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Surface-Area-Normalized *Kt/V*: A Method of Rescaling Dialysis Dose to Body Surface Area—Implications for Different-Size Patients by Gender

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Abstract

Dialysis is measured as *Kt/V*, which scales the dose (*Kt*) to body water content (*V*). Scaling dialysis dose to body surface area (S_{dub}) has been advocated, but the implications of such rescaling have not been examined. We developed a method of rescaling measured *Kt/V* to S_{dub} and studied the effect of such alternative scaling on the minimum adequacy values that might then be applied in male and female patients of varying body size. We examined anthropometric estimates of *V* and *S* (Watson vs. Dubois estimates) in 1765 patients enrolled in the HEMO study after excluding patients with amputations. An *S*-normalized target std*Kt/V* was defined, and an adequacy ratio (*R*) was computed for each patient as *R* = *D/N* where *D* = delivered std*Kt/V* (calculated using the Gotch–Leypoldt equation for std*Kt/V*) and *N* = the *S*-normalized minimum target value. In the HEMO data set, we determined the extent to which baseline (prerandomization) std*Kt/V* values would have exceeded such an *S*-based minimum target std*Kt/V*. The median V_{wat}:S_{dub} ratios were significantly higher in men (21.34) than in women (18.50). The average of these (20) was used to normalize the current suggested minimally adequate value (std*Kt/V* ≥ 2.0 / week) to the *S*-normalized target value (std*Kt/S* ≥ 40 *L/M*^{2}), assuming that average modeled *V* = average anthropometric *V*. To achieve this *S*-normalized target, the required single-pool (sp) *Kt/V* was always higher in women than in men at any level of body size. For small patients (V_{wat} = 25*L*), required std*Kt/V* values were 2.05 and 2.21/week for men and women, respectively, corresponding to sp*Kt/V* values of 1.31 and 1.52/session. On the other hand, large (V_{wat} = 50*L*) male patients would need sp*Kt/V* values of only 1.0/session. Prerandomization baseline dialysis sessions in the HEMO study were found to meet such a new *S*-based standard in almost all (766/773) men and in 885/992 women. An analysis of scaling dose to anthropometrically estimated liver size (*L*) showed similar gender ratios for V_{wat}:*L* and V_{wat}:S_{dub}, providing a potential physiologic explanation underpinning *S*-based scaling. *S*-based scaling of the dialysis dose would require considerably higher doses in small patients and in women, and would

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allow somewhat lower doses in larger male patients. Current dialysis practice would largely meet such an *S*-based adequacy standard if the dose were normalized to a V_{wat}:S_{dub} ratio of 20.

Hemodialysis therapy is commonly scaled to the urea distribution volume (*V*). The choice of *V* is governed by the fact that urea, which is distributed in body water, was initially chosen as the marker solute. Elimination of urea by dialysis more or less follows first-order kinetics with an elimination constant equal to *K/V*, where *K* is the dialyzer clearance and *V* is the urea distribution volume, approximately equal to total body water content (1). The product of *K/V*, which can be considered a measure of dialysis intensity, and *t*, the dialysis session length (time), has been accepted as a measure of dialysis dose independent of body size. Concern has been raised about the relatively low dialysis dose (when expressed as *Kt* or liters of plasma cleared) provided to smaller patients and in particular, women (2,3); such patients have relatively low values for*V* compared to body surface area (*S*).

Alternative methods of scaling *Kt/V* have been proposed, including no scaling, providing the same *Kt* to all patients (4), scaling*Kt* to*S* (5), or scaling *Kt* to basal metabolicrate (6,7).Scaling to visceral mass as the presumptive source of uremic toxins has also been proposed. (8). Native kidney function is measured as the glomerular filtration rate (GFR).In a recent study, some of us examined the impact of scaling native kidney GFR, measured with ^{125}iothalamate, to anthropometric estimates of *V* or *S* in healthy kidney donors. When men were compared with women, GFR/*S* values were similar in men and women, but GFR/*V* values were substantially different (9).

One problem with scaling dialysis dose (*Kt*) to *S* is that currently, in most dialysis centers in the United States.*Kt/V* is measured, instead of *Kt*, with *Kt/V* calculated from the ratio pre/post BUN weight change during dialysis, and session length; *V* and *Kt* cannot easily be disentangled without accurate measures of dialyzer clearance. Direct, reliable measures of *Kt* are becoming available from dialysis machines with conductivity-measuring devices, but their presence is not yet universal. Thus, monthly measurements of the blood urea reduction ratio from which *Kt/V* measurements are derived remain the current standard. Given this reality, we attempted to develop an algebraic method of putting a “wrapper” around the delivered *Kt/V* in order to “rescale” *Kt/V* to anthropometric estimates of *S*. We further examined the implications of surface-area-based scaling to KDOQI-recommended minimum values for session (3/week) and standard *Kt/V*, based on the relationships among anthropometric estimates of *V* and *S* observed in patients studied prior to randomization in the HEMO study.

Materials and Methods

Anthropometric and modeling data were drawn from a prerandomization modeling session performed in 1846 patients who were accepted into the baseline phase of the HEMO study (10). The characteristics of these patients have been described previously (10). Both men and women were well represented, the mean age of the patients was 57.6 (14.0) years, and African Americans made up 62.6% of the study population. For this analysis, 81 patients with amputations were excluded, leaving 1765 for analysis. For each subject, body surface area was computed from postdialysis weight and height measured during the baseline period using the equations of Dubois and Dubois (11). Anthropometric *V* (V_{wat}) was determined from the Watson equations for men and women (12). Equations of the form $S = aV^b$ were fit by applying orthogonal regression (13) to relate logarithmically transformed values of *S* and *V* separately for men and women. These regression equations were used to calculate expected ratios of *V:S* when *V* = 25, 30, 35, 40, 45, and 50 l. A value close to the average of the median values in men and women for *V:S* ratio, namely $20 L/M^2$ was used as a normative ratio to calculate target std*Kt/S* values corresponding to a std*Kt/V* value of 2.0.

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The std*Kt/V* was computed for each patient from single-pool *Kt/V*, dialysis session length (*t*), and dialysis frequency (*N*) using a modification of the Leypoldt equation (14) as described in the KDOQI 2006 guidelines (15).

$$\mathrm{std}Kt/V = \frac{10080\frac{1-e^{-eKt/V}}{t}}{\frac{1-e^{-eKt/V}}{\mathrm{sp}Kt/V}+\frac{10080}{Nt}-1}$$

The equilibrated *Kt/V* (e*Kt/V*) was computed from sp*Kt/V* using the Tattersall equation (16):

$$eKt/V = \mathrm{sp}Kt/V(t/(t+35))$$

where *t* is dialysis session length in minutes. For each patient, an "adequacy ratio" (*R*) was computed as *D/N*, where *D* is the delivered std*Kt/V*, and *N* the *S*-normalized minimum target std*Kt/V*. The latter was calculated as:

$$N = 2.0 \times 20 \times S_{dub}/V_{wat}$$

where 2.0 is the current std*Kt/V* minimum standard, 20 is the normalizing V_{wat}:S_{dub} ratio (described in the Results section), and S_{dub} and V_{wat} are the Dubois and Watson estimates of surface area and body water, respectively, calculated for each patient based on weight, height, gender, and age. *R* was then plotted against the sp*Kt/V* for both men and women to determine the extent to which dialysis doses delivered to HEMO patients before randomization would meet the new *S*-normalized target (*N*).

The exponential regressions of S_{dub} vs. V_{wat} were then used to compute estimated V_{wat}:S_{dub} values in men and women when *V* is 25–50*L*, and these values were used to compute the average std*Kt/V* as well as 3/week session sp*Kt/V* that would be required to achieve *S*-normalized minimum target values of std*Kt/V* for each value of *V*. The relationship between sp*Kt/V* and std*Kt/V* is dependent on session length (*t*). In determining the required sp*Kt/V* values for patients with V_{wat} levels of 25–50*L*, values for *t* were derived based on an estimated dialyzer clearance of 250 ml/minute. The session length was set accordingly unless it was less than 180 minutes; in such a case a 180 minute session length was used.

Results

Relationship between Dubois *S* and Watson *V*

These results are shown in Fig. 1. The median values for Watson *V* were 38.85 and 31.07*L* for men and women, respectively. The corresponding median values for Dubois *S* were 1.82 and 1.68. Exponential regressions of the form $S = aV^b$ fit the data well, with coefficients for men (a = 0.104, b = 0.770) and women (a = 0.085, b = 0.866) being substantially different.

In Fig. 2, the same data are replotted as V_{wat}:S_{dub} vs. V_{wat}. As can be seen, the V_{wat}:S_{dub} ratio increases with increasing body size (the latter expressed as V_{wat}), but the ratios are different between the genders, with median values of 21.34 in men and 18.50 in women. The average of these two numbers is close to 20, and this value was used as the normalizing factor to adjust the dialysis dose from a *V*-based approach to *S*-based scaling.

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Extent to Which HEMO Prerandomization Therapy Would Meet the New Target

In the HEMO study, baseline (prerandomization) values for the adequacy ratio, *R*, calculated as described in the Materials and Methods section, are shown in Fig. 3 for men and in Fig. 4 for women, each plotted against delivered sp*Kt/V*. It is clear that in most instances, the std*Kt/V* that was delivered to these patients prior to randomization would still exceed an *S*-based minimum target defined in this way, as *R* was ≥1.0 in almost all men and in the great majority of women. However, in men this occurred when sp*Kt/V* > 1.05/ session, whereas in women, a considerably higher level of sp*Kt/V* was required, approximately 1.5/session. A nonnegligible percentage of the women patients, especially those with sp*Kt/V* < 1.5, would not meet the minimum *S*-normalized std*Kt/V* target (e.g., *R* < 1.0).

Calculation of Minimum Required Values for std*Kt/V* Based on Body Size and Gender

Using the regression equations for S_{dub} vs. V_{wat}, predicted average V_{wat}:S_{dub} ratios were estimated in men and women for values of *V* ranging from 25 to 50 l. These were used to compute values for the *S*-normalized minimum target values (*N*) for std*Kt/V* according to gender and size (*V*). These results are shown in Table 1.

These results are plotted graphically in Fig. 5 and Fig. 6. Required std*Kt/V* values range from 8%to 13% higher in women than in men, with the increase across genders becoming greater with larger body size. When considering required session *Kt/V* values, the results are very session-length dependent, but again, are 16–19% higher in women than in men. For very small patients, the required sp*Kt/V* targets are in the range of 1.31 formen, and 1.52 for women. In large (e.g., V_{wat} = 50*L*) male patients, this method of *S*-normalization suggests that session sp*Kt/V* values ≥1.0may be sufficient (Fig. 6).

Discussion

Our results describe a method of moving from a *V*-based system of dialysis dosing, which is required if uremic toxin generation rate were to scale to total body water volume, to one in which the dose of dialysis is normalized to anthropometric body surface area. If this approach were accepted, such an adjustment would obligate a higher dose of dialysis for smaller patients, and an additional across the board increase in dialysis dose for women. Also, it would allow a somewhat reduced dose of dialysis in men.

The practical implications of *S*-based dosing can be seen in Fig. 5 and Fig. 6, where values from Table 1 and Table 2 are plotted in the form of a nomogram. They show the minimum std*Kt/V* and 3/week session sp*Kt/V* values that would be required. This computation involves at least three assumptions: (i) that KDOQI minimums apply to an average size patient, with a V_{wat}:S_{dub} ratio of 20, (ii) that the dialysis dose for patients of other sizes and gender should be equivalent to this normative patient in terms of body surface area, and (iii) that modeled and anthropometric *V* are identical or at least that the relationships between modeled *V* and S_{dub} are similar to those between V_{wat} and S_{dub}. The analysis suggests that this method of *S*-normalization, when applied to a continuous clearance like std*Kt/V*, would require a 16–19% higher session sp*Kt/V* (3/week) for women vs. men of the same anthropometric body surface area as well as higher *Kt/V* values for smaller patients.

While the relationship between required session sp*Kt/V* and body size and gender shown in Fig. 6 is the consequence of *S*-adjustment, the actual values of sp*Kt/V* depend on the particular V_{wat}:S_{dub} normalization factor that is chosen. In the current *S*-normalization strategy, a V_{wat}:S_{dub} ratio of 20 was chosen, close to the average of the median value in men and the median value in women. This resulted in a lower recommended minimal sp*Kt/V* in larger men than current KDOQI guidelines. For example, the minimum target std*Kt/V* for a male with

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V_{wat} = 40*L* is 1.848 /week, with a corresponding sp*Kt/V* of 1.1/session when three sessions per week are being given. One could normalize all values to a V_{wat}:S_{dub} ratio of 21.4, close to the median value in men. This would increase the std*Kt/V* minimum targets by 21.4/20 = 1.07, or 7%. This would bring the std*Kt/V* target for a male with V_{wat} = 40*L* up to the more familiar 1.98/week, and sp*Kt/V* close to 1.2/session. However, it would also raise the std*Kt/V* target for a small woman with $V_{wat} = 25_L$ (one can think of this as moving the nomogram curves in Fig. 5 and Fig. 6 to the right), such that an sp*Kt/V* value greater than 1.7/session would be required.

Another issue with these proposed minimum targets is the method used to compute standard *Kt/V*. For the purposes of this paper, we have been using the Gotch–Leypoldt simplified equation as modified by theKDQOI 2006 update (14,15). When using this equation, an sp*Kt/V* of 1.2 with a 3/week schedule and a 240 minute session length translates into a std*Kt/V* of 2.0. For this reason, in the KDOQI clinical practice recommendations, a std*Kt/V* of at least 2.0 was suggested to guide treatment in patients with residual renal function and when using other than 3/week schedules. Recently, some of us have analyzed the performance of this simplified equation against std*Kt/V* derived from formal two-pool modeling (where weekly traces of serum urea nitrogen vs. time were generated) and found that it underestimates modeled std*Kt/V* by about 8%, on average (17). There is a simple fix: multiplying the old std*Kt/V* by $1/(1 - 0.9 \times Qf \times t/V)$, where *Qf* is the ultrafiltration rate in ml/minute, *t* is the session length in minutes, and *V* is the urea distribution volume in ml. Were this new equation to be used, the values of std*Kt/V* would, on average, increased by 7–8%. With the new formula, for someone in whom $Qf \times t/V$ = ~0.08 (for example, 2800 ml of fluid removal in a patient with *V* = 35,000 ml), the std*Kt/V* value corresponding to an sp*Kt/V* of 1.2 given over 240 minutes 3/week becomes about 2.16 instead of 2.0. So with the new formula, the *S*-normalized target (*N*) would also need to be increased proportionately, from = $2.0 \times 20 \times S_{dub}/V_{wat}$ to = $2.16 \times 20 \times S_{dub}/V_{wat}$. The net result would be that the std*Kt/V* values in Table 1 would all go up by 7–8%, but the sp*Kt/V* values in Table 2 would remain largely unchanged.

One issue with any new proposed dialysis standard is to what extent it would be achievable in current practice. Analysis of baseline (prerandomization) modeling sessions in HEMO study patients shows that the amount of therapy delivered would have largely met such a new *S*-based adequacy standard (normalizing to V_{wat}: S_{dub} = 20). This occurred because in practice higher amounts of sp*Kt/V* are routinely delivered to women and to small patients. For example, only 7 of 772 male patients were below the proposed *S*-normalized minimum target (*D/N*) ratio of 1.0, and in 3 of these, the ratio was above 0.98. An sp*Kt/V* of 1.05 or so was sufficient to ensure that the *S*-normalized target would be consistently met (Fig. 3). In contrast, in the women patients, 107 of 992 patients were below a *D/N* ratio of 1.0. Admittedly, many of these were very close to 1.0, but from Fig. 4, it is clear that an sp*Kt/V* of 1.5 is required to insure that such a new *S*-normalized target is being consistently met, although a considerable percentage of women with sp*Kt/V* in the range of 1.3–1.5 were able to meet the new target as well.

Are there any outcomes data that suggest that women and/or smaller patients may be relatively underdialyzed, to the point that they have a worse outcome? A large, cross-sectional study of the dialysis dose vs. mortality relationship by Owen et al. suggested that there was a gender difference, with dose impacting mortality more strongly in women than in men (2). Lowrie et al. published a number of cross-sectional analyses of dialysis dose vs. mortality, and their conclusions were that *Kt/V* may be giving too little dialysis to smaller patients (4,5). They also suggested normalizing dialysis dose to body surface area (5).

The NIH HEMO trial compared mortality in patients dialyzed to urea reduction percentages of approximately 63% vs. 75% (corresponding to equilibrated *Kt/V* values of 1.05 and 1.45). Mortality was similar in the two randomized groups (10) but women randomized to the higher dose of dialysis survived better than those in the lower dose group (3). Subsequent to the release

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of the data showing a gender effect in the HEMO trial, analysis of the USRDS data revealed a concordant effect—mortality was lower at higher dose in women, but not nearly so much in men (18). So there are data from a randomized trial as well as data from observational studies suggesting that women may benefit from more dialysis than currently recommended doses that are indexed by *V*.

On the other hand, the data suggesting that women and smaller patients are relatively underdialyzed are not strong or necessarily consistent. The HEMO study analysis by gender is subject to the standard limitations of subgroup analyses in randomized trials, and may have represented a Type I error (i.e., a false-positive result) in the context of several subgroup analyses that were performed for this trial (3). Moreover, in the HEMO analysis by gender cited above, the gender effect of randomized dose could not be linked to any of multiple measures of body size. When the dose effect on outcome was controlled for body size, a gender effect remained, but when controlled for gender, the body size effect was no longer significant (3). Analysis of observational data purporting to show a link between gender or body size and the effect of dose on outcome is fraught with the confounding effects of delivered dose on mortality, the so-called “dose-targeting bias” (19). Analysis of delivered doses in the HEMO trial also showed that dose targeting bias was stronger in women than in men (19),making interpretation of gender effects on dose vs. outcome in cross-sectional studies problematic. Nevertheless, examination of delivered dose in the HEMO study (10) shows that delivered dose in the standard-dose group was close to an sp*Kt/V* of 1.3. It is clear from an examination of Fig. 3 and Fig. 4 that, whereas almost all men with an sp*Kt/V* of 1.3 would be above the new *S*-normalized minimum target, most of the women would fall below the $R = 1.0$ line. Whether this might explain the discrepant results in outcomes between men and women (3) is amatter of conjecture.

Another issue is the question of modeled *V* vs. anthropometric *V*. The present analysis makes an assumption that they are equal, whereas experimental data suggest that the modeled urea volume may be only about 85% of the anthropometric total body water estimate (20). This will not affect the relative changes in dialysis dose when moving to a surface-based analysis, as long as the relationships between modeled $V{:}S_{dub}$ and $V_{wat}{:}S_{dub}$ are similar and first order. However, this relationship is important if one were to move from a urea-modeled approach (corrected or not for body surface area) to a completely anthropometric approach, where only *Kt* is measured, and where the only denominator is either anthropometric *V* or anthropometric *S*.

Other denominators have been considered. One proposal is to scale GFR, as well as dialysis dose, to the patient’s metabolic rate rather than *V* or *S* (6,7,21). When scaling to body surface area, the assumption is that a man and woman of the same height and weight will require the same GFR or *Kt*. But when scaling to metabolic rate this is no longer true, as men have consistently higher metabolic rates than women of the same body size. So if *Kt* were scaled to metabolic rate, the gender effect, so prominent with *S*, would be reduced. Also, physiologically, it may not be likely that metabolism per se requires a higher GFR, especially metabolism of tissues that are simply oxidizing carbohydrates and fats, such as muscle. There is little evidence that activity level substantially affects GFR, an observation not in keeping with an important role of metabolic rate in determining GFR among humans.

Another approach is to scale the dialysis dose to visceral body mass (8), as the latter may best predict the generation rate of uremic toxins, assuming that control of toxin concentrations is the ultimate goal of dialysis. The visceral mass represents a greater portion of the body weight in small patients, and is also a greater portion of the body water in women than in men (8).

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One additional, focusing hypothesis might be that the main organ contributing uremic toxins is specifically the liver, as this is where compounds are detoxified and solubilized, and this is a major site of metabolism of nitrogenous compounds. The liver accounts for only about 20% of the resting energy expenditure (22), so scaling dialysis dose to metabolic rate vs. to liver size or functional activity may not be equivalent strategies. One could therefore assume that liver function is related to its size, and to scale dialysis to liver size. Many authors have developed anthropometric equations predicting liver size from body height and weight (23–25). In most of these equations, liver size is simply a function of body surface area and is not gender dependent (23,24), although in one study liver size was gender dependent in patients younger than 50 years of age (25). We did examine the relationship of predicted liver (*L*)mass (in grams) or volume (in ml) and the ratio of V_{wat}:*L* in men vs. women, using the same baseline HEMO data set as described in the Materials and Methods section. The results are presented in Table 3 and are compared with the ratio of V_{wat}:S_{dub}. For a comparison of liver size and other alternative rescaling measures, see the accompanying article in this issue (26).

It can be seen that in general, the ratio of median values of V_{wat}:*L* between men and women, regardless of the equation used, is similar to the gender ratio of the median values of V_{wat}:S_{dub}. This means that, for any level of *V*, a woman will have a larger estimated liver size, as well as a larger body surface area, compared to a similarly sized male. Thus, liver size may be a physiological underpinning explaining why scaling both GFR and dialysis dose to *S* is a more appropriate strategy than scaling to *V*.

In summary, the present data identify a practical method of rescaling the dose of dialysis from a system based on urea distribution volume, *V*, to one based on body surface area. Rescaling to surface area would obligate more dialysis for smaller patients, more dialysis for women, and potentially, less dialysis for larger, male patients. The present analysis can be used as a guide to estimate how much more dialysis might be indicated as a minimum for women and for small patients and might be used to justify slightly less dialysis for larger male patients. However, additional research may be required before the current minimum targets for hemodialysis dosing are revised. Assuring that current standards are sufficient for all major dialysis subpopulations should be a high priority goal for future quality improvement efforts.

References

1. Gotch FA. Kinetics of solute removal in hemodialysis. Adv Exp Med Biol 1987;223:227–237. [PubMed: 3328954]
2. Owen WF Jr, Chertow GM, Lazarus JM, Lowrie EG. Dose of hemodialysis and survival: differences by race and sex. JAMA 1998;280:1764–1768. [PubMed: 9842952]
3. 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. Hemodialysis Study Group: Dialysis dose and the effect of gender and body size on outcome in the HEMO Study. Kidney Int 2004;65:1386–1394. [PubMed: 15086479]
4. Lowrie EG, Li Z, Ofsthun N, Lazarus JM. Body size, dialysis dose and death risk relationships among hemodialysis patients. Kidney Int 2002;62:1891–1897. [PubMed: 12371994]
5. Lowrie EG, Li Z, Ofsthun N, Lazarus JM. The online measurement of hemodialysis dose (*Kt*): clinical outcome as a function of body surface area. Kidney Int 2005;68:1344–1354. [PubMed: 16105070]
6. Singer MA. Of mice and men and elephants: metabolic rate sets glomerular filtration rate. Am J Kidney Dis 2001;37:164–178. [PubMed: 11136185]
7. McKnab, BK. Water and Salt Exchange in Terrestrial Vetebrates. Ithaca, NY: Cornell University Press; 2002. The Physiological Ecology of Vertebrates: A View from Energetics Chapter 7; p. 205
8. Sarkar SR, Kuhlmann MK, Kotanko P, Zhu F, Heymsfield SB, Wang J, Meisels IS, Gotch FA, Kaysen GA, Levin NW. Metabolic consequences of body size and body composition in hemodialysis patients. Kidney Int 2006;70:1832–1839. [PubMed: 17021607]

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9. Daugirdas JT, Meyer KH, Greene T, Poggio E. Scaling of iothalamate GFR in kidney donor candidates by anthropometric estimates of body surface area,metabolic rate, or body water: Gender equivalence when scaling to body surface area, but not to the others. ASN Abstr. 2008(in press)
10. 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. Hemodialysis (HEMO) Study Group: Effect of dialysis dose and membrane flux in maintenance hemodialysis. N Engl J Med 2002;347:2010–2019. [PubMed: 12490682]
11. Dubois D, Dubois EF. A formula to estimate the approximate surface area if height and weight be known. Arch Intern Med 1916;17:863–871.
12. 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. [PubMed: 6986753]
13. Fuller, W. Measurement Error Models. Section 1.3: Ratio of Measurement Variances Known. New York: Wiley; 1987. p. 30-49.
14. Leypoldt JK, Jaber BL, Zimmerman DL. Predicting treatment dose for novel therapies using urea standard *Kt/V*. Semin Dial 2004;17:142–145. [PubMed: 15043617]
15. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis 2006;48:S2–S90. [PubMed: 16813990]
16. Tattersall JE, DeTakats D, Chamney P, Greenwood RN, Farrington K. The post-hemodialysis rebound: predicting and quantifying its effect on *Kt/V*. Kidney Int 1996;50:2094–2012. [PubMed: 8943495]
17. Depner TA, Daugirdas JT, Greene T, Schulman G. for the FHN Trial Network: Improved simplified formula for estimating hemodialysis standard *Kt/V*-urea. ASN Abstr. 2008(in press)
18. Port FK, Wolfe RA, Hulbert-Shearon TE, McCullough KP, Ashby VB, Held PJ. High dialysis dose is associated with lower mortality among women but not among men. Am J Kidney Dis 2004;43:1014–1023. [PubMed: 15168381]
19. Greene T, Daugirdas J, Depner T, Allon M, Beck G, Chumlea C, Delmez J, Gotch F, Kusek JW, Levin N, Owen W, Schulman G, Star R, Toto R, Eknoyan G. Hemodialysis Study Group: Association of achieved dialysis dose with mortality in the hemodialysis study: an example of “dose-targeting bias”. J Am Soc Nephrol 2005;16:3371–3380. [PubMed: 16192421]
20. Daugirdas JT, Greene T, Depner TA, Chumlea C, Rocco MJ, Chertow GM. Hemodialysis (HEMO) Study Group: Anthropometrically estimated total body water volumes are larger than modeled urea volume in chronic hemodialysis patients: effects of age, race, and gender. Kidney Int 2003;64:1108–1119. [PubMed: 12911564]
21. Morton AR, Singer MA. The problem with *Kt/V*: dialysis dose should be normalized to metabolic rate not volume. Semin Dial 2007;20:12–15. [PubMed: 17244112]
22. Gallagher D, Belmonte D, Deurenberg P, Wang Z, Krasnow N, Pi-Sunyer FX, Heymsfield SB. Organ-tissue mass measurement allows modeling of REE and metabolically active tissue mass. Am J Physiol 1998;275(2 Pt 1):E249–E258. [PubMed: 9688626]
23. Heinemann A, Wischhusen F, Püschel K, Rogiers X. Standard liver volume in the Caucasian population. Liver Transpl Surg 1999;5:366–368. [PubMed: 10477836]
24. Yoshizumi T, Gondolesi GE, Bodian CA, Jeon H, Schwartz ME, Fishbein TM, Miller CM, Emre S. A simple new formula to assess liver weight. Transplant Proc 2003;35:1415–1420. [PubMed: 12826175]
25. Choukèr A, Martignoni A, Dugas M, Eisenmenger W, Schauer R, Kaufmann I, Schelling G, Löhe F, Jauch KW, Peter K, Thiel M. Estimation of liver size for liver transplantation: the impact of age and gender. Liver Transpl 2004;10:678–685. [PubMed: 15108261]
26. 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 2008:377–384. [PubMed: 18945324]

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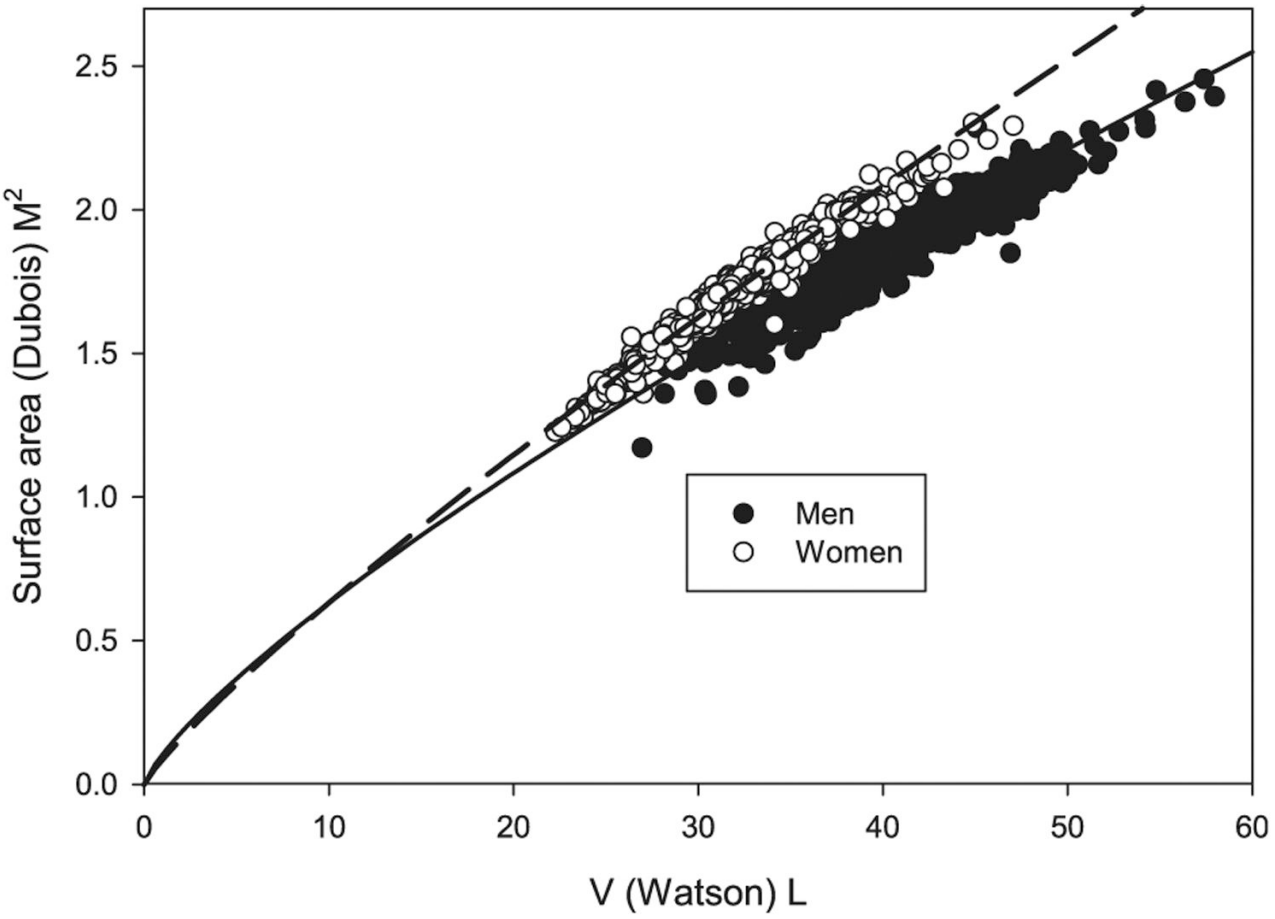

Fig. 1.
Plot of Dubois *S* vs. Watson *V*. Equations of the form $S = aV^b$ were used to fit the data. Coefficients for *a* were 0.104 and 0.085 and for *b* were 0.780 and 0.866 for men and women, respectively.

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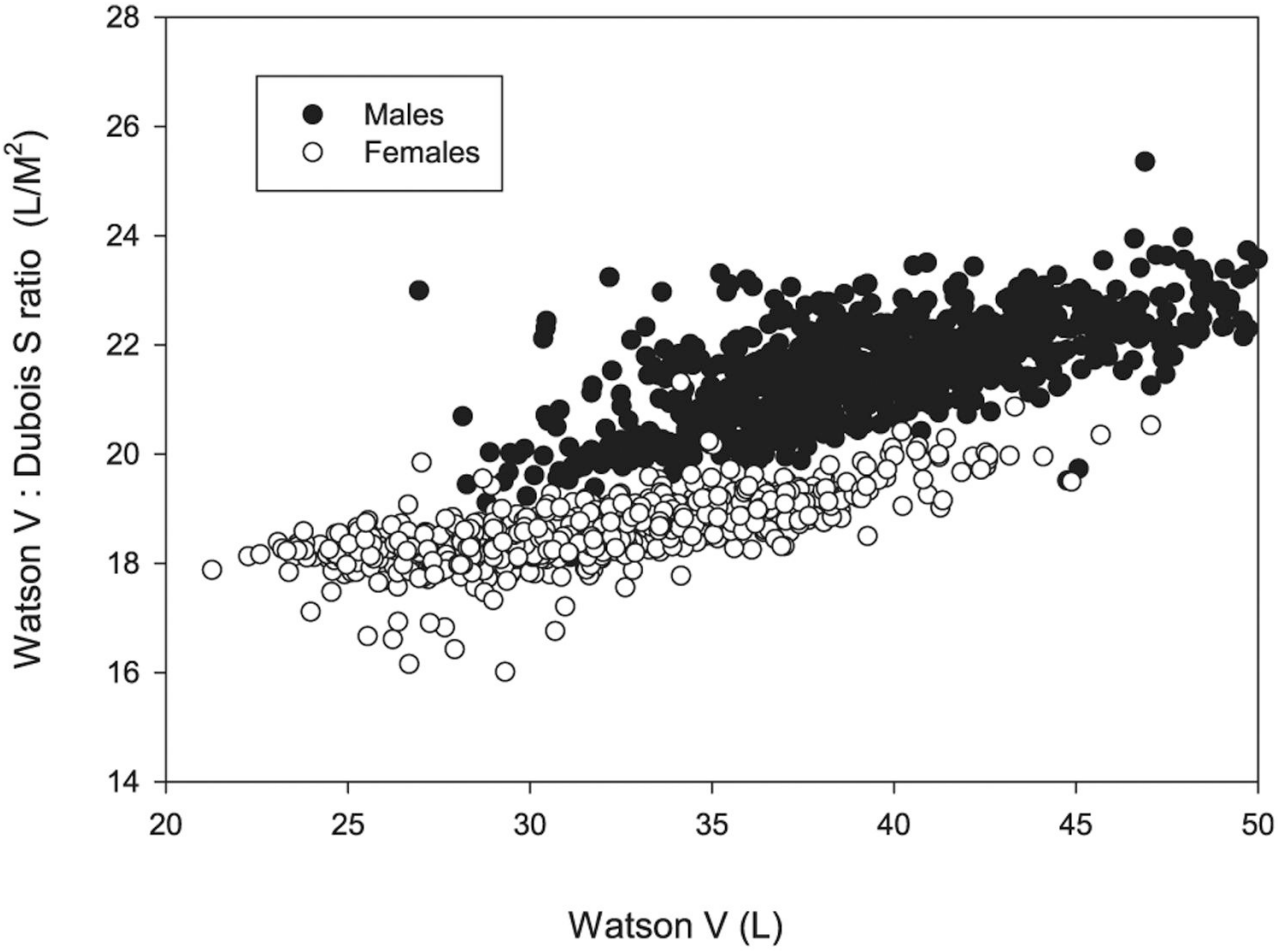

Fig. 2.
Relationship of V_{wat}:S_{dub} ratio to V_{wat} (by gender), The relationships were close to linear, V_{wat}:S_{dub} increased as V_{wat} increased, and V_{wat}:S_{dub} was higher in men than in women.

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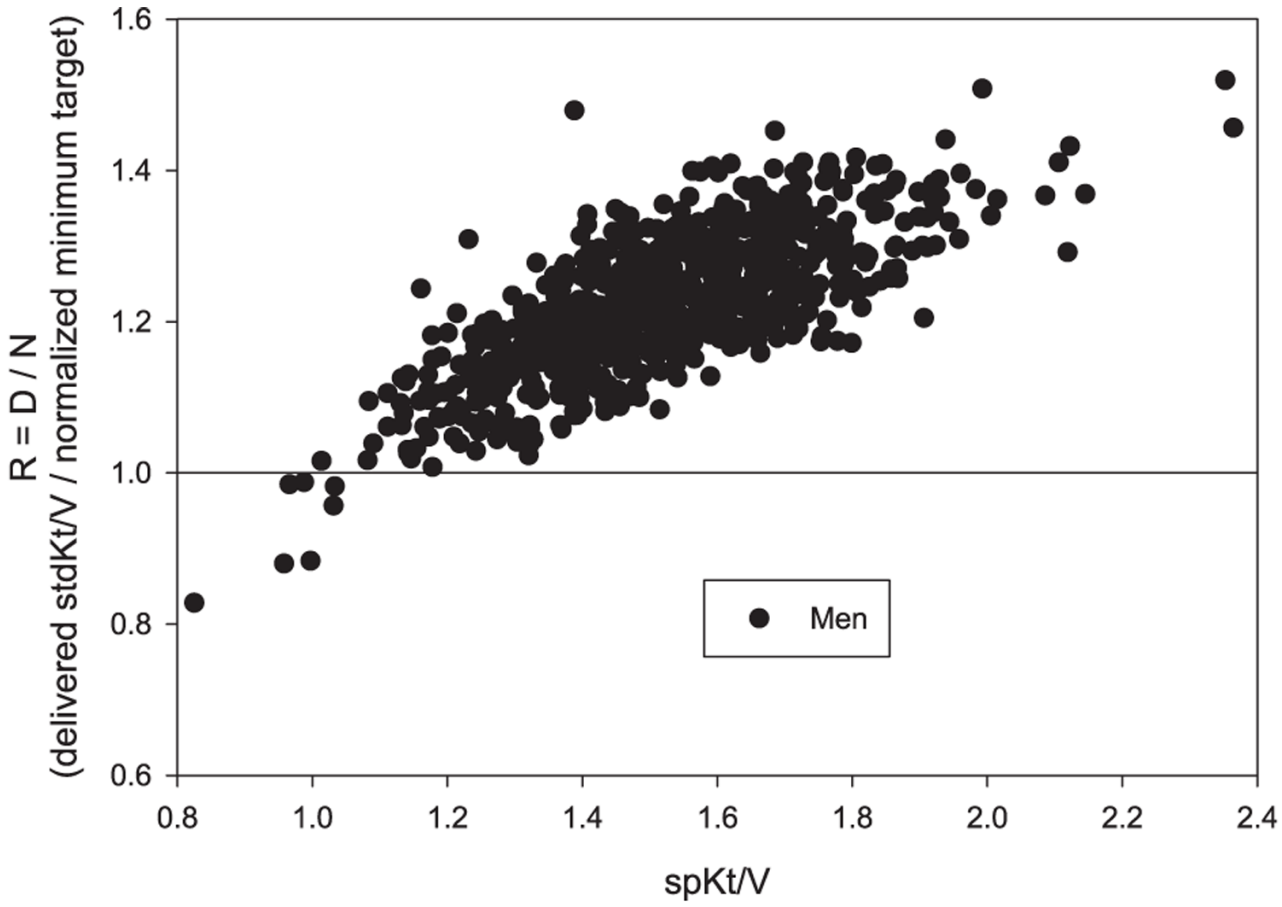

Fig. 3.

Plot of adequacy ratio *R* (delivered std*Kt/V* divided by *N*, the *S*-normalized minimum target std*Kt/V*) in the HEMO baseline patients (men) against sp*Kt/V*. *D* was computed using the fixed volume Gotch–Leypoldt std*Kt/V* equation. The normalized target (*N*) = 40 × S_{dub}/V_{wat}. The data show that almost all men (766/773) would achieve the new target, and that a minimum sp*Kt/V* value in the range of 1.05 was all that was required.

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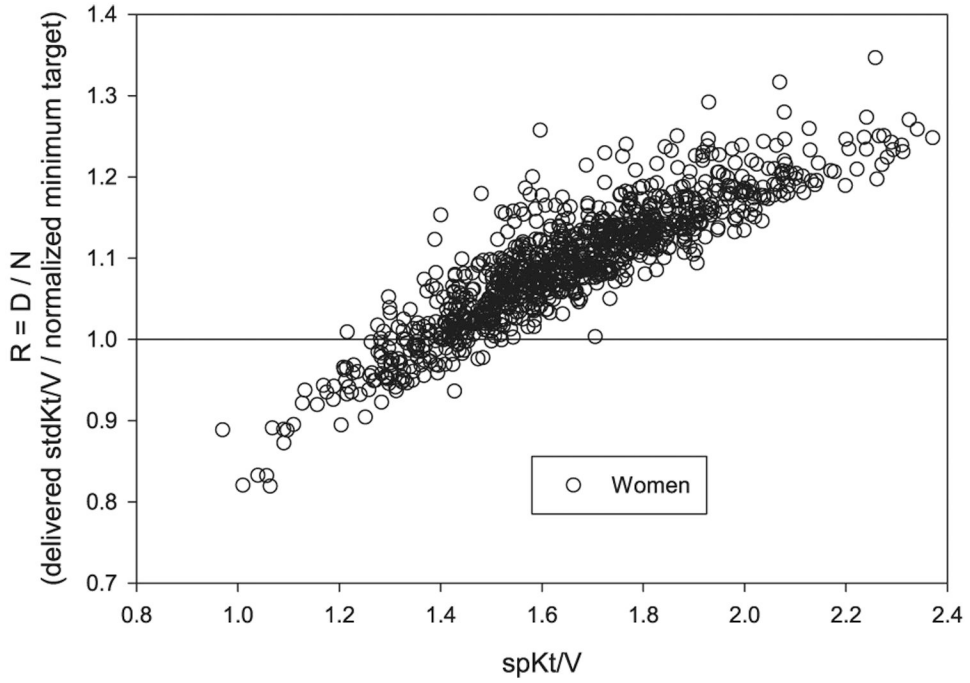

Fig. 4.

Plot of adequacy ratio *R* (delivered std*Kt/V* divided by *N*, the *S*-normalized target std*Kt/V*) in the HEMO baseline patients (women) against sp*Kt/V*. The data show that almost all women (885/992) would achieve the new *S*-normalized minimum target, but that an sp*Kt/V* value of 1.5 or higher would be necessary.

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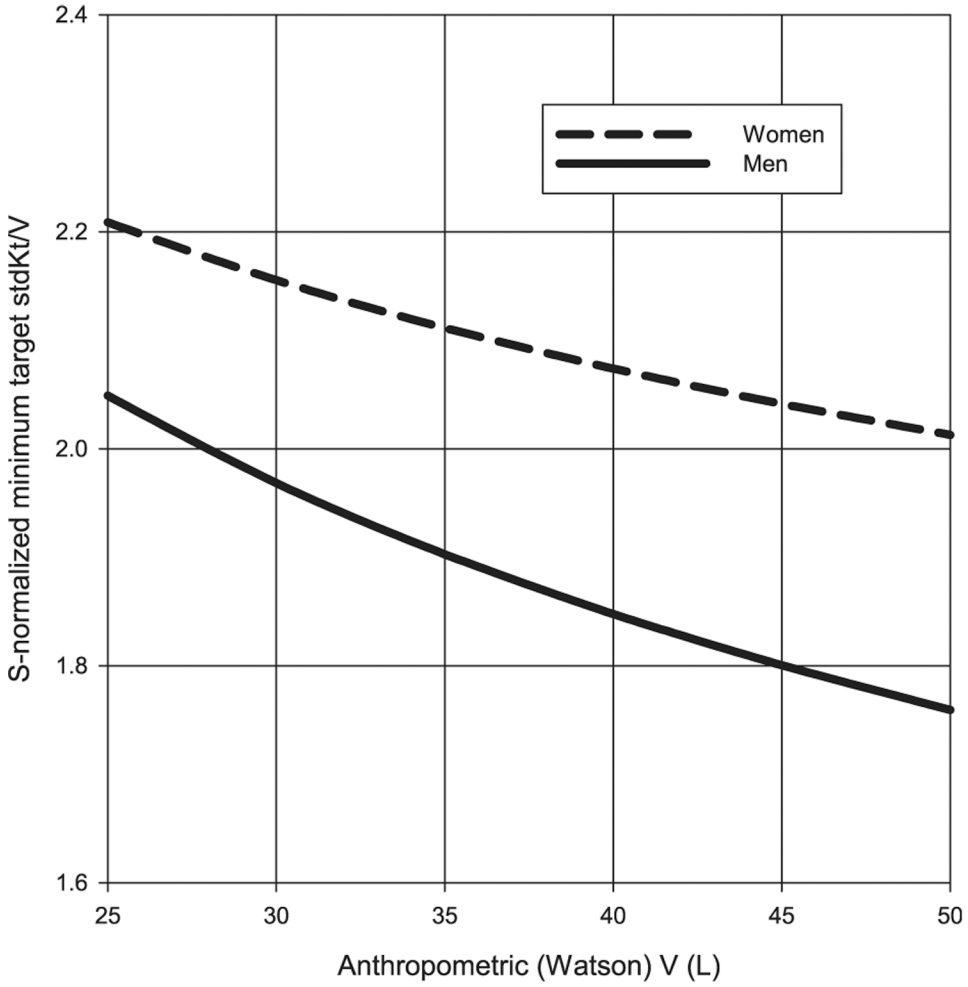

Fig. 5.

Predicted *S*-normalized std*Kt/V* minimum targets in men and women based on body size, with the latter expressed in terms of Watson *V*. This assumes that std*Kt/V* is being calculated using the fixed-volume Gotch–Leypoldt simplified equation (see text for details).

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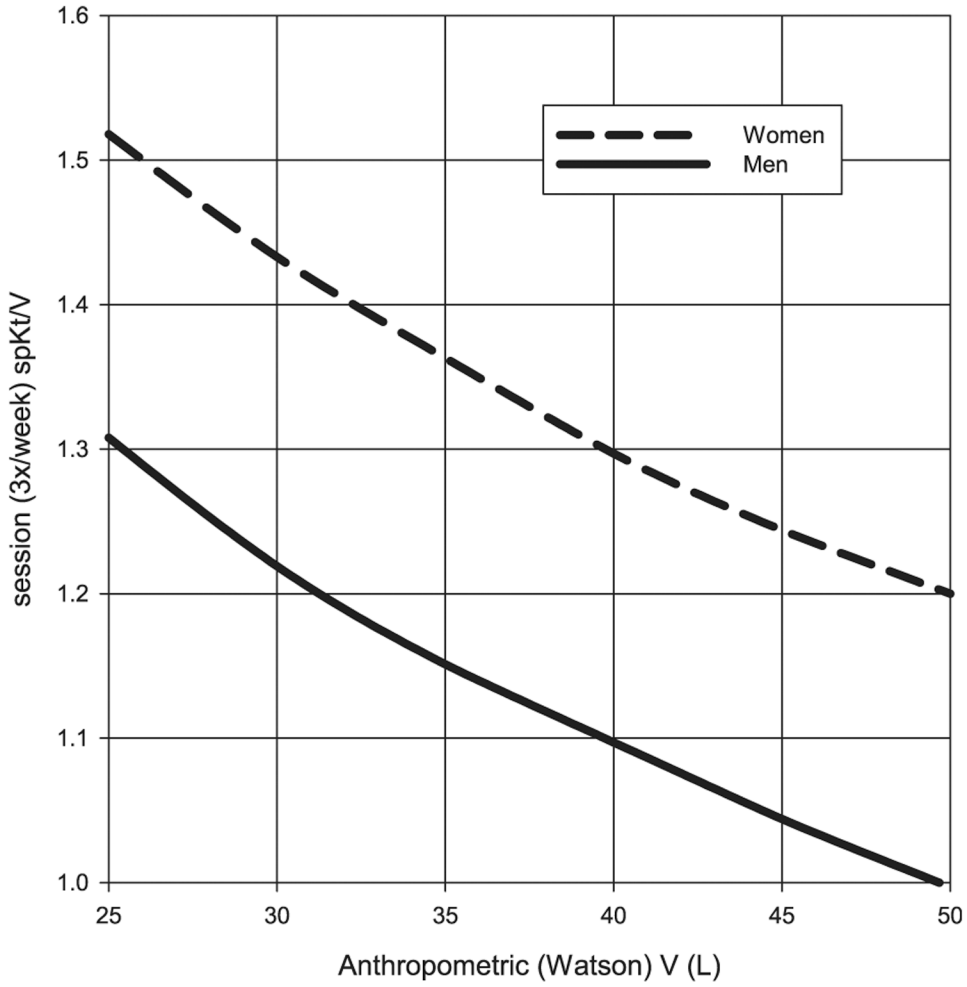

Fig. 6.

Session (3/week) sp*Kt/V* values that would be required to achieve the *S*-normalized std*Kt/V* minimum targets shown in Fig. 5. Session length was set as 180 minutes or higher; in the latter case, session length used to calculate std*Kt/V* corresponded to a dialyzer clearance of 250 ml/minute.

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TABLE 1

S-normalized minimum target std*Kt/V* values (*N*) by body size and gender

Watson *V*	**25**	**30**	**35**	**40**	**45**
Men	2.049	1.968	1.902	1.848	1.800
Women	2.209	2.155	2.111	2.074	2.041

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TABLE 2

Session (3/week) sp*Kt/V* values by body size and gender required to achieve values of *N* shown in Table 1

Watson *V*	**25**	**30**	**35**	**40**	**45**
Men	1.308 (180)[a]	1.219 (180)	1.151 (180)	1.097 (180)	1.044 (188)
Women	1.518 (180)	1.433 (180)	1.363 (191)	1.297 (208)	1.244 (224)

[a]Values in parentheses reflect the session length (minutes) used to calculate the std*Kt/V*.

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TABLE 3

V_{wat}:*S* and V_{wat}*L* in baseline HEMO patients and their ratios in men vs. women

Ratio	Equation	Men (median)	Women (median)	Men/women[a]
$V_{wat}S_{dub}$	Watson,Dubois	21.34	18.50	1.153
$V_{wat}L$ (l/ml)	Heinemann (23)	0.0244	0.0215	1.135
$V_{wat}L$ (l/g)	Yoshizumi (24)	0.0279	0.0240	1.162
$V_{wat}L$ (l/g)	Chouker (25)	0.0222	0.0189	1.175

[a]Median ratio inmen divided by the median ratio in women.