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Peritoneal urea and creatinine clearances in continuous peritoneal dialysis patients with different types of peritoneal solute transport

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Peritoneal clearances in peritoneal dialysis patients with different peritoneal transport types. We studied whether anuric subjects on continuous ambulatory peritoneal dialysis (CAPD) who achieve the target Kt/V urea of 2.0 weekly will also achieve the target normalized creatinine clearance (NC_{Cr}) of 60 liter/1.73 m^2 weekly, and the reasons of discrepancy between the two clearances in anuric subjects, by analyzing 476 clearance studies performed in 309 CAPD patients within 12 months of the performance of a peritoneal equilibration test (PET). On the basis of the PET, peritoneal solute transport was classified as low (37 clearance studies), low-average (199 studies), high-average (186 studies) and high (54 studies). We found that weekly values of Kt/V urea in the low transport group (LTG) was 1.74 ± 0.51, in the low-average transport group (LATG) was 1.66 ± 0.41, in the high-average transport group (HATG) 1.68 ± 0.41, and in the high transport group (HTG) 1.73 ± 0.46 (NS, variance analysis). Weekly values for NC_{Cr}, liter/1.73 m^2 were: LTG, 37.8 ± 9.0; LATG, 44.0 ± 9.2; HATG, 49.2 ± 10.0; HTG 56.8 ± 13.3 ($P <$ 0.0001). The ratios of raw (not-normalized) peritoneal creatinine clearance to peritoneal urea clearance were: LTG, 0.65 ± 0.14; LATG, 0.76 ± 0.09; HATG, 0.84 ± 0.09; HTG, 0.91 ± 0.12 ($P <$ 0.0001). Linear regression with Kt/V urea as x and NC_{Cr} as y revealed the following results: LTG, y = 19.486 + 10.500x, r = 0.591 [if x = 2.0, y = 40.5, 95% confidence interval (95% CI) of y 25.3 to 55.7]; LATG, y = 15.004 + 17.482x, r = 0.774 (if x = 2.0, y = 50.0, 95% CI of y 38.4 to 61.6); HATG, y = 15.285 + 20.162x, r = 0.829 (if x = 2.0, y = 55.6, 95% CI of y 44.4 to 66.8); HTG, y = 14.945 + 24.134x, r = 0.839 (if x = 2.0, y = 63.2, 95% CI of y 48.4 to 78.1). Peritoneal solute transport type has a major effect on peritoneal creatinine clearance, but an insignificant effect on peritoneal urea clearance. Consequently, the majority of anuric patients who achieve a weekly Kt/V urea of 2.0 will have a weekly NC_{Cr} lower than 60 liter/1.73 m^2 and will require a Kt/V urea much higher than 2.0 to achieve the target NC_{Cr} of 60 liter/1.73 m^2 weekly. The current targets of urea and creatinine clearance are not compatible in anuric patients on CAPD.

The relationship between adequacy of small solute clearance and clinical outcomes in continuous ambulatory peritoneal dialysis (CAPD) has been the subject of study since 1985 [1]. The current indicators for adequacy of clearance include both urea and creatinine [2, 3], and Table 1 contains the abbreviated clearance terms. Initially, the target (lowest acceptable) level for total (peritoneal plus renal) urea clearance ($K_{pr}t/V_{ur}$) was set at 1.7 weekly, whereas that for total creatinine clearance ($C_{pr}N_{cr}$) was set at 50 liters weekly [2]. Recent studies have suggested that higher clearances are needed to improve survival and decrease hospitalization [4, 5]. Consequently, recent guidelines have set as weekly targets for adequate clearance in CAPD 2.0 for $K_{pr}t/V_{ur}$ and 60 liters for $C_{pr}N_{cr}$ [3, 6].

The critical question raised by the designation of two different indices of adequacy is whether a dose of CAPD sufficient for urea clearance will also be sufficient for creatinine clearance. The relationship between the two clearances, therefore, acquires importance. In general, the two clearances correlate [7–9]. However, discrepancies (one clearance above the target value and the other clearance below the target value) were reported in approximately 20% of the clearance studies when the older target levels of 1.7 weekly for $K_{pr}t/V_{ur}$ and 50 to 55 liters weekly for $C_{pr}N_{cr}$ were studied [8, 10]. The physiological causes of these discrepancies are residual renal function and peritoneal solute transport type: Subjects with substantial residual renal function and adequate $C_{pr}N_{cr}$ may be at risk for low $K_{pr}t/V_{ur}$; those with low or even low-average transport and adequate $K_{pr}t/V_{ur}$ may be at risk for low $C_{pr}N_{cr}$ [8, 10]. A preliminary report suggested that the discrepancy between the two clearances is more frequent, around 30%, when the recent weekly targets of 2.0 for $K_{pr}t/V_{ur}$ and 60 liters for $C_{pr}N_{cr}$ are tested [11].

The quantitative differences between urea and creatinine clearance are important because currently it appears prudent to maintain both clearances above the target levels [3]. The present report addressed potential discrepancies between urea and creatinine clearance in anuria. For this purpose, we studied peritoneal urea and creatinine clearances in patients with varying peritoneal solute transport. We anticipated that peritoneal solute transport type will result in substantial differences between the two peritoneal clearances. This anticipation was based on both the analysis of the discrepancies between the two clearances [8, 10] and our

Key words: creatinine clearance, urea clearance, peritoneal dialysis, anuria, CAPD, adequacy of dialysis, Kt/V.

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Table 1. Clearance terms

Abbreviation	Explanation
Kt_{ur}	Raw (not normalized) urea clearance, K_pt_{ur} peritoneal, K_rt_{ur} renal, $K_{pr}t_{ur}$ total (peritoneal plus renal)
Kt/V_{ur}	Urea clearance normalized to body water (V), K_pt/V_{ur} peritoneal, K_rt/V_{ur} renal, $K_{pr}t/V_{ur}$ total
C_{cr}	Raw creatinine clearance, C_{pcr} peritoneal, C_{rcr} renal, C_{prcr} total
CN_{cr}	Creatinine clearance normalized to 1.73 m^2 of body surface area (BSA), C_pN_{cr} peritoneal, C_rN_{cr} renal, $C_{pr}N_{cr}$ total
Kt/V_{cr}	Creatinine clearance normalized to body water, K_pt/V_{cr} peritoneal, K_rt/V_{cr} renal, $K_{pr}t/V_{cr}$ total

From the abbreviations, $C_{cr} = Kt_{cr}$. Therefore, the ratios C_{pcr}/K_pt_{ur} (raw peritoneal clearance ratios) and $(K_pt/V_{cr})/(K_pt/V_{ur})$ are both equal to K_{pcr}/K_{pur} ($V_{cr} = V_{ur}$ = body water)

previous findings that peritoneal solute transport type is a predictor of $C_{pr}N_{cr}$ [8], but not of $K_{pr}t/V_{ur}$ [12]. We were particularly interested in defining the frequency and the conditions under which a normalized peritoneal urea clearance (K_pt/V_{ur}) of 2.0 will correspond to a normalized peritoneal creatinine clearance (C_pN_{cr}) less than 60 liters in anuric subjects.

METHODS

Patients and studies

The study population consisted of 309 patients on CAPD followed between 1994 and 1996 at the Albuquerque Veterans Affairs Medical Center and Dialysis Clinics Incorporated, the University of Pittsburgh and the University of Toronto. The majority of these patients (275 or 89%) were on the standard CAPD schedule of four daily exchanges with two liters exchange volume. Among the remaining 24 patients, 7 were on four daily exchanges with 2.5 or 3.0 liters exchange volume, 6 were on five daily exchanges with 2.0 liters exchange volume and the remaining 11 were on three daily exchanges with 2.0 to 3.0 liters exchange volume.

All patients had at least one peritoneal equilibration test (PET) performed by a slight modification of the method of Twardowski et al [13]. Briefly, after an overnight exchange was drained completely while the patient was in a sitting position for over 20 minutes, 2 liters of dialysate containing 2.5% dextrose were infused intraperitoneally and after four hours the dialysate was drained completely, also while the patient was in a sitting position, and drain volume and dialysate creatinine concentration were measured. Serum creatinine concentration was measured on the same day, usually at the beginning or midway through the PET. Based on the four-hour dialysate-to-plasma creatinine concentration ratio (D/P_{4cr}), the peritoneal solute transport type was classified as low when D/P_{4cr} was < 0.50, low-average when D/P_{4cr} was 0.50 to 0.65, high-average when D/P_{4cr} was 0.65 to 0.82 and high when D/P_{4cr} was > 0.82 [13, 14].

The patients had 476 clearance studies within 12 months of a PET. Clearance studies were performed by standard methods [8, 12, 15]. After a collection of 24-hour drained dialysate, a blood sample was obtained for the measurement of serum urea and creatinine concentrations. Dialysate volume was measured and a dialysis specimen was obtained for determination of dialysate urea and creatinine concentration after thorough mixing of all the drained dialysate bags. The methods used for dialysate creatinine determination did not receive interference from glucose.

The following weekly peritoneal clearances were calculated in each study: urea clearance, raw (K_pt_{ur}) and normalized for size by body water (V) (K_pt/V_{ur}); and creatinine clearance, raw (C_{pcr}) and normalized for size to both 1.73 m^2 BSA (C_pN_{cr}) and body water (V) (K_pt/V_{cr}). The size indicator V was obtained from the Watson formulae [16], while BSA was calculated by the Dubois formula [17]. Daily drain volume normalized by body water (Dv/V), which is a mathematical determinant of $K_{pr}t/V_{ur}$ and $K_{pr}t/V_{cr}$ as well as a predictor of $K_{pr}t/V_{ur}$ [12], $C_{pr}N_{cr}$ [8] and $K_{pr}t/V_{cr}$ [8], fractional deviation of body wt from ideal [18, 19] and body mass index were also calculated.

Statistical analysis

Continuous variables were expressed as mean ± SD and if they had a normal distribution were compared between the low, low-average, high-average and high transport groups by one-way analysis of variance. When the analysis of variance produced significant differences, we used the Student-Neuman-Keuls test, the Bonferroni test, the Tukey studentized range method and the Scheffe method to identify which transport groups differed. The Kruskall-Wallis analysis of variance by ranking was used to compare continuous variables without a normal distribution.

The relationship between two individual clearances, for example, the normalized peritoneal urea and creatinine clearances, was examined by linear regression. The purpose of this study was to analyze potential differences in peritoneal creatinine and urea clearance between different peritoneal transport types, not patients. Therefore, the analysis included all clearance studies, regardless of the number of studies from each patient. To test for potential bias introduced by using multiple clearance studies from a number of patients, analysis of variance was repeated twice, once using the mean value from each patient and a second time using only the first clearance study from each patient.

RESULTS

Table 2 shows demographic variables, anthropometric measurements and serum chemistry values. The percent of females was higher in the two lower transport groups, while the percent of diabetics was higher in the two higher transport groups. Duration of CAPD increased from the low to the high transport group. There were no differences between the four transport groups in height, weight, V, BSA, fractional weight deviation from ideal weight, body mass index, and serum urea and creatinine concentrations.

Table 3 shows dialysate parameters and clearance values when all 476 studies were entered in the analysis. Dialysate drain volume, dialysate urea concentration, and raw and normalized peritoneal urea clearances did not differ between the four transport groups. Between the low and high transport groups, normalized dialysate drain volume (Dv/V) progressively decreased, while dialysate creatinine concentration, 24-hour dialysate-to-plasma urea and creatinine concentration ratios, raw and normalized peritoneal creatinine clearances and the ratio of peritoneal creatinine clearance to peritoneal urea clearance (K_{pcr}/K_{pur}) progressively increased. This last increase was substantial: Compared to the mean K_{pcr}/K_{pur} in the low transport group, the mean K_{pcr}/K_{pur} was 17% greater in the low-average group, 29% greater in the high-average group, and 40% greater in the high transport

Table 2. Demographic variables, anthropometric measurements and serum chemistries

Group	Low	Low-average	High-average	High
N %	37 (7.8%)	199 (41.8%)	186 (39.1%)	54 (11.3%)
Females %	19 (51.4%)	83 (41.7%)	68 (36.6%)	13 (24.1%)[a]
Diabetics %	14 (37.8%)	61 (30.7%)	95 (51.1%)	27 (50.0%)[b]
CAPD duration, *months*	6.8 ± 12.2	15.4 ± 21.4	20.5 ± 25.0	25.8 ± 24.1[c]
Age *years*	52.6 ± 16.1	51.6 ± 15.7	56.7 ± 14.0	51.4 ± 14.1[d]
Height *cm*	166.0 ± 11.3	166.1 ± 11.2	167.6 ± 9.7	167.7 ± 9.6[NS]
Weight *kg*	66.3 ± 16.5	70.9 ± 18.1	72.6 ± 16.3	68.6 ± 13.9[NS]
V *liter*	35.0 ± 7.8	36.8 ± 7.6	37.3 ± 6.8	37.4 ± 6.1[NS]
BSA m^2	1.73 ± 0.25	1.78 ± 0.25	1.81 ± 0.22	1.77 ± 0.2[NS]
FΔW	0.10 ± 0.22	0.17 ± 0.29	0.16 ± 0.28	0.08 ± 0.20[NS]
BMI kg/m^2	23.8 ± 4.6	25.5 ± 5.5	25.8 ± 5.3	24.3 ± 3.9[NS]
Serum urea *mmol/liter*	19.5 ± 7.6	19.3 ± 5.6	18.6 ± 5.9	19.5 ± 6.7[NS]
Serum creatinine *μmol/liter*	725 ± 325	854 ± 325	820 ± 292	843 ± 278[NS]

Abbreviations are: V, urea and creatinine volume of distribution (body water); BSA, body surface area; FΔW, fractional deviation of body weight from ideal; BMI, body mass index. Differences between the high-average and each one of the other three transport groups were identified by the Bonferroni, Tukey and Scheffe tests.

[a] Females as percent within each group; chi-square, $P = 0.037$

[b] Diabetics as percent within each group; chi-square, $P < 0.001$

[c] Kruskall-Wallis analysis of variance, $P < 0.001$

[d] Analysis of variance, $P = 0.0047$

[NS] Analysis of variance not significant.

Table 3. Dialysate parameters and clearance values in all studies analyzed

Group	Low	Low-average	High-average	High
Dv *liter/24 hr*	9.84 ± 1.68	9.57 ± 1.77	9.56 ± 1.69	9.49 ± 1.58[NS]
Dv/V *liter/liter per 24 hr*	0.295 ± 0.084	0.270 ± 0.071	0.263 ± 0.058	0.259 ± 0.055[a]
D_{cr} *μmol/liter*	402 ± 197	565 ± 210	622 ± 219	729 ± 281[b]
D_{ur} *mmol/liter*	16.7 ± 7.0	17.1 ± 5.3	17.0 ± 6.7	18.8 ± 6.6[NS]
D/P_{24cr}	0.55 ± 0.11	0.67 ± 0.08	0.76 ± 0.08	0.86 ± 0.11[b]
D/P_{24ur}	0.86 ± 0.18	0.89 ± 0.10	0.92 ± 0.09	0.95 ± 0.09[c]
C_{pcr} *liter weekly*	37.8 ± 9.3	44.6 ± 8.4	50.9 ± 9.0	57.3 ± 11.8[b]
K_pt_{ur} *liter weekly*	59.1 ± 14.2	59.1 ± 11.2	61.1 ± 11.3	63.3 ± 13.0[NS]
K_{pcr}/K_{pur}	0.65 ± 0.14	0.76 ± 0.09	0.84 ± 0.09	0.91 ± 0.12[b]
C_pN_{cr} *liter weekly*	37.8 ± 9.0	44.0 ± 9.2	49.2 ± 10.0	56.8 ± 13.3[b]
K_pt/V_{cr} *weekly*	1.10 ± 0.31	1.25 ± 0.31	1.40 ± 0.33	1.57 ± 0.41[b]
K_pt/V_{ur} *weekly*	1.74 ± 0.51	1.66 ± 0.41	1.68 ± 0.41	1.73 ± 0.46[NS]

Abbreviations are: Dv, 24-hr drain volume; Dv/V, drain volume normalized by body water (Watson formulae); D_{cr} and D_{ur}, dialysate creatinine and urea concentration, respectively; D/P_{24cr} and D/P_{24ur}, dialysate (in 24 hr drain volume) to plasma concentration ratios for creatinine and urea, respectively.

[a] Analysis of variance, $P = 0.0416$; localizing differences found by the Bonferroni, Tukey and Scheffe tests between low, high-average and high groups.

[b] Analysis of variance, $P < 0.0001$; differences found between all four transport groups by all four localizing tests.

[c] Analysis of variance, $P < 0.0001$; differences found by all four localizing tests between the two lower transport groups and each of the two higher transport groups and between high-average and high transport groups.

[NS] Analysis of variance not significant.

group. When all four transport groups were analyzed together, K_{pcr}/K_{pur} was 0.80 ± 0.12. Table 4 shows clearance values when only the mean value from each subject was entered in the analysis. The results were indistinguishable from those in Table 3. Analysis of variance using only the first study from each patient produced essentially the same results.

A series of linear regressions was performed using as the independent variable (x) 24-hour drain volume (Dv), raw and normalized peritoneal urea clearance, and as the dependent variable (y) raw and normalized urea or creatinine clearance. Each regression was performed in each transport group and in a group including all the studies. Table 5 shows the regressions performed with Dv and raw peritoneal urea clearance (K_pt_{ur}) as the independent variables. From the regression equations, we calculated the values, with their 95% confidence interval, of raw peritoneal urea and creatinine clearance corresponding to a Dv of 10 liter/24 hr and the raw peritoneal creatinine clearance corresponding to a raw urea clearance of 62.7 liter/24 hr (the value corresponding to a Dv of 10 liter/24 hr when all studies were analyzed together). The 95% confidence intervals were broad and overlapped between the different peritoneal solute transport types.

Figure 1 shows the linear regression of peritoneal creatinine clearance, normalized by BSA (C_pN_{cr}) on K_pt/V_{ur} in the four transport groups. Figure 2 shows the corresponding regressions of K_pt/V_{cr} on K_pt/V_{ur}. Figure 3 shows estimates of C_pN_{cr} (Fig. 3A) and K_pt/V_{cr} (Fig. 3B) corresponding by the regression equations to a weekly K_pt/V_{ur} of 2.0 and their 95% confidence intervals. The 95% confidence intervals indicate that the majority of CAPD patients with a weekly K_pt/V_{ur} of 2.0 are expected to have a weekly C_pN_{cr} less than 60 liters. This majority includes all patients with low transport, almost all subjects with low-average transport,

Table 4. Clearance values; only the mean values from each patient analyzed

Group	Low	Low-average	High-average	High
N %	30 (9.7%)	124 (40.1%)	126 (40.8%)	29 (9.4%)
D/P_{24cr}	0.55 ± 0.10	0.67 ± 0.07	0.77 ± 0.08	0.87 ± 0.10
D/P_{24ur}	0.87 ± 0.17	0.89 ± 0.09	0.91 ± 0.08	0.95 ± 0.09
K_{pcr}/K_{pur}	0.65 ± 0.13	0.76 ± 0.07	0.84 ± 0.07	0.92 ± 0.10
C_pN_{cr} *liters weekly*	38.3 ± 8.6	44.1 ± 9.9	49.2 ± 9.2	58.6 ± 13.0
K_pt/V_{cr} *weekly*	1.12 ± 0.30	1.26 ± 0.30	1.39 ± 0.31	1.63 ± 0.38
K_pt/V_{ur}, *weekly*	1.76 ± 0.51	1.67 ± 0.41	1.67 ± 0.39	1.79 ± 0.49

Analysis of variance revealed exactly the same results as in Table 3.

Table 5. Linear regressions with drain volume and urea clearance as the independent variables

Group	Regression	Correlation	y *(95% CI)*
A. Independent variable (x) Dv, dependent variable (y) K_pt_{ur}			
All studies	y = 8.011 + 4.085x	0.792	62.7 (48.6–76.8)[a]
Low	y = 18.876 + 4.085x	0.484	59.7 (33.8–85.6)[a]
Low-average	y = 9.109 + 5.221x	0.821	61.3 (48.6–74.0)[a]
High-average	y = 6.927 + 5.668x	0.847	63.6 (51.7–75.5)[a]
High	y = −4.865 + 7.182x	0.874	67.0 (54.1–79.9)[a]
B. Independent variable (x) Dv, dependent variable (y) K_pt_{cr}			
All studies	y = 9.675 + 3.999x	0.652	49.7 (34.1–65.3)[a]
Low	y = 4.218 + 3.408x	0.617	38.3 (23.1–53.5)[a]
Low-average	y = 8.993 + 3.721x	0.778	46.2 (35.7–56.7)[a]
High-average	y = 10.573 + 4.218x	0.793	52.8 (41.9–63.7)[a]
High	y = −0.332 + 6.075x	0.809	60.4 (46.1–74.7)[a]
C. Independent variable (x) K_pt_{ur}, dependent variable (y) K_pt_{cr}			
All studies	y = 7.705 + 0.667x	0.750	49.5 (35.9–63.1)[b]
Low	y = 13.686 + 0.408x	0.623	39.3 (24.2–54.4)[b]
Low-average	y = 8.688 + 0.608x	0.809	46.8 (36.8–56.8)[b]
High-average	y = 10.055 + 0.668x	0.841	51.9 (42.2–61.6)[b]
High	y = 9.874 + 0.750x	0.820	56.9 (43.0–70.8)[b]

Abbreviation 95% CI is 95% confidence interval.
[a] x = 10 liter/24 hr, [b] x = 62.7 liter weekly
All correlations were significant at $P \leq 0.002$.

most of the subjects with high-average transport and even a substantial minority of the subjects with high peritoneal solute transport type. An even higher percent of CAPD patients with a K_pt/V_{ur} of 2.0 will have inadequate peritoneal creatinine clearance if creatinine clearance is normalized by body water rather than BSA.

DISCUSSION

The relationship between peritoneal urea and creatinine clearance is critical if both clearances are to be kept above specified levels in CAPD. That these clearances may be discrepant because of differences in peritoneal solute transport has been repeatedly shown [3, 6, 8–10, 20–22]. For anuric subjects, it is important to know the range of peritoneal creatinine clearance corresponding to a weekly K_pt/V_{ur} of 2.0 which is the current lowest acceptable clearance in CAPD [3]. Both theoretical analyses and calculations from patient data have been applied in the determination of these levels of creatinine clearance.

Theoretically, Gotch, disregarding peritoneal solute transport differences and assuming that K_{pcr}/K_{pur} equals 0.8 and that a V of 35 liter corresponds to a BSA of 1.73 m^2, calculated that a C_pN_{cr} of 56 liter corresponds to a K_pt/V_{ur} equal to 2.0 [3]. Remarkably, when all clearance studies were analyzed together in our study the mean K_{pcr}/K_{pur} was exactly 0.80.

Linear regression analysis using clearance data also suggests that the average C_pN_{cr} corresponding to a K_pt/V_{ur} of 2.0 is less than 60 liter. In the present study, which contained only CAPD patients, a mean C_pN_{cr} of 52.9 liter corresponded to a K_pt/V_{ur} of 2.0 when all studies were analyzed together (Fig. 3). In our previous study, which in addition to the patients on CAPD contained some patients on peritoneal dialysis with shortened dwell times, a C_pN_{cr} of 52.1 liter corresponded to a K_pt/V_{ur} of 2.0 [8]. Flanigan, Lim and Langholt [9] reported a logarithmic relation between C_pN_{cr} and K_pt/V_{ur}. From their regression, we calculated that a mean C_pN_{cr} of 52.8 liter corresponds to a K_pt/V_{ur} of 2.0. A higher value for the mean C_pN_{cr} (59.5 liter) corresponding to a K_pt/V_{ur} equal to 2.0 is calculated from the linear regression in the study of Durand et al [20]. The percent of different peritoneal solute transport types in a study will affect the relationship between K_{pur} and K_{pcr}.

The potential causes of discrepancy between the normalized peritoneal urea and creatinine clearances are physiologic (differences in the peritoneal transport of the two azotemic substances) and mathematical, created by the use of two different size indicators, V and BSA, to normalize respectively urea and creatinine clearance in CAPD. We have shown that the relationship between V and BSA is not linear: In a patient developing obesity, the increase in V will be disproportionately greater than the increase in BSA creating a relatively larger decline in $K_{pr}t/V_{ur}$ than in $C_{pr}N_{cr}$ if obesity does not affect $K_{pr}t_{ur}$ and C_{prcr} [23]. In

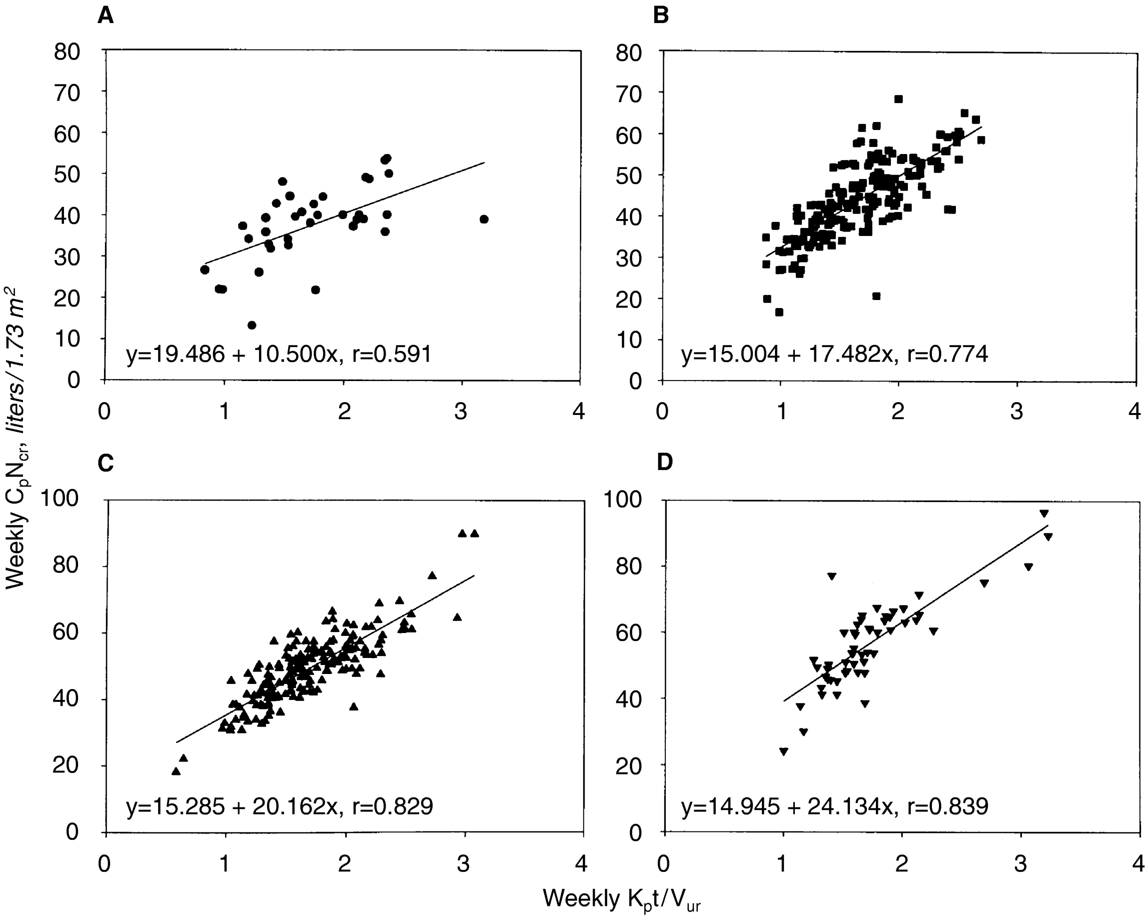

Fig. 1. Linear regression of peritoneal creatinine clearance normalized to 1.73 m^2 of body surface area (C_pN_{cr}) on peritoneal urea clearance normalized by body water (K_pt/V_{ur}) in the four transport groups: A, low; B, low-average; C, high-average; D, high transport group. When all studies were analyzed together, y = 15.449 + 18.749x, r = 0.715.

addition, gender affects the relationship between V and BSA. V will be substantially greater in a man than in a woman with the same height, weight and, consequently, BSA [23]. The mathematical distortion of the relationship between the normalized clearances is eliminated when either raw clearances are compared or the same size indicator is used to normalize both clearances [23]. Elimination of the mathematical distortions was the reason for comparing C_{pcr} to K_pt_{ur} and K_pt/V_{cr} to K_pt/V_{ur} in the present study. Normalization of creatinine clearance by V has been applied in two other studies [8, 24].

The present study reports a major effect of peritoneal solute transport type on peritoneal creatinine clearance. On comparable CAPD prescriptions and body sizes (Tables 1 and 2), subjects with high transport characteristics had approximately 50% higher peritoneal creatinine clearances than those with low transport characteristics. This is not surprising given the fact that D/P_{4cr} in the PET was used to characterize peritoneal solute transport. What is remarkable is the minimal effect of peritoneal solute transport on peritoneal urea clearance. Note that small, but significant, differences, approximately 10% between the high and low transport groups, were found in $D/P_{24\ ur}$ (Tables 3 and 4) and that this effect was blunted in the K_pt_{ur} and K_pt/V_{ur} because normalized drain volume (Dv/V) decreased from low to high transport groups (Table 3). Drain volumes are affected by peritoneal solute transport in CAPD. Subjects with higher transport types tend to have lower drain volumes than those with lower transport types [13, 14] and are consequently at risk of fluid retention [25]. However, even when we calculated the peritoneal clearances corresponding to the same Dv (10 liter/24 hr), K_pt_{ur} differed between the low and high transport groups by only 12% while K_pt_{cr} differed by 58% (Table 5).

The findings of the present study are applicable only to patients on CAPD, who have long dwell times. For continuous or intermittent peritoneal dialysis with shortened dwell times, the relationship between peritoneal creatinine and urea clearance differs from that in patients on CAPD. Nolph, Twardowski and Keshaviah [7] showed that the ratio K_{prcr}/K_{prur} is lower in nocturnal intermittent peritoneal dialysis than in CAPD. Piraino and Bernardini [26] reported different D/P_{24cr} and $D/P_{24\ ur}$ in patients on CAPD, continuous cycling peritoneal dialysis (CCPD) and nocturnal peritoneal dialysis (NPD). From their data we calculated that mean K_{pcr}/K_{pur} was 0.80 in CAPD, 0.74 in CCPD and 0.69 in NPD. The effects of peritoneal solute transport type on the relationship K_{pcr}/K_{pur} in peritoneal dialysis with short dwell times have been studied in only a preliminary report [20], to our knowledge.

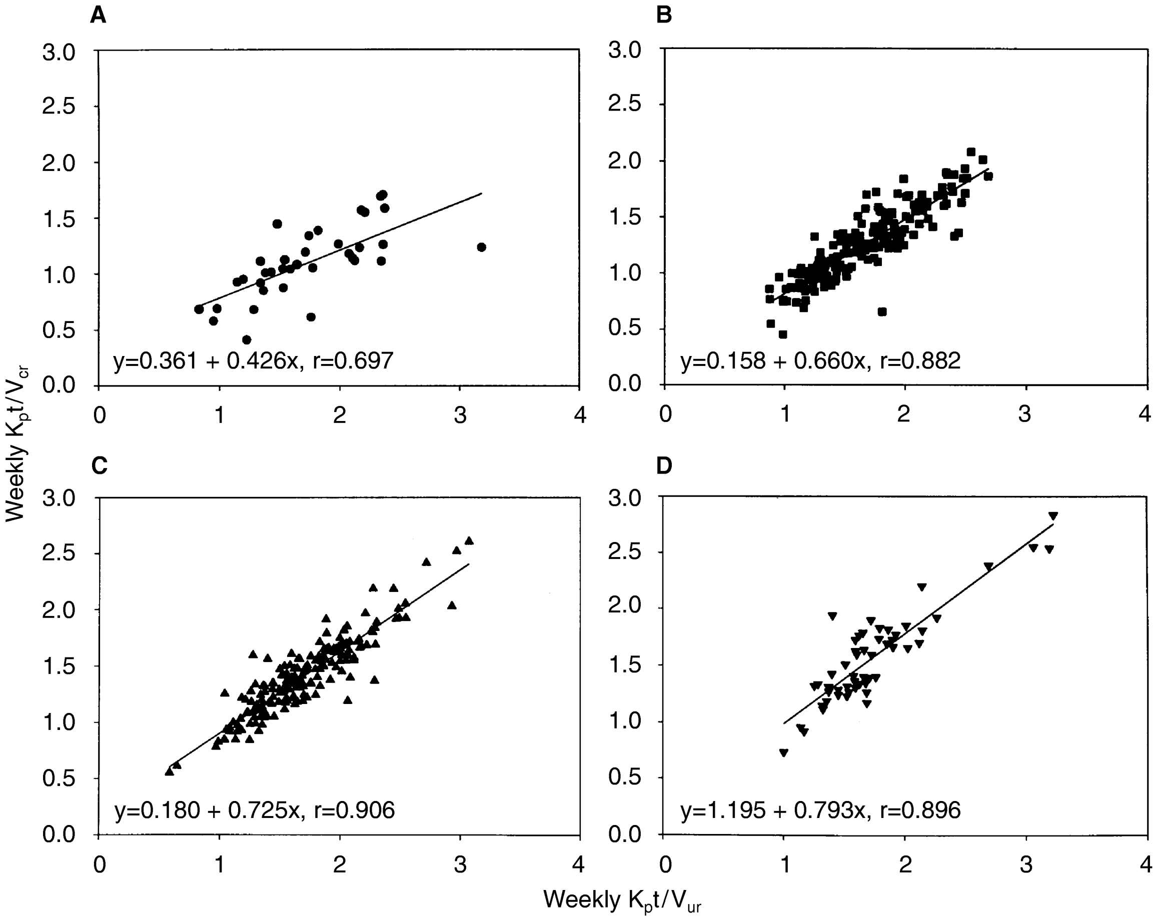

Fig. 2. Linear regression of peritoneal creatinine clearance normalized to body water (K_pt/V_{cr}) on peritoneal urea clearance normalized to body water (K_pt/V_{ur}) in the four transport groups: A, low; B, low-average; C, high-average; D, high transport group. When all studies were analyzed together, y = 0.192 + 0.679x, *r* = 0.824.

The DOQI guidelines set 2.0 weekly as adequate $K_{pr}t/V_{ur}$ and 60 liters weekly as adequate $C_{pr}N_{cr}$ in CAPD [3]. Our study as well as that of Flanigan, Lim and Langholt [9] showed that the majority of anuric CAPD patients with a K_pt/V_{ur} of 2.0 will have a C_pN_{cr} less than 60 liter. Only subjects with high peritoneal solute transport and a K_pt/V_{ur} of 2.0 have a reasonable probability of having a C_pN_{cr} of 60 liter. From the regression equations, the estimated average weekly K_pt/V_{ur} required for a C_pN_{cr} of 60 liter is 2.22 for high-average transport, 2.57 for low-average transport and 3.86 for low transport. Achieving these K_pt/V_{ur} values with CAPD may be feasible only in small individuals tolerating large exchange volumes [8, 27, 28].

Currently, there is no clear-cut justification to aim at the very high K_pt/V_{ur} targets calculated in the previous paragraph. The selection of the current clearance targets was influenced by the CANUSA study [5], which showed an increase in mortality as residual renal clearance decreased while peritoneal clearance remained unchanged in CAPD. Both total urea and total creatinine clearance were predictors of mortality, while only total creatinine clearance was a predictor of hospitalization. It is conceivable that creatinine clearance was a better predictor of outcomes than urea clearance in the CANUSA study because an average of urinary creatinine and urinary urea clearance is a more sensitive index of residual renal function than urinary urea clearance in CAPD [29, 30]. Whether creatinine clearance, which is greatly affected by peritoneal solute transport type, or urea clearance, which is only minimally affected by peritoneal solute transport type, is a better predictor of outcomes in anuric CAPD patients will need to be investigated by an interventional study. Such a study may lead to the use of a single peritoneal clearance as the index of adequacy of azotemic solute clearance in CAPD.

In summary, differences in peritoneal transport type cause major discrepancies between peritoneal urea and creatinine clearance. Consequently, anuria magnifies the discrepancies between Kt/V_{ur} and CN_{cr}. Only a small fraction of the anuric subjects who achieve the target Kt/V_{ur} will also achieve the target CN_{cr}. The current targets for urea and creatinine clearance in CAPD are not compatible.

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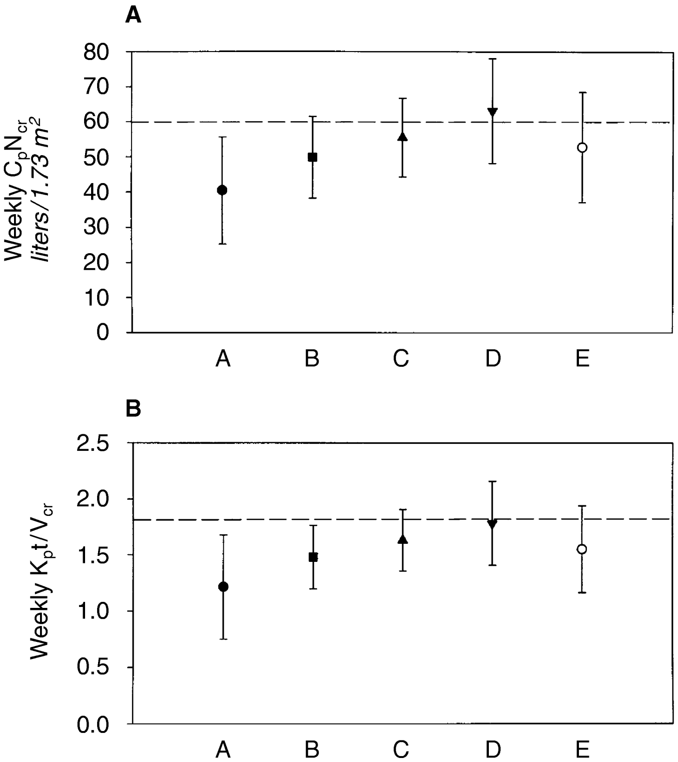

Fig. 3. Estimates of C_pN_{cr} (*A*) and K_pt/V_{cr} (*B*) corresponding by linear regression to a K_pt/V_{ur} of 2.0 and their 95% confidence intervals. Symbols are: (●)group A, low transport; (■) group B, low-average transport; (▲) group C, high-average transport; (▼) group D, high transport; (○) group E, all studies analyzed together. Interrupted horizontal lines are the lower acceptable creatinine clearance levels [2]. The acceptable level of K_pt/V_{cr} (1.80 weekly) was set as follows: by linear regression including all 476 studies, $K_pt/V_{cr} = -0.060 + 0.031(C_pN_{cr})$, $r = 0.944$. From this regression a K_pt/V_{cr} of 1.8 corresponds to a C_pN_{cr} of 60 liters.

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