it means for a dialysis patient who has an estimated TBW of 35 L and a calculated Kt/V of 1.7, the 95% CI of this measurement would be a Kt/V 1.44-1.94. This will vary by bioimpedance manufacturer and 12 different devices were reported (see caption to Table 2 for details); however this study was not designed to ascribe superiority of any particular device.

*Comparison of Watson (adults) and Mellits & Cheek (children) formulae with isotopic dilution*

3 studies in non-dialysis subjects and 10 in dialysis patients (127 HD, 379 PD) are included in Table 3. The mean difference between the methods for non-dialysis subjects was 0.43L ±0.92, and -0.01 L ±1.78 for dialysis patients. The 95% limits of agreement for non-dialysis subjects were -12%, 14.4% of TBW and for dialysis subjects ranged from -17.6%, +18.0%, see Table 3 and Figure 2. Translating this into what it means for a patient who has an estimated TBW of 35 L and a calculated Kt/V of 1.7 in, the 95% CI of this measurement would be a Kt/V of 1.44-2.06. This pooled estimate excludes a large data set comparing the use of anthropometric equations with 2H2O/3H2O dilution methods across a wide age range and, more importantly white versus black ethnic haemodialysis patients.(13) In this study the Watson equation typically underestimated TBW by 2.3-11 L in white men (n=604), 6.5-11 L in black men (n=128), -0.3-0.9 L in white women (n=772 ), 1.5-6.9 L in black women (n=191), the degree depending on age range. These estimates are not presented as paired data with limits of agreement, so cannot be directly compared to other studies, but they strongly suggest that the Watson equation underestimates TBW in all black people and older white men on dialysis.

*Comparison of Watson formula with bioimpedance*

3 studies in non-dialysis subjects and 9 in dialysis patients (3696 HD, 718 PD) are included in Table 4. The mean difference between the methods for non-dialysis subjects was -1.12L ±0.57, and -1.01L ±2.22 for dialysis patients. The 95% limits of agreement for non-dialysis subjects were -15.3%, 8.9% of TBW and for dialysis subjects ranged from -17.4%, +12%, see Table 4 and Figure 3. Translating this into what it means for a patient who has an estimated TBW of 35 L and a calculated Kt/V of 1.7 in, the 95% CI of this measurement would be a Kt/V of 1.51-2.05. In the large dataset of 3009 US HD patients there was a high proportion of African Americans who had a significantly higher TBW, 41.6L, than Caucasians, 40.4L, and Hispanics, 39.0L, and other ethnicities, 37.2L (ANOVA <0.0001).

**Discussion**

This meta-analysis of studies comparing the three main methods of estimating TBW, namely gold standard isotope dilution, bioimpedance and anthropometric equations found that in each case that the limits of agreement were relatively wide. Typically for dialysis patients the 95%CI ranged ±12-18% of the TBW translating into a Kt/V range of 1.4-2.05 in an individual whose TBW is 35L and a measured Kt/V of 1.7. This in-built lack of accuracy in estimating the Kt/V in an individual patient has to be taken into account when setting guidance on measuring dialysis dose for clinicians and how this estimate should be used to inform the dialysis prescription; equally commissioners or regulators of dialysis care need to understand the significance this has for setting a ‘one size fits all’ dialysis dose target.

Despite these wide limits of agreement the mean difference between all the measures is relatively small, even across quite a wide range of averaged TBW volumes. In other words, population averages are quite reliable and it is the individual variation in body composition that is driving the wide limits of agreement. There was a tendency for these LOAs to be wider in the dialysis than the non-dialysis populations, the latter being predominantly healthy subjects of different ages and physical fitness, in contrast with the more varied health of the dialysis group and in particular the well documented risk of muscle wasting that occurs in advanced kidney failure, especially over time on dialysis.(10,14) Obesity is also also a concern, being common in the dialysis population and this is illustrated by the greater bias observed when comparing bioimpedance estimates with isotopic methods in otherwise healthy subjects, Table 2.(15) Equations developed for application of the BCM bioimpedance device do minimise this error, Tables 2 and 3,(16) but clinicians should take this into account when estimating dialysis dose. This is especially an issue in PD, as false underestimation of the Kt/V in obese patients may lead to inappropriate increases in dialysis dose that inevitably lead to more peritoneal glucose exposure and glucose absorption from the dialysate that will worsen the obesity.

Ethnicity is clearly a source of bias for the population averages, with higher TBW in African Americans or Afro-Caribbeans compared to whites, entirely in keeping with known racial differences in average muscle mass.(17) This was especially noticeable for the comparisons with the Watson formula which underestimated TBW in these populations but overestimated it in subjects of Asian origin, being most accurate in white populations (see especially Table 2). Given that the Watson formula was developed from predominantly white cohorts this is not surprising, and has led to the development of other regression equations, notably those of Chumlea (18) or Chertow.(19) Application of these equations may help to reduce the population level bias associated with ethnic origin but will not solve the issue of individual variation which was seen with all methods, comparisons and the different bioimpedance devices. Of note the new formula for children developed by Morgenstern *et al*. specifically for children on dialysis is more accurate than the formula of Mellits and Cheek, and its use is now recommended by the Pediatric Peritoneal Dialysis Study Consortium.(7,20)

An alternative approach to avoiding the V problem in normalising the dialysis dose is to normalise to body surface area (BSA) as is typically done for creatinine clearance or glomerular filtration rate. Advocates for this approach would argue that it is more appropriate to normalise metabolic functions to BSA. However this approach is not without problems in PD patients. The ADEMEX trial,(3) which used creatinine clearance normalised to BSA as its target found no relationship between the peritoneal clearance targets and survival or health related quality of life, and peritoneal transport characteristics will influence the achieved creatinine clearance but in such a way as they will be more easily achieved in high transport patients who paradoxically have an increased mortality risk.(21,22) There is also still the problem of malnourished patients, being below their desirable body weight, which will affect both V and BSA such that they more easily achieve a ‘target’ dialysis dose. One other solution that has been proposed is normalisation of the dialysis dose to another measure of metabolic activity, for example resting or total energy expenditure. As would be expected from Kleiber’s law, which relates metabolic rate to mass across many species, energy expenditure is not linearly related to volume.(5,23) The predicted consequences of this would be that smaller people, e.g. women, or more physically active patients should require proportionally more dialysis, itself an argument for stratifying dialysis dose,(4) although there is not much evidence that these particular patient groups are at risk. Clinical studies indicate that malnourished patients of whatever size with low levels or absent residual kidney function and poorly controlled uremic symptoms are the greater cause of concern. Estimations of V are likely to be especially unreliable in these patient groups, given their abnormal body composition.

The strengths of this review and meta-analysis are that it is by far the largest synthesis of comparative methods used to determine TBW (V) in both non-dialysis and dialysis populations published to date and it gives a consistent estimate of LOA across a wide range of methodologies. The weaknesses are that within the broad comparisons made there is considerable heterogeneity (for example 12 different bio-impedance devices, 3 isotopic methods, different anthropometric equations, variable reporting methodology) which prevented more sophisticated analysis (e.g. weighting by sample size, sub-analysis by gender).

*Conclusions and recommendations:*

*Implications for dialysis providers and healthcare commissioners*

1. In setting a Kt/V target for the individual patient, defining an acceptable range that recognises the uncertainty of the measurement, rather than applying a single cut-off value is more appropriate. Grade: 1A
2. Given the uncertainty of a the estimation of V, clinicians should be encouraged to alter the prescribed dialysis dose in response to symptoms and treatment goals, rather than solely equating a single value cut-off value with adequate treatment.

Grade: 1A

1. Despite the limitation in estimating V, there is no clear evidence that using this to normalise the dialysis dose is better or worse than other methods (e.g. BSA, energy expenditure). Clinicians may wish to use more than one method, but all have their limitations. Grade: 2C
2. When reporting prescribed dialysis dose at the population level, this should be as population mean and range of Kt/V rather than as the proportion of patients who are above an arbitrary cut-off value (e.g. 1.7); this will allow comparison at the population level while recognising limitations of the measurement

Grade:2C

*Implications for patients*

While measuring the amount of your dialysis is helpful in guiding prescription, there is no precise way or simple formula for knowing exactly how much dialysis you need. This is because individuals differ in their size, shape, state of nutrition, activity and symptoms. Your clinical team should work with you to adjust your dialysis does so as to take all these factors into account.

*Audit recommendation*

Clinicians should record that the diaysis dose prescription is discussed with the patient, that it is informed but not solely dictated by dialysis dose measurement that is incorporated into a joint decision process. Extremes of dose and prescription should be justified and documented.

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**Captions for Figures:**

**Figure 1.** Modified Bland and Alman plot to show agreement between bioimpedance and isotopic dilution (gold standard) estimated TBW, in which each data point (mean difference ±95% CI for limits of agreement) refects a different study as summarised in Table 2, (o) non-dialysis subjects, (•) dialysis patients. Agreementt tends to be better for non-dialysis subjects across a wider range of TBW.

**Figure 2.** Modified Bland and Alman plot to show agreement between anthropometrically (\*Watson in adults or Mellits & Cheek formulae in chlidren) and isotopic dilution (gold standard) estimated TBW, in which each data point (mean difference ±95% CI for limits of agreement) refects a different study as summarised in Table 3, (o) non-dialysis subjects, (•) dialysis patients.

**Figure 3.** Modified Bland and Alman plot to show agreement between bioimpedance and anthropometrically (Watson equation) estimated TBW, in which each data point (mean difference ±95% CI for limits of agreement) refects a different study as summarised in Table 4, (o) non-dialysis subjects, (•) dialysis patients.

**Table 1. The Problems of Kt/V as an estimate of adequate dialysis dose.**

|  |  |
| --- | --- |
| **Type of problem** | **Why Kt/V is potentially flawed** |
| **Lack of evidence** |  |
| Kt/V target as a surrogate for adequate dialysis dose | The peritoneal Kt/V is poorly correlated to the relevant outcomes of adequate treatment, e.g. uremic symptoms, maintenance of nitrogen balance, nutritional state, physical function and survival |
| **Conceptual** |  |
| Residual kidney function does not equate to peritoneal clearance | Residual and peritoneal Kt/V are usually summed but there is no justification for this – residual associates with survival benefit, peritoneal does not with any certainty |
| It assumes stable body composition | Weight loss or gain, by altering the calculated V, will alter Kt/V in the opposite direction, encouraging the wrong prescription intervention |
| It estimates small molecular weight clearance only | Many uremic toxins are of a significantly higher molecular weight than urea |
| What denominator should the dialysis dose should be scaled to? | It can be argued that dialysis dose should be normalised to metabolic activity rather than a static measure of body composition such as V. Alternatively the estimate of V should be made using ideal rather than actual body weight |
| Urea kinetic modelling is based on nitrogen metabolism/protein losses | Kt/V was developed from urea kinetic modelling and the balance between urea generation (indicative or protein catabolic rate) and urea removal. However, this ignores calorie intake (to include dialysis calories) which can play a role in maintaining nitrogen balance despite peritoneal protein losses. |
| **Accuracy and precision of measurement** |  |
| Accurate estimate of V | Usually estimated from methods that rely on population derived equations, often in healthy subjects and thus of limited accuracy when applied to the individual, especially when over or under hydration is present. |

**Table 2: Bioimpedance methods compared to isotopic water dilution measurement (gold standard)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Source** | **N** | **Population** | **Bioimpedance Device** | **Mean TBW (L) (Isotope Dilution**§**)** | **Difference (ID-BIA in L)** | **95% Limits of agreement (L)** |
| Smith, 2002 (24) | 24 | Healthy subjects (12 men) | Xitron1 | 39.2 | 2.18 | -3.15, 7.5 |
| Engel, 2004 (25) | 24 | Healthy subjects at 12 months | Xitron1 | 40.4 | 3.1 | -2.25, 8.5 |
| Moissl, 2006 (16) | 120 | Healthy subjects | BCM2 | 39.4 | 0.2 | -4.4, 4.8 |
| Vaché, 1998 (26) | 58 | Healthy elderly (27 men) | Analycor-33 | 34.2 | 1.3 | -3.8, 6.4 |
| Ritz, 2001 (27) | 169 | Geriatric inpatients with varying hydration status | Analycor-33 | 29.3 | 0.48 | -4.1, 5.0 |
| * Steijaert, 1997 (15) | 55 | 20 Lean healthy subjects  25 Obese healthy subjects | Human IM-Scan4 | 31.3  34.5 | -1.7\*  -3.4\* | -5.1, 1.97  -5.44, 1.52 |
| Kerr A, 2015 (28) | 29 | Elite male athletes (BMI>25) | Impedimed SFB75 | 55.9 | 0.5 | -5.57, 5.09 |
| Khan, 2012 (29) | 200 | Bangladeshi children, 7-10 yrs | Tanita-300MA6 | 13.1 | 0.22 | -0.09, 0.52 |
| Dasgupta, 2018 (30) | 61 | Healthy children 6-14 years, 32 male | BCM2 | 20.5 | -0.6 | -3.2, 2.0 |
| Mendley, 2005¶ (8) | 14 | Paediatric PD patients | RJL Systems 101A7 | 35.0 | -0.4 | -3.4, 2.6 |
| Milani, 2017 (31) | 16 | Paediatric PD & HD patients | BCM2 | 19.2 | -0.1 | -2.2, 1.9 |
| Chertow, 1995 (32) | 33 | HD patients (15 men) | RJL Systems 101A7 | 40.6 | -3.0 | -9.2, 3 |
| Wong, 1995 (33) | 20 | PD patients (6 men) | RJL Systems 101A7 | 38.8 | 1.7 | -10.3, 13.7 |
| Arkouche, 1997 (34) | 10 | PD patients (5 men) | IMP BO8 | 32.4 (18O)  33.8 (2H2O) | 8.6  10 | 0.1, 16.8  1.2, 18 |
| Cooper, 2000 (35) | 54 | 35 PD, 14 HD, 5 Transplant | ﻿ SFB2 MF9 | 36.8 | -1.2 | -2.75, 0.31 |
| Konings, 2002 (36) | 40 | PD patients (29 men) | Xitron1 | 38.8 | 2.0 | -5.6, 9.6 |
| Moissl, 2006 (16) | 54 | HD patients | BCM2 | 38 | 0.3 | -5.7, 6.3 |
| Chan, 2009 (10) | 59 | HD Baseline (42 men) | InBody S2010 | 44.2 | 1.62 | -4.47, 7.7 |
| John, 2010 (37) | 46 | PD patients (16 men) | Xitron1 | 36.5 | 2.02 | -4.45, 8.49 |
| Raimann, 2013 (38) | 49 | HD patients (29 men) | Xitron1  Xitron1 (SF 50kHz) | 40  40 | 1.9  -2.1 | -1.3, 5.1  -5.3, 1.1 |

§2H2O unless otherwise indicated. \*Mean of 5 different models used. ¶ 28 observations, Kushner model for bioimpedance

﻿1 Xitron 4200, Xitron Technologies, CA) MF = Multifrequency, SF, single frequency

2 Body Composition Monitor, Fresenius Medical Care, Bad Homberg, Germany

3 Analycor-3 analyzer, Spengler, Cachan, France, using the Wisser model equations

4 Human IM-Scan Impedance Analyser, Dietosystem Milan, Italy

5 ImpediMed Limited, Pinkenba, Queensland, Australia

﻿6 Tanita TBF-300MA Body Composition Analyzer, Tanita Corporation, Tokyo, Japan.

7 Quantum, RJL systems, MI. USA.

8IMP BO, L’Impulsion, Caen, France

9SFB2 Multifrequency Analyser, SEAC, Brisbane, Australia

﻿10InBody series, Body Composition Analysis, Biospace, Seoul, South Korea.

﻿11STA-BIA, Akern, Florence, Italy

﻿12Quadscan 4000, Bodystat, UK

**Table 3: Anthropometric equations (example Watson Formula based on actual weight) compared to isotopic water dilution measurement (gold standard)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Source** | **N** | **Population** | **Mean TBW (L) (Isotope Dilution)** | **Difference (ID-Watson in L)** | **95% Limits of agreement (L)** |
| Smith, 2002 (24) | 24 | Healthy subjects (12 men) | 39.2 | 1.47 | -2.52, 5.5 |
| Moissl, 2006 (16) | 120 | Healthy subjects | 39.4 | 0.1 | -7.2, 7.5 |
| Woodrow, 2003 (39) | 32 | Healthy subjects (15 men) | 37.03 | -0.29 | -4.19, 3.6 |
| Wong, 1995 (33) | 20 | PD patients (6 men) | 38.8 | 4.21 | -8.1, 16.5 |
| Arkouche, 1997 (34) | 10 | PD patients (5 men) | 32.4 (18O)  33.8 (2H2O) | -0.8  0.6 | -6.6, 5.1  -5, 6.2 |
| Johansson, 1998 (40) | 165 | PD patients | 38.2 (3H2O) | 0.4 | -6.2, 7.2 |
| Cooper, 2000 (35) | 54 | 35 PD, 14 HD, 5 Transplant | 36.8 | -1.75 | -3.1, -0.4 |
| Konings, 2002 (36) | 40 | PD patients (29 men) | 38.8 | -2.3 | -8.7, 4.2 |
| Woodrow, 2003 (39) | 31 | PD Patients (15 men) | 35.04 | -0.87 | -7, 5.27 |
| Morgenstern, 2005 (7) | 64 | Paediatric PD patients | 16.9 | 0.001\* | -4.2, 4.2 |
| Mendley, 2005 (8) | 14¶ | Paediatric PD patients | 35 | 0.0 | -4.3, 4.3 |
| Moissl, 2006 (16) | 54 | HD patients | 38 | 0.7 | -5.77, 7.2 |
| Chan, 2009 (10) | 59 | HD Baseline and at 12 months | 44.2 | -0.29 | -7.1, 7.2 |

\*Child specific formulas developed by the Paediatric PD Study Consortium (9) ¶ 28 observations

**Table 4. Anthropometric equations (example Watson Formula based on actual weight) compared to Bioimpedance methods**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Source** | **N** | **Population** | **Bioimpedance Device\*** | **Mean TBW (L) (Bioimpedance)** | **Difference (L) (BIA-Watson)** | **95% Limits of agreement (L)** |
| Lee, 2001 (41) | 67 | Healthy adults (44 men) | InBody 210 | 34.6 | -1.8 | -6.64, 3.08 |
| Smith, 2002 (24) | 24 | Healthy adults (12 men) | Xitron1 | 39.2 | -0.71 | -6.9, 5.5 |
| Kim, 2005 (42) | 720 | Health Korean subjects, 404 men, 316 women | InBody 10 | 37.9 (male)  28.2 (female) | -1.4  -0.59 | -4.6, 1.8  -3.3, 2.1 |
| Lee, 2001 (41) | 101 | HD Patients (49 men) | InBody 210 | 29.9 | -1.4 | -5.93, 3.19 |
| Chertow, 1997 (19) | 3009 | HD patients | Quantum RJL7 | 40.8 | 4.8 | -1.1, 8.7 |
| Chiu, 2005 (43) | 54 | HD patients | InBody 310 | 32.34 | -2.63 | -13.1, 2.6 |
| Donadio, 2005 (44) | 19 | HD patients (12 men) | STA-BIA SF11  Quadscan MF12 | 39.9  38.8 | -1.72  -1.69 | -7.07, 3.6  -5.8, 2.45 |
| Moissl, 2006 (16) | 54 | HD patients | BCM2 |  | 0.3 | -5.7, 6.3 |
| Davenport, 2011 (45) | 600 | PD patients of mixed ethnicities  Caucasian  South Asian  African/Afro-Caribbean | InBody 720 *or*  BCM1 | 36.4  32.3  36.5 | -0.67  -3.5  0.73 | -1.12, 0.22  -4.1, 3.0  -0.4, 1.86 |
| Kumar, 2013 (46) | 371 | HD patients of mixed ethnicities (225 men) | InBody 72010 | 35.1 | -1.45 | -9.9, 6.66 |
| El-Kateb, 2016 (4) | 118 | PD patients (75 men) | InBody 72010 | 40.6 | 0.72 | -9.2, 10.7 |
| Noori, 2018 (47) | 184 | HD patients (109 men) | BCM1 | 31.1 | -4.6 | -11.6, 2.5 |

\*For sources of bio-impedance devices see footnote to Table 2

**Figure 1**

**Figure 2**

**Figure 3**

**Supplementary Table describing Search Strategy**

|  |  |
| --- | --- |
| **Search term (MeSH)** | **Number of abstracts** |
| Body Water | 15,363 |
| Body Water + deuterium | 742 |
| Body Water + isotope dilution | 439 |
| Body Water + anthropometry | 4495 |
| Body Water + deuterium + electric impedance | 48\* |
| Body Water + isotope dilution + electric impedance | 27\* |
| Body Water + anthropometry + electric impedance | 143\* |
| Body Water + electric impedance + peritoneal dialysis | 76\* |
| Body Water + electric impedance + hemodialysis | 213\* |
| **Final Search Results** (included studies) |  |
| Studies comparing isotope dilution with bioimpedance (ALL) | 20 |
| Studies comparing isotope dilution with bioimpedance (Dialysis) | 11 |
| Studies comparing isotope dilution with anthropometrics (ALL) | 13 |
| Studies comparing isotope dilution with anthropometrics (Dialysis) | 10 |
| Studies comparing anthropometrics with bioimpedance (ALL) | 12 |
| Studies comparing anthropometrics with bioimpedance (Dialysis) | 9 |

\*Full abstracts were read to establish if they compared two or more of the methods (isotope dilution, bioimpedance or anthropometric equations). Abstracts were rejected if they were reviews, non-human studies.

If they fulfilled these criteria the full paper was read and included if they reported limits of agreement (or if this information could be extracted, e.g. from graphs) but not if they only reported different methods (e.g. Mean differences, Root Mean Square Errors)